Prepared for the Independent Hospital Pricing Authority

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

Final Report

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Executive summary

The study context

The Australian Government established the Clinical Trials Action Group (CTAG), in October 2009, to boost Australia's profile as a preferred destination for conducting clinical trials. The CTAG report, containing 11 recommendations endorsed by the Australian Government, was released by Ministers Roxon and Carr in March, 2011 with a commitment to implementation. Recommendation C of that report requires that the Independent Hospital Pricing Authority (IHPA) be directed to develop a table of standard costs associated with conducting clinical trials in Australia. Accordingly, Minister Plibersek issued a Ministerial Direction to IHPA, dated 28th November 2012, to determine the national efficient price (NEP) for a list of standard items (developed by the National Health and Medical Research Council (NHMRC)) associated with conducting clinical trials in Australia.

Methodology

HealthConsult was engaged by IHPA on 5th March, 2013, to undertake a project to *"develop a table of standard costs for conducting Clinical Trials in Australia"*. The project objective was to develop, in consultation with stakeholders, a robust set of calculations and NEPs for the NHMRC's list of standard items associated with conducting clinical trials in Australia. The methodology used to complete the project featured the development of a discussion paper as the basis of a call for public submissions; a broad stakeholder consultation process involving visits to 10 public and three private hospitals, three organisations involved in clinical trials in the primary and community services sector, as well as discussions with representatives of trial sponsors, trial collaboratives, and other key interested parties; and a detailed analysis of the information generated to determine a standard cost for each of the 61 items on the NHMRC list.

Developing the table of standard costs

HealthConsult observed that the 61 items on the list do not reflect a classification for a relatively homogenous set of services (even at the level of the three sub-lists). Accordingly, the study started by developing draft definitions for each item on the NHMRC list (by supplementing what was in the NHMRC paper defining the list), and then seeking stakeholder input into finalising the definitions. It should be noted that, consistent with the Ministerial Direction, there was no scope to alter the list for the purpose of developing the table of standard costs, so the study concentrated on defining the scope of services to be included in each item on the list.

A mixture of approaches was needed to derive standard costs for each item on the NHMRC list. Standard costs for some items are based on an analysis of prevailing fees (as the items were defined as fees incurred or charged) whereas standard costs for other items are determined from first principles using activity based costing. Where activity based costing was used, the study examined current practice in designing and implementing clinical trials in Australia through the visits to clinical trial host sites. The information generated through the investigative processes was used to determine the standard costs by application of a series of best practice costing principles that were applied to determine the approach to costing each item on the NHMRC list.

Importantly, the methodology focussed on determining the cost experienced by trial host sites, as the concern expressed in the CTAG report was that the perceived increase in the costs of hosting trials had detracted from Australia's competitiveness as a potential destination for multi-national clinical trials. Through the fieldwork and the public submissions process, it became clear that

there are a number of items on the NHMRC where the associated costs are typically not incurred by trial host sites (they are incurred by the trial sponsor or the sponsor's agent). For many of these items, there was insufficient evidence to determine a standard cost. The items for which standard costs have not been derived are clearly indicated as 'not determined' in the table of standard costs.

Where a determination was possible, a typical or representative standard cost for each item has been derived. The standard cost for each item is intended to be the NEP for the item, consistent with the cost recovery principle required by the Ministerial Direction. It is recognised that in specific trial circumstances, the actual cost may be different from the standard cost. However, by publishing a reference standard cost, it leaves potential trial host sites and trial sponsors free to use the standard cost as a starting point for discussing the unique features of the trial being proposed and the associated costs, as part of negotiating the trial budget.

Using the table of standard costs

In using the table of standard costs, it is important to note that this study was required to focus on the NHMRC list of items that was developed as a result of the CTAG process (which enjoyed substantial input from the pharmaceutical industry, but lower levels of participation from other commercial trial sponsors). This costing study deliberately pursued broad stakeholder consultation, including with commercial and non-commercial trial sponsors. In that process, some stakeholders, including the Medical Technology Association of Australia (MTAA), were concerned that the NHMRC list was largely focussed on pharmaceutical trials. As a result, it is considered that further work is required to ensure the applicability of the NHMRC list to medical device trials, and until such time as this work is carried out, the table of standard costs should not be used for device trials.

In any case, there is not expected to be any compulsion to use the table of standard costs in negotiating trial budgets, it is intended only as a guideline or reference point. Nonetheless, it is considered that there is considerable value in the Australian table of standard costs, particularly if users of the table have regard to the following factors in negotiating trial budgets:

- **Standard care versus trial specific care.** It is important to note that the standard costs are intended to be applied only for those activities that are over and above standard of care i.e. the determined standard costs should not be applied to services that patients would have received in any case, if they had not been enrolled in a clinical trial.

- **Type of trial**. Although, the standard costs have been developed without reference to the type of trial, there may be a need to consider adjustments to the standard costs depending on the nature of the intervention on trial (e.g. pharmaceutical trials, radiation oncology trials, surgical trials, service model trials, observational trials, etc.).

- **Target population of trial.** Some trials will target populations where there will be different costs experienced relative to the typical adult population, there may be a need to consider adjustments to the standard costs for trials that are likely to involve high proportions of participants from smaller target groups.

- **Phase of trial**. Pharmaceutical trials are normally categorised into phases from Phase 1 through to Phase 4. The phase of the trial was found to impact on costs, so there may be a need to consider adjustments to the standard costs depending on trial phase.

- **Setting for the trial.** The auspice organisations conducting clinical trials represent a range of settings, from hospitals to primary and community services, through to purpose built facilities. The study found that there are different experiences of the cost of trials depending on the setting, so there may be a need to consider adjustments to the standard costs based on the setting in which the clinical trial will be conducted.

- **Location of trial sites/trial participants**. Some trial sites may be located in regional/ rural areas, where there may be higher cost experiences. Also, metropolitan area-based trials may provide access to participants residing in regional/rural areas through the use of tele-health technology, or subsidised travel to and from the regional/rural location. Accordingly, there may be a need to consider adjustments to the standard costs for trials where the trial site and/or the trial participants are in located in regional/rural areas.

- **Complexity of trial**. There are potentially a number of factors associated with trial complexity that may impact on cost. It is considered that the judgement about trial complexity needs to be made in context as general rules are too difficult to develop, but it may be relevant to consider an adjustment to the standard costs based on trial complexity.

A number of the public submissions also made reference to the potential to adjust the standard costs depending on the trial sponsor (e.g. industry, collaborative, or investigator initiated). The study found that in most situations the trial sponsor is not a cost issue, rather it is a funding issue. It was observed that trial sites often did not seek the same level of funding to host collaborative or investigator initiated trials that they did to host industry sponsored trials. But the activities involved were generally very similar, and so were their associated costs. It is a matter for trial sites to decide whether they will negotiate trial budgets at levels lower than the standard costs for collaborative and investigator initiated trials, it is not a matter that influences the standard costs.

Opportunities to refine the NHMRC list of items

The study has identified seven opportunities to improve the NHMRC list of activities associated with conducting clinical trials, as follows:

- develop a clearer definition of the scope of activities to be included on the list (i.e. only costs incurred by trial host sites, or all costs, including sponsor costs, associated with clinical trials);
- reworking the list so all items are defined as activities associated with conducting clinical trials, and all references to fees in item definitions are removed;
- restructuring the list so that it is based on the clinical trial life cycle, compared to whether the activity is a clinical service, a clinical support service, or a non-clinical support service;
- extending sub-list one so that it is more inclusive of clinical services not covered by the MBS, as well as services associated with overnight stay and outpatient/day stay;
- specifically including activities undertaken by the supporting departments (in addition to the pharmacy department) on the list; and
- removing the overlap in some of the activities listed in sub-list two, with a particular focus on the pharmacy and biospecimen items; and
- removing the duplication between items on sub-lists two and three, which would be partly addressed by eliminating the fee based items.

Opportunities to refine the costing of the NHMRC list of items

Three opportunities have been identified for improving the costing of the items on any revised list of activities associated with clinical trials, as follows:

- re-costing all the items on the revised list that were previously defined as fee items on the basis of the resource units required for the underlying activities, rather than the typical fees charged;
- undertaking the costing on a prospective basis, so as to generate data that can be used to determine loading factors for the standard costs that reflect trial characteristics (e.g. paediatric trials, drug, device, or service model trials, hospital versus community based trials, etc.); and
- developing costing templates for clinical trials (different templates reflecting key variations in trial characteristics) that could be used by trial sponsors and trial host sites to determine trial budgets (i.e. mirror the related developments in the UK).

Maintenance of the table of standard costs

Like any schedule of costs/prices there will be a need to maintain the currency of the table of standard costs. This work may be as simple as ensuring appropriate escalation of the standard costs to reflect the increases in input prices experienced in the health system. However, the environment in which clinical trials are being conducted is changing fairly rapidly. There are efforts across the country to streamline the processes associated with obtaining ethics and institutional approvals for clinical trials. There are also the initiatives that will result from implementation of the other ten recommendations of the CTAG report. These developments are likely to impact on the costs of conducting clinical trials. In the circumstances, it is suggested that recalculation of the standard costs, over and above reflecting input price escalation, may be required two-yearly.

Evaluating the impact of the table of standard costs

Although the fieldwork found widespread support for the development of the table of standard costs, there were a few stakeholders who expressed concerns about the possible negative impact of the initiative. Like any significant intervention, there is a need to formally evaluate the impact of the table of standard costs on both the number and costs of clinical trials conducted in Australia. It is noted that the initial work on evaluating the production of costing templates for clinical trials in the UK (the parallel initiative in the UK to the production of the table of standard costs in Australia) has generally produced positive results. Accordingly, it is suggested that an evaluation of the impact of the table of standard costs on clinical trials in Australia be undertaken within three years of the publication of this report.

1 Introduction

HealthConsult was engaged by the Independent Hospital Pricing Authority (IHPA) on 5th March, 2013, to undertake a project to:

"develop a table of standard costs for conducting Clinical Trials in Australia"

This Chapter presents the project background and objectives; and summarises the methodology used by HealthConsult to conduct the assignment.

1.1 BACKGROUND – COMPETITIVE CLINICAL TRIALS IN AUSTRALIA

Clinical trials represent a vital component of the Australian health care system. Their conduct confers many benefits including improved access for patients to leading edge treatment and care; creating an environment that fosters research and innovation thereby attracting and/or retaining high quality scientists and clinicians to the Australian health care system; and attracting research and development funds to Australian hospitals. Like any enterprise in this global environment, there is competition for clinical trials funds. Recognising the need to remain world-competitive, in October 2009, the Australian Government established the Clinical Trials Action Group (CTAG) to boost Australia's profile as a preferred destination for conducting clinical trials.

The CTAG report was released by Ministers Roxon and Carr in March, 2011. The report contains 11 recommendations endorsed by the Australian Government. Ministers Roxon and Carr committed the relevant Government departments and agencies to work on implementing those 11 recommendations in the time-frames outlined in the CTAG report. Specific to this project, Recommendation C requires that IHPA be directed to develop a table of standard costs associated with conducting clinical trials in Australia. To that end, Minister Plibersek issued a Ministerial Direction to IHPA on the Performance of its Functions (No. 1 of 2012), dated 28th November 2012, to determine the national efficient price (NEP) for a list of standard items (developed by the National Health and Medical Research Council (NHMRC)) associated with conducting clinical trials in Australia.

It is relevant to note that the Australian Government's Industry and Innovation Statement, *A Plan for Australian Jobs*, included $9.9 million over five years for a new initiative, *Expediting Clinical Trial Reform in Australia*[1]. This initiative aims to accelerate the implementation of recommendations from the CTAG report to ensure Australia maintains its competitive advantage as a global leader in clinical research and improves its attractiveness as a destination for investment in clinical research. The initiative includes funding to support the work being done by IHPA on the development of the table of standard costs for conducting clinical trials in Australia.

[1] http://www.aussiejobs.innovation.gov.au/programs/Pages/clinical-trial-reform.aspx

1.2 PROJECT OBJECTIVES

The project objective was to develop, in consultation with stakeholders, a robust set of calculations and National Efficient Prices (NEP) for the NHMRC's list of standard items associated with conducting clinical trials in Australia. This overall objective was specifically set in the context of addressing the requirements of Schedule 1 of the Ministerial Direction, which stated:

1. Functions

(i) By 30th June 2013, the Pricing Authority must determine the national efficient price for a list of standard items (provided to it by the NHMRC) associated with conducting clinical trials in Australia.

(ii) At the first meeting of the Standing Council on Health after 30th June 2013, the Pricing Authority must provide a report on its performance of the activity referred to in Item 1(i) of this Direction to the Minister for Health and Ageing and to the Minister having responsibility for health in each State and Territory.

2. Matters the Pricing Authority is to have regard to

(i) In performing the activity described in Item 1 of this Schedule, the Pricing Authority must have regard to the matters set out in subsection 131(3) of the Act.

(ii) In addition, the Pricing Authority may, so far as the Act permits, have regard to the following matters:

a. the actual activity of each item;
b. principles of cost-recovery; and
c. submissions from relevant parties, including clinical trial sponsors and private hospitals.

1.3 PROJECT METHDOLOGY

Figure 1.1 presents the six stage methodology designed by HealthConsult to achieve the outcomes sought by the IHPA. Briefly, the six stages were:

(1) **Stage 1:** Project planning which included the development of stakeholder engagement and risk management plans;

(2) **Stage 2:** First round stakeholder consultations with CTAG and NHMRC representatives; and the development of a discussion paper, which was used as the basis of a call for public submissions. This paper provided stakeholders with the opportunity to comment on the draft definitions developed by HealthConsult on the scope of services to be included in each of the 61 items on the standard list, as well as the proposed approach to costing each item;

(3) **Stage 3:** A brief literature review to examine the international experience in costing the activities associated with clinical trials, which input into the development of the infrastructure necessary to ensure that the best value would be derived from the site visit process;

(4) **Stage 4:** Broad stakeholder consultation which included one to two day visits to ten public and three private hospitals, three organisations involved in clinical trials in the primary and community services sector, as well as discussions with representatives of trial sponsors (e.g. pharmaceutical companies) and other key interested parties (e.g. Medical Technology Association of Australia, Centre for Biostatics and Clinical Trials, Victorian Comprehensive Cancer Centre, Cancer Trials Australia);

(5) **Stage 5:** Analysis of the gathered data (from written submissions; secondary data sources (e.g. Medicare Benefits Schedule(MBS), Awards), site visits, etc.) to determine a standard cost for each item on the NHMRC list of activities associated with clinical trials in

Australia, including review by the Steering Committee (using a modified version of the Delphi process);

(6) **Stage 6:** Preparation of the final report (this document).

Figure 1.1: Overview of the six stage methodology used

1.4 PURPOSE OF VISITS TO CLINICAL TRIAL HOST SITES

As there was not sufficient time to conduct a prospective study to measure costs for each item on the standard list across trial sites; a protocol based costing methodology was used. The evidence for the costing process was derived principally from a series of visits to 13 hospitals and three organisations operating in the primary and community service sector involved with the design and implementation of clinical trials. Analysis of the information obtained from these site visits became the basis for refining the draft definitions developed by HealthConsult and for determining the standard cost for each item on the NHMRC list.

For the items on the NHMRC list where costing from first principles (i.e. activity based costing) was attempted, the site visit information was used to develop process maps, identify resource units required for each process step, and then apply (externally sourced) standard unit costs, to derive an overall standard cost. For other items, the standard costs were based on external reference points including labour rates (e.g. relevant Awards), fee schedules (e.g. MBS fees, prevailing HREC fees) and costs measured for other purposes (e.g. the National Hospital Costs Data Collection).

1.5 ORGANISATIONS SELECTED FOR SITE VISITS

Two members of the HealthConsult team visited the 13 hospitals and three organisations operating in the primary and community service sector to generate the evidence base to underpin the development of the standard table of costs (see Table 1.1). All sites visited were involved with the design and implementation of clinical trials.

Table 1.1: Organisations participating in the study site visits

State/Territory	Public Hospitals	Private Hospitals	Primary and community health organisations
New South Wales	Prince of Wales	Sydney Adventist	Family Planning NSW
	The Children's Westmead		Hornsby Hospital (in respect of community-based trials)
	Dubbo Base (by teleconference only)		Northern Clinical School, University of Sydney (in respect of trials based in general practices)
Victoria	Royal Melbourne	Cabrini	
	Royal Children's		
	Barwon Health		
Queensland	Royal Brisbane	Greenslopes	
Western Australia	Royal Perth		
South Australia	Royal Adelaide		
Northern Territory	Royal Darwin		

It was intended that the nominated sites would be reasonably representative of the settings in which clinical trials are conducted in Australia (i.e. provide coverage across trial and site characteristics including type of intervention in clinical trial (e.g. drug, surgical, diagnostic), jurisdiction (six states and two territories), type of site (general hospital, specialist hospital, primary and community health service); location of site (metropolitan, regional); and sector of site (public, private)). Due to the logistics associated with organising the site visits in a short timeframe, paediatric hospitals were over-represented, and regional hospitals were under-represented in the final sites visited.

2

Definitions for the list of standard items for clinical trials

This Chapter presents the NHMRC list of standard items associated with clinical trials and the definitions for each item on the list.

2.1 DEVELOPMENT OF THE NHMRC LIST OF STANDARD ITEMS

The NHMRC list was developed in 2012 in response to recommendation C of the CTAG report. HealthConsult's analysis of the list identified 61 individual items (at the most granular level), which group up into 16 categories, and then into three sub-lists titled *"Clinical – Tests and Procedures", "Clinical – Trial Support Services"* and *"Non clinical services"*. To set the context for the costing study, the explanatory notes provided by the NHMRC to accompany the list were;

- *"The CTAG report states that the purpose of the list is to reduce uncertainty around clinical trial costs in the public health system.*
- *The term 'standard item' has been interpreted as referring to those items that are common to the conduct of clinical trials generally, including non-clinical items such as resources, project review, start-up and ongoing administrative costs. Items that are uncommon or common only to a narrow range of clinical trials are not included. It is acknowledged that all items included on the list do not apply to all clinical trials.*
- *The items listed may be items that are standard clinical trial costs of commercial sponsors, trial coordination groups and/or institutions conducting a trial. The items in the list are not categorised or distinguished in this respect.*
- *The item "institutional overhead" or "departmental overhead" was not included as a separate item due to the difficulties in defining the scope of this item, particularly in addition to the items listed.*
- *Costing issues are not within the scope of this document. Nevertheless, in developing this list, NHMRC recognises that stakeholders have raised a number of issues related to the costing of clinical trials such as*
  - *the use of the list for both commercially-sponsored and non-commercial clinical trials, including differential costing applied in those contexts*
  - *the complexities involved in determining which tests, procedures or services are provided pursuant to standard care for a patient who is also a trial participant, and which items are trial-specific tests, procedures or services provided to a participant as part of a clinical trial."*

The costing study took the NHMRC advice into account in designing and executing the costing methodology. As there were no definitions provided by the NHMRC, the study needed to start by formulating draft definitions of the scope of services to be included in each item in the classification.

2.2 OVERVIEW OF THE NHMRC LIST OF STANDARD ITEMS

For the purposes of the costing study, HealthConsult developed a reference numbering for the NHMRC list. The reference numbers are structured as a.b.c, where 'a' is the sub-list number, 'b' is the category number, and 'c' is the item number within each category. Table 2.1 presents a brief description of the features of the list, including the number of sub-lists; and the number of categories and items within each sub-list.

Table 2.1: Brief descriptive analysis of NHMRC list of standard items associated with clinical trials

Sub-list Number	Sub-list label	Number of categories	Number of items	Comments
1	Clinical – Tests and procedures	7	8	Represents the clinical services provided to participants in a clinical trial. Most items are defined using the MBS, which suggests the use of the MBS fee as a surrogate for the standard cost for most items. The standard costs are presented on a per service basis (i.e. not per trial). For those items not on the MBS (e.g. some PET scans), alternative approaches were investigated for deriving the standard cost per service.
2	Clinical – Trial support services	6	21	Represents a diverse mix of support services, some of which occur only once (e.g. Departmental reviews of the Trial Protocol), whereas others occur numerous times (e.g. bio-specimen collection and processing) in the course of a clinical trial. Stakeholder consultation and investigation was used to establish clear definitions; then develop processes maps (where necessary), assign resource units and identify appropriate standard unit costs, in order to derive a standard costs for each item.
3	Non clinical services	3	32	Represents a very diverse mix of services that again includes one-off and repeated activities; also includes participant related costs. Some services were difficult to define (e.g. staff training, data analysis and recruitment activity) whereas others reflect fees paid or charged (e.g. Lead HREC/Lead site fee, participant/carer parking). Again, stakeholder consultation and investigation was used to establish clear definitions; then develop processes maps (where necessary), assign resource units and identify appropriate standard unit costs, in order to derive a standard costs for each item.
Total		**16**	**61**	

HealthConsult observed that the 61 items on the list do not reflect a classification for a relatively homogenous set of services (even at the level of each sub-list). Accordingly, the study started by developing draft definitions for each item on the NHMRC list (by supplementing what was in the NHMRC paper), and seeking stakeholder input into finalising the definitions via the public consultation process; through site visits to 13 hospitals and discussion with three organisations involved in trials conducted in the primary and community services sector; and through a number of consultation with interested stakeholder groups (including industry and trial collaboratives). It should be noted that, consistent with the Ministerial Direction, there was no scope to alter the list for the purpose of developing the table of standard costs (the NHMRC undertook a stakeholder consultation process in 2012 as part of developing the list), so the study concentrated on drafting and refining definitions of the scope of services to be included in each item on the list.

2.3 THE CLINICAL – TESTS AND PROCEDURES ITEMS

The first sub-list itemises clinical tests and procedures (including clinical services). Table 2.2 shows that there are eight items on this sub-list in seven different categories. It contains the refined definitions for each item, commentary on how the standard cost associated with the item might be used in formulating clinical trial budgets, as well as suggestions as to how the definition of the item could be further refined in any subsequent review of the NHMRC list.

Table 2.2: The NHMRC sub-list of standard items associated with clinical trials for clinical – tests and procedures with the refined definitions and associated comments

Major category	Item	Reference number	Definition	Comments
Screening Visit and Health Assessment	Clinical services provided specifically for the purposes of screening and health assessment	1.1.1	• Comprises a range of clinical services provided for the purposes of trial participant screening including physical examination, obtaining a medical history, measuring vital signs, diagnostic tests, imaging examinations, confirmation of diagnosis (which may include genomic eligibility confirmation), providing information about the clinical trial, explaining the requirements of involvement, ensuring understanding and, where appropriate, obtaining consent to participate in the clinical trial.	• The screening visit and health assessment might overlap as the baseline visit for some eligible participants. • The screening visit and health assessment often includes a range of procedures and/or consultations from sub-list one: 1.2.1 – 1.7.1. • Screening visit and health assessment may include consultation (where clinical services are not provided) with the principal investigator, research nurse and/or clinical research coordinator, which should be determined based on the hourly rate in items 2.6.3, 2.6.4 and 2.6.5 respectively.
Laboratory Tests/Procedures	Laboratory tests and procedures itemised under the MBS	1.2.1	• As per the MBS Schedule Groups P1-P9. For example, includes pathology, histopathology, haematology, chemical, microbiology, immunology, tissue pathology, cytology, genetics, etc.	• Any laboratory activities related to biospecimen collection, processing, analysis, storage and/or destruction for the sole purpose of the clinical trial that are not tested locally should be included under items 2.5.1 – 2.5.4, as applicable.
Medical Imaging	Imaging examinations and procedures itemised under the MBS	1.3.1	• Includes diagnostic radiology (e.g. plain radiography, computed tomography (CT), magnetic resonance imaging (MRI), ultrasound and nuclear medicine).	• No comment.
	PET-FDG/FLT scans not itemised under the MBS	1.3.2	• Includes Positron Emission Tomography (PET) scans using the radiopharmaceuticals fluorodeoxyglucose (FDG) or fluorothymidine (FLT)	• PET-FLT scans are not currently covered under any MBS item numbers.
Radiation Therapy	Radiation therapy planning and treatment itemised under the MBS	1.4.1	• Includes radiation therapy planning, external beam radiation therapy, brachytherapy, etc.	• Only for non-standard of care radiation therapy planning and treatment.
Other Clinical Tests or Procedures	Other clinical tests or procedures itemised under the MBS	1.5.1	• Includes surgical and non-surgical procedures (e.g. diagnostic and treatment related procedures) performed by clinically and/or scientifically qualified staff.	• This item does not cover instances where a trial protocol may require tests and/or procedures not covered by the MBS. Such instances are not covered in the current NHMRC list.
Specialist Medical Consultations	Specialist medical consultations itemised under the MBS	1.6.1	• Includes all specialist medical consultations (including GPs, dentists, etc.).	• Only for non-standard of care specialist medical consultations.

Major category	Item	Reference number	Definition	Comments
Nursing / Allied Health Consultations	Nursing/Allied Health consultations not itemised under the MBS	1.7.1	• Includes all nursing and allied health services.	• Only for non-standard of care nursing and allied health services.

2.4 THE CLINICAL – TRIAL SUPPORT SERVICES

The second sub-list itemises clinical trial support services. Table 2.3 shows that there are 21 items on this sub-list in six different categories. It contains the refined definitions for each item, commentary on how the standard cost associated with the item might be used in formulating clinical trial budgets, as well as suggestions as to how the definition of the item could be further refined in any subsequent review of the NHMRC list.

Table 2.3: The NHMRC sub-list of standard items associated with clinical trials for clinical – trial support services with refined definitions and associated comments

Major category	Item	Reference number	Definition	Comments
Departmental Protocol Review	Departmental Protocol Review	2.1.1	• Includes the Heads (or nominees) within the clinical trial host unit (e.g. oncology unit, respiratory unit, etc.) in addition to the supporting departments (e.g. pharmacy, pathology, radiology, radiation therapy, other clinical specialties, clinical trials office/governance office, etc.) reviewing the clinical trial protocol. The process may involve individuals or a panel drawn from the above mentioned departments to review the protocol for scientific merit and local feasibility.	• Departmental protocol review is often considered one aspect of the site selection including site feasibility assessment process.
Departmental Establishment/Set up Fees	Departmental Establishment/Set up Fees	2.2.1	• The Departmental Establishment/Set up Fees includes the fees associated with each Department involved in clinical trial set up activities which may include, but not restricted to preparing trial specific request forms, coordination with investigators and/or meeting with sponsors, instructions and identification of locations for storage of samples, development of supporting documentation and/or IT/data management.	• Fee practices for this item vary by site but often cover activities of items covered elsewhere on the NHMRC list. Hence caution should be given to this item as there is potential to duplicate the activities of other items (i.e. item 2.3.1, 3.1.2, 3.1.3, 3.1.4, 3.1.8, 3.1.9 and 3.2.1).
Departmental Ongoing Administration Fees	Departmental Ongoing Administration Fees	2.3.1	• This is a fixed fee that covers all activities associated with the ongoing administration of a clinical trial including: ➢ organising and making available materials for monitors visits (i.e. includes printing and photocopying, etc.); and ➢ management of clinical trial resources including human and infrastructure.	• Fee practices for this item vary by site but often cover activities of items covered elsewhere on the NHMRC list. Hence caution should be given to this item as there is potential to duplicate the activities of other items (i.e. item 2.6.1, 2.6.2, 2.6.3, 2.6.4, 3.2.6, 3.2.9 and 3.2.10).

Major category	Item	Reference number	Definition	Comments
Pharmacy / Investigational Drug-related	Staff training (drug specific)	2.4.1	• Includes training undertaken by pharmacy staff on the protocol (including site specific dispensing guidelines), use of Interactive Voice Response System (IVRS)/Interactive Web Response System (IWRS) randomisation systems, as well as educating other pharmacists (i.e. those on wards etc.) as well as doctors, nurses etc. on the drug-specific aspects of the clinical trial protocol (e.g. in drug handling etc.).	• This item should not get confused with item 3.1.9 which is for general staff training which is not specific to the pharmacy department.
	On call and call in/call back fees	2.4.2	• Includes fees associated with being on call, call in or call backs of pharmacy staff to deal with events specifically associated with the clinical trial.	• These fees typically include the first three hours of labour following call in/call back, with any additional hours being charged at an hourly rate.
	Drug stocking	2.4.3	• Includes the receiving of pharmacy stock for the clinical trial, completing an inventory check (online or manual), downloading temperature log (if applicable), sending any required data (e.g. checked inventory list) about the receipt of stock to trial sponsor and transferring the stock to the required storage location (e.g. shelf, fridge, freezer etc.). The drug stocking activity also includes stock management which includes expiry management activities (e.g. recording and storing used/returned drugs; data entry associated with returning any expired or unused drugs, returning unused/used drugs to sponsor etc.)	• Any review of the NHMRC list of activities should consider consolidating some of the pharmacy items as there are a number of closely related item which are difficult to make mutually exclusive. For example, the process of "drug storage and temperature monitoring" (item 2.4.7) and "drug dispensing and accountability" (item 2.4.5) are often thought to be part of drug stocking (item 2.4.3).
	Drug preparation, labelling and re-labelling	2.4.4	• Includes the manufacturing of the drugs (if applicable) or the preparation of the drugs (e.g. aseptic, cytotoxic or placebo preparation) required for the clinical trial as well as the associated general consumables (e.g. intravenous fluids, filters, etc.); the development and maintenance of special dosage forms (including the activities associated with the randomisation process if applicable), labelling and re-labelling (e.g. due to extension of the expiry date of the drug) of all drugs involved in the clinical trial.	• Wide variation in the activities involved (e.g. not all clinical trials involve drug manufacturing) which are dependent on the type of drug trial (e.g. cytotoxic drug vs. tablet) and number of drugs involved in the trial. • For the purposes of mutual exclusivity between items 2.4.4 and 2.4.5, the activities associated with "preparation" (which includes labelling) is included under item 2.4.4 but the activity associated with "giving out" the drug (including the associated pharmacy consult) is included under item 2.4.5. • Any review of the NHMRC list of activities should consider consolidating some of the pharmacy items as there are a number of closely related item which are difficult to make mutually exclusive. For example, the process of "drug dispensing and accountability" (item 2.4.5) are often thought to be part of "drug preparation, labelling and re-labelling" (item 2.4.4).
	Drug dispensing and accountability	2.4.5	• Includes the conduct of dispensing (including the provision of counselling to clinical trial participants), review of clinical trial participants' adherence to the trial protocol and recording details of the clinical trial in the participant's medical record (paper based or electronic).	• It was recognised that drug preparation and labelling is often part of the drug dispensing process. • Development of trial specific protocols, manuals, procedures etc. should be captured under the Departmental Establishment/Set up Fee (item 2.1.1).

Major category	Item	Reference number	Definition	Comments
	Drug transfer	2.4.6	• Includes the cost associated with drugs being transferred from one institution to another, or delivered to patients by courier, which would involve: ➢ transport costs; ➢ education/information; ➢ quality assurance for handling/transport; and ➢ administration/paperwork.	• Not all pharmacies are involved in drug transfer.
	Drug storage and temperature monitoring	2.4.7	• Includes the shelf, fridge and/or freezer storage of medications/drugs being used throughout the clinical trial; storage of returned stock and temperature monitoring (including log recording) of the refrigeration and/or freezer facilities.	• Often not related to any specific clinical trial.
	Drug destruction	2.4.8	• Involves the destruction of drugs according to the institutions policy, sponsor requirements (if applicable), safe operating practices and the requirements of the trial.	• Drug destruction processes varies depending on the type of drugs involved in the clinical trial (e.g. from emptying the vials down the sink to transferring drugs to commercial facilities for destruction (e.g. high temperature incinerators). • This process is sometimes covered by the pharmacy department ongoing administration fee (item 2.3.1).
Biospecimen-related	Biospecimen collection and processing (central and local)	2.5.1	• Includes the collection, processing and transport costs (e.g. quarantine permits, etc.) of clinical trial biospecimens. Examples of biospecimens include blood and other body fluids, tissues, nucleic acids, and other direct derivatives from human tissues. Processing of biospecimens includes those activities involved in preparing the biospecimen for analysis following collection and those activities involved in the arrangement of transfer of the biospecimen(s) to local or central laboratories.	• Activities related to training/accreditation for biospecimen related activities should be captured under item 3.1.9.
	Biospecimen analysis (central and local)	2.5.2	• Includes the analysis and reporting of biospecimens (including blood and other body fluids, tissues, nucleic acids, and other direct derivatives from human tissues) collected as part of the clinical trial where the test/procedure is not covered under the MBS.	• Activities related to training/accreditation for biospecimen related activities should be captured under item 3.1.9.
	Biospecimen storage (central and local)	2.5.3	• Includes the storage and management of biospecimens (including blood and other body fluids, tissues, nucleic acids, and other direct derivatives from human tissues) collected as part of the clinical trial that are not covered under the MBS.	• Activities related to training/accreditation for biospecimen related activities should be captured under item 3.1.9.
	Biospecimen destruction (central and local)	2.5.4	• Includes the destruction of biospecimens (including blood and other body fluids, tissues, nucleic acids, and other direct derivatives from human tissues) collected as part of the clinical trial that are not covered under the MBS.	• Activities related to training/accreditation for biospecimen related activities should be captured under item 3.1.9.

Major category	Item	Reference number	Definition	Comments
	Tissue repository set-up and management	2.5.5	• Includes the central project management set up, tracking and administration for establishing the tissue repository and ongoing management.	• No clinical trial site that was visited was involved in the establishment or management of a tissue repository.
Clinical Staff/Resource Allocation	Coordinating principal investigator surcharge	2.6.1	• The stated additional time multiplied by unit labour cost (*hourly rate plus on-costs, overtime, overheads and CPI increases)* that the coordinating principal investigator is expected to spend on coordinating the clinical trial.	• Principal investigators are almost always senior medical doctors.
	Investigator allocation	2.6.2	• The stated time allocation multiplied by unit labour cost (*hourly rate plus on-costs, overtime, overheads and CPI increases)* for each investigator (who is listed on the ethics approval) is expected to be involved in the clinical trial.	• Investigators tend to be senior medical doctors.
	Research nurse allocation	2.6.3	• The stated time allocation multiplied by unit labour cost (*hourly rate plus on-costs, overtime, overheads and CPI increases)* for the research nurses that are expected to be involved in the clinical trial.	• Research nurses will be involved in the majority of the activities included in sub-lists 2 and 3.
	Clinical research coordinator (non-research nurse) allocation	2.6.4	• The stated time allocation multiplied by unit labour cost (*hourly rate plus on-costs, overtime, overheads and CPI increases)* for the clinical research coordinator (e.g. personnel with scientific qualification, etc.) that are expected to be involved in the clinical trial.	• Clinical research coordinators will be involved in the majority of the activities included in sub-lists 2 and 3.
	Clinic/theatre usage	2.6.5	• The estimated amount of time (in hours) clinic and/or theatre usage is expected to be required to conduct the clinical trial	• No site visited had factored clinic/theatre usage charges, as a stand-alone item, into a clinical trial budget.

2.5 THE NON-CLINICAL SERVICES

The third sub-list itemises non-clinical trial services. Table 2.4 shows that there are 32 items on this sub-list in three different categories. It contains the refined definitions for each item, commentary on how the standard cost associated with the item might be used in formulating clinical trial budgets, as well as suggestions as to how the definition of the item could be further refined in any subsequent review of the NHMRC list.

Table 2.4: The NHMRC sub-list of standard items associated with clinical trials for non-clinical services with the refined definitions and associated comments

Major category	Item	Reference number	Definitions	Comments
Project Development	Preparation of research proposal	3.1.1	• Includes the preparation of the initial research synopsis, research proposal, grant application, the detailed clinical trial protocol and other material required for an ethics submission (e.g. Investigators Brochure, Patient Information and Consent Form, advertising and information materials, etc.).	• This item refers to activities undertaken only for investigator initiated clinical trials (i.e. non-industry sponsored clinical trials).

Major category	Item	Reference number	Definitions	Comments
	Site selection including site feasibility assessment process	3.1.2	• Includes the: ➢ assessment of study feasibility at a site including the completion of feasibility questionnaire/s; ➢ budget review and negotiation; ➢ legal review and institutional sign off; and ➢ the site selection/feasibility visit.	• Some clinical trial sites capture the activities associated with site selection in their Departmental Establishment/Set Up fees.
	Preparation and submission of applications to HREC and institutions	3.1.3	• **Preparation and submission of applications to HREC:** Includes the preparation and submission of the human research ethics committee (HREC) application form (or equivalent) and supporting documentation which includes the site specific participant information and consent form (PICF), processing of country specific regulatory documents (e.g. the Clinical Trial Notification (CTN) Scheme form), insurance and indemnity documents, trial agreements, recruitment and advertising materials, etc. Also includes revisions to applications according to ethics committee requests. • **Preparation and submission of applications to institutions:** Includes the preparation and submission of the Site Specific Assessment (SSA) application forms which involves completion of the form, obtaining authorising signatures, liaising with inter-institutional Departments (e.g. radiology, pharmacy, etc.), adapting the Lead HREC approved master PICF(s) with site specific letterhead and contact details; submission of SSA to the research governance officer (RGO) for review; liaison with sponsor, responding to RGO queries, forwarding copies of relevant authorisations and associated correspondence/documentation to sponsor.	• Some sites include the activities associated with preparation and submission of applications to HREC and institution in the "departmental establishment/set up fee" (item 2.2.1). • The additional time taken to prepare and submit the HREC application by a lead site should be captured under this item. However the additional time involved in managing the ongoing coordination of the clinical trial, due to being the lead site, should be captured under the Lead HREC/Lead site fee which is item 3.1.7.
	Radiation safety and/or biosafety reports	3.1.4	• Includes the preparation and submission of the safety and/or biosafety reports	• No comment.
	HREC (ethical) review fee	3.1.5	• Is the fee charged by the Ethics Committee for the review of the HREC application	• The activities associated with preparation and submission of applications to HREC and institutions should be captured under item 3.1.3 and not this item. • The activities associated with the review of the site assessment application should be captured under item 3.1.6.
	Institutional (site assessment) review fee	3.1.6	• Is the fee charged by the research governance office for the review of the site specific assessment (or equivalent) application	• The activities associated with preparation and submission of applications to HREC and institutions should be captured under item 3.1.3 and not this item. • The activities associated with the review of the HREC (ethical) application fee should be captured under 3.1.5.

Major category	Item	Reference number	Definitions	Comments
	Lead HREC/Lead site fee	3.1.7	• Is the fee charged by the lead site for the ongoing coordination and management of all the nominated sites participating in the clinical trial	• The additional personnel time required for the preparation and submission of the lead HREC application to the HREC and institutions should be captured under item 3.1.3 and not 3.1.7. • The activities associated with the review of the lead HREC (ethical) application should be captured under 3.1.5 and not this item.
	Investigator meetings	3.1.8	• Includes the organisation and the attendance of principal or co-investigators and/or Clinical Trials Manager/Coordinator at meetings about the clinical trial	• No comment.
	Staff training	3.1.9	• Includes any training (e.g. detailed protocol, eCRF, GCP) of staff directly involved in the clinical trial (excluding staff training that occurs during the start-up meeting).	• Activities associated with pharmacy staff undertaking training specific to pharmacy work involved in clinical trials is included under item 2.4.1. • Staff training that occurs on the day of the start-up meeting should be captured under item 3.2.1.
	Trial-specific equipment hire/purchase	3.1.10	• Includes the hire and/or purchase of any equipment (excluding IT infrastructure) required for the purposes of conducting the clinical trial.	• This item excludes any activities required to maintain trial-specific equipment or time required to return trial specific equipment that has been 'loaned'. These activities should be captured under item 3.2.6 "ongoing administration, monitoring and reporting" and 3.2.11 "Study close-out activity including preparation for audit" respectively.
	IT set-up, equipment and maintenance	3.1.11	• Includes the purchasing and/or hiring of the IT equipment required for the clinical trial as well as the required set-up/customisation of the IT infrastructure so that it is suitable for use in the clinical trial.	• Any staff training related to IT equipment should be captured under item 3.1.9 "staff training". • This item excludes any activities required to maintain trial-specific IT equipment or activities required to return trial specific IT equipment that has been 'loaned. These activities should be captured under item 3.2.6 "ongoing administration, monitoring and reporting" and 3.2.11 "Study close-out activity including preparation for audit" respectively.
	Trial centre set-up and development	3.1.12	• Including the central (i.e. across all trial sites) set up and development of all clinical trial support materials including grants, budgets, Case Report Forms (CRFs), databases, randomisation procedures, statistical plan, quality assurance, etc.	• The inclusion of this item in the list should be reviewed as no clinical trial sites visited were involved in this activity.
Project Implementation	Start-up meeting	3.2.1	• The meeting that occurs at the start of the clinical trial, where the sponsor representative attends the clinical trial site for a series of meetings with personnel to be involved in the trial.	• Any staff training that occurs at the start-up meeting should be captured under this item and not item 3.1.9 "staff training".

Major category	Item	Reference number	Definitions	Comments
	Pre-screening activity	3.2.2	• Involves the activities directly linked with clinical trial cohort identification which includes: ➢ database and medical records review; ➢ the development of recruitment plans including suggested strategies, timelines and costs; ➢ the development and execution of consultation plan to support study recruitment as well as provide opportunities to increase awareness about clinical research and opportunities to participate; ➢ interviewing potential participants which includes asking questions to address the specific inclusion/exclusion criteria for the study and other issues of suitability (either by telephone or face-to-face); and ➢ documenting pre-screening trial activity (irrespective of eligibility).	• The boundary between pre-screening activities, recruitment and the clinical tests and procedures conducted as part of the screening/health assessment visit is not always clear. Caution should be taken so as to not double count these activities. • Activities where screening of patient records was undertaken when reviewing the protocol initially should be captured under item 2.1.1 "Departmental Protocol Review". • Activities where screening of patient records takes place as part of feasibility assessment should be captured under "site selection including site feasibility assessment process" (i.e. item 3.1.2). • Activities where a patient may attend a site for further pre-screening assessment (i.e. pre recruitment activities) should be captured under this item and not under item 3.2.3 "recruitment activity".
	Recruitment activity	3.2.3	• Includes all activities involving potential and recruited clinical trials participants between the completion of pre-screening and the final determination of the assessment for suitability. Such activities include the provision of education and information to possible clinical trial participants, the informed consent process, organising the screening visit (which includes any required assessments and/or tests), and documenting all the recruitment activity (irrespective of the number of potentially eligible participants that fail the screening assessment).	• The boundary between pre-screening activities, recruitment and the clinical tests and procedures conducted as part of the screening/health assessment visit is not always clear. Caution should be taken so as to not double count these activities. • In particular the line between pre-screening and recruitment is blurred – therefore activities pre gaining informed consent (which includes a consultation with the PI and/or CTC/M prior to informed consent being obtained) should be captured under item 3.2.2.
	Medical records set-up, access and storage	3.2.4	• Includes the work undertaken by the medical records departments to access the medical record, for the purposes of the clinical trial only, and provide to the clinical trial host unit for clinical trial monitoring requirements.	• Some sites include the activities associated with the establishment of the medical and/or clinical trial record, as well as accessing and storing the medical record under item 2.2.1 "Departmental Establishment/Set up Fees". To prevent double counting it is suggested that the activities associated with the setup of the medical and/or clinical trial record is included under the establishment fee/set up fee (item 2.2.1).
	Interpreter services	3.2.5	• Includes the fees associated with using interpreter services for the purposes of the clinical trial.	• Few instances of interpreter services in clinical trials were reported at the site visits.

Major category	Item	Reference number	Definitions	Comments
	Ongoing administration, monitoring and reporting	3.2.6	• **Ongoing administration** activities include administration tasks that occur post the establishment phase and includes managing clinical trial documentation, retrieving medical and/or clinical records, invoicing, preparing materials for monitoring visit, VPN access etc.; • **Ongoing monitoring** activities include liaison with investigators and/or sponsor (including the monitors), CRF completion, data entry, endpoint recording, involvement in monitor visits, review of SAE reports, etc.; and • **Ongoing reporting** activities include: accrual reporting, safety and adverse event reporting, annual reporting, annual ethics report, etc.	• This item overlaps with the "Departmental Ongoing Administration fee" (item 2.3.1) and the "Departmental Establishment/set up fee" (item 2.2.1). Care should be taken to not double count administration activities. • It is suggested that in any review of the NHMRC list that may be commissioned specifically consider whether it is necessary to continue to have both items 2.3.1 and 3.2.6. There may be an opportunity to consolidate these items or remove the administration component from item 3.2.6 so it just represents the ongoing monitoring and reporting required for clinical trials.
	Data analysis (+/- study report)	3.2.7	• Includes the time spent in undertaking the clinical trial data analysis and/or producing the study report.	• Not an activity typically undertaken by the clinical trial site.
	Trial centre data management, data analysis and ongoing administration, monitoring and reporting	3.2.8	• Includes the CRF design, CRF annotation, database designing, data-entry, data validation, discrepancy management, medical coding, data extraction, and database locking in compliance with regulatory standards. It also includes the continual monitoring and reporting of the data in the trial centre database.	• Not an activity typically undertaken by the clinical trial site.
	Amendment preparation and submission	3.2.9	• Includes the preparation and submission of protocol amendments to the HREC and RGO including amendments to the PICFs, investigator brochures and any other trial information which has been updated/amended	• This item does not capture the activity associated with the RGO and/or HREC reviewing the submitted amendments. Review of the amendments by the RGO and/or HREC is included under item 3.2.10 "amendment review".
	Amendment review	3.2.10	• This includes the fee charged by the RGO and/or HREC to review an amendment. The time spent by the clinical trials unit to prepare and submit the amendment to the RGO and/or HREC is included under item 3.2.9.	• This item does not capture the activities associated with the clinical trials units preparing and submitting the amendments to the RGO and/or HREC. These activities are included under item 3.2.9 "amendment preparation and submissions".
	Study close-out activity including preparation for audit	3.2.11	• Includes the activities undertaken to confirm that each site's clinical trial obligations have been met and post study obligations are understood. The closeout activities include verifying that the study procedures have been completed, data is collected, and, if relevant, study intervention is returned to the responsible party or prepared for destruction. For example, if the clinical trial is a randomised, double-blind clinical trial, the close-out should include plans to unblind/unmask and debrief site staff and subjects upon trial completion. The boxing up of all trial material ready for archiving/storage is also included under this item.	• The activities associated with preparing records for archiving are included in this item.
	Archiving of trial records	3.2.12	• Includes the storage fee charged for archiving of clinical trial related documents for up to the agreed number of years of storage.	• No comment.

Major category	Item	Reference number	Definitions	Comments
Participant-related	Participant payment	3.3.1	• Includes a payment made to clinical trial participants to join in the clinical trial. Such payments are generally described in the Clinical Trial Agreement and in the Patient Information and Consent Form and may be paid in a lump sum at the beginning of the trial or the conclusion of the trial or in instalments at each visit.	• Any activities associated with invoicing participant payments should be captured under item 3.2.6 "ongoing administration, monitoring and reporting". • There is need for this item to be reviewed along with all participant payment related items. The only activities that are relevant to trial sites are the activities associated with administering the participant payment process. The amount of participant payments, where they are considered ethical, is discretionary, and should be properly be determined by the trial sponsor.
	Participant/carer time and inconvenience reimbursement	3.3.2	• Includes a payment, provided to a clinical trial participant, which is linked to the time involved in participating in the clinical trial and inconvenience created. Such payments are generally described in the Clinical Trial Agreement and in the Patient Information and Consent Form and may be paid in a lump sum at the beginning of the trial or the conclusion of the trial or in instalments at each visit.	• Comments as per item 3.3.1.
	Participant/carer travel	3.3.3	• Includes participant/carer out-of-pocket travel costs as described in the Clinical Trial Agreement and in the Patient Information and Consent Form.	• Sites often include the participant/carer parking allowance under participant/carer travel. Further sites often include the participant/carer meals allowance under participant/carer travel. Care should be taken to not double count. • Comments as item 3.3.1.
	Participant/carer parking	3.3.4	• Includes participant/carer out-of-pocket parking costs as described in the Clinical Trial Agreement and in the Patient Information and Consent Form.	• Sites often include the participant/carer parking allowance under participant/carer travel. Care should be taken to not double count. • Comments as per item 3.3.1.
	Participant/carer meals	3.3.5	• Includes participant/carer out-of-pocket meal costs as described in the Clinical Trial Agreement and in the Patient Information and Consent Form.	• Sites often include the participant/carer meals allowance under participant/carer travel. Care should be taken to not double count. • Comments as per item 3.3.1.
	Participant/carer accommodation	3.3.6	• Includes participant/carer out-of-pocket accommodation costs as described in the Clinical Trial Agreement and in the Patient Information and Consent Form.	• Comments as per item 3.3.1.

Major category	Item	Reference number	Definitions	Comments
	Participant inpatient/overnight stay	3.3.7	• Includes any out-of-pocket costs incurred by clinical trial participants for an overnight stay in a participating clinical trial institution.	• Overnight stays form part of a clinical services and should be captured in sub-list one. However, currently, no items on sub-list 1 relate to the non-health professional costs associated with overnight stays, as there is a reliance on the MBS for almost all the clinical tests and procedures items. • There is no place in the list to deal with the hospital accommodation cost. The trial site can cover the cost of the professional service (medical, nursing or allied health time) but not the institution cost. • This issue should be dealt with as part of a review of the NHMRC list, to eliminate redundancy in the categories and to ensure that all necessary clinical services are exhausted by the categories
	Participant outpatient/day stay	3.3.8	• Includes any out-of-pocket costs incurred by clinical trial participants for an outpatient visit or day stay in a participating clinical trial institution.	• Outpatient/day stays form part of a clinical services and should be captured in sub-list one. However, currently, no items on sub-list 1 relate to the non-health professional costs associated with outpatient/day stays, as there is a reliance on the MBS for almost all the clinical tests and procedures items. • There is no place to deal with the day procedure suite cost, if the clinical tests and procedures service requires admission as a day patient. The trial site can cover the cost of the professional service (medical, nursing or allied health time) but not the institution cost. • This issue should be dealt with as part of a review of the NHMRC list, to eliminate redundancy in the categories and to ensure that all necessary clinical services are exhausted by the categories.

3

Literature review on experiences in costing of clinical trials

This Chapter reports on a brief review of the international literature that examined developments in measuring costs and/or setting prices associated with clinical trials.

3.1 COSTING COMMERCIAL RESEARCH STUDIES IN THE NHS

Similar to Australia, the UK National Health Services (NHS) noted wide variation in processes and prices for commercial trials; as well as widely variable operating overheads; and prolonged set up times (due to cost negotiations). Other issues identified included that England has a comparatively higher cost of living to the United States and parts of Europe; and that the cost effectiveness associated with undertaking clinical trials in the UK was lagging behind other developed nations.[2] As a result, it was decided to develop a clinical trials costing template in the UK, which aimed to:

- increase investment and commitment in clinical research by addressing industry's needs and aligning strategies;
- enable industry to quickly cost research for the UK and, engage investigators at an earlier stage;
- greatly increase the UK's profile as innovators and help ensure buy-in with future global drug development programs;
- increase the amount and diversity of research and treatments available to patients; and
- ensure that the NHS is fully reimbursed for undertaking all commercial research.

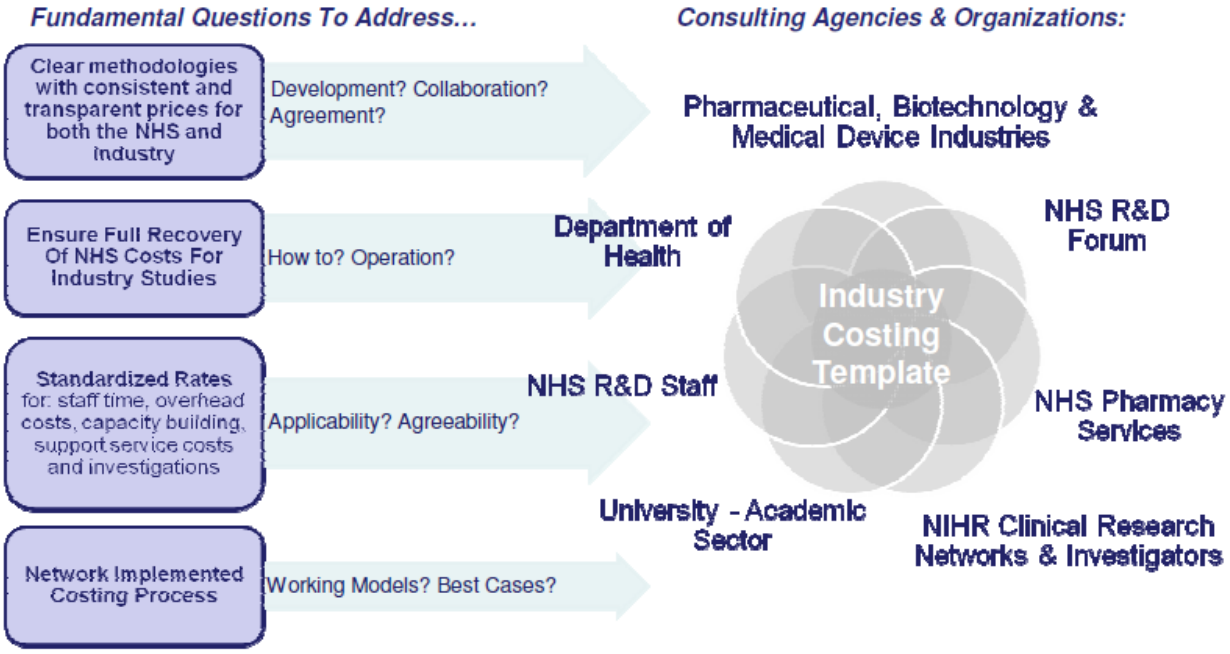
- As a result, in early 2007, the National Institute of Health Research (NIHR) costing project set objectives and goals for the development of its costing model3:
- provide clear methodologies and transparent prices for both the NHS and industry;
- ensure that the NHS is fully reimbursed for commercial research activities, in accordance with operating and financial requirements;
- identify standard rates for essential research activities that are both common and differing across the whole of the NHS;
- create a focused negotiating framework to facilitate timely and accurate study costing;
- supplement all costing activities with clear guidance and support; and
- ensure that costing process and negotiations can be implemented through the NIHR networks.

The costing project was developed with the advice and support of three key groups: the UK Clinical Research Collaborative Industry Road Map Group, the UK Clinical Research Network Costing Group and the UK Clinical Research Network Pharmacy Sub Group. Representatives included pharmaceutical industry, Contract Research Organisations, NHS R&D Forum, NHS R&D staff, Department of Health, University/academic sector, NIHR Topic and

[2] Burdette C, Using and implementing the industry costing template within the NHS; NHS R&D Forum Annual Conference. Available from: http://www.rdforum.nhs.uk/confrep/annual09/CBurdette.pdf
[3] Ibid.

Comprehensive Clinical Research Networks, and NHS Pharmacy Services.[4] Figure 1 outlines the costing project including consulting agencies involved in informing the final output, which was the costing template.

Figure 1: Agencies and organisations engaged in developing the Industry Costing Template



Source: Burdette C, Using and implementing the industry costing template within the NHS; NHS R&D Forum Annual Conference. Available from: http://www.rdforum.nhs.uk/confrep/annual09/CBurdette.pdf

Following wide consultation and the development of the costing template it was tested in two parts:

- **retrospective benchmarking**: to ascertain what research is actually costing in the UK and why there is such variability – in total 85 iterations were developed, five companies involved, 11 studies were provided, and five potential rates for overheads and capacity building were tested; and
- **Piloting the template:** a real-time benchmarking six-month pilot completed in January 2008, 12 studies were run through the template; nine companies were involved, and all Translational Research Cancer Networks were involved.

In trying to address the variability in overhead charges, the costing template built in research overheads and tested them through the benchmarking studies. Benchmarking demonstrated that 70% overheads and 20% capacity building elements added to direct, best fit commercial research costs.[5] The overhead rate is to cover the cost of infrastructure (indirect costs), which allows clinical trial activity to take place. The capacity building overhead of 20% is added to basic staff costs intended to contribute to the development of research activities by the Trusts i.e. training,

[4] UK Clinical Research Unit, Costing Industry Sponsored Studies through the NIHR Networks (Pharma/biotech contract research in secondary care). Available from: http://www.sabp.nhs.uk/aboutus/policies/A-C/clinical-trials/0010%20Appendix%20D%20-%20Costing%20Clinical%20Trials.pdf/at_download/file

[5] Burdette C, Using and implementing the industry costing template within the NHS; NHS R&D Forum Annual Conference. Available from: http://www.rdforum.nhs.uk/confrep/annual09/CBurdette.pdf

education, material and equipment. The work on the costing template is ongoing with regular updates and benchmarking activities.

As a result, the NHS has developed a set of costing templates for commercial research to provide transparency, consistency and predictability for companies, whilst ensuring full cost recovery for the healthcare site.[6] There are four current versions of the industry costing templates covering drug or device based research in either a primary care (e.g. GP practice) or secondary care (e.g. hospital) setting.[7] The templates generate set-up, per patient and additional costs that are based on the time taken to perform a task using standardised hourly rates and price lists. To account for location cost weighting when using national rates, the Department of Health's Payments by Results Market Forces Factor is applied.[8]

The costs are guidance only and local negotiation may still be needed to agree a suitable price with each site involved to reflect the site facilities and practice. To date the costing templates have been reviewed positively by commercial companies and NHS trusts. They appear to have improved the negotiation process, by providing a good and transparent starting point for negotiations.[9] No evaluation or further research on the impact of the costing template was identified.

3.2 LITERATURE ON MEASURING COSTS IN CLINICAL TRIALS

The following section briefly describes some of the literature on the measurement of costs in clinical trials. The material is not as relevant as that identified for the UK, because it mainly attempts to measure the aggregate cost of a clinical trial, rather than cost the activities associated with conducting clinical trials.

3.2.1 Approach undertaken by University of California

The University of California, San Francisco published guidelines on best practice in clinical trial budgeting.[10] Factors affecting budgets include: (1) research personnel and composition and (2) the type, phase, acuity, or complexity of the protocols involved, the actual time it takes to do the work, organisation of clinical trial research services within the research centre, long-term follow-up (particularly if the end-point is death) and indirect costs. They also note that industry sponsored trials tend to be more labour intensive and cooperative trials are more driven by disease site.

The university finds that measuring actual work (task times) instead of the number of patients or protocols managed by a Clinical Research Centre (CRC) seems to be the best approach. However, the National Institute of Health (NIH)/ National Cancer Institute (NCI) recommends:

- one FTE manages 25 patients on study and 50 in follow-up (not clear on whether this covers only data management or also includes nursing and regulatory activities).

The Society of Clinical Research Associates recommends:

[6] National Institute for Clinical Research (NICR), 2013 Commercial Study Costing Templates. Available from: http://www.crncc.nihr.ac.uk/Life+sciences+industry/Set-up/costing
[7] Ibid
[8] Clinical Discovery, Counting the cost of clinical trials in the NHS, 5 march 2009. Available from: http://www.clinicaldiscovery.com/readArticle.aspx?articleId=117
[9] Ibid.
[10] Kellen JL, Clinical Trials Budgeting: methods and best practice. Available from: http://or.ucsf.edu/cg/7893-DSY/version/default/part/4/data/

- one FTE handling all responsibilities (i.e. regulatory, IRB, patient monitoring, data management, sponsor encounters/audits) could effectively manage approximately 30 new patients per year.

The Universities ballpark recommendations around study team labour include:

- allow 4-12 hours per visit or 1-2 hours per time point for CRC labour;
- allow 1-3 hours per visit for faculty labour;
- allow 1-2 hours per visit for nursing, if applicable; and
- screening for accrual: 10 patients will need to be screened in order to accrue one participant.

Missed costs tend to include: a lengthy consent form process; screening for accrual (10 patient screens for every one patient); supplies (office supplies, furniture, etc.); pharmacy costs; storage costs; and principal investigator conference calls.

3.2.2 Measuring oncology clinical trial costs

A study conducted by Penberthy et al[11] measured the effort required in screening for cancer clinical trials through the Clinical Trial Eligibility Database (CTED) used at the Virginia Commonwealth University. The estimation of cost was based on the following:

- cost for eligibility determination per enrolled patient was attributed according to the average salary for a research nurse or clinical research associate;
- hourly cost was allocated based on an 80% attribution of effort associated with eligibility screening by research nurses and 20% by clinical research staff (CRS).

This estimated cost per enrolled patient was then used in combination with the number of enrolled patients and evaluations from CTED to calculate the total cost of screening for each clinical trial phase during the study period as well, as the annualised total eligibility screening cost to the cancer centre. The average time spent to find, screen, and enrol a patient varied from 3.4 to 8.8 hours, and cost varied from $129 to $336, respectively. The hours per enrolment were greatest for phase one trials and lowest for observational trials. Time taken to enrol patients was longer for phase three over phase two trials. The published literature estimates screening costs from $120 to $2,508 per enrolled patient. This difference relates to variations in cost estimation methods used in the published literature, such as retrospective data capture, inclusion of non-therapeutic trials, and inclusion of recruitment-related costs (e.g., advertising).
Emanuel et al[12] collected data from 21 clinical sites, on the numbers of hours associated with 13 activities necessary to the conduct of clinical research. The hours were based on enrolling 20 patients in a 12-month randomised placebo-controlled trial of a new chemotherapeutic agent. This study systematically determined the actual time and non-clinical costs required to initiate and manage successfully a clinical research trial. The hours spent on each activity by specified staff were converted into costs using the actual 1999 salary and fringe benefit rates provided by each site. Table 3.1 provides a breakdown of findings by activity and institute type.

[11] Penberthy, L. T., B. A. Dahman, et al. (2012). "Effort Required in Eligibility Screening for Clinical Trials." Journal of Oncology Practice **8**(6): 365-370.

[12] Emanuel Ej et al, The costs of conducting clinical research, Journal of Clinical Oncology; 21 (22); 4145-4150; 2003

Table 3.1: Average time required for conducting randomised, controlled clinical research study

Activity	Number of hours to enrol and treat 20 subjects			
	NIH sponsored		Industry sponsored	
	Hours	Range	Hours	Range
Pre-IRB submission and initiation of study	57	5-177	117	6-223
Subject recruitment and informed consent	201	63-453	190	63-223
Randomisation and dispensing of drugs	113	10-295	156	17-487
Office visits	2,846	1,047-10,809	2,691	988-11,611
Management of adverse events	69	1.5-225	72	14-225
Data management and analysis	640	1.5-225	652	40-3,301
Audits and communications with the sponsor	65	2-156	112	12-235
Post study follow-up and meetings	21	2-120	48	1-155
Total hours	**4,012**	**1,512-13,319**	**3,998**	**1,735-15,699**

Source: Emanuel Ej et al, The costs of conducting clinical research, Journal of Clinical Oncology; 21 (22); 4145-4150; 2003

On average, slightly less than 4,000 cumulative hours (range, 1,512 to 13,319 hours) were required to conduct a randomised, controlled clinical trial of 20 subjects. There was no significant difference in the total hours between the NIH- and industry-sponsored clinical studies. The distribution of hours by the three major types of professionals involved in clinical research showed that physicians account for about 9% of the hours; nurses 32%, and data managers, 36%. Other professionals, such as pharmacists and administrative staff, contribute the remaining time. Non-clinical activities accounted for 28% of NIH sponsored trials and 32% of industry sponsored trials.

Overall, it costs it just over $6,000 (range, $2,098 to $19,285) per oncology subject to participate in the randomised controlled trial, excluding costs for diagnostic tests, blood work, and overhead. Of this amount non-clinical services cost $2,000 on average. The authors note considerable variation in the overall time and costs required to conduct clinical research trials between group practices and academic and cancer centres.

3.3 SUMMARY OF FINDINGS

Overall, the literature is limited in this field. Although it is likely that pharmaceutical companies and other clinical trial sponsor groups have a basis for determining trial costs and/or have done benchmarking work to understand trial costs, this information is not publically available. This literature review has found that the work undertaken by the NHS in developing costing templates represents the most comprehensive contribution to the field, and is relevant to Australia. The issues identified regarding variations in clinical trial costs around the UK in the mid-2000s parallel those currently faced by Australia. And, it is reported that the templates developed to improve the transparency of costs and to ensure cost recovery by trial sites seem be having a positive impact.

In terms of informing this study, it is noted that there are similarities between the NHS items and the current NHMRC items. But, the NHS costing templates are only for industry trials whereas the Australian study must consider all clinical trials, whether industry, collaborative groups or investigator driven. For commercial trials, the NHS has produced four costing templates that recognise differences in costs between device and drug trials, as well as in trials conducted in primary and secondary care settings. The main difference between the templates is that set-up and close-out fees for trials conducted in primary care services are less than for trials in secondary health services. Also of note, the medical device template includes costs associated with the supply and management of the device, but the parallel costs are not included on the drug trial template.

The NHS costs for clinical and non-clinical activities associated with clinical trials are mainly derived by estimating the time of the key personnel involved. There is an institutional overhead (70%) and a capacity building overhead (20%) charged on top of the hourly rate for clinical, nurse, pharmacy and other departmental staff. Costs and fees have been allocated for set-up, close out, archiving, and administration. In the NHS templates, pharmacy costs accord a separate tab, and the main differentiating feature in determining the cost relates to the type of drug dispensed i.e. aseptic vs. dispensary based (if required). The NHS costing template also makes clear distinctions between per patient costs, variable costs and set-up costs, which are bundled under these headings.

There are many important lessons from the NHS approach that have been taken forward into the methodology developed for the current study. There is one key difference, the NHS costing templates are designed for determining the full cost of a trial with the end product being the 'study budget total.' The templates are intended to be used by sponsors first and then by clinical trial units with the aim of providing a more streamlined approach to negotiations. The current study is designed only to produce a standard cost for each item on the NHMRC list, with the decision of how the list is used to determine a trial budget being left to trial sponsors and trial host sites. Given the NHS work, a natural extension of the current study would be to build costing templates (probably multiple templates to take account of the variety of factors that impact on clinical trial costs) to assist with the negotiation of the trial budget (as per the UK approach).

4

Costing the list of standard items for clinical trials

This Chapter presents the approach taken to derive a standard cost for each item on the NHMRC list. It starts with a discussion of the costing principles used, and then presents the three sub-lists along with the approach used to derive a standard cost for each item.

4.1 PRINCIPLES TO BE USED IN COSTING THE LIST OF STANDARD ITEMS FOR CLINICAL TRIALS

HealthConsult's assessment of the NHMRC list was that a mixture of approaches was needed to derive standard costs for each item. Accordingly, standard costs for some items are based on an analysis of prevailing fees (as the items were defined as fees incurred or charged) whereas standard costs for other items are determined from first principles using activity based costing. Where activity based costing was used, the study examined current practice in designing and implementing clinical trials in Australia through a series of visits to clinical trial host sites and consultation with other key stakeholders. The information generated through the investigative processes was used to determine the standard costs by application of the following principles:

- **Activity based costing based on developed process maps for each item on the list was used wherever possible**. Where possible, items were costed on an activity basis from first principles. A protocol based approach was used that developed process maps (where necessary), defined the resource units associated with each step in the process map, and determined standard unit costs for each resource. These three pieces of information were then used to derive an overall standard cost for items on the NHMRC list where activity based costing was used.

- **Unit costs were externally derived.** Where items on the NHMRC list were costed from first principles, the unit costs for the resource units used to determine standard costs came from secondary sources (e.g. the MBS or other published fee schedules; the National Hospital Costs Data Collection (Round 15) held by the IHPA; various Awards, classifications and pay rates under which hospital staff are employed; various charges levied by ethics committees, clinical trial auspice/coordinating bodies; and so on). Local (i.e. those measured at trial host sites) unit costs were not used (i.e. the local rate of pay for the principal investigator), but local resource units were used (i.e. the number of hours required by the principal investigator to complete the activities associated with various items on the list (e.g. preparation of ethics submissions, attendance at project start-up meeting, etc.)).

- **Standard costs were based on normal (typical) practices**. The timeframe and resources available to the study were such that constructing a prospective data collection to measure actual costs for each item across a series of clinical trials was not possible. The study determined standard costs by investigating the actual processes used across a series of trial sites, but the standard costs were not be based on the mean of a series of measurements. Rather, standard costs were based on a synthesis of the process maps derived from the fieldwork that identified normal or typical practices.

- **Standard costs/price schedules were used without amendment.** Where costing from first principles was not possible, generally accepted standard cost/price schedules (e.g. MBS fees for diagnostic tests) were used without amendment, as there was insufficient time and resources available to the study to validate pre-existing cost/price schedules. The use of a multiplier to reflect the fact that there may be a different cost experience associated with services provided in the clinical trial context (compared to a standard care context) was contemplated, but the relativities in the published price schedules were not altered. Where there were multiple cost/price schedules available for an item, all available cost/price schedules were examined and the most commonly accepted cost or price was used to determine an estimate of the standard cost.

- **Actual practices were investigated in a number of clinical trial sites through fieldwork**. As, for items costed from first principles, the standard costs were not calculated as the mean of a series of measures, purposeful random selection of fieldwork sites was not required. However, the sampling strategy ensured that the sites selected for fieldwork were reasonably representative of the settings in which clinical trials are conducted in Australia (i.e. provided coverage across trial and site characteristics including (type of intervention in clinical trial (e.g. drug, surgical, diagnostic), jurisdiction (six states and two territories), type of site (general hospital, specialist hospital, community organisation); location of site (metropolitan, regional); and sector of site (public, NGO, private)). Most of the selected sites were hospitals, consistent with fact that the great majority of clinical trials are based in hospitals.

- **The standard costs were developed on a fully absorbed cost basis**. Consistent with the other costing processes conducted by the IHPA, the standard costs were derived on a fully absorbed basis. This approach is also consistent with the NHMRC decision to not include specific institutional or departmental overhead items on the standard list. So all the determined standard costs include absorbed overheads (both salary related overheads and other institutional overheads); it is not intended that the standard costs be loaded by a factor that reflects overheads. Knowing that the table of standard costs includes overheads, users are free to refer to it as they wish for the processes of negotiating budgets for the establishment of clinical trials.

- **The costing process is transparent**. For each item on the NHMRC list, potential users of the table of standard costs know the basis on which the standard cost was derived, including any associated limitations. Where external (to the study) cost/price schedules and/or unit costs are used to derive the standard cost of an item, they will be referenced (subject only to any limitations imposed by commercial confidentiality). Appendices A to C provide all of the information needed to understand the basis for determination of the standard cost for each item on the NHMRC list.

- **Standard costs were measured, not prices.** The study has produced a table of standard costs, of necessity some standard costs are based on an analysis of prevailing fees or charges, as that is the way some items were defined by the NHMRC. However, in all cases, there is no mark-up on measured costs for pricing purposes (i.e. as with the NEP for public hospitals set by the IHPA, the NEP for items associated with clinical trials, that IHPA is required to produce by Ministerial Direction, equals the measured standard cost). Users of the table of standard costs are free to refer to it as they wish for the purposes of negotiating budgets for the establishment of clinical trials.

These principles were used to determine the best approach to costing each item on the NHMRC list. For some items, costing options were limited by the available evidence. Importantly, the methodology focussed on determining the cost experienced by trial host sites, as the concern expressed in the CTAG report was that the perceived increase in the costs of hosting trials had detracted from Australia's competitiveness as a potential destination for multi-

national clinical trials. Through the field work and the public submissions process (see, in particular, the submission by the Centre for Biostatics and Clinical Trials at the Peter MacCallum Cancer Institute), HealthConsult observed that there are a number of items on the NHMRC where the associated costs are typically not incurred by trial host sites (they are incurred by the trial sponsor or the sponsor's agent).

For many of these items, there was insufficient evidence to determine a standard cost, as the methodology focussed on trial host sites. As a number of these items related to costs that are typically incurred by trial sponsors or their agents, for industry sponsored trials, in particular, it is unlikely that the costs would have been made available for the purposes of the study (to preserve commercial confidentiality). The items for which standard costs have not been derived are clearly indicated as 'not determined' in the tables that follow. It is suggested that any future review of the NHMRC list consider again the question of the scope of the activities on the standard list, and whether the list should be restricted to activities where the cost is typically incurred by trial host sites, or whether it should cover all costs associated with clinical trials. If it is the former, based on the evidence gathered in this study, some items could be removed from the list, and if it is the later some items would need to be added to the list and the commercial confidentiality issue would need to be resolved.

4.2 COSTING THE CLINICAL TESTS AND PROCEDURE SUB-LIST

Table 4.1 provides details of the method used to determine the standard costs for the eight items on the clinical tests and procedures (including clinical consultation services) sub-list.

Table 4.1: The NHMRC sub-list of standard items for clinical tests and procedures (including clinical consultation services) with associated costing method

Item number	Item	Costing method	Costing basis	Develop process map?	Method for determining resource units and unit costs	Method for determining standard cost
1.1.1	Clinical services provided specifically for the purposes of screening and health assessment	Reference to standard cost for relevant items on NHMRC list	per service	No	• Use the trial protocol to identify applicable items on the NHMRC list and the associated standard cost	• Multiply the number of services required by the standard cost for each service for the relevant items on the NHMRC list, then sum to arrive at trial-specific standard cost
1.2.1	Laboratory tests and procedures itemised under the MBS	Reference to MBS fees	per service	No	• Identify applicable items on the MBS	• Use the relevant MBS fee and the multiplier to derive the standard cost
1.3.1	Imaging examinations and procedures itemised under the MBS	Reference to MBS fees	per service	No	• Identify applicable items on the MBS	• Use the relevant MBS fee and the multiplier to derive the standard cost
1.3.2	PET-FDG/FLT scans not itemised under the MBS	Reference to MBS fees	per service	No	• Identify nearest equivalent PET-FDG/FLT item on the MBS	• Use the chosen MBS fee and the multiplier to derive the standard cost
1.4.1	Radiation therapy planning and treatment itemised under the MBS	Reference to MBS fees	per service	No	• Identify applicable items on the MBS	• Use the relevant MBS fee and the multiplier to derive the standard cost
1.5.1	Other clinical tests or procedures itemised under the MBS	Reference to MBS fees	per service	No	• Identify applicable items on the MBS	• Use the relevant MBS fee and the multiplier to derive the standard cost

Item number	Item	Costing method	Costing basis	Develop process map?	Method for determining resource units and unit costs	Method for determining standard cost
1.6.1	Specialist medical consultations itemised under the MBS	Reference to MBS fees	per service	No	• Identify applicable items on the MBS	• Use the relevant MBS fee and the multiplier to derive the standard cost
1.7.1	Nursing/Allied Health consultations not itemised under the MBS	Reference to IHPA published prices	per service	No	• Identify applicable categories on the NHCDC Tier 2 Clinic list	• Use the published price weight multiplied by the national efficient price to derive the standard cost

4.3 COSTING THE CLINICAL TRIALS SUPPORT SERVICES SUB-LIST

Table 4.2 provides details of the method used to determine the standard costs for the 21 items on the clinical trials support services sub-list.

Table 4.2: The NHMRC sub-list of standard items for clinical trials support services with associated costing method

Item number	Item	Costing method	Costing basis	Develop process map?	Method for determining resource units and unit costs	Method for determining standard cost
2.1.1	Departmental Protocol Review	Primary costing, activity based	per protocol review	yes	• Identify resource units (minutes of labour) based on the process map and determine fully absorbed unit labour cost from external source	• Choose typical labour hours (median of observations) and multiply by unit labour cost, then sum to derive the standard cost
2.2.1	Departmental Establishment/Set up Fees	Reference to typical fees	per involved department per trial	no	• Identify typical fees charged by the involved departments to appropriately establish a clinical trial	• Choose typical fee (25th percentile of observations) for each involved department as basis for standard cost
2.3.1	Departmental Ongoing Administration Fees	Reference to typical fees	per department per trial per annum	no	• Identify typical fees charged by the involved departments for ongoing clinical trial administration	• Choose typical fee (25th percentile of observations) for each involved department as basis for standard cost
2.4.1	Staff training (drug specific)	Primary costing, activity based	per trial	yes	• Identify resource units (minutes of labour) based on the process map and determine fully absorbed unit labour cost from external source	• Choose typical labour hours (25th percentile of observations) and multiply by unit labour cost, then sum to derive the standard cost
2.4.2	On call and call in/call back fees	Reference to typical fees	per service (call in/call back)	no	• Identify typical fees charged by the pharmacy department for call in/call back of a clinical trial pharmacist	• Choose typical fee (median of observations) as the basis for standard cost
2.4.3	Drug stocking	Primary costing, activity based	per stock shipment received	yes	• Identify resource units (minutes of labour) based on the process map and determine fully absorbed unit labour cost from external source	• Choose typical labour hours (minimum of observations) and multiply by unit labour cost, then sum to derive the standard cost

Item number	Item	Costing method	Costing basis	Develop process map?	Method for determining resource units and unit costs	Method for determining standard cost
2.4.4	Drug preparation, labelling and re-labelling	Primary costing, activity based; and Reference to typical fees	per drug preparation; and per batch labelled/re-labelled	yes (for drug preparation only)	• For drug preparation, identify resource units (minutes of labour) based on the process map and determine fully absorbed unit labour cost from external source • For drug labelling and relabelling, identify typical fees charged by the pharmacy department per batch	• For drug preparation, choose typical labour hours (25th percentile of observations) and multiply by unit labour cost, then sum to derive the standard cost • For drug labelling and relabelling, choose typical fee (25th percentile of observations) as the basis for standard cost
2.4.5	Drug dispensing and accountability	Primary costing, activity based	Per participant per service	yes	• Identify resource units (minutes of labour) based on the process map for dispensing (simple and complex), accountability, and counselling separately; and determine fully absorbed unit labour cost from external source	• Choose typical labour hours (median of observations) and multiply by unit labour cost, then sum to derive the standard cost for dispensing (simple and complex), accountability, and counselling separately
2.4.6	Drug transfer	Primary costing, activity based	per service (drug transfer)	yes	• Identify resource units (minutes of labour) based on the process map and determine fully absorbed unit labour cost from external source	• Choose typical labour hours (median of observations) and multiply by unit labour cost, then sum to derive the standard cost
2.4.7	Drug storage and temperature monitoring	Primary costing, activity based	per trial per annum	no	• Identify resource units (minutes of labour) based on the process map and determine fully absorbed unit labour cost from external source	• Choose typical labour hours (median of observations) and multiply by unit labour cost, then sum to derive the standard cost, then adjust for the likely number of trial and non-trial drugs stored per annum
2.4.8	Drug destruction	Primary costing, activity based	per service (drug destruction)	yes	• Identify resource units (minutes of labour) based on the process map and determine fully absorbed unit labour cost from external source	• Choose typical labour hours (minimum of observations) and multiply by unit labour cost, then sum to derive the standard cost
2.5.1	Biospecimen collection and processing (central and local)	Primary costing, activity based	per service (biospecimen collection and processing)	yes	• Identify resource units (minutes of labour) based on the process map and determine fully absorbed unit labour cost from external source	• Choose typical labour hours (25th percentile of observations) and multiply by unit labour cost, then sum to derive the standard cost

Item number	Item	Costing method	Costing basis	Develop process map?	Method for determining resource units and unit costs	Method for determining standard cost
2.5.2	Biospecimen analysis (central and local)	Reference to MBS fees	per service (biospecimen analysis)	No	• Identify nearest equivalent test item on the MBS	• Use the chosen MBS fee and the multiplier to derive the standard cost
2.5.3	Biospecimen storage (central and local)	Not costed	N/A	yes (but not used in costing)	• Not determined	• Not determined (deemed to be included with biospecimen analysis)
2.5.4	Biospecimen destruction (central and local)	Not costed	N/A	yes (but not used in costing)	• Not determined	• Not determined (deemed to be included with biospecimen analysis)
2.5.5	Tissue repository set-up and management	Not costed	N/A	no	• Not determined	• Not determined (cost typically not incurred at trial host sites)
2.6.1	Coordinating principal investigator surcharge	Reference to external Awards	per hour	no	• Agree coordinating principal investigator hours and determine fully absorbed unit labour cost using AMA published full-time Specialists Minimum Remuneration levels	• Multiply agreed coordinating principal investigator hours by unit labour cost to derive the standard cost
2.6.2	Investigator allocation	Reference to external Awards	per hour	no	• Agree investigator hours and determine fully absorbed unit labour cost using AMA published full-time Specialists Minimum Remuneration levels	• Multiply agreed investigator hours by unit labour cost to derive the standard cost
2.6.3	Research nurse allocation	Reference to external Awards	per hour	no	• Agree research nurse hours and determine fully absorbed unit labour cost using the National Nurses Award	• Multiply agreed research nurse hours by unit labour cost to derive the standard cost
2.6.4	Clinical research coordinator (non-research nurse) allocation	Reference to external Awards	per hour	no	• Agree clinical research coordinator hours and determine fully absorbed unit labour cost using the NSW and Victorian Medical Scientists Award	• Multiply agreed clinical research coordinator hours by unit labour cost to derive the standard cost
2.6.5	Clinic/theatre usage	Not costed	N/A	no	• Not determined	• Not determined (no reasonable basis, and cost typically not charged by trial host sites, theatre use is usually for standard of care services)

4.4 COSTING THE NON-CLINICAL SERVICES SUB-LIST

Table 4.3 provides details of the method used to determine the standard costs for the 32 items on the non-clinical services sub-list.

Table 4.3: The NHMRC sub-list of standard items for non-clinical services with associated costing method

Item number	Item	Costing method	Costing basis	Develop process map?	Method for determining resource units and unit costs	Method for determining standard cost
3.1.1	Preparation of research proposal	Primary costing, activity based	per research proposal	yes	• Identify resource units (minutes of labour) based on the process map and determine fully absorbed unit labour cost from external source	• Choose typical labour hours (median of observations) and multiply by unit labour cost, then sum to derive the standard cost
3.1.2	Site selection including site feasibility assessment process	Primary costing, activity based	per site selection	yes	• Identify resource units (minutes of labour) based on the process map and determine fully absorbed unit labour cost from external source	• Choose typical labour hours (median of observations) and multiply by unit labour cost, then sum to derive the standard cost
3.1.3	Preparation and submission of applications to HREC and institutions	Primary costing, activity based	per application per clinical trial for lead and non-lead sites	yes	• Identify resource units (minutes of labour) based on the process map and determine fully absorbed unit labour cost from external source	• Choose typical labour hours (median of observations) and multiply by unit labour cost, then sum to derive the standard cost
3.1.4	Radiation safety and/or biosafety reports	Primary costing, activity based	per report	yes	• Identify resource units (minutes of labour) based on the process map and determine fully absorbed unit labour cost from external source	• Choose typical labour hours (median of observations) and multiply by unit labour cost, then sum to derive the standard cost
3.1.5	HREC (ethical) review fee	Reference to typical fees	per HREC application	no	• Identify typical fees charged by the HREC to review a clinical trial application	• Choose typical fee (median of observations) as the basis for standard cost
3.1.6	Institutional (site assessment) review fee	Reference to typical fees	per institutional assessment	no	• Identify typical fees charged by the Research Governance Office to review a clinical trial application	• Choose typical fee (25th percentile of observations) as the basis for standard cost
3.1.7	Lead HREC/Lead site fee	Reference to typical fees	per additional site per annum	no	• Identify typical fees charged by the lead HREC/lead site to administer and/or coordinate the activities associated with the clinical trial	• Choose typical fee (median of observations) as the basis for standard cost

Item number	Item	Costing method	Costing basis	Develop process map?	Method for determining resource units and unit costs	Method for determining standard cost
3.1.8	Investigator meetings	Primary costing, activity based	per trial per attendee per trial location (overseas or domestic)	yes	• Identify resource units (minutes of labour) based on the process map and determine fully absorbed unit labour cost from external source	• Choose typical labour hours (median of observations for overseas, minimum of observations for domestic) and multiply by unit labour cost, then sum to derive the standard cost
3.1.9	Staff training	Primary costing, activity based	per trial per participant	yes	• Identify resource units (minutes of labour) based on the process map and determine fully absorbed unit labour cost from external source	• Choose typical labour hours (median of observations) and multiply by unit labour cost, then sum to derive the standard cost
3.1.10	Trial-specific equipment hire/purchase	Primary costing, activity based	per equipment item (set-up and check only)	no	• Identify resource units (minutes of labour) needed to set up and check the equipment item and determine fully absorbed unit labour cost from external source	• Choose typical labour hours (median of observations) and multiply by unit labour cost, then sum to derive the standard cost
3.1.11	IT set-up, equipment and maintenance	Primary costing, activity based	per IT equipment item (set-up and check only)	no	• Identify resource units (minutes of labour) needed to set up and check the IT equipment item and determine fully absorbed unit labour cost from external source	• Choose typical labour hours (median of observations) and multiply by unit labour cost, then sum to derive the standard cost
3.1.12	Trial centre set-up and development	Not costed	N/A	no	• Not determined	• Not determined (no reasonable basis, and the cost is typically not incurred by trial host sites)
3.2.1	Start-up meeting	Primary costing, activity based	per start-up meeting	yes	• Identify resource units (minutes of labour) based on the process map and determine fully absorbed unit labour cost from external source	• Choose typical labour hours (25th percentile of observations) and multiply by unit labour cost, then sum to derive the standard cost
3.2.2	Pre-screening activity	Primary costing, activity based	per trial	yes	• Identify resource units (minutes of labour) based on the process map and determine fully absorbed unit labour cost from external source	• Choose typical labour hours (median of observations) and multiply by unit labour cost, then sum to derive the standard cost
3.2.3	Recruitment activity	Primary costing, activity based	per potential trial participant	yes	• Identify resource units (minutes of labour) based on the process map and determine fully absorbed unit labour cost from external source	• Choose typical labour hours (25th percentile of observations) and multiply by unit labour cost, then sum to derive the standard cost

Item number	Item	Costing method	Costing basis	Develop process map?	Method for determining resource units and unit costs	Method for determining standard cost
3.2.4	Medical records set-up, access and storage	Reference to typical fees	per medical record accessed	yes	• Identify typical fees charged by the medical record department to retrieve a record solely for the purposes of the clinical trial	• Choose typical fee (25th percentile of observations) as the basis for standard cost
3.2.5	Interpreter services	Reference to external Awards	per hour	no	• Agree interpreter hours and determine fully absorbed unit labour cost using the NSW Health Employee's Interpreters State Award	• Multiply agreed interpreter hours by unit labour cost to derive the standard cost
3.2.6	Ongoing administration, monitoring and reporting	Primary costing, activity based	per trial participant per annum	yes	• Identify resource units (minutes of labour) based on the process map and determine fully absorbed unit labour cost from external source	• Choose typical labour hours (25th percentile of observations) and multiply by unit labour cost, then sum to derive the standard cost
3.2.7	Data analysis (+/- study report)	Not costed	N/A	no	• Not determined	• Not determined (no reasonable basis, and the cost is typically not incurred by trial host sites)
3.2.8	Trial centre data management, data analysis and ongoing administration, monitoring and reporting	Not costed	N/A	no	• Not determined	• Not determined (no reasonable basis, and the cost is typically not incurred by trial host sites)
3.2.9	Amendment preparation and submission	Primary costing, activity based	per amendment	yes	• Identify resource units (minutes of labour) based on the process map and determine fully absorbed unit labour cost from external source	• Choose typical labour hours (25th percentile of observations) and multiply by unit labour cost, then sum to derive the standard cost
3.2.10	Amendment review	Reference to typical fees	per amendment	no	• Identify typical fees charged by the HREC or RGO to review an amendment to the clinical trial protocol	• Choose typical fee (median of observations) as the basis for standard cost
3.2.11	Study close-out activity including preparation for audit	Primary costing, activity based	per trial	yes	• Identify resource units (minutes of labour) based on the process map and determine fully absorbed unit labour cost from external source	• Choose typical labour hours (median of observations) and multiply by unit labour cost, then sum to derive the standard cost
3.2.12	Archiving of trial records	Reference to typical fees	per trial	no	• Identify typical fees charged by the clinical trial host site to archive the trial records	• Choose typical fee (25th percentile of observations) as the basis for standard cost
3.3.1	Participant payment	Not costed	N/A	no	• Not determined	• Not determined (any payments made at discretion of the trial sponsor)

Item number	Item	Costing method	Costing basis	Develop process map?	Method for determining resource units and unit costs	Method for determining standard cost
3.3.2	Participant/carer time and inconvenience reimbursement	Not costed	N/A	no	• Not determined	• Not determined (any payments made at discretion of the trial sponsor)
3.3.3	Participant/carer travel	Not costed	N/A	no	• Not determined	• Not determined (any payments made at discretion of the trial sponsor)
3.3.4	Participant/carer parking	Not costed	N/A	no	• Not determined	• Not determined (any payments made at discretion of the trial sponsor)
3.3.5	Participant/carer meals	Not costed	N/A	no	• Not determined	• Not determined (any payments made at discretion of the trial sponsor)
3.3.6	Participant/carer accommodation	Not costed	N/A	no	• Not determined	• Not determined (any payments made at discretion of the trial sponsor)
3.3.7	Participant in-patient/overnight stay	Not costed	N/A	no	• Not determined	• Not determined (no evidence of participants being charged in practice was found)
3.3.8	Participant outpatient/day stay	Not costed	N/A	no	• Not determined	• Not determined (no evidence of participants being charged in practice was found)

5

Determination of the table of standard costs

This Chapter presents the determination of the table of standard costs. It begins by describing the factors that have been considered in determining the standard costs; presents the table of standard costs and associated comments for each item on the NHMRC list; and then discusses a series of issues that should be considered if trial sponsors and trial host sites decide to use the standard costs to determine trial budgets.

5.1 DETERMINING THE TABLE OF STANDARD COSTS

In making the determination, IHPA is required to have regard to the matters set out in Section 131(3) of the *National Health Reform Amendment (Independent Hospital Pricing Authority) Act 2011*, as well as additional matters specific to the *Ministerial Direction to the Independent Hospital Pricing Authority on the Performance of its Functions (No. 1 of 2012)*. These matters are set out in Table 5.1.

Table 5.1: Matters to be considered by IHPA in determining the table of standard costs for activities associated with clinical trials in Australia.

Matters set out in Section 131(3) of the *National Health Reform Amendment (Independent Hospital Pricing Authority) Act 2011*	Matters set out in the *Ministerial Direction to the Independent Hospital Pricing Authority on the Performance of its Functions (No. 1 of 2012)*
(a) relevant expertise and best practice within Australia and internationally; *(b) submissions made at any time by the Commonwealth, a State or a Territory;* *(c) the need to ensure:* *(i) reasonable access to health care services; and* *(ii) safety and quality in the provision of health care services; and* *(iii) continuity and predictability in the cost of health care services; and* *(iv) the effectiveness, efficiency and financial sustainability of the public hospital system;* *(d) the range of public hospitals and the variables affecting the actual cost of providing health care services in each of those hospitals.*	*(iii) In addition, the Pricing Authority may, so far as the Act permits, have regard to the following matters:* *a. the actual activity of each item;* *b. principles of cost-recovery; and* *c. submissions from relevant parties, including clinical trial sponsors and private hospitals.*

These factors were carefully considered in developing the table of standard costs. In respect of clause 131(3) of the Act, a literature review was conducted to address sub-clause (a); a process of inviting public submissions was undertaken to address sub-clause (b); actual costs were measured and used to determine standard costs to address sub-clause (c); and visits to ten different public hospitals covering a range of characteristics were conducted to address sub-clause

(d). In respect of the Ministerial Direction, the actual activity of each item was considered, which resulted in a determination not being made for some items where there was typically no activity in the trial host sites (sub-clause (iii)(a)); the standard cost is based on the typical cost incurred (sub-clause (iii)(b)); and public submissions were invited, with the 25 submissions received influencing the final determination of the table of standard costs (sub-clause (iii)(c)).

In particular, there was a choice between determining one standard cost (with no (or minimal) variation) or determining a range for the standard cost for each item (i.e. lowest to highest) for each item on the NHMRC list. Given that this study had to be done in a short time period and the fieldwork was necessarily restricted, it was not considered possible to publish a range for the standard cost (a prospective costing study would have been better for this purpose). Although there were estimates made of the actual costs using data derived from the site visits, as already explained the sample of sites was not representative, and the logistics of the process prevented the cost of all the items being measured at all visited sites. For this reason, the observed range of costs may not be fully representative of actual practice, and in any case the range was generally so wide that publishing it as the standard cost would add little value, and would not be consistent with clause 131(3)(c)(iii) of the Act, which discusses the need for continuity and predictability in the cost of health care services.

For these reasons, it was thought that determining a single typical or representative standard cost for each item on the NHMRC list was the best approach. The standard cost for each item is intended to be the national efficient price for the item, consistent with the cost recovery principle required by the Ministerial Direction. It is recognised that in specific trial circumstances, the actual cost may be different from the standard cost. However, by publishing a reference standard cost, it leaves potential trial host sites and trial sponsors free to use the standard cost as a starting point for discussing the unique features of the trial being proposed and the associated costs, as part of negotiating the trial budget. Some matters that trial sponsors and trial host sites might wish to have regard to when using the standard cost as part of the budget negotiation process are discussed in section 5.3.

5.2 THE TABLE OF STANDARD COSTS

The costing information for all 61 items on the NHMRC standard list of activities associated with clinical trials is presented in the same format, in Appendix A (clinical tests and procedures), B (clinical – trial support services) and C (non-clinical services) of this report. Within the relevant Appendix, there are between one and three pages for each NHMRC list item, with the headings and content for each item being as shown in Table 5.2.

Table 5.2: Description of the contents of the standard cost determination for each item

Category of information	Summary of content
Identifying data including the determined standard cost	Includes the item's reference number, description, sub-list, category, definition (modified as a result of the fieldwork and consideration of submissions) and the determined standard cost.
Related items	Describes the items that are related to the item being presented, as a number of items on the list were found to have possible overlapping content.
Learning from site visits	Summarises the key learning relevant to determining the standard cost that was derived from the site visits.
Derived process map	For those items where primary costing is attempted, the process map that has been derived from the information generated by the site visits is presented as the basis of the standard cost estimate.
Considerations for deriving the cost	Discusses the options considered for deriving the cost of the item, including a summarised presentation of any secondary data that was accessed.
Table of standard costs	Describes the determination that has been made, including where available presenting a summary of the data points (observations) used. Includes a discussion of the rationale for the choice of the representative standard cost.

In determining the standard cost, it was found that the 61 items on the NHMRC list represent a mixture of services and activities for which costs can be derived using activity based costing, as well as a number of items that simply describe prevailing fees. These fees are often levied to cover one or more activities that appear elsewhere on the list. For example, the 'Departmental Establishment/Set-up Fee' often covers 'Site Selection Including Site Feasibility Assessment', and 'Preparation and Submission of Applications to HREC and Institutions' both of which appear as items elsewhere on the list. The 'Departmental Ongoing Administration Fees' often covers 'Pre-screening Activity', Amendment Preparation and Submission', and 'Ongoing Administration, Monitoring and Reporting, all three of which appear elsewhere on the list. In the short term, this potential duplication means that some items on the list should not be used together with other specific items on the list when negotiating budgets (otherwise there will be duplication of costs). These items are highlighted in the determined table of standard costs (see Table 5.3) so that users may take the potential for duplication into account in negotiating trial budgets.

Table 5.3: Table of standard costs for the NHMRC list of items associated with conducting clinical trials in Australia

Major category	Item	Reference number	Standard cost	Comments to guide use of the standard cost
Sub-List 1 – Clinical Tests and Procedure Items				
Screening Visit and Health Assessment	Clinical services provided specifically for the purposes of screening and health assessment	1.1.1	• Calculated per service based on trial protocol using standard costs for items 1.2.1, 1.3.1, 1.3.2, 1.5.1, 1.6.1, 1.7.1, 2.6.2, 2.6.3, and 2.6.4	• The cost of undertaking a "screening visit and health assessment" is trial protocol dependent and will vary according to the nature of the tests and procedures undertaken and the consultations required with staff involved in the clinical trial. • The cost of undertaking a "screening visit and health assessment" will also vary according to whether components of the screening visits and health assessment are considered standard of care or are in addition to standard of care. • The screening visit and health assessment often includes a range of procedures and/or consultations from sub-list one: 1.2.1 – 1.7.1. All these activities should be costed according to their respective items.

Major category	Item	Reference number	Standard cost	Comments to guide use of the standard cost
Laboratory Tests/Procedures	Laboratory tests and procedures itemised under the MBS	1.2.1	• 140% of the MBS fee per laboratory test and/or procedure	• The MBS loading reflects the additional reporting requirements required for the clinical trial and/or different procedures (e.g. non-standard parameters for paediatric trials) that need to be followed to meet the protocol requirements. • In some instances, there are tests undertaken locally, for which there is no item listed on the MBS. The costs of these tests should be dealt with under items 2.5.1 – 2.5.4. • Only for non-standard of care laboratory tests and procedures.
Medical Imaging	Imaging examinations and procedures itemised under the MBS	1.3.1	• 140% of the MBS fee per imaging examination and/or procedure	• The MBS loading reflects the additional reporting requirements associated with imaging examinations and/or procedures on trial participants. • There are a number of trial specific issues (e.g. imaging examinations in paediatric trials generally take longer and hence are more costly), which may need to be dealt with on a case by case basis with reference to the standard cost. • Only for non-standard of care imaging examinations and/or procedures.
	PET-FDG/FLT scans not itemised under the MBS	1.3.2	• 140% of the nearest equivalent MBS fee for PET-FDG per scan	• PET-FLT scans are not currently covered under any MBS item numbers. The principal difference in the cost of PET-FDG and PET-FLT would be in the costs of the radiopharmaceutical. It was not possible to obtain data that allowed this cost difference, if there is any, to be quantified. • In the interim, where PET-FLT is used as an alternative to PET-FDG, the PET-FDG MBS fee for that same site should be used. • Only for non-standard of care radiation therapy planning and treatment.
Radiation Therapy	Radiation therapy planning and treatment itemised under the MBS	1.4.1	• 140% of the MBS fee including ROHPG component per service	• The MBS loading reflects the trial specific activities (e.g. extra reporting, image transfer) associated with radiotherapy services provided to trial participants. • Only for non-standard of care radiation therapy planning and treatment.
Other Clinical Tests or Procedures	Other clinical tests or procedures itemised under the MBS	1.5.1	• 140% of the MBS fee per service	• The MBS loading reflects the trial specific activities (e.g. extra reporting, image transfer) provided to trial participants. • Only for non-standard of care other clinical tests or procedures.
Specialist Medical Consultations	Specialist medical consultations itemised under the MBS	1.6.1	• 140% of the MBS fee per specialist medical (including GP) service • 100% of ADA fee per specialist dental service	• The MBS loading reflects the trial specific activities (e.g. extra reporting, extra information) provided to trial participants. • The ADA Fee is unadjusted because it allows for a return on investment component in setting the fee. • Only for non-standard of care specialist medical consultations.
Nursing / Allied Health Consultations	Nursing/Allied Health consultations not itemised under the MBS	1.7.1	• 100% of the published IHPA price for public hospital outpatient services	• Only for non-standard of care nursing and allied health services.
Sub-List 2 – Clinical Trial Support Services				
Departmental Protocol Review	Departmental Protocol Review	2.1.1	• $171 per protocol review	• The costs associated with the departmental protocol review are often not included in any clinical trial budget, as the activities occur before site selection, and are considered part of the tendering process for site selection.

Major category	Item	Reference number	Standard cost	Comments to guide use of the standard cost
Departmental Establishment /Set up Fees	Departmental Establishment/Set up Fees	2.2.1	• $2,000 for clinical trial unit per clinical trial • $990 for pharmacy department per clinical trial • $425 for pathology department per clinical trial • $550 for radiology department per clinical trial	• Fee practices for this item vary by site but often cover costs of items covered elsewhere on the NHMRC list. Hence caution should be exercised in using this item as there is potential to duplicate the cost of other items (i.e. item 2.3.1, 3.1.2, 3.1.3, 3.1.4, 3.1.8, 3.1.9 and 3.2.1). • Fee charged once per clinical trial by host department (i.e. clinical trial unit) as well as by most supporting departments (i.e. pathology, pharmacy, imaging etc.). • Generally if a Departmental Establishment/Set up fee is charged then the Departmental Ongoing Administration Fee (2.3.1) is not charged until year two of the clinical trial.
Departmental Ongoing Administration Fees	Departmental Ongoing Administration Fees	2.3.1	• $1,005 for clinical trial unit per annum (from year two of the clinical trial) • $500 for pharmacy department per annum (from year two of the clinical trial) • $398 for pathology department per annum (from year two of the clinical trial) • $200 for radiology department per annum (from year two of the clinical trial)	• Fee practices for this item vary by site but often cover costs of items covered elsewhere on the NHMRC list. Hence caution should be exercised in using this item as there is potential to duplicate the cost of other items (i.e. item 2.6.1, 2.6.2, 2.6.3, 2.6.4, 3.2.6, 3.2.9 and 3.2.10). • This fee is generally charged annually by host department as well as by most supporting departments (i.e. pathology, pharmacy, imaging etc.). • Generally if a Departmental Establishment/Set up fee is charged (item 2.2.1) then the Departmental Ongoing Administration Fee is not charged until year two of the clinical trial.
Pharmacy / Investigational Drug-related	Staff training (drug specific)	2.4.1	• $224 per clinical trial	• Charged by pharmacy department only.
	On call and call in/call back fees	2.4.2	• $400 per call in/call back	• This fee includes the first three hours of labour following call in/call back, with any additional hours being charged at an hourly rate.
	Drug stocking	2.4.3	• $45 per stock shipment received	• Often included as part of the dispensing fee (item 2.4.5).
	Drug preparation, labelling and re-labelling	2.4.4	• $37 per drug preparation • $85 per 25 containers either labelled or relabelled	• There is wide variation in drug preparation time dependent on the type of drug trial and number of drugs involved in the trial, these costs may need to be negotiated on a per trial basis with some reference to this standard cost.
	Drug dispensing and accountability	2.4.5	• Dispensing – simple $37.00 per participant per service • Dispensing – complex $92.50 per participant per service • Accountability - $12.75 per participant per service • Counselling - $14.80 per participant per service	• Developing a standard cost for dispensing activities was difficult due to the wide variation which is dependent on the type and number of drugs involved in the trial. • Clinical trial budgets may need to be negotiated on a per trial basis with reference to the standard cost.
	Drug transfer	2.4.6	• $49 per drug transfer (excluding transport/courier costs)	• Costs associated with drug transfer activities is variable depending on the number of drugs that need to be packaged and sent, the type of drugs (e.g. tablets vs. cytotoxic drugs); the transport fees (which varies depending on type of drug and requirements of transfer (e.g. ambient temperature or -20^{o}C etc.). These variations will need to be considered when negotiating clinical trial budgets.

Major category	Item	Reference number	Standard cost	Comments to guide use of the standard cost
	Drug storage and temperature monitoring	2.4.7	• $50 per annum per clinical trial	• Standard cost assumes about 40 different types of drugs will be monitored at any one time per clinical trial site. • This cost is often included under "departmental ongoing administration fees" (item 2.3.1) or "Drug dispensing and accountability" (item 2.4.5).
	Drug destruction	2.4.8	• $77 per drug destruction service (excluding off-site destruction fees)	• Drug destruction is not always undertaken by the clinical trial sites, and may in fact be undertaken by the CRA, which results in no cost being incurred by the clinical trial site. This practice should be reflected in the clinical trial budget negotiated. • The cost of drug destruction is sometimes included in the pharmacy department ongoing administration fee (item 2.3.1).
Biospecimen-related	Biospecimen collection and processing (central and local)	2.5.1	• $30 per biospecimen collected for analysis by central laboratories (excludes transport costs (e.g. courier costs, any required quarantine permits, etc.) as these costs vary depending on the amount of biospecimens being transported, the delivery location (e.g. within Australia or overseas) as well as the temperature at which the biospecimens need to be transported at).	• The cost associated with this item only applies when clinical trial staff are collecting and processing biospecimens which will be analysed by central laboratories (i.e. no MBS fee (or equivalent) is charged by the clinical trial site). • When clinical trial staff collect and process a biospecimen that will be analysed by the local laboratory, then the cost incurred by the clinical trial site is covered by the MBS fee (particularly when the suggested 1.4 loading is applied).
	Biospecimen analysis (central and local)	2.5.2	• 140% of the MBS fee for the nearest equivalent test listed on the MBS	• The MBS loading associated with item 1.2.1 "Laboratory Tests/Procedures" and item 1.5.1 "Other Clinical Tests or Procedures" already incorporates the additional time and hence costs associated with biospecimen analysis for tests covered under the MBS.
	Biospecimen storage (central and local)	2.5.3	• Not determined, deemed to be included in 2.5.2	• Comment as per item 2.5.2. • The nearest equivalent MBS fee and loading associated with item 2.5.2 "Biospecimen analysis (central and local)" already incorporates the additional time and hence costs associated with biospecimen analysis for tests and procedures not covered under the MBS. Hence item 2.5.3 should include biospecimen storage for only biospecimens that are not tested and reported locally.
	Biospecimen destruction (central and local)	2.5.4	• Not determined, deemed to be included in 2.5.2	• No relevant data could be obtained from sites. Hence the fee for local analysis (testing and reporting) of the biospecimen includes the cost of biospecimen destruction. This fee would be charged under either items 1.2.1, 1.5.1 or 2.5.2. No separate standard cost for this item has been determined.
	Tissue repository set-up and management	2.5.5	• Not determined as cost is typically not incurred at trial sites	• As no relevant data were able to be obtained from sites, no separate standard cost for tissue repository, set up and management has been determined. • The inclusion of this item in the list should be reviewed. If the intention is to capture or set reasonable costs to assist in the setting of budgets for sites involved in clinical trials, as no sites visited are involved in the set up or management of tissue repositories, inclusion of this item on the list does not seem warranted.

Major category	Item	Reference number	Standard cost	Comments to guide use of the standard cost
Clinical Staff/Resource Allocation	Coordinating principal investigator surcharge	2.6.1	• $215 per hour	• This item should only be used where the clinician is acting in his/her capacity as an investigator and should not include items costed on a per service basis (i.e. sub-list 1). • The quoted hourly rate represents a fully absorbed costs which is made up of: 60% for direct salary costs + 15% for salary on-costs + 25% for institutional overheads.
	Investigator allocation	2.6.2	• $215 per hour	• This item should only be used where the clinician is acting in his/her capacity as an investigator and should not include items costed on a per service basis (i.e. sub-list 1). • This item is used to set the reasonable unit cost for investigator time, which is then used to calculate the costs of many of the other activities in sub-lists 2 and 3. If item 2.6.2 is used together with items such as site selection including feasibility and preparing ethics submissions care should be taken to avoid double counting. • The quoted hourly rate represents a fully absorbed costs which is made up of: 60% for direct salary costs + 15% for salary on-costs + 25% for institutional overheads.
	Research nurse allocation	2.6.3	• $60 per hour	• This item should only be used where the research nurse is acting in his/her capacity as an researcher and should not include items costed on a per service basis (i.e. sub-list 1). • This item is used to set the reasonable unit cost for research nurse researcher time, which is then used to calculate the costs of many of the other activities in sub-lists 2 and 3. • The quoted hourly rate represents a fully absorbed costs which is made up of: 60% for direct salary costs + 15% for salary on-costs + 25% for institutional overheads.
	Clinical research coordinator (non-research nurse) allocation	2.6.4	• $75 per hour	• This item is used to set the reasonable unit cost for a clinical research coordinator time, which is then used to calculate the costs of many of the other activities in sub-lists 2 and 3. • The quoted hourly rate represents a fully absorbed costs which is made up of: 60% for direct salary costs + 15% for salary on-costs + 25% for institutional overheads.
	Clinic/theatre usage	2.6.5	• Not determined, as there was no reasonable basis, and cost typically not charged by trial host sites, theatre use is usually for standard of care services	• As no relevant data were able to be obtained from sites, no separate standard cost for clinic/theatre usage has been determined. • The need for this item should be reviewed with regard to how the clinical tests and procedures items are handled and whether the clinic/theatre resources needed to provide those services should be an absorbed cost.
Sub-List 3 – Non clinical services				
Project Development	Preparation of research proposal	3.1.1	• $80,858 per research proposal (for non-industry sponsored trials only)	• Only applicable to investigator initiated clinical trials (i.e. non-industry sponsored clinical trials). • No cost is incurred by clinical trial sites for the preparation of a research proposal for industry sponsored clinical trials as this activity is undertaken by the industry sponsor.
	Site selection including site feasibility assessment process	3.1.2	• $2,597 per site selection (including site feasibility assessment process)	• The costs associated with site selection including the site feasibility assessment process is not often included in any budget negotiated with clinical trials sponsors (or their agents) as the activities occur before the clinical trial begins. • However some clinical trial sites capture the cost associated with site selection in their "Departmental Establishment/Set Up fees" (item 2.2.1). Hence care should be taken to avoid duplication.

Major category	Item	Reference number	Standard cost	Comments to guide use of the standard cost
	Preparation and submission of applications to HREC and institutions	3.1.3	• HREC (non-lead) and SSA = $3,098 per application per clinical trial • HREC (lead) and SSA $3,953 per application per clinical trial	• Some sites include the costs associated with personnel time spent on preparing and submitting the applications to HREC and institution in the "departmental establishment/set up fee" (i.e. item 2.2.1). Hence care should be taken to avoid duplication. • The costs associated with the extra time taken to prepare and submit the HREC application by a lead site should be captured under this item. However the costs associated with the additional time involved in managing the ongoing coordination of the clinical trial, due to being the lead site, should be captured under the Lead HREC/Lead site fee (item 3.1.7).
	Radiation safety and/or biosafety reports	3.1.4	• $99 per radiation safety and/or biosafety report	• No comment
	HREC (ethical) review fee	3.1.5	• $3,000 per HREC (ethics) application	• The cost associated with preparation and submission of applications to HREC and institutions is included under item 3.1.3 and not this item. • The fee associated with the review of the site assessment application is included under item 3.1.6.
	Institutional (site assessment) review fee	3.1.6	• $750 per institutional (site assessment) application	• The cost associated with preparation and submission of applications to HREC and institutions are included under item 3.1.3 and not this item. • The fee associated with the review of the HREC (ethical) application fee is included under 3.1.5.
	Lead HREC/Lead site fee	3.1.7	• $400 per additional site per annum	• This standard costs represents the input time of the lead site in the ongoing coordination and management of all the nominated sites participating in the clinical trial • The additional cost associated with personnel time required for the preparation and submission of the lead HREC application to the HREC and institutions are included under item 3.1.3 and not 3.1.7. • The fee associated with the review of the lead HREC (ethical) application are included under 3.1.5 and not this item.
	Investigator meetings	3.1.8	• $1,020 per Clinical Trials Manager/Coordinator attending an international investigator meeting • $3,440 per Principal Investigator attending an international investigator meeting OR • $287 per Clinical Trials Manager/Coordinator attending a domestic investigator meeting • $882 per Principal Investigator attending an domestic investigator meeting	• The standard costs exclude travel time and travel expenses. Travel expenses are generally covered by the trial sponsor whereas travel time is generally not covered by the sponsors. • The costs of a PI and/or CTC/M attending the investigator meeting is generally not charged by clinical trials sites for the following reasons: ➢ most PI's and/or CTC/M consider it inappropriate to have their time paid for at the investigator meetings as it could be seen as 'conflict of interest'; ➢ most PI and/or CTC/M see it as an important networking and professional development exercise; ➢ most CTC/M are not highly paid personnel and see it as a benefit of the job; ➢ most sites recognise that the costs of travel from Australia to Europe and/or Asia are much greater than from other potential trial host countries, and most Australian sites do not want to lose access to this privilege so do not ask for their time to be covered.

Major category	Item	Reference number	Standard cost	Comments to guide use of the standard cost
	Staff training	3.1.9	• $638 per Clinical Trials Manager / Coordinator required to undertake staff training per clinical trial. • $430 per Principal Investigator required to undertake staff training per clinical trial.	• For the purposes of determining standard costs for items on the list, it has been assumed that no staff training is included in the "Departmental Establishment/Set up Fees" (item 2.2.1) and/or "Departmental Ongoing Administration fees" (item 2.3.1). • Costs associated with pharmacy staff undertaking training specific to pharmacy work involved in clinical trials is included under item 2.4.1. • The costs associated with staff training that occurs on the day of the start-up meeting is included under item 3.2.1.
	Trial-specific equipment hire/purchase	3.1.10	• $75 per trial-specific equipment hire/purchase for a biomedical engineering check	• The costs associated with any time required to maintain trial-specific equipment or time required to return trial specific equipment that has been 'loaned' are not included. These costs are included under item 3.2.6 "ongoing administration, monitoring and reporting" and 3.2.11 "Study close-out activity including preparation for audit" respectively.
	IT set-up, equipment and maintenance	3.1.11	• $37.50 per trial-specific IT equipment item for set-up	• Any staff training related to IT equipment should be captured under item 3.1.9 "staff training". • The costs associated with any time required to maintain trial-specific IT equipment or time required to return trial specific IT equipment that has been 'loaned' are not included. These costs are included under item 3.2.6 "ongoing administration, monitoring and reporting" and 3.2.11 "Study close-out activity including preparation for audit" respectively.
	Trial centre set-up and development	3.1.12	• Not determined, as cost typically not incurred by trial sites	• If intention is to capture or set reasonable costs to assist in the setting of budgets for sites involved in clinical trials, then the item is not required as trial sites are typically not involved in the set up or management of a trial centre.
Project Implementation	Start-up meeting	3.2.1	• $1,815 per start-up meeting	• The costs associated with the start-up meeting are generally not charged by clinical trial sites or are included under the "Departmental Establishment/Set up fees" (i.e. item 2.2.1). • The costs associated with any staff training that occurs at the start-up meeting are included in this item and not under item 3.1.9 "staff training".
	Pre-screening activity	3.2.2	• $4,003 per clinical trial	• It is recognised that the cost associated with pre-screening is trial-dependent (e.g. in some trials, patients are recruited from an existing relatively small patient group that was already attending the site regularly for treatment compared to involving extensive review of a large number of patient records). • Variations should be negotiated on a per trial basis with reference to the standard cost.
	Recruitment activity	3.2.3	• $349 per potential clinical trial participant screened and assessed	• Reasonable cost is based on explaining the clinical trial, gaining informed consent, organising the tests and procedures, and providing the potential clinical trial participant with the results.

Major category	Item	Reference number	Standard cost	Comments to guide use of the standard cost
	Medical records set-up, access and storage	3.2.4	• $10 per medical record accessed (for clinical trial visits only i.e. excluding standard of care visits)	• For non-standard of care needs only. • This standard cost excludes the cost associated with the setup of the medical and/or clinical trial record, as this cost is included under the establishment fee/set up fee (item 2.2.1). • This item represents a cost borne by the medical records department only. The costs associated with (1) the clinical trials unit requesting the medical records; or (2) storing the clinical trials record long term is included in the standard costs for item 3.2.6 "ongoing administration, monitoring and reporting" and item 3.2.12 "archiving of trial records" respectively. • The cost incurred by medical records departments to retrieve a medical record for the sole purpose of the clinical trial is often not charged.
	Interpreter services	3.2.5	• $52 per hour	• The quoted hourly rate represents a fully absorbed costs which is made up of: 60% for direct salary costs + 15% for salary on-costs + 25% for institutional overheads.
	Ongoing administration, monitoring and reporting	3.2.6	• $470 per participant per annum	• As this item overlaps with the "Departmental Ongoing Administration fee" (item 2.3.1) and the "Departmental Establishment/set up fee" (item 2.2.1), the standard cost has been determined, as far as was possible, on the ongoing monitoring and reporting requirements.
	Data analysis (+/- study report)	3.2.7	• Not determined, as cost typically not incurred by trial sites	• Not a cost typically incurred by clinical trial sites. • The inclusion of this item in the list should be reviewed. If the intention is to capture or set reasonable costs to assist in the setting of budgets for sites involved in clinical trials, then the item is not required as trial sites are typically not involved in data analysis and/or preparation of the study report.
	Trial centre data management, data analysis and ongoing administration, monitoring and reporting	3.2.8	• Not determined, as cost typically not incurred by trial sites	• Not a cost typically incurred by clinical trial sites. • The inclusion of this item in the list should be reviewed. If the intention is to capture or set reasonable costs to assist in the setting of budgets for sites involved in clinical trials, then the item is not required as trial sites are typically not involved in the activities covered by trial centre data management.
	Amendment preparation and submission	3.2.9	• $343 per amendment (excluding fee charged by the RGO and/or HREC for review)	• This standard cost does not capture the fee charged by the RGO and/or HREC for review of the amendments. The fee charged by the RGO and/or HREC for review of the amendments is included under item 3.2.10 "amendment review".
	Amendment review	3.2.10	• $275 per amendment reviewed	• This standard cost does not capture the time spent by clinical trials units to prepare and submit the amendments to the RGO and/or HREC. The cost associated with personnel in the clinical trials unit preparing the amendment submissions is included under item 3.2.9 "amendment preparation and submissions".

Major category	Item	Reference number	Standard cost	Comments to guide use of the standard cost
	Study close-out activity including preparation for audit	3.2.11	• $693 for study close out per clinical trial	• The costs associated with preparing the clinical trial records for archiving is included in this standard cost. • The fees for archiving trial records is included under item 3.2.12 "archiving of trial records". • If study close out activities are undertaken by the CRAs then this cost should either not be present in the clinical trial budget or reduced to reflect the actual time required by the clinical trial site personnel involved in assisting the CRA in study close out activities.
	Archiving of trial records	3.2.12	• $750 per clinical trial	• The storage fee associated with archiving the clinical trials records is included in this item. The costs associated with preparing clinical trials records for archiving is included under item 3.2.11 'study close-out activity including preparation for audit".
Participant-related	Participant payment	3.3.1	• Not determined, any payments made at discretion of the trial sponsor	• The standard costs associated with any invoicing of participant payments is included under item 3.2.6 "ongoing administration, monitoring and reporting". • There is need for this item to be reviewed along with all participant payment related items. The only costs that are relevant to trial sites are the costs of administering the participant payment process. The amount of participant payments, where they are considered ethical, is discretionary, and should be properly be determined by the trial sponsor.
	Participant/carer time and inconvenience reimbursement	3.3.2	• Not determined, any payments made at discretion of the trial sponsor	• Comments as per item 3.3.1.
	Participant/carer travel	3.3.3	• Not determined, any payments made at discretion of the trial sponsor	• Comments as per item 3.3.1.
	Participant/carer parking	3.3.4	• Not determined, any payments made at discretion of the trial sponsor	• Comments as per item 3.3.1.
	Participant/carer meals	3.3.5	• Not determined, any payments made at discretion of the trial sponsor	• Comments as per item 3.3.1.
	Participant/carer accommodation	3.3.6	• Not determined, any payments made at discretion of the trial sponsor	• Comments as per item 3.3.1.
	Participant inpatient/overnight stay	3.3.7	• Not determined, as no evidence of participants being charged in practice was found.	• There is no place in the list to deal with the hospital accommodation cost. The trial site can cover the cost of the professional service (medical, nursing or allied health time) but not the institution cost.
	Participant outpatient/day stay	3.3.8	• Not determined, as no evidence of participants being charged in practice was found.	• Outpatient day stays form part of a clinical services and should be captured in sub-list one. • There is no place to deal with the day procedure suite cost, if the clinical tests and procedures service requires admission as a day patient. The trial site can cover the cost of the professional service (medical, nursing or allied health time) but not the institution cost.

5.3 USING THE TABLE OF STANDARD COSTS

In using the table of standard costs, it is important to note that this study was required to focus on the NHMRC list of items that was developed as a result of the CTAG process (which enjoyed substantial input from the pharmaceutical industry, but lower levels of participation from other commercial trial sponsors). This costing study deliberately pursued broad stakeholder consultation, including with commercial and non-commercial trial sponsors. In that process, some stakeholders, including the Medical Technology Association of Australia (MTAA), were concerned that the NHMRC list was largely focussed on pharmaceutical trials. As a result, it is considered that further work is required to ensure the applicability of the NHMRC list to medical device trials, and until such time as this work is carried out, the table of standard costs should not be used for device trials.

In any case, there is not expected to be any compulsion to use the table of standard costs in negotiating trial budgets, it is intended only as a guideline or reference point. It is recognised that the determination of a single standard cost for each item on the NHMRC list is an over-simplification of reality (e.g. compare to the UK approach where four costing templates are produced that cover only industry sponsored trials, one template for each combination of pharmaceutical and device trials conducted in primary and secondary care settings). Nonetheless, it is considered that there is considerable value in the Australian table of standard costs, particularly if users of the table costs have regard to the following factors in negotiating trial budgets.

- **Standard care versus trial specific care.** Although strictly speaking this is not a costing issue, it is important to note that the standard costs are intended to be applied only for those activities that are over and above standard of care i.e. the determined standard costs should not be applied to services that patients would have received in any case if they had not been enrolled in the trial. It was not possible within the context for the study to develop guidance on what services represent standard of care, as this concept was found to be trial-specific. Thus, users of the table of standard costs should determine whether a service is standard of care in a given trial context, before applying a standard cost and seeking to include that cost in the trial budget.

- **Type of trial**. It was observed that the NHMRC list was constructed mainly with reference to the experience of pharmaceutical trials, an observation that was also made by a number of authors of public submissions. Although, the standard costs have been developed without reference to the type of trial, there may be a need to consider adjustments to the standard costs depending on the nature of the intervention on trial (e.g. pharmaceutical trials, radiation oncology trials, surgical trials, service model trials, observational trials, etc.).

- **Target population of trial.** Some trials will target populations where there will be different costs experienced relative to the typical adult population. For example, the study found that it is usually more expensive to conduct paediatric trials (although separate standard costs for paediatric trials are not published). It was also found that trials that involve significant participation of patients from known special need groups e.g. people from Indigenous or culturally and linguistically diverse backgrounds are likely to have higher costs. Accordingly, there may be a need to consider adjustments to the standard costs for trials that are likely to involve high proportions of participants from smaller target groups.

- **Phase of trial**. Pharmaceutical trials are normally categorised into phases from Phase 1 where researchers test an experimental drug or treatment in a small group of people (typically 20 to 80) for the first time to evaluate its safety, determine a safe dosage range, and identify side effects through to Phase

4 which are post-marketing studies that delineate additional information, including the treatment risks, benefits, and optimal use. The Phase of the trial was found to impact on costs, so there may be a need to consider adjustments to the standard costs depending on trial phase (e.g. there are typically higher pre-screening costs associated with for Phase 1 trials).

- **Setting for the trial.** The auspice organisations conducting clinical trials represent a range of settings, from hospitals (public or private) through to primary and community services, through to purpose built facilities (particularly for Phase 1 trials). The study found that there are different experiences of the cost of trials depending on the setting in which it is conducted. It is also relevant to note that separate costing templates have been developed in the UK for trials conducted in primary and secondary care settings. Accordingly, there may be a need to consider adjustments to the standard costs depending on the setting in which the clinical trial will be conducted.

- **Location of trial sites/trial participants**. Some trial sites may be located in remote regional and rural areas, where it is known that there may be higher cost experiences (e.g. for participant travel, or for the unit cost of clinical labour). It may also be relevant for a metropolitan area-based trial to consider providing access to participants residing in regional/rural areas through the use of telehealth technology, or perhaps to subsidise (pay for) travel to and from the regional/rural location. Accordingly, there may be a need to consider adjustments to the standard costs for trials where the trial site and/or the trial participants are in located in regional/rural areas.

- **Complexity of trial**. There are potentially a number of factors potentially associated with trial complexity that may impact on cost. A few of the public submissions made reference to this point, but it is considered that the judgement about trial complexity needs to be made in context, general rules are too difficult to develop. In some cases it may be clear, for example, some pharmaceutical trials might require complex on-site preparation of a medicine, whereas other involve only standard dispensing of a pre-prepared medicine. But there will be other cases, for example, trials targeted at very small population groups (e.g. patients with rare diagnoses) that need to be assessed in context. So it may be relevant to consider an adjustment to the standard costs based on the complexity of the trial.

A number of the public submissions also made reference to the potential to adjust the standard costs depending on the trial sponsor (e.g. industry, collaborative, or investigator initiated). The study found that in most circumstances the trial sponsor is not a cost issue, rather it is a funding issue. It was observed that trial sites often did not seek the same level of funding to host collaborative or investigator initiated trials that they did to host industry sponsored trials. But the activities involved were generally very similar and so were their associated costs. It is a matter for trial sites to decide as to whether they will negotiate trial budgets at levels lower than the standard costs for collaborative and investigator initiated trials, it is not a matter that influences the standard costs.

6

Opportunities for further development

The study gathered a very considerable evidence base relating to the activities on the NHMRC list and the costs of conducting clinical trials in Australia. This Chapter discuses a number of identified opportunities to improve the list and the associated table of standard costs.

6.1 REFINEMENTS TO THE NHMRC LIST OF ITEMS

The study has identified a number of opportunities to improve the NHMRC list of activities associated with conducting clinical trials. First, a clearer definition of the scope of activities to be included on the list is required. Most of the activities on the current list are undertaken by clinical trial host sites (e.g. protocol review) but some are not (e.g. trial centre set-up and development). If it is intended to include all work associated with conducting clinical trials, then a number of activities typically not undertaken by clinical trial sites need to be included in the list (e.g. those carried out by the sponsor). Otherwise, if restricted to activities undertaken by clinical trial host sites, then a number of items need to be removed from the list (e.g. set up or management of a trial centre).

The second opportunity involves reworking the list so all items are defined as activities associated with conducting clinical trials. If this opportunity is pursued, all references to fees in the definition of the items would be removed, and hence the observed duplication between the 'umbrella' fee items and the activity items would be eliminated. In some circumstances this rework would involve changing the fee items (e.g. HREC fee) to the underlying activity i.e. review of the ethics application by an appropriately constituted HREC, and then costing this item on an activity basis. In other circumstances, it may be that the fee item is deleted from the list and the implied activity is covered by another item (e.g. medical records set-up, access and storage).

The third opportunity would be to restructure the list so that it is based on the typical life cycle (or different stages) of a clinical trial, as opposed to whether the activity is a clinical service, a clinical support service, or a non-clinical support service. This opportunity was also identified in a number of public submissions. An alternative structure would be to reflect the, at least, four distinct stages in a clinical trial including:

- Development stage;
- Establishment stage;
- Implementation stage; and
- Close out stage.

By re-structuring the list using this suggested framework (or something similar) it is considered that the current duplication of activities (e.g. Departmental Establishment/Set up fees (item, 2.2.1), Department Ongoing Administration Fees (2.3.1) and ongoing administration, monitoring and reporting (item 3.2.6)) would be removed. The restructured list would then provide a more transparent basis for allocation of costs to particular activities, rather than drafting definitions that attempt to remove overlap in closely related items, so as to allow partitioning of costs.

The fourth opportunity is to extend sub-list 1 so that it is more inclusive of clinical services not covered by the MBS, as well as services associated with overnight stay and outpatient/day stay. There is currently no place in the list to deal with hospital accommodation cost or day procedure suite cost (if the clinical tests and procedures service requires admission as a day patient). The trial site can cover the cost of the professional service (medical, nursing or allied health time) under the current sub-list 1 but not the institution cost. It is thought that these items were not included, as it is expected that they would normally represent standard of care, but this may not be the case for all trials, and their inclusion would make the lists of items exhaustive of clinical services.

The fifth opportunity would be to specifically include activities undertaken by the supporting departments on the list. The current list has a strong focus on pharmacy activities, at the exclusion of other supporting departments (e.g. imaging, pathology, etc.). Depending on the type of clinical trial, pharmacy departments may not be involved (or be less important). For example, in a radiation oncology clinical trial, the radiation therapy and imaging departments would be more involved and undertake specific activities for the clinical trial (e.g. radiology feasibility studies which include activities such as staff qualification checking; and quality and transmission testing of the technical equipment). Ensuring that the list includes activities undertaken by supporting departments would enable better costing of these activities to be undertaken, rather than relying on them being covered by umbrella fees (e.g. department establishment/set up fees, etc.).

The sixth opportunity would be to remove the overlap in some of the activities listed in sub-list 2. For example, under the Pharmacy related/investigational drug related activities (i.e. items 2.4.1 to 2.4.8), the process of "drug storage and temperature monitoring" (item 2.4.7) and "drug dispensing and accountability" (item 2.4.5) are often thought to be part of drug stocking (item 2.4.3). There is also considerable overlap in some of the activities listed under the Pharmacy related/investigational drug related activities (i.e. items 2.4.1 to 2.4.8) and the "Department Establishment/Setup fee" (item 2.2.1). Accordingly, it is suggested that in any review of the NHMRC list, the opportunity to consolidate pharmacy related items should be considered.

The seventh opportunity would be to remove the duplication between sub-lists 2 and 3, which would be partly addressed by removing fee based items. For example, some sites include the activities associated with preparation and submission of applications to HREC and institution (item 3.1.3) in the "departmental establishment/set up fee" (item 2.2.1). Also, staff training (item 3.1.9) creates considerable confusion with item 2.4.1 staff training (drug specific). In developing the definitions, it has been attempted to create mutually exclusivity between the items, as the list could not be altered. However, a better process would be to remove duplication in the item labels themselves, which would in turn result in simplified definitions.

6.2 REFINEMENTS TO THE TABLE OF STANDARD COSTS

There are also a number of opportunities for improving the costing of the items on any revised list of activities associated with clinical trials. The first is to re-cost all the items on the revised list that were previously defined as fee items on the basis of the activities that those items cover (e.g. the 'Institutional (site assessment) Review Fee' would be costed based on the typical hours required for the review, rather than the typical fee charged). A similar activity based costing approach to that used in this current study would be appropriate. This development would meant that the only use of prices as the basis for costing would be for those services that are acquired by trial host sites (e.g. archival of trial records), i.e. where the cost to the trial host site is a purchased service.

The second opportunity is to undertake the costing on a prospective basis. Prospective costing would be much more labour intensive than this study. It would involve the design of purpose specific data collection infrastructure, and the roll-out of that infrastructure across an appropriately representative sample of clinical trial sites across Australia. The collection would be managed over, say, a six to twelve month period, and the resultant data would be centrally collated and analysed. Such an approach would produce statistically more reliable measures of the cost of each item than the current study, and also provide the potential to quantify loading factors (as IHPA currently does for the NEP for public hospital services using the NHCDC). The merit of such a study would need to be considered on a cost benefit basis.

The third opportunity is to develop costing templates for clinical trials that could be used by trial sponsors and trial host sites. Such an approach would mirror developments in the UK. Specific templates could be produced that reflect the circumstances of clinical trials (e.g. the trial type, the trial setting, the trial location, the trial phase, and so on). The standard costs developed in this study could be used to partially populate the templates, supplemented as required by additional information that would be derived through the template development process. Again the merit of developing clinical trial costing templates would need to be considered on a cost benefit basis, but pursuing this opportunity would put Australia on a par with the UK.

6.3 MAINTENANCE OF THE TABLE OF STANDARD COSTS

Like any schedule of costs/prices there will be a need to maintain the currency of the table of standard costs. This work may be as simple as ensuring appropriate escalation of the standard costs to reflect the increases in input prices experienced in the health system. However, the environment in which clinical trials are being conducted is changing fairly rapidly. There are efforts across the country to streamline the processes associated with obtaining ethics and institutional approvals for clinical trials. There are also the initiatives that will result from implementation of the other ten recommendations of the CTAG report. These developments are likely to impact on the costs of conducting clinical trials. In the circumstances, it is suggested that recalculation of the standard costs, over and above reflecting input price escalation, may be required two-yearly.

6.4 EVALUATING THE IMPACT OF THE TABLE OF STANDARD COSTS

Although the fieldwork found widespread support for the development of the table of standard costs, there were a few stakeholders who expressed concerns about the possible negative impact of the initiative. Like any significant intervention, there is a need to formally evaluate the impact of the table of standard costs on both the number and costs of clinical trials conducted in Australia. It is noted that the initial work on evaluating the production of costing templates for clinical trials in the UK (the parallel initiative in the UK to the production of the table of standard costs in Australia) has generally produced positive results. Accordingly, it is suggested that an evaluation of the impact of the table of standard costs on clinical trials in Australia be undertaken within three years of the publication of this report.

Appendix A – Clinical tests and procedure items

Reference number	1.1.1
Item	Clinical services provided specifically for the purposes of screening and health assessment
Sub-list	Clinical tests and procedures items
Category	Screening visit and health assessment
Definition	Comprises a range of clinical services provided for the purposes of trial participant screening including physical examination, obtaining a medical history, measuring vital signs, diagnostic tests, imaging examinations, confirmation of diagnosis (which may include genomic eligibility confirmation), providing information about the clinical trial, explaining the requirements of involvement, ensuring understanding and, where appropriate, obtaining consent to participate in the clinical trial.
Standard Cost	Calculated per service based on trial protocol using standard costs for items 1.2.1, 1.3.1, 1.3.2, 1.5.1, 1.6.1, 1.7.1, 2.6.2, 2.6.3, and 2.6.4

Related items

Table A.1 presents other items which are related (i.e. not necessarily mutually exclusive from) to item 1.1.1 "Screening Visit and Health Assessment".

Table A.1: Items related to screening visit and health assessment

Item	Reference Number	Comment
Laboratory Tests/Procedures	1.2.1	Screening visit and health assessment typically involves a range of laboratory tests and procedures.
Medical Imaging	1.3.1 and 1.3.2	Screening visit and health assessment often includes medical imaging services.
Other Clinical Tests or Procedures	1.5.1	Screening visit and health assessment often includes other clinical tests and procedures (e.g. lung function, ECG, etc.).
Specialist Medical Consultations	1.6.1	Screening visit and health assessment typically includes a consultation with a medical specialist.
Nursing/Allied Health Consultations	1.7.1	Screening visit and health assessment often includes consultation with nursing and/or allied health professionals
Investigator allocation	2.6.2	Screening visit and health assessment may include consultation with the principal investigator. The cost of this time may be captured under item 1.6.1 if the investigator is a medical specialist, otherwise it is costed into the screening and health assessment item at the hourly rate in 2.6.2.
Research nurse allocation	2.6.3	Screening visit and health assessment may include consultation with the research nurse. The cost of this time may be captured under item 1.7.1 if the research nurse also provides clinical nursing services, otherwise it is costed into the screening and health assessment item at the hourly rate in 2.6.3.
Clinical research coordinator	2.6.4	Screening visit and health assessment may include consultation with the clinical research coordinator (who may or may not be the research nurse). This time should be costed into the screening and health assessment item at the hourly rate in 2.6.4.

Learnings from site visits

Screening visits are often the longest visit in the trial and could overlap as the baseline visit for eligible participants. Reports on the duration of screening visits across sites ranged from one hour to a full day (i.e. eight hours) and typically included consultations with multiple staff involved in the clinical trial and a range of medical (including physical and psychological) assessments. The trial coordinator/manager was often involved in arranging participant attendance and booking appropriate tests and consultations. At the time of the screening visit, or sometimes prior to the screening visits, informed consent was obtained from the participants and this task often involved time with the principal investigator in addition to the clinical trial coordinator/manager.

The screening visit is used to determine or confirm a participant's eligibility to participate in the trial and not all people attending screening visits will go on to be included in the trial (i.e. they may fail to meet a part of the inclusion criteria). Those participants identified as ineligible for trial participation are termed 'screen fails'. Trial sites were typically paid per enrolled participant therefore some trial budgets included a fee for 'screen fails' at a rate negotiated during the development of the trial contract (e.g. all potential participant screening is paid up to a capped 20% screen failure rate). This fee was to cover the cost of consultations, tests and procedures undertaken for screening participants that was in addition to or above usual standard of care. Screen fail rates reported by trials ranged zero to 80%.

Derived process map for "screening visit and health assessment"

Not applicable

Considerations for deriving the cost of "screening visit and health assessment"

The cost of undertaking a "screening visit and health assessment" is trial protocol dependent and will vary according to the nature of the tests and procedures undertaken and the consultations required with staff involved in the clinical trial. It will also vary according to whether components of the screening visits and health assessment are considered standard of care or are in addition to standard of care. Thus cost of the 'screening visit and health assessment will be made up of the costs of other items in the Clinical –Tests and Procedure items including those items listed in Table A.1 as appropriate to each trial.

Table of standard costs for "screening visit and health assessment"

The standard costs for the screening and health assessment services in a trial will be calculated using Table A.2, based on the trial protocol.

Table A.2: Typical personnel, resources and unit costs for "screening visit and health assessment"

Reference Number	Item	Service volume	Unit cost	Standard cost
1.2.1	Laboratory tests/procedures	No. services	as per 1.2.1	volume * unit cost
1.3.1	Imaging services itemised under MBS	No. services	as per 1.3.1	volume * unit cost
1.3.2	PET FDG/FLT scans not itemised under the MBS	No. services	as per 1.3.2	volume * unit cost
1.5.1	Other clinical tests or procedures	No. services	as per 1.5.1	volume * unit cost
1.6.1	Specialist medical consultations*	No. services	as per 1.6.1	volume * unit cost
1.7.1	Nursing/allied health consultations*	No. services	as per 1.7.1	volume * unit cost
2.6.2	Investigator allocation	No. hours	as per 2.6.2	hours * unit cost
2.6.3	Research nurse allocation	No. hours	as per 2.6.3	hours * unit cost
2.6.4	Clinical research coordinator	No. hours	as per 2.6.4	hours * unit cost
1.1.1	**Screening visit and health assessment**	**per service**	**N/A**	**Sum of above**

* Where available, the MBS items that reflect an initial (rather than subsequent visit) should be used

As can be seen, Table A.2 provides a basis for using the standard costs determined for the clinical service items and the relevant labour rates, together with the trial protocol to determine a trial specific cost for the screening and health assessment item. Given the wide variation in the complexity, and hence resource usage, of the services that make up the screening visit and health assessment, determination of a single standard cost to be applied across all clinical trials is not considered appropriate.

Reference number	1.2.1
Item	Laboratory tests and procedures itemised under the MBS
Sub-list	Clinical tests and procedures items
Category	Laboratory tests/procedures
Definition	As per the MBS Schedule Groups P1-P9. For example, includes pathology, histopathology, haematology, chemical, microbiology, immunology, tissue pathology, cytology, genetics, etc.
Standard Cost	140% of the MBS fee per laboratory test and/or procedure

Related items

Table A.3 presents other items which are related (i.e. not necessarily mutually exclusive from) to item 1.2.1 "Laboratory tests and procedures itemised under the MBS".

Table A.3: Items related to laboratory tests and procedures

Item	Reference Number	Comment
Biospecimen collection and processing (central and local)	2.5.1	The cost involved in the collection and processing of biospecimens collected for the sole purpose of a clinical trial that are not tested locally, is included under item 2.5.1 and not 1.2.1. The term "processing" in this context is not related to the processing of the biospecimen in an analytical instrument or examination in the laboratory, but rather activities associated with the labelling, recording and centrifugation (if required) of the biospecimen.
Biospecimen analysis (central and local)	2.5.2	The cost involved in any additional analysis required of biospecimens collected for the sole purpose of clinical trials, that are not tested locally, is included under item 2.5.2 not item 1.2.1.
Biospecimen storage (central and local)	2.5.3	The cost involved in the storage of biospecimens collected for the sole purpose of a clinical trial, that are stored locally (whether or not part of the biospecimen is processed centrally) is included under item 2.5.3 not item 1.2.1.
Biospecimen destruction (central and local)	2.5.4	The cost involved in the destruction of biospecimens collected for the sole purpose of a clinical trial, that are stored locally (whether or not part of the biospecimen is processed centrally) is included under item 2.5.4 not item 1.2.1.

Learnings from site visits

Most clinical trials will involve pathology testing of biospecimens from clinical trial participants at multiple points during the trial. The required pathology tests and required testing time points are detailed in the trial protocol. In some instances trial personnel are responsible for collecting the sample, storing, packing and sending (via courier) to a central laboratory (e.g. within Australia or overseas). In other instances, pathology testing and analysis is completed at the facility/site where the clinical trial is being undertaken.

Most consulted sites invest time in identifying pathology tests that are considered part of standard of care and those that are considered clinical trial specific. Those laboratory tests and procedures considered as part of standard of care, are billed according to normal hospital practices. Whereas, those tests that are considered clinical trial specific are included in the costs of, and hence budget for the trial. A small proportion of sites did not make any distinction and passed on all test/procedure costs to the trial sponsor, irrespective if it was usual standard of care. Some of these sites argued that although the test may be considered part of standard of care the reporting was clinical trial specific and therefore the full cost was included in the clinical trial budget.

Derived process map for "laboratory tests and procedures"

Not applicable.

Considerations for deriving the cost of "laboratory tests and procedures"

Discussions at site visits indicated that some pathology laboratories had developed local measures of the unit costs of common tests. However, this practice was not widespread, and it was not possible to verify these costs (task too complex within the time and resources available). Accordingly, research was undertaken to ascertain alternative secondary sources for the cost of pathology tests that could be used for the process of costing a clinical trial.

Most sites consulted stated that the budget derived for pathology testing often referred to the MBS but included a loading on the MBS to reflect the additional reporting requirements required for the clinical trial and/or different procedures (e.g. non-standard parameters for paediatric trials) that need to be followed to meet the protocol requirements. It should be noted that the MBS has a number of features that reflect its use for reimbursement under Medicare. In particular, there are complex rules regarding multiple supply and episode linking of tests, when they are performed concurrently. These rules as not considered relevant to clinical trials (i.e. the test is trial specific and so called 'coning rules' should not apply). Consequently, the reference point for the purposes of setting the standard costs is the individual cost of tests being drawn from the MBS.

It is important to note, however, that in some instances there are tests undertaken for the purposes of a clinical trial are not listed on the MBS. Where the costs of such tests are not directly met by the trial sponsor, an estimate will need to be made on a test by test basis and dealt with under item 1.5.1 'Other clinical tests or procedures itemised under the MBS'.

Table of standard costs for "laboratory tests and procedures"

MBS is a system for determining benefits payable to patients, it has regard to costs but it is not based on costs. But, it is appropriate for use in this circumstance, as bottom up costing could not be attempted, and most sites negotiate trial budgets based on an MBS multiplier. Table A.4 presents a number of reference points for the MBS multipliers applied by the visited sites.

Table A.4: MBS multipliers for laboratory tests and procedures

Item	Basis	Resource Unit (MBS multiplier)					Unit cost	Multiplier to derive standard cost
		Min	25th percentile	Median	75th percentile	Max		
Laboratory Tests/Procedures	MBS fee with adjustment factor	0.5	1.0	1.2	1.4	2.5	N/A	1.4

As can be seen, there were very different MBS multipliers applied by sites to set trial budgets often depending on whether the trial was investigator initiated, collaborative sponsored, or industry sponsored. Hence, the wide range between the min and max multipliers, where the min is more often applied to investigator initiated trials (usually including collaborative sponsored trials) and the max is more often applied to industry sponsored trials. This practice reflects cross-subsidisation by trial sites and is not relevant to a study seeking to determine reasonable costs.

For this reason, multipliers at the lower and higher end of observed practice are not considered relevant. The site visits clearly show that there are often trial specific processes (e.g. extra reporting) associated with tests on trial participants that would justify an MBS multiplier greater than one. There are also a number of trial specific issues (e.g. lab tests in paediatric trials are generally more costly), which may need to be dealt with on a case by case basis with reference to the standard cost. On this basis the multiplier of 1.4 is considered reasonable to reflect a standard cost, with variations to be negotiated based on the relative complexity of the testing processes required by the trial.

Reference number	1.3.1
Item	Imaging examinations and procedures itemised under the MBS
Sub-list	Clinical tests and procedures items
Category	Medical imaging
Definition	Includes diagnostic radiology (e.g. plain radiography, computed tomography (CT), magnetic resonance imaging (MRI), ultrasound and nuclear medicine)
Standard Cost	140% of the MBS fee per imaging examination and/or procedure

Related items

Table A.5 presents other items which are related (i.e. not necessarily mutually exclusive from) to item 1.3.1 "imaging examinations and procedures".

Table A.5: Items related to imaging examinations and procedures

Item	Reference Number	Comment
PET-FDG/FLT scans	1.3.2	Item 1.3.2 covers PET-FDG/FLT scans not itemised under the MBS, whereas item 1.3.1 covers PET-FDG/FLT scans covered under the MBS (note that PET-FLT scans are not covered under any MBS item number).

Learnings from site visits

Many clinical trials require imaging examinations and procedures to be performed as part of the trial protocol. These services were typically performed using the hospital's normal arrangements for imaging, either onsite or through an external provider. Discussions with participating sites indicated that imaging costs need to be considered as a mix of reimbursement for the procedure (where these do not form part of standard of care) and payment for additional services/activities beyond those normally included in the imaging procedure (such as additional reporting).

Process map for "imaging examinations and procedures itemised under the MBS"

Not applicable.

Considerations for deriving the cost of "imaging examinations and procedures itemised under the MBS"

As with pathology, perhaps even more so, most sites consulted stated that the clinical trial budget derived for imaging examinations and procedures referred to the MBS with some adjustment. The adjustment was either an additional fixed amount (e.g. range $50-$100 per imaging activity) or an add-on loading to the MBS fee to cover the extra work associated with any different processes that need to be followed to meet the trial protocol, additional reporting requirements, tracking requests, billings, etc. Putting a loading on MBS fee was the more common approach, particularly where the trial host site outsourced the imaging service to another (usually private) provider.

Trial sites advised that there were other activities relating to trial specific imaging examinations and procedures that required additional time and costs including:

- protocol review;
- staff training;
- setting up request stationery and billing procedures;
- additional reporting such as Response Evaluation Criteria In Solid Tumors (RECIST) reporting, which is usually charged based on time;

- production of CD containing images; and
- data extracts which is usually charged based on time.

Some sites covered the "additional costs" in their fixed establishment/set up fee or the ongoing administration fees. For simplicity, and to level the playing field between sites that provide the imaging services 'in-house' and those that outsource, it is considered, as with laboratory tests, that these costs are best reflected by using a multiplier on the MBS fee.

Table of standard costs for "imaging examinations and procedures itemised under the MBS"

MBS is a system for determining benefits payable to patients, it has regard to costs but it is not based on costs. But, it is appropriate for use in this circumstance, as bottom up costing could not be attempted, and most sites negotiate trial budgets based on an MBS multiplier. Table A.6 presents a number of reference points for the MBS multipliers applied by the visited sites.

Table A.6: MBS multipliers for imaging examinations and procedures

Item	Basis	Resource Unit (MBS multiplier)					Unit cost	Multiplier to derive standard cost
		Min	25th percentile	Median	75th percentile	Max		
Imaging examinations and procedures	MBS fee with adjustment factor	1	1	1.2	1.3	1.8	N/A	1.4

As can be seen, there were different MBS multipliers applied by sites to set trial budgets often depending on whether the trial was investigator initiated, collaborative sponsored, or industry sponsored. Hence, the wide range between the min and max multipliers, where the min is more commonly applied to investigator initiated trials (usually including collaborative sponsored trials) and the max is more commonly applied to industry sponsored trials. This practice reflects cross-subsidisation by trial sites and is not relevant to a study seeking to determine reasonable costs.

For this reason, multipliers at the lower and higher end of observed practice are not considered relevant. The site visits clearly show that there are often trial specific processes (e.g. extra reporting) associated with imaging examinations on trial participants that would justify an MBS multiplier greater than one. There are also a number of trial specific issues (e.g. imaging examinations in paediatric trials generally take longer and hence are more costly), which may need to be dealt with on a case by case basis with reference to the standard cost. On this basis the multiplier of 1.4 is considered reasonable to reflect a standard cost, with variations to be negotiated based on the relative complexity of the imaging examinations required by the trial.

Reference number	1.3.2
Item	PET-FDG/FLT scans not itemised under the MBS
Sub-list	Clinical tests and procedures items
Category	Medical imaging
Definition	Includes Positron Emission Tomography (PET) scans using the radiopharmaceuticals fluorodeoxyglucose (FDG) or fluorothymidine (FLT)
Standard Cost	140% of the nearest equivalent MBS fee for PET-FDG per scan

Related items

Table A.7 presents other items which are related to item 1.3.2 "PET-FDG/FLT scans not itemised under the MBS". Although, given the way they are defined, these items are mutually exclusive, it is considered that subsequent versions of the standard list of items associated with clinical trials should include all PET services under one item.

Table A.7: Items related to imaging examinations and procedures

Item	Reference Number	Comment
Imaging examinations and procedures itemised under the MBS	1.3.1	Item 1.3.1 covers PET-FDG/FLT scans itemised under the MBS, whereas item 1.3.2 covers PET-FDG/FLT scans not itemised under the MBS (note that PET-FLT scans are not covered under any MBS item number).

Learnings from site visits

PET scans are often included in oncology clinical trial protocols. There are MBS items for PET scans however they are only for those where the contrast media is FDG not FLT. It is important to note that the FDG-PET scans currently listed under the MBS are for specific clinical indications only (e.g. performed for the staging of proven non-small cell lung cancer, for the evaluation of suspected residual, metastatic or recurrent colorectal carcinoma or melanoma in patients considered suitable for active therapy etc.).

It was also observed that some sites manufacture their own contrast media (e.g. FDG or FLT) whereas others buy the contrast media from a manufacturer.

Derived process map for "PET-FDG/FLT scans not itemised under the MBS"

Not applicable

Considerations for deriving the cost of "PET-FDG/FLT scans not itemised under the MBS"

There were only a few sites where information was able to be obtained about PET scans. As with other imaging examinations, there was a disposition to use an adjusted MBS fee to set the clinical trial budget. The issue is that MBS only covers PET scans using FDG as the contrast medium. From first principles, the cost of PET scans can be considered is three parts:

- **Radiopharmaceutical costs:** the cost of the radioactive element that is used to produce the images (FDG or FLT);
- **Procedure costs:** the cost of conducting the procedure covering facility, labour, and equipment; and
- **Professional Fees:** the cost associated with having the radiologist interpret the test result.

On this basis the principal difference in the cost of PET-FDG and PET-FLT should be in the costs of the radiopharmaceutical. It was not possible to obtain data within the time available for this study that allowed this cost difference to be quantified.

Table of standard costs for "PET-FDG/FLT scans not itemised under the MBS"

MBS is a system for determining benefits payable to patients, it has regard to costs but it is not based on costs. But, in the absence of any other data, it is appropriate for use in this circumstance, as bottom up costing could not be attempted. Table A.8 indicates that insufficient data on the charging practices applied in the visited sites was able to be obtained.

Table A.8: MBS multipliers for PET-FDG/FLT scans not itemised under the MBS

Item	Basis	Resource Unit (MBS multiplier)					Unit cost	Multiplier to derive standard cost
		Min	25th percentile	Median	75th percentile	Max		
PET procedures	MBS fee for nearest equivalent PET-FDG procedure with adjustment factor	N/A	N/A	N/A	N/A	N/A	N/A	1.4

In the absence of any other data it is considered that the best approach is to use the MBS fee for the nearest equivalent PET procedure using FDG contrast medium. Where PET-FDG is used for tumour sites where there is no MBS item, the PET FDG fee for the most similar site should be used. Where PET-FLT is used as an alternative to PET-FDG, the PET-FDG MBS fee for that same site should be used. This arrangement is not entirely satisfactory, as it is known that FLT is better than FDG for certain tumours and vice versa for others.

As the main difference in the cost is likely to be the contrast medium (i.e. the costs of the procedure and the costs of the radiologist interpreting the image are likely to be fairly independent of the contrast medium used), the use of the PET-FDG MBS fee as a base for estimating the cost of PET-FLT scans is the best available option. As with other imaging examinations and procedures a multiplier of 1.4 is considered reasonable to reflect a standard cost, with variations to be negotiated based on the relative complexity of the PET examinations required by the trial.

Reference number	1.4.1
Item	Radiation therapy planning and treatment itemised under the MBS
Sub-list	Clinical tests and procedures items
Category	Radiation Therapy
Definition	Includes radiation therapy planning, external beam radiation therapy, brachytherapy etc.
Standard Cost	140% of the MBS fee including ROHPG component per service

Related items

None.

Learnings from site visits

Radiation therapy procedures are often a component of oncology clinical trials. Although the majority of procedures are standard of care, some additional services may be required to satisfy the trial protocol. Additional time to undertake certain trial specific activities was noted at the sites visited (e.g. time taken to upload files/images to sponsors).

Derived process map for "radiation therapy planning and treatment"

Not applicable.

Considerations for deriving the cost of "radiation therapy planning and treatment"

The MBS was the only source for information relating to radiotherapy costs that was identified. It includes items related to all types of radiation therapy services and represents the most logical basis for estimating costs and setting trial budgets. Similar to imaging services, some sites adjust the relevant MBS fee when developing their clinical trials budgets either using an additional fixed amount (e.g. $50-$100 per service) or an add-on percentage to the MBS fee to cover the extra work associated with services provided to trial participants (e.g. reporting, tracking requests, and billings).

It should also be noted that the current MBS fee does not incorporate a payment for the capital cost of the radiation therapy machines (e.g. linear accelerators, CTs for treatment planning, etc.). Capital costs are reimbursed through a separate Radiation Oncology Health Program Grant (ROHPG) that provides a fixed amount according to the MBS item (range $8 to $1,145 per treatment). The amount of ROHPG payable for the equipment is determined from time to time by the Department of Health and Ageing and the per service amount is paid for each service (in addition to the MBS fee) until the capital balance is exhausted.

Table of standard costs for "radiation therapy planning and treatment"

MBS is a system for determining benefits payable to patients, it has regard to costs but it is not based on costs. But, it is appropriate for use in this circumstance, as bottom up costing could not be attempted, and most sites negotiate trial budgets based on an MBS multiplier. Table A.9 indicates that insufficient data on the multipliers applied in the visited sites was able to be obtained.

Table A.9: MBS multipliers for radiation therapy planning and treatment

Item	Basis	Resource Unit (MBS multiplier)					Unit cost	Multiplier to derive standard cost
		Min	25th percentile	Median	75th percentile	Max		
Radiation therapy planning and treatment itemised under the MBS	MBS fee including the ROHPG capital component with adjustment factor	N/A	N/A	N/A	N/A	N/A	N/A	1.4

As can be seen, it is considered appropriate to add the MBS per service fee to the ROHPG per service fee to derive the standard cost, irrespective of the funded status of the equipment (i.e. fully amortised or not) used to provide the service. Such an approach is justified as the basis of the study is reasonable costs, which would normally include an amortised capital cost.

Consistent with the other clinical services items, the site visits clearly show that there are often trial specific activities (e.g. extra reporting, image transfer) associated with radiotherapy services provided to trial participants that would justify an MBS multiplier greater than one. There are also a number of trial specific issues (e.g. radiotherapy services in paediatric trials generally take longer and hence are more costly), which may need to be dealt with on a case by case basis with reference to the standard cost. As with other clinical service items, an MBS multiplier of 1.4 is considered reasonable to reflect a standard cost, with variations to be negotiated based on the relative complexity of the radiotherapy services required by the trial.

Reference number	1.5.1
Item	Other clinical tests or procedures itemised under the MBS
Sub-list	Clinical tests and procedures
Category	Other clinical tests or procedures
Definition	Includes surgical and non-surgical procedures (e.g. diagnostic and treatment related procedures) performed by clinically and/or scientifically qualified staff
Standard Cost	140% of the MBS fee per service

Related items

Table A.10 presents other items which are related (i.e. not necessarily mutually exclusive from) to item 1.5.1 "other clinical tests or procedures itemised under the MBS".

Table A.10: Items related to other clinical tests or procedures itemised under the MBS

Item	Reference Number	Comment
Laboratory tests and procedures itemised under the MBS	1.2.1	Costed according to MBS fee adjusted by a loading
Imaging examinations and procedures itemised under the MBS	1.3.1	Costed according to MBS fee adjusted by a loading
PET-FDG/FLT scans not itemised under the MBS	1.3.2	Costed according to the MBS fee for the nearest equivalent PET-FDG item adjusted by a loading
Radiation therapy planning and treatment itemised under the MBS	1.4.1	Costed according to MBS fee adjusted by a loading

It is also possible that a trial protocol may require tests or procedures to be performed that are not covered by the MBS. Such tests would not be covered by this item, but they are not obviously covered elsewhere. It was not possible to fully investigate this situation in site visits, so the nature of such tests or procedures is unknown. Perhaps the issue could be further considered in any future revision to the standard list of items associated with undertaking clinical trials.

Learnings from site visits

A number of trials required tests or procedures that fit into this category (e.g. respiratory function tests, ECGs, etc.). These services were typically provided on-site by the relevant hospital service (e.g. respiratory laboratory, echocardiography laboratory, etc.). Similar arrangements to the other diagnostic services (i.e. laboratory tests, imaging examinations and procedures, etc.) that might be used for participants in a clinical trial generally applied.

Derived process map for "other clinical tests or procedures itemised under the MBS"

Not applicable.

Considerations for deriving the cost of "other clinical tests or procedures itemised under the MBS"

The MBS was the only source for information relating to the costs of "other clinical tests or procedures itemised under the MBS" that was identified. By definition it will include all the services covered by this item and represents the most logical basis for estimating costs and setting trial budgets. Similar to other types of clinical tests and procedures, sites seem to adjust the relevant MBS fee when developing their clinical trials budgets, usually by applying an add-on percentage to cover the extra work associated with services provided to trial participants (e.g. reporting, tracking requests, and billings).

Table of standard costs for "other clinical tests or procedures itemised under the MBS"

MBS is a system for determining benefits payable to patients, it has regard to costs but it is not based on costs. But, it is appropriate for use in this circumstance, as bottom up costing could not be attempted, and most sites negotiate trial budgets based on an MBS multiplier. Table A.11 indicates that insufficient data on the multipliers applied in the visited sites was able to be obtained.

Table A.11: MBS multipliers for other clinical tests or procedures itemised under the MBS

Item	Basis	Resource Unit (MBS multiplier)					Unit cost	Multiplier to derive standard cost
		Min	25th percentile	Median	75th percentile	Max		
Other clinical tests or procedures itemised under the MBS	MBS fee with adjustment factor	N/A	N/A	N/A	N/A	N/A	N/A	1.4

Consistent with the other clinical services items, the site visits clearly show that there are often trial specific activities (e.g. extra reporting, test results transfer) associated with "other clinical tests or procedures itemised under the MBS" provided to trial participants that would justify an MBS multiplier greater than one. As with other clinical service items, an MBS multiplier of 1.4 is considered reasonable to reflect a standard cost, with variations to be negotiated based on the relative complexity of the "other clinical tests or procedures itemised under the MBS" services required by the trial.

Reference number	1.6.1
Item	Specialist medical consultations
Sub-list	Clinical tests and procedures items
Category	Specialist medical consultations
Definition	Includes all specialist medical consultations (including GPs, dentists, etc.)
Standard Cost	140% of the MBS fee per specialist medical (including GP) service 100% of ADA fee per specialist dental service

Related items

None.

Learnings from site visits

Specialist medical consultations featured in clinical trials in one of three ways:

- a clinical trial participant attends a consultation considered part of standard of care;
- a clinical trial participant attends a consultation considered for the most part as standard of care but additional time is required due to clinical trial requirements; or
- a clinical trial participant attends a consultation only for the purpose of meeting clinical trial requirements.

In the case of the third option, when an additional consultation is scheduled that is not part of standard of care the trial budget usually includes the full cost of the medical consultation. In the case where additional activities and time is added to a consultation that is part of standard of care the proportional cost (or usually time) is identified and included in the trial budget.

Derived process map for "specialist medical consultations"

Not applicable.

Considerations for deriving the cost of "specialist medical consultations"

The investigation into a basis for setting the standard cost of specialist medical services identified a number of options. The MBS, the Australian Medical Association (AMA) Fee Schedule, and the Department of Veterans' Affairs (DVA) Fee Schedule all represent approaches that are consistent with common billing practices. Table A.12 provides a comparison of some relevant items from the three Schedules. It is noted that the AMA is consistently highest (representing a premium of 75% to 86% of MBS), with the DVA fee in the middle of the range.

Table A.12: Comparison of Fee Schedules (amounts rounded)

Item	MBS	AMA	DVA
Item 36 GP Attendance Level C (20-39 minutes)	$70	$126	$81
Item 104 Specialist Consultation Initial	$86	$150	$116
Item 105 Specialist Consultation Follow up	$43	$80	$58

For simplicity MBS is best used as the reference point as IT systems will generally be set up with the MBS listing. Through the site visits, examples of sites using the MBS fee with an add-on percentage to recognise that additional administrative time is required to manage the trial billings as a reference for setting the trial budget were found. There were also examples of sites using the AMA fee with an add-on percentage. In short, trial budget setting practices varied significantly.

Although only one site was identified as undertaking any clinical trials relating to dentistry, it is important to note that generally, the MBS does not cover any dental clinical tests or procedures. In circumstances where dental services are provided to clinical trial participants, then either the DVA Dental Fee Schedule or Australia Dental Association (ADA) Fee Schedule are referenced.

Table of standard costs for "specialist medical consultations"

MBS is a system for determining benefits payable to patients, it has regard to costs but it is not based on costs. There are other Fee Schedules for medical specialist services, notably the AMA and DVA Schedules. To retain consistency with the other items in the clinical test and procedures sub-list, MBS is also used as the basis for classifying and setting the standard costs for specialist medical services (except dental services). Use of the MBS fee as a reference point is appropriate, as bottom up costing could not be attempted, and most sites negotiate trial budgets based on an MBS multiplier. Table A.13 indicates that insufficient data on the multipliers applied in the visited sites (not all sites used MBS) was able to be obtained.

Table A.13: MBS multipliers for specialist medical services

Item	Basis	Resource Unit (MBS multiplier)					Unit cost	Multiplier to derive standard cost
		Min	25th percentile	Median	75th percentile	Max		
Specialist medical consultations	MBS fee with adjustment factor	N/A	N/A	N/A	N/A	N/A	N/A	1.4
Specialist dental consultations	ADA fee, unadjusted	N/A	N/A	N/A	N/A	N/A	N/A	1.0

Consistent with the other clinical services items, the site visits clearly show that there are often trial specific activities (e.g. extra reporting, extra information to be provided to trial participants) associated with specialist medical consultations that would justify an MBS multiplier greater than one. It is difficult to justify a multiplier of around 1.8 which is typical of the relevant items in the AMA Fee Schedule (it is argued that at this level, there is a return on investment component included, i.e. not just reasonable costs). Therefore, as with the other clinical service items, an MBS multiplier of 1.4 is considered reasonable to reflect a standard cost, with variations to be negotiated based on the relative complexity of the medical specialist services required by the trial.

The same approach cannot be used for dental services as there are no MBS items for most services. In the circumstances, the use of the ADA Fee Schedule is considered appropriate. The ADA Fee Schedule is considered similar to the AMA Fee Schedule, in that it allows for a return on investment component in setting the fee (i.e. it is not a measure of costs). The investigations conducted for the purposes of the study did not produce any basis for adjusting the fees in the ADA Schedule, so it is considered that the best approach is to use the Schedule without a multiplier (i.e. the return on investment component of the ADA fee is considered roughly equal to the additional cost of providing dental service to clinical trial participants). Variations to the ADA fee can then be negotiated based on the relative complexity of the dental services required by the trial.

Reference number	1.7.1
Item	Nursing/Allied Health Consultations
Sub-list	Clinical tests and procedures items
Category	Nursing/Allied Health Consultations
Definition	Includes all nursing and allied health services
Standard Cost	100% of the published IHPA price for public hospital outpatient services

Related items

None.

Learnings from site visits

Nursing consultations feature in the vast majority of clinical trials and allied health consultations feature to a lesser degree. Either the participant is seen for trial activities as part of a standard of care visit or as a separate clinical trial specific visit. In the latter case, the trial budgets typically include the cost of a full nursing/allied health consultation service. In the case of a shared visit, and where the time on trial activities is material, a proportion of the cost of the nursing/allied health service is often included in the trial budget.

The issue of setting the costs for consultation services provided by a pharmacist was raised by a few of the sites visited. For the purposes of this list, it is considered that a pharmacist is an allied health professional, and that the same process for deriving a standard cost should apply. Note that it is consultation services provided by a pharmacist that are addressed here, not the drug dispensing related services that are covered under sub-list 2 "Clinical – Trial Support Services".

Derived process map for "nursing/allied health consultations"

Not applicable.

Considerations for deriving the cost of "nursing/allied health consultations"

The investigation into a basis for setting the standard cost of nursing and allied health services identified a number of options. The MBS, and the Australian Medical Association (AMA) Fee Schedule represent approaches that are consistent with common billing practices. Table A.14 provides a comparison of some relevant items for fees associated with nursing consultations. Both these items relate to assessment services, and their MBS fees are very similar. The AMA fees are in a range, with the maximum representing a premium of about 30% over the MBS fee.

Table A.14: Comparison of Fee Schedules, Nurse Consultations (amounts rounded)

Item	MBS	AMA
Item 10986-Practice Nurse Consultation	$58	$34-$76
Item 82215-Nurse Practitioner Consultation	$59	$34-$76

Allied health consultation fee schedules are generally state based rates, particularly for occupational therapy and physiotherapy. For comparison purposes only NSW, Vic and WA are included along with national rates taken from the Comcare website in Table A.15. There is wide variation in these fees and for practical purposes, it is difficult to set a reference point. There are also some items in the MBS that can be claimed by allied health professionals (e.g. the provision of psychological therapy services by a psychologist or clinical psychologist, or the provision of services by a physiotherapist to a person with a chronic condition who has complex care needs).

Table A.15: Allied health fee schedules

Allied health professional	Type of consultation	NSW	Vic	WA	National
Psychology	Initial consult (1-15 mins)	n.a	n.a	n.a	$61.00
	Initial consult (16-30 mins)	n.a	n.a	n.a	$119.00
	Subsequent consult (1-15 mins)	n.a	n.a	n.a	$61.00
	Subsequent Consult (16-30 mins)	n.a	n.a	n.a	$119.00
Occupational therapy	Initial consultation < 1 hour	n.a	$53.23	$127.55	n.a
	Standard consultation < 30 minutes	n.a	$42.84	$51.60	n.a
Physiotherapy	Initial consult	$83.70	$92.26	$75.40	n.a
	Standard consult	$70.90	$48.45	$60.55	n.a

Source: http://www.comcare.gov.au/claims/benefits__and__entitlements/medical_expenses/medical_service_rates/allied_health_rates

Another possible source of data is the national efficient price determined by the Independent Hospital Pricing Authority (IHPA) for the purposed of activity based funding in public hospitals. These prices are determined based on the average costs derived National Hospital Costs Data Collection, which covers a very large proportion of public hospital services provided in Australia. Table A.16 sets out the prices published by IHPA for 2013/14 for allied health and nursing clinics.

Table A.16: Nursing and allied health outpatient clinic costs, as published by IHPA for 2013/14

Item	Price weight	Price (based on NEP of $4,993)
Nursing		
Pre-admission and pre-anaesthesia (indicator for nursing)	0.0595	$297
Pharmacy		
Clinical Pharmacy	0.0762	$380
Allied Health		
Audiology	0.0800	$399
Neuropsychology	0.1071	$535
Nutrition/Dietetics	0.0261	$130
Occupational Therapy	0.0379	$189
Optometry	0.0212	$106
Orthoptics	0.0267	$133
Physiotherapy	0.0376	$188
Podiatry	0.0713	$356
Psychology	0.0577	$288
Social Work	0.0506	$253
Speech Pathology	0.0434	$217

Table of standard costs for "nursing/allied health consultations"

There are wide variations in cost/prices of nursing/allied health services derived from the potential sources investigated. While it may be appropriate to use MBS as the basis for the classification of the services, as MBS has been used for all the other clinical services, there is insufficient information in the MBS to cover all nursing and allied health services. On that basis use of the prices published by IHPA is the preferred option. Table A.17 indicates the preferred approach (it is not based on data on the cost in the visited sites), as such data were not obtainable.

Table A.17: Approach to determining standard cost for nursing/allied health services

Item	Basis	Resource Unit					Unit cost	Multiplier to derive standard cost
		Min	25th percentile	Median	75th percentile	Max		
Nursing/allied health consultations	IHPA price with no adjustment	N/A	N/A	N/A	N/A	N/A	N/A	1.0

In the circumstances, the use of the IHPA prices, which are based on average cost, is considered most appropriate. There is variation in these costs relative to the other possible indicators of cost examined, but the NHCDC is considered the most robust source, and the accuracy of the costs will improve as IHPA carries out further, more detailed, costing studies (a study is in progress).

Appendix B – Clinical Trial Support Services

Reference number	2.1.1
Item	Department Protocol Review
Sub-list	Clinical Trial Support Services
Category	Department Protocol Review
Definition	Includes the Heads (or nominees) within the clinical trial host unit (e.g. oncology unit, respiratory unit, etc.) in addition to the supporting departments (e.g. pharmacy, pathology, radiology, radiation therapy, other clinical specialties, clinical trials office/governance office, etc.) reviewing the clinical trial protocol. The process may involve individuals or a panel drawn from the above mentioned departments to review the protocol for scientific merit and local feasibility.
Standard Cost	$171 per protocol review

Related items

Table B.1 presents other items which are related to item 2.1.1 "Departmental Protocol Review".

Table B.1: Items related to Departmental Protocol Review

Item	Reference Number	Comment
Site selection including site feasibility assessment process	3.1.2	Departmental protocol review is often considered one aspect of the site selection including site feasibility assessment process. However to create mutual exclusivity between 3.1.2 and 2.1.1, item 2.1.1 does not include any activities covered under 3.1.2.

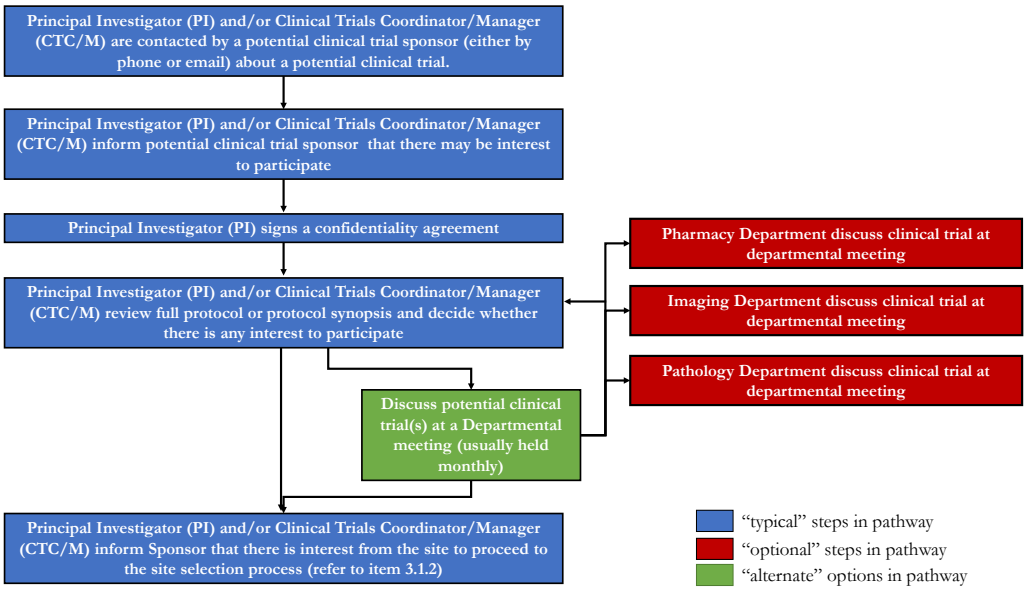
Learnings from site visits

According to informants at the site visits, the costs associated with the departmental protocol review are not included in any budget negotiated by the trial site with the trial sponsor (or nominee), as the activities occur before site selection. The time spent reviewing a protocol depends on a range of factors such as the length of the protocol (i.e. a protocol may vary from a few page summary to a full 100 pages), the complexity of the trial and the relationship between the sponsor (or nominee) and the clinical trial host department. In cases where the host department and the sponsor have a long-standing relationship, the time required to review the protocol is minimal. In addition to a potential lead investigator on-site being directly approached by a clinical trial sponsor, some clinical trials units hold monthly meetings to discuss/assess clinical trial interest; others consult more broadly (i.e. with supporting departments to make sure there is capacity and interest), whereas others involve the potential on-site lead investigator and/or clinical trials manager only reviewing a synopsis of a clinical trial protocol. There was no consistency between or within sites.

Derived process map for "Departmental Protocol Review"

Figure B.1 presents the typical process involved in reviewing a trial protocol.

Figure B.1: Process map of the activities involved under "Departmental Protocol Review"



Considerations for deriving the cost

In order to derive a reasonable cost associated with protocol review, time (in hours) was chosen as the most suitable basis due to the activities involved various personnel reviewing a protocol. As the process varied in terms of who was involved in the initial protocol review, costing for this activity was based on the typical process which involved the potential principal investigator and the clinical trials coordinator/manager (who was a registered nurse in 75% of cases and a medical scientist in 25% of site visits). The referenced unit cost is the hourly rate determined in item 2.6.2 for the Principal Investigator and a combination of the hourly rate determined for items 2.6.3 Research Nurse (75% allocation) and 2.6.4 Clinical Research Coordinator (25% allocation). Only industry or collaborative sponsored trials undertake protocol review. For investigator initiated trials (i.e. those funded under NHMRC grants etc.), the costs associated with protocol development and review are included in item 3.1.1.

It was not possible to cost the involvement of other departments reviewing the protocol as there was too much variability, in that supporting departments were not always involved in protocol review and who within the department would review the protocol also varied.

Table of standard costs for "Departmental Protocol Review"

Table B.2 presents the resource units, in hours, required for each activity by specific personnel. Only the typical steps in the process map (i.e. those in **blue**) are costed.

Table B.2: Typical personnel, resources and unit cost involved in Departmental Protocol Review

Item	Basis	Resource unit (hours)					Unit cost (per labour hour)	Standard cost (median)
		Min	25th percentile	Median	75th percentile	Max		
Departmental protocol review	Principal Investigator	0.3	0.5	0.5	1.0	42.0	$215.00	$107.50
	Clinical Trials Coordinator/Manager	0.3	1.0	1.0	2.0	48.0	$63.75	$63.75
	Other departmental input	0.5	1.3	2.0	3.5	6.0	n/a	n/a
Total								**$171.00**

The "max" was driven by two sites, one was a paediatric clinical trial unit that stated that thorough investigation of all protocols (e.g. they investigate patient population, possible eligible

patient numbers, reviewing logistic of specimen collection and storage etc.) is undertaken prior to moving to the site feasibility and selection phase (covered under item 3.1.2) and the other was a metropolitan hospital reviewing a Phase 1 trial protocol.

The most typical process identified at the sites was an exchange of confidentiality agreements and a review of the synopsis or summary of the protocol by the potential lead investigator on-site, and the potential study coordinator on-site. This time has been costed at the observed median, and on that basis the standard cost is set at $171.

Reference number	2.2.1
Item	Departmental Establishment/Set up Fees
Sub-list	Clinical Trial Support Services
Category	Departmental Establishment/Set up Fees
Definition	The Departmental Establishment/Set up Fees includes the fees associated with each Department involved in clinical trial set up activities which may include, but not restricted to preparing trial specific request forms, coordination with investigators and/or meeting with sponsors, instructions and identification of locations for storage of samples, development of supporting documentation and/or IT/data management.
Standard Cost	$2,000 for clinical trial unit per clinical trial
	$990 for pharmacy department per clinical trial
	$425 for pathology department per clinical trial
	$550 for radiology department per clinical trial

Related items

Table B.3 presents other items which are related to item 2.2.1 "Departmental Establishment/Set up Fees".

Table B.3: Items related to Departmental Establishment/Set up Fees

Item	Reference Number	Comment
Departmental Ongoing Administration Fee	2.3.1	If ongoing administrative tasks (i.e. post the set up phase of a clinical trial) are included in the Departmental Establishment/Set up Fees (i.e. item 2.2.1), then activities described under item 2.3.1 would also be captured in item 2.2.1. Hence only one fee should be charged in the first 12 months.
Site selection including site feasibility assessment process	3.1.2	Activities associated with site selection should be captured under item 3.1.2 and not 2.2.1.
Preparation and submission of applications to HREC and institutions	3.1.3	Activities associated with preparing and submitting the ethics application and/or governance application should be captured under item 3.1.3 (for personnel time) and 3.1.5 (for associated ethics and/or governance fees) and not 2.2.1.
Radiation safety and/or biosafety reports	3.1.4	Activities associated with preparing the radiation safety and/or biosafety reports should be captured under item 3.1.4 and not 2.2.1.
Investigator meetings	3.1.8	Any activities/costs associated with personnel attending the investigator meeting should be captured under item 3.1.8 and not 2.2.1.
Staff training	3.1.9	Any staff training activities associated with the start up of a clinical trial (e.g. GCP, eCRF, etc.) or other protocol requirements should be captured under item 3.1.9 and not 2.2.1.
Start-up meeting	3.2.1	Attendance of any study personnel at site initiation meeting should be excluded from item 2.2.1 and should be captured under 3.2.1.

Learnings from site visits

Most clinical trial host departments charge an establishment/set up fee that covers various activities. In addition most supporting departments (i.e. pathology, pharmacy, imaging etc.) also charge a departmental establishment/set up fee. The fee charged is usually varied depending whether the site is a lead or non-lead site and how many different activities are attempted to be captured under the "Departmental Establishment/Set up Fee" (e.g. preparation of ethics applications were sometimes included under the Departmental Establishment/Set up Fees and other times a separate fee for the ethics application was included).

As we identified that the activities included under the establishment/set up fee varies from departments within the same hospital to departments across hospitals Table B.4 attempts to capture the activities that we believe should be included under the establishment/set up fee by each type of department to prevent any duplication.

Table B.4: Activities included under Departmental Establishment/Set up Fees

Department	Activity
Clinical trial unit	• Review and familiarisation of protocol and the investigator brochure by all study personnel; • Preparation of documents/proformas required for the study; • Liaison with investigator(s), clinical trial/study coordinator(s) and/or clinical trial research associates; • Liaison with supporting departments (e.g. radiology, pathology, pharmacy etc.); • Development of information leaflets for participants or health professionals about the study; • Provision of education to medical, nursing, allied health personnel outside the clinical trial unit as a means of promoting the study; and • Receipt, acknowledgement, storage of clinical trials materials prior to commencement of trial.
Pathology department	• Review and familiarisation of protocol and the investigator brochure by all study personnel; • Review and/or development of any pathology - clinical trial specific manuals (including any logistic planning); • Preparation of clinical trial specific request and/or reporting forms; • Identifying and sourcing (i.e. hire and/or purchase) additional equipment (if required); and • Identification of appropriate storage areas (if required).
Pharmacy department	• Review and familiarisation of protocol and the investigator brochure by all study personnel; • Review and/or development of any pharmacy - clinical trial specific protocols/manuals/procedures (e.g. randomisation guidelines, dispensing guidelines, inventory log, IVRS and eCRF accounts, logistic planning etc.); • Preparation of clinical trial specific request and/or reporting forms (e.g. prescription forms, drug accountability, manufacture of special dose forms, etc.); • Preparation of other clinical trial specific forms (e.g. subject/carer education cards, study information sheets, etc.); • Identifying and sourcing (i.e. hire and/or purchase) additional equipment and/or medicines; • Identification of appropriate storage areas (if required).
Radiology department	• Review and familiarisation of protocol and the investigator brochure by all study personnel; • Review and/or development of any radiology - clinical trial specific manuals (including any logistic planning); • Preparation of clinical trial specific request and/or reporting forms; • Identifying and sourcing (i.e. hire and/or purchase) additional equipment; and • Identification of appropriate storage areas (if required).

Derived process map for "Departmental Establishment/Set up fees"

Not applicable.

Considerations for deriving the cost

As this item was a fees item, the relevant consideration was the range of fees charged by the visited sites rather than the cost associated with activities captured under item 2.2.1. In fact, it was not possible to cost the activities that might underlie each component of the fee to assess if the set fees were reasonable, as there was considerable variability as to what sites included in the department establishment/set up fees and whether they charged a department establishment/set up fee or not. However the basis for the units/departments setting the fee seemed to, in most cases, have little reference to cost. Some pharmacy departments have attempted to cost the set-up fee they were charging but there was so much variability in terms of the requirements based

on phase of trial and complexity of the clinical trial that the published fees did not necessarily match the charged fees for specific trials.

Table of standard costs for "Departmental Establishment/Set up fees"

Table B.5 presents the fee range charged by various visited clinical trials sites around Australia. In determining the standard cost it was considered that the fee practices observed at the sites visited often covered the costs for items that are dealt with elsewhere on the NHMRC list (for which a separate standard cost has been determined). Also, determination of the standard cost needed to take account of the fact that a number of exclusions from what is covered by the Departmental Establishment/Set up fee (as described in Table B.3) have been suggested to improve the homogeneity, and narrow the scope of the work, covered by this item on the NHMRC list. For these reasons, the standard cost, which is actually a reasonable establishment fee for each of the Departments participating in the clinical trial, is determined based on the 25th percentile of the observed range.

Table B.5: Typical fees associated with Departmental Establishment/Set up fees

Item	Basis	Resource unit (fee)					Unit cost	Standard cost (25th percentile)
		Min	25th percentile	Median	75th percentile	Max		
Clinical trial unit	Typical fees	$500	$2,000	$3,000	$5,000	$40,000	n/a	$2,000
Pharmacy department	Typical fees	$500	$990	$1,150	$1,400	$2,000	n/a	$990
Pathology department	Typical fees	$200	$425	$550	$650	$800	n/a	$425
Radiology department	Typical fees	$500	$550	$600	$900	$1,200	n/a	$550

The large variation seen in the establishment/start up is due to the inclusion of some phase 1 trials. If a Departmental establishment fee is used, it should be negotiated between the trial site and trial sponsor with reference to the reasonable costs, and the number of cost based items that are to be included in the trial budget.

Reference number	2.3.1
Item	Departmental Ongoing Administration Fees
Sub-list	Clinical Trial Support Services
Category	Departmental Ongoing Administration Fees
Definition	This is a fixed fee that covers all activities associated with the ongoing administration of a clinical trial including: • organising and making available materials for monitors visits (i.e. includes printing and photocopying, etc.); and • management of clinical trial resources including human and infrastructure.
Standard Cost	$1,005 for clinical trial unit per annum (from year two of the clinical trial)
	$500 for pharmacy department per annum (from year two of the clinical trial)
	$398 for pathology department per annum (from year two of the clinical trial)
	$200 for radiology department per annum (from year two of the clinical trial)

Related items

Table B.6 presents other items which are related to item 2.3.1 "Departmental Ongoing Administration Fees".

Table B.6: Items related to Departmental Ongoing Administration Fees

Item	Reference Number	Comment
Coordinating principal investigator surcharge	2.6.1	Time required by the coordinating principal investigator for attendance at meetings with the monitors should be captured under 2.3.1 and not 2.6.1.
Investigator allocation	2.6.2	Time required by any investigator for attendance at meetings with the monitors should be captured under 2.3.1 and not 2.6.2.
Research nurse allocation	2.6.3	Time required by the research nurse to manage ongoing clinical trial documentation; organise and making available materials for monitors visits and attend meetings with the monitors should be captured under 2.3.1 and not 2.6.3.
Clinical research coordinator (non-research nurse) allocation	2.6.4	Time required by the clinical research coordinator to manage ongoing clinical trial documentation; organise and making available materials for monitors visits and attend meetings with the monitors should be captured under 2.3.1 and not 2.6.4.
Ongoing administration, monitoring and reporting	3.2.6	Activities associated with submission and review of serious adverse event; and/or ongoing maintenance of training and qualifications should be captured under 3.2.6 and not 2.3.1.
Amendment preparation and submission	3.2.9	Activities associated with amendment preparation and submission should be captured under 3.2.9 and not 2.3.1.
Amendment review	3.2.10	Any fee associated with amendment review should be captured under 3.2.10 and not 2.3.1.

Learnings from site visits

Not all departments at the sites consulted, although some did, included a "Departmental Ongoing Administration Fee" in their clinical trial budgets. Some sites captured the expected time to be spent on administrative tasks as part of their per patient time allocation by the specified personnel. Other sites stated they just had an establishment fee which attempted to capture their ongoing administration costs. Those sites with ongoing administration fees sometimes charged them in the first year but most often they started in the second year of the trial as they felt their establishment/set up fee captured the first year administration costs. For those sites that had an ongoing annual administration fee, they also typically added a yearly increase which varied from 3% to 10%.

Derived process map for "Departmental Ongoing Administration Fees"

Not applicable.

Considerations for deriving the cost

Again, as this item was a fees item, the relevant consideration was the range of fees charged by the visited sites rather than the cost associated with activities captured under item 2.3.1. It was not possible to cost each component of the fee to assess if the set fees were reasonable or not. In fact, there was considerable variability as to what sites included in the departmental ongoing administration fees, and whether they charged a departmental ongoing administration fee or not. However the basis for the units/departments setting the ongoing administration fee seemed to, in most cases, have little reference to cost.

Table of standard costs for "Departmental Ongoing Administration Fees"

Table B.7 presents the fee range charged by various visited clinical trials sites around Australia. In determining the standard cost it was considered that the fee practices observed at the sites visited often covered the costs for items that are dealt with elsewhere on the NHMRC list (for which a separate standard cost has been determined). Also, determination of the standard cost needed to take account of the fact that a number of exclusions from what is covered by the Departmental ongoing administration fee (as described in Table B.6) have been suggested to improve the homogeneity, and narrow the scope of the work, covered by this item on the NHMRC list. For these reasons, the standard cost, which is actually a reasonable ongoing administration fee for each of the Departments participating in the clinical trial, is determined based on the 25th percentile of the observed range.

Table B.7: Typical fees associated with Departmental Ongoing Administration Fees

Item	Basis	Resource unit (fee per annum)					Unit cost	Standard cost (25th percentile)
		Min	25th percentile	Median	75th percentile	Max		
Clinical trial unit fee	Typical fee	$385	$1,005	$1,500	$2,000	$3,000	n/a	$1,005
Pharmacy department fee	Typical fee	$195	$500	$630	$1,025	$2,200	n/a	$500
Pathology department fee	Typical fee	$295	$398	$500	$850	$1,200	n/a	$398
Radiology department fee	Typical fee	$200	$200	$200	$225	$250	n/a	$200

If a Departmental ongoing administration fee is used, it should be negotiated between the trial site and trial sponsor with reference to the reasonable costs. It should also not duplicate the cost for other items that that have been determined on an activity basis.

Reference number	2.4.1
Item	Staff training (drug specific)
Sub-list	Clinical trial support services
Category	Pharmacy/Investigational Drug-related
Definition	Includes training undertaken by pharmacy staff on the protocol (including site specific dispensing guidelines), use of Interactive Voice Response System (IVRS)/Interactive Web Response System (IWRS) randomisation systems, as well as educating other pharmacists (i.e. those on wards etc.) as well as doctors, nurses etc. on the drug-specific aspects of the clinical trial protocol (e.g. in drug handling etc.).
Standard Cost	$224 per clinical trial

Related items

No related items, however this item should not get confused with 3.1.9 which is for general staff training which is not specific to the pharmacy department.

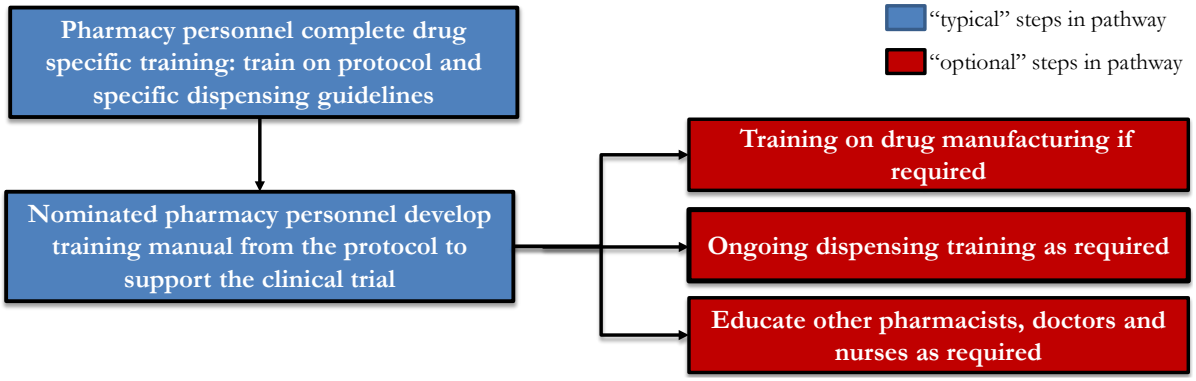
Learnings from site visits

According to the representatives consulted during the site visits, currently the cost associated with drug specific training is either absorbed by the pharmacy department or captured in the ongoing administrative fee or start-up fee which some pharmacy departments charge. The amount of time spent on drug specific training varied depending on the complexity of the drug (e.g. cytotoxic drugs vs. drugs of dependence, etc.) being manufactured and/or dispensed. Anywhere between two to four pharmacists may undertake drug specific training per trial. There may also be instances where the trials pharmacist has to train nurses, doctors or other pharmacists on the specific trial drug. Again this is dependent on the type and complexity of the drug being dispensed.

Derived process map for "staff training (drug specific)"

Figure B.2 presents the typical process involved in drug specific training. The **blue** boxes represent the typical process. The **red** boxes represent the optional processes in the typical pathway that are dependent on the actual clinical trial (e.g. complexity of drugs being prepared and dispensed).

Figure B.2: Process map of activities included under staff training (drug specific)"



Considerations for deriving the cost

The reasonable cost was based on two pharmacists (one grade 2 and one grade 3) undertaking the pharmacy specific training for each trial. As not all trials involve training for manufacturing, no cost has been allocated, although the variables collected are presented in Table B.8.

The fully absorbed hourly rate for the grade 2 and 3 pharmacist was calculated using an average of the NSW and Victorian pharmacist awards. We calculated a fully absorbed hourly rate (based on five days per week, 7.5 hours per day) for a grade 2 pharmacist to be $61 (Vic) to $75 (NSW) and $74 (Vic) to $87 (NSW) per hour for a grade 3 pharmacist. The average for a grade 2 pharmacist used was $68 and for a grade 3 pharmacist ($81).

Table of standard costs for "staff training (drug specific)"

Table B.8 presents the resource units, in hours, required for staff training drug specific resulting in a standard cost of $224 per clinical trial.

Table B.8: Typical personnel, resources and unit cost involved staff training (drug specific)

Activities	Personnel Involved	Resource unit (hours)					Unit cost	Standard cost (25th percentile)
		Min	25th percentile	Median	75th percentile	Max		
Staff training (drug specific)	Pharmacist - Grade 2	0.5	1.5	2.25	3	11	$68	$102
	Pharmacist - Grade 3	0.5	1.5	2.25	3	11	$81	$122
	Manufacturing Pharmacist	0.5	0.5	1	1	1	n/a	n/a
Total								**$224**

The typical cost is chosen at the 25th percentile for staff training (drug specific), as it was considered that there was an observational bias in the responses to the question (i.e. the times provided tended to relate to the more complicated instances of training).

Reference number	2.4.2
Item	On call and call in/call back fees
Sub-list	Clinical trial support services
Category	Pharmacy/investigational drug related
Definition	Includes fees associated with being on call, call in or call backs of pharmacy staff to deal with events specifically associated with the clinical trial.
Standard Cost	$400 per call in/call back

Related items

No related items were identified

Learnings from site visits

On call and call in/back events were not found to be common to clinical trials involving drugs. However if they are incurred they are usually charged per occasion at the on-call fee for the specified pharmacist. The professional discipline of the pharmacist on call is usually a grade two or three pharmacist (or equivalent). We found that on-call fees range from $200 to $640 charged on a per-event basis. Some sites also charge an on-call telephone recall fee which is usually in the range of $100-$170 per call. We also found that some sites will include a minimum number of hours in the call out fee (e.g. minimum of three hours) independent of the hours actually worked.

Most sites advised that this item should include more than just pharmacy staff as other clinical trial staff (e.g. trial coordinators, principal investigators etc.) often work outside of "normal" working hours (e.g. weekends etc.) recruiting patients etc. However as this item is specific to pharmacy, and it is outside the scope of this project to modify the items, such activities would need to be captured under items 2.6.2 (principal investigator allocation), 2.6.3 (research nurse allocation) and/or 2.6.4 (clinical research coordinator allocation).

Derived process map for "on call and call in/call back fees"

Not applicable.

Considerations for deriving the cost

Again, as this item was a fees item, Table B.9 represents the fees charged by the sites rather than the cost associated with activities captured under item 2.4.2. It was not possible to cost each component of the fee to assess if the set fees were reasonable or not as it is variable depending on the type of clinical trial and minimum hours to be paid based on State based awards. There were only two sites visited that had a specified "on-call telephone recall" charge. This fee was lower than there call in/call back fee as it did not require the on call pharmacist to attend the clinical trial site. We have not factored in the "on-call telephone recall" fee within the "on call and call in/call back fees" due to very few sites providing this information, however we have kept this information in Table B.9 for information. It is important to note that this fee is seen as a loading on the hours actually worked by the pharmacist, although it usually covers up to the first three hours before the usual hourly rate is applied.

Table of standard costs for "on call and call in/call back fees"

Table B.9 presents the typical minimum on call and call in/call back fee for pharmacy personnel.

Table B.9: Typical fee charged for on call and call in/call back fees

Activities	Basis	Fee (per call in/call back)					Unit cost	Standard cost (median)
		Min	25th percentile	Median	75th percentile	Max		
On call and call in/call back fees	Typical fee	$200	$360	$400	$450	$640	n/a	$400
On-call telephone recall	Typical fee	$100	$118	$135	$153	$170	n/a	n/a

These fees typically include the first three hours of labour following call in/call back, with any additional hours being charged at an hourly rate.

Reference number	2.4.3
Item	Drug stocking
Sub-list	Clinical trial support services
Category	Pharmacy/Investigational Drug-related
Definition	Includes the receiving of pharmacy stock for the clinical trial, completing an inventory check (online or manual), downloading temperature log (if applicable), sending any required data (e.g. checked inventory list) about the receipt of stock to trial sponsor and transferring the stock to the required storage location (e.g. shelf, fridge, freezer etc.). The drug stocking activity also includes stock management which includes expiry management activities (e.g. recording and storing used/returned drugs; data entry associated with returning any expired or unused drugs, returning unused/used drugs to sponsor etc.)
Standard Cost	$45 per stock shipment received

Related items

Table B.10 presents other items which are related but are consider mutually exclusive from item 2.4.3 "drug stocking".

Table B.10: Items related to drug stocking

Item	Reference Number	Comment
Drug preparation, labelling and re-labelling	2.4.4	The labelling, in addition to preparation and re-labelling, of received clinical trials stock is included in item 2.4.4 as opposed to 2.4.3 "drug stocking"
Drug storage and temperature monitoring	2.4.7	The process of storage and temperature monitoring is not considered part of 2.4.3 "drug stocking" but should be captured under 2.4.7.

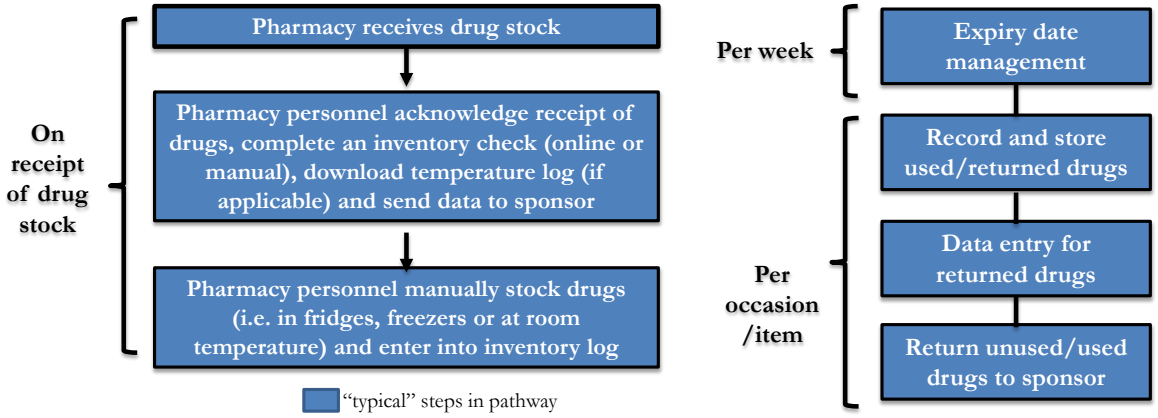
Learnings from site visits

Most sites stated that the cost associated with drug stocking is either absorbed by the pharmacy department (i.e. not charged to the sponsor or captured in the ongoing administrative fee or establishment/start-up fee, which some pharmacy departments charge). The cost associated with drug stocking is influenced by the amount of stock (i.e. a large stock delivery will take much more time to unpack and process compared to a smaller delivery). Drug stocking may be automated or require a pharmacy technician to do the inventory by hand. Some sites commented that although web-capture and automated processes have advantages in terms of 'real time' and interactive data management they are not always time-efficient. Most sites commented that drug stocking is undertaken by a pharmacy technician with some over sight from a grade 2 or 3 level pharmacist.

Derived process map for "drug stocking"

Figure B.3 presents the typical process involved in the drug stocking process. The **blue** boxes represent the typical process.

Figure B.3: Process map of activities included under "drug stocking"



Considerations for deriving the cost

As stated, the amount of time required to undertake the drug stocking (including expiry date management) is variable with the amount of stock received. Typically, sites reported that drugs would most often arrive in smaller rather than larger quantities. Accordingly, the most suitable basis for setting the standard costs was thought to be the hours spent by a pharmacy technician, with oversight from a grade 2/3 pharmacist. The costs associated with storage (shelf-space) in the pharmacy were considered to immaterial due to the fact that just-in-time inventory approaches are increasingly being used, therefore there is no need to stock large quantities.

The fully absorbed hourly rate for the grade 2 and 3 pharmacist was calculated using an average of the NSW and Victorian pharmacist awards. We calculated a fully absorbed hourly rate (based on five days per week, 7.5 hours per day) for a grade 2 pharmacist to be $61 (Vic) to $75 (NSW) and $74 (Vic) to $87 (NSW) per hour for a grade 3 pharmacist. The average for a grade 2/3 pharmacist used was $74. The fully absorbed hourly rate for the pharmacy technician was based on a grade 1 pharmacist (using an average between NSW and Victoria again) and was calculated at $51/hour.

Table of standard costs for "drug stocking"

Table B.11 presents the resource units, in hours by pharmacy staff, required for each stock shipment received. The fact that dugs are typically received in small quantities and that there is increased use of just-in-time inventory approaches to drug stocking led to the minimum of the observed range being assessed as the most suitable basis for setting the standard costs.

Table B.11: Typical personnel, resources and unit cost involved in drug stocking

Item	Personnel Involved	Resource Unit (hours)					Unit Cost	Standard cost (minimum)
		Min	25th percentile	Median	75th percentile	Max		
Drug stocking	Pharmacy technician	0.5	1.25	2.5	3.75	16	$51	$26
	Pharmacist - Grade 2/3	0.25	0.25	1	1	3	$74	$19
Total								**$45**

The extreme between the maximum and minimum indicated the degree variation reported by sites for drug stocking activity involves. It is considered that part of the reason for the observed variation the fact there are a number of closely related items for pharmacy activities associated with clinical trials. In any review of the NH&MRC list of activities, the opportunity to consolidate some of the pharmacy items should be considered.

Reference number	2.4.4
Item	Drug preparation, labelling and re-labelling
Sub-list	Clinical trial support services
Category	Pharmacy/Investigational Drug-related
Definition	Includes the manufacturing of the drugs (if applicable) or the preparation of the drugs (e.g. aseptic, cytotoxic or placebo preparation) required for the clinical trial as well as the associated general consumables (e.g. intravenous fluids, filters, etc.); the development and maintenance of special dosage forms (including the activities associated with the randomisation process if applicable), labelling and re-labelling (e.g. due to extension of the expiry date of the drug) of all drugs involved in the clinical trial.
Standard Cost	$37 per drug preparation $85 per 25 containers either labelled or relabelled

Related items

Table B.12 presents other items which are related to item 2.4.4 "drug preparation, labelling and re-labelling".

Table B.12: Items related to "drug preparation, labelling and re-labelling"

Item	Reference Number	Comment
Drug dispensing and accountability	2.4.5	Drug preparation and labelling is often a part of drug dispensing (i.e. medicines are prepared and giving out as one process). For the purposes of mutual exclusivity between items 2.4.4 and 2.4.5, the activities associated with "preparation" (which includes labelling) is included under item 2.4.4 but the activity associated with "giving out" the drug (including the associated pharmacy consult) is included under item 2.4.5.

Learnings from site visits

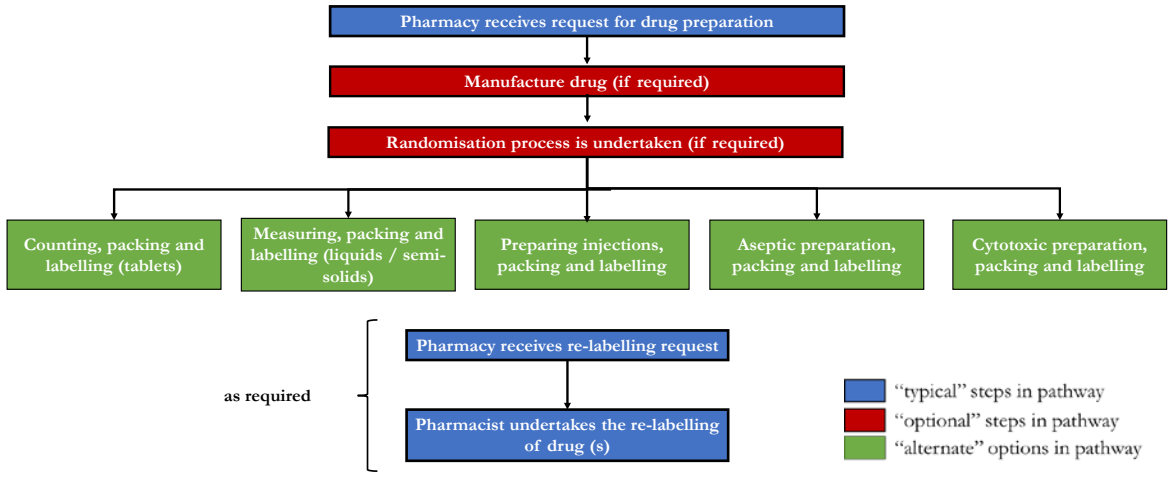
Drug preparation, labelling and re-labelling comprises a number of steps depending on whether there are requirements to make a placebo; whether patients are being randomised; whether drugs are being manufactured on-site (e.g. cytotoxic drugs manufactured on-site require closed system facilities), as well as the type of drug being manufactured (i.e. tablets; injections; cytotoxic drugs). Manufacturing drugs on-site adds substantially to pharmacy labour costs. A number of sites reported avoiding drug manufacture for clinical trials, as they felt the cost of this service is not adequately covered. Some sites charge a preparation fee for manufacturing (e.g. $100 for an industry sponsored trial and $80 for an investigator initiated trial).

Re-labelling tends to be invoiced as it occurs with charges typically around $100 per hour, or a charge base on the number of items that are required to be re-labelled (e.g. $54 for every ten labels). Not all sites charge for re-labelling, where not charged the cost was reported as being absorbed into ongoing administrative fees. Re-labelling can occur several times during the one clinical trial.

Derived process map for "drug preparation, labelling and re-labelling"

Figure B.4 presents the typical process involved in drug preparation, labelling and re-labelling process. The **blue** boxes represent the typical process. The **red** boxes represent the optional processes in the typical pathway that are dependent on the actual clinical trial (e.g. if double blind RCT, then a randomisation process would need to be followed). The **green** boxes represent the optional processes in the typical pathway that are dependent on the actual clinical trial (e.g. cancer drug trial would involve preparation of cytotoxic drugs).

Figure B.4: Process "drug preparation, labelling and re-labelling"



Considerations for deriving the cost for "drug preparation, labelling and re-labelling"

Wide variation was identified in the "drug preparation, labelling and re-labelling" activities depending on the type of drug trial and number of drugs involved in the trial. Also, most sites found it difficult to separate the time spent on preparation and dispensing activities. Typically, we were advised that two pharmacists were required for preparation and dispensing activities. To disaggregate the reported cost, the standard cost is set on the basis that only one pharmacist is involved in preparation activities.

Again, the fully absorbed hourly rate for the grade 2 and 3 pharmacist was calculated using an average of the NSW and Victorian pharmacist awards. The fully absorbed hourly rate (based on five days per week, 7.5 hours per day) for a grade 2 pharmacist was calculated as $61 (Vic) to $75 (NSW) and $74 (Vic) to $87 (NSW) per hour for a grade 3 pharmacist. The average for a grade 2/3 pharmacist was used, which was calculated at $74 per hour.

It is also important to note that labelling and re-labelling fees (which were often not distinguished, i.e. same fee set) were often charged per event and included on average 25 containers. Given that a per container approach to charging labelling fees reflects prevailing practice, this approach has been used to set the standard cost.

Table of standard costs for "drug preparation, labelling and re-labelling"

Table B.13 presents the resource units, in hours, required for drug preparation, labelling and re-labelling. Given the differences in prevailing practices, the standard costs for drug preparation is set separately to that for labelling/re-labelling activities.

Table B.13: Typical resources and unit cost involved in drug preparation, labelling and re-labelling

Item	Basis	Resource Unit (hours or fee)					Unit Cost	Standard cost (25th percentile)
		Min	25th percentile	Median	75th percentile	Max		
Drug preparation	Pharmacist - Grade 2/3	0.5	0.5	3	3	6	$74	$37
Labelling/re-labelling fee	Typical fee per 25 containers	$85	$85	$100	$119	$125	n/a	$85

For drug preparation, the typical cost is based on the 25th percentile, as it was considered that many of the observations made at the site visits were of the more complex instances of drug preparation (i.e. respondents tended to answer in respect of the more complex drug trials).

Reference number	2.4.5
Item	Drug dispensing and accountability
Sub-list	Clinical trial support services
Category	Pharmacy/Investigational Drug-related
Definition	Includes the conduct of dispensing (including the provision of counselling to clinical trial participants), review of clinical trial participants' adherence to the trial protocol and recording details of the clinical trial in the participant's medical record (paper based or electronic).
Standard Cost	Dispensing – simple $37.00 per participant per service
	Dispensing – complex $92.50 per participant per service
	Accountability - $12.75 per participant per service
	Counselling - $14.80 per participant per service

Related items

Table B.14 presents other items which are related to item 2.4.5 "drug dispensing and accountability".

Table B.14: Items related to "drug dispensing and accountability"

Item	Reference Number	Comment
Departmental Establishment/ Set up Fees	2.1.1	The review and/or development of any pharmacy - clinical trial specific protocols/manuals/procedures (e.g. randomisation guidelines, dispensing guidelines etc.) should be captured under item 2.1.1.
Drug preparation, labelling and re-labelling	2.4.4	It is recognised that drug preparation and labelling is often part of the drug dispensing process. For the purposes of mutual exclusivity between items 2.4.5 and 2.4.4, the activities associated with "preparation" (which includes labelling) is included under item 2.4.4 but the activity associated with "giving out" the drug (including the associated pharmacy consult) is included under item 2.4.5.

Learnings from site visits

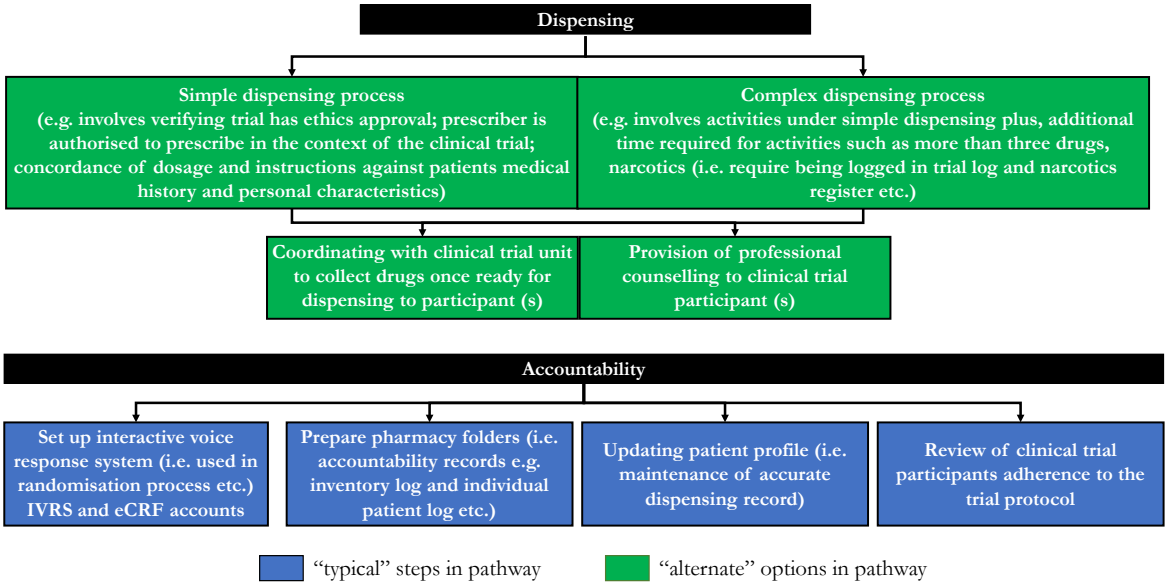
Most sites commented it is impossible to cost drug dispensing and accountability as it varies depending on whether it is a simple (e.g. provision of tablets) or a complex dispensing procedure (e.g. involves narcotics, or the pharmacy department conducts the randomisation process, or it is a Phase 1 trial, or multiple packs are involved); and whether the pharmacy or the clinical trial unit is providing the participant counselling on the medication. Typically, we were advised that two pharmacists were required for preparation and dispensing activities.

Most representatives from the site visits also commented about the confusion in the list in regards to "drug preparation, labelling and re-labelling" and "drug dispensing and accountability". However as changing any of the items is out of scope of the current project, work was done with sites to create at least some separation in items 2.4.4 and 2.4.5. Any future revisions to the list should consider some consolidation of the items relating to pharmacy.

Derived process map for "drug dispensing and accountability"

Figure B.5 presents the typical activities/processes involved in s drug dispensing and accountability. The **blue** boxes represent the typical process. The **green** boxes represent the optional processes in the typical pathway that are dependent on the actual clinical trial (e.g. whether the pharmacy is involved in dispensing of the drug to the trial participant or whether the clinical trial unit is involved in the dispensing of the drug to the trial participant, etc.).

Figure B.5: Process map of the activities included under "drug dispensing and accountability"



Considerations for deriving the cost

Wide variation was identified in the "drug dispensing and accountability" activities depending on the type and number of drugs involved in the trial. Also, most sites found it difficult to separate the time spent on preparation and dispensing activities. However representatives of trial sites were asked to estimate the average time spent on various drug dispensing and accountability activities and the types of personnel involved. There were broad ranges provided, and Table B.13 presents the sites best estimates of typical times, recognising the difference between simple and complex dispensing (no criteria were set, the distinction is left as a matter of judgement).

Again, the fully absorbed hourly rate for the grade 2 and 3 pharmacist was calculated using an average of the NSW and Victorian pharmacist awards. We calculated a fully absorbed hourly rate (based on five days per week, 7.5 hours per day) for a grade 2 pharmacist to be $61 (Vic) to $75 (NSW) and $74 (Vic) to $87 (NSW) per hour for a grade 3 pharmacist. The average for a grade 2/3 pharmacist was used, which was calculated as $74 per hour. The fully absorbed hourly rate for the pharmacy technician was based on a grade 1 pharmacist (using an average between NSW and Victoria again) and was calculated at $51 per hour.

Table of standard costs for "drug dispensing and accountability"

Table B.15 presents the resource units, in hours, required for drug dispensing and accountability. Given the differences in resources used, separate standard costs have been set for dispensing (simple and complex), accountability, and counselling activities at the median of the observations.

Table B.15: Typical personnel, resources and unit cost involved in drug dispensing and accountability

Activities	Personnel Involved	Resource Unit (hours)					Unit cost	Standard cost (median)
		Min	25th percentile	Median	75th percentile	Max		
Dispensing - simple	Two Pharmacists - Grade 2/3	0.10	0.13	0.25	0.25	1.00	$74.00	$37.00
Dispensing -complex	Two Pharmacist - Grade 2/3	0.25	0.44	0.63	1.00	3.00	$74.00	$92.50
Accountability	Pharmacy technician	0.10	0.25	0.25	0.50	1.50	$51.00	$12.75
Counselling	Pharmacist - Grade 2/3	0.10	0.18	0.20	0.20	0.25	$74.00	$14.80

Reference number	2.4.6
Item	Drug transfer
Sub-list	Clinical trial support services
Category	Pharmacy/Investigational Drug-related
Definition	Includes the cost associated with drugs being transferred from one institution to another, or delivered to patients by courier, which would involve: • transport costs; • education/information; • quality assurance for handling/transport; and • administration/paperwork.
Standard Cost	$49 per drug transfer (excluding transport/courier costs)

Related items

None.

Learnings from site visits

Not all pharmacies are involved in drug transfer. Some pharmacies (sometimes referred to as "central clinical trials pharmacies") are involved in the preparation and labelling of clinical trials drugs for clinical trials units in locations other than where the pharmacy is situated. Central pharmacies usually exist in circumstances where there is either no pharmacy at other clinical trials sites; or the sponsor wants to centralise the pharmacy process; or other clinical trial site pharmacies do not have the capacity to undertake the work. It is in any of these circumstances that drug transfer activities are undertaken by the nominated "central pharmacy". The other circumstance where drug transfer may occur is when some clinical trial sites are running low on clinical trial drugs whereas other sites have an over-supply, so clinical trials drugs are transferred from the over-supplied site to the under supplied site.

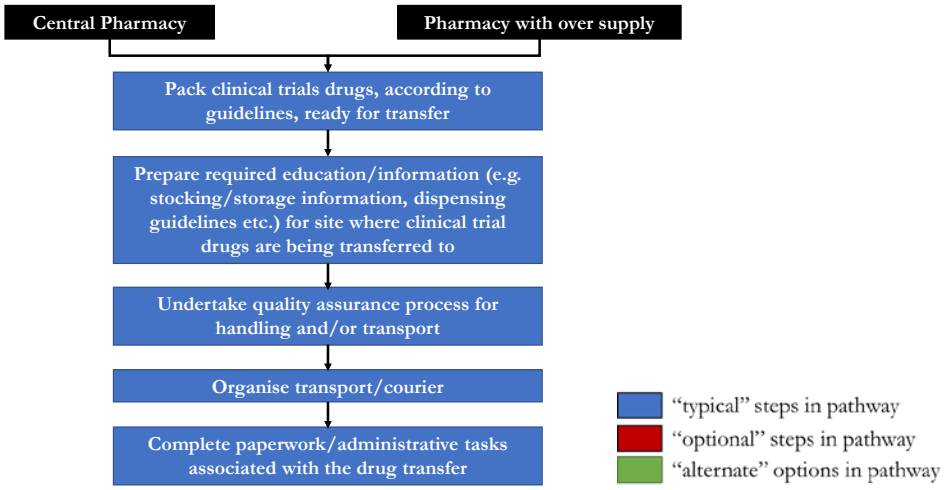
The actual drug transfer activity involves the packaging of the trial drugs, organisation of the courier/transport, the courier/transport fees, undertaking quality assurance for handling and transport purposes, provision of education/information to the site where the clinical trial drugs are being transferred to and the administration/paperwork associated with drug transfer.

Again the costs associated with any one of these above mentioned steps is variable depending on the number of drugs that need to be packaged and sent, the type of drugs (e.g. tablets vs. cytotoxic drugs); the transport fees (which varies depending on type of drug and requirements of transfer (e.g. ambient temperature or -20^{o}C etc.).

Derived process map for "drug transfer"

Figure B.6 presents the typical activities/processes involved in drug transfer.

Figure B.6: Process map for the activities included under drug transfer



Considerations for deriving the cost

Sites were asked to estimate the average time each resource would spend on various activities involved in a drug transfer. A broad range of values was provided, with Table B.16 presenting various estimates of typical times for each activity involved in a drug transfer.

Again, the fully absorbed hourly rate for the grade 2 and 3 pharmacist was calculated using an average of the NSW and Victorian pharmacist awards. We calculated a fully absorbed hourly rate for a grade 2 pharmacist to be $61 (Vic) to $75 (NSW) and $74 (Vic) to $87 (NSW) per hour for a grade 3 pharmacist. The average for a grade 2/3 pharmacist was used, which was calculated as $74 per hour. The fully absorbed hourly rate for the pharmacy technician was based on a grade 1 pharmacist (again using an average of NSW and Victoria) and was calculated at $51 per hour.

It is important to note that the "transport costs" associated with the drug transfer are not captured in Table B.16 due to the variability in the charge, based on the size of the package and the temperature that it needs to be delivered at (e.g. ambient vs. refrigerated). These charges are levied by the courier, and typically met directly by the trial sponsor, and therefore not included.

Table of standard costs for "drug transfer"

Table B.16 presents the resource units, in hours, required for drug transfer, which result in a standard cost of $49 per drug transfer (excluding transport/courier costs) based on the median of the observations from trial host sites.

Table B.16: Typical personnel, resources and unit cost involved in drug transfer

Activities	Personnel Involved	Resource Unit (hours)					Unit Cost	Standard costs (median)
		Min	25th percentile	Median	75th percentile	Max		
Pack clinical trials drugs, according to guidelines	Pharmacy technician	0.2	0.25	0.25	0.25	0.25	$51	$13
Prepare required education/information	Pharmacist - Grade 2/3	0.2	0.2	0.2	0.275	0.5	$74	$15
Quality assurance process for handling and/or transport	Pharmacist - Grade 2/3	0.1	0.1	0.1	0.25	0.25	$74	$7
Organise transport/courier	Pharmacy technician	0.1	0.1	0.175	0.3125	1	$51	$9
Complete paperwork /administrative tasks	Pharmacy technician	0.1	0.1	0.1	0.2125	1	$51	$5
Total - Drug transfer								**$49**

Reference number	2.4.7
Item	Drug storage and temperature monitoring
Sub-list	Clinical trial support services
Category	Pharmacy/Investigational Drug-related
Definition	Includes the shelf, fridge and/or freezer storage of medications/drugs being used throughout the clinical trial; storage of returned stock and temperature monitoring (including log recording) of the refrigeration and/or freezer facilities.
Standard Cost	$50 per annum per clinical trial

Related items

Table B.17 presents other items which are related to item 2.4.7 "drug storage and temperature monitoring".

Table B.17: Items related to "drug storage and temperature monitoring"

Item	Reference Number	Comment
Drug stocking	2.4.3	The activities associated with the transfer of stock from the delivered packages to the required storage location (e.g. shelf, fridge, freezer, etc.) are included under item 2.4.3.
Drug dispensing and accountability	2.4.5	Some sites reported that temperature monitoring was a cost included in the fee for drug dispensing and accountability.
Departmental Ongoing Administration Fees	2.3.1	A number of sites included drug storage and temperature monitoring in their annual administration fee.

Learnings from site visits

Medications/drugs associated with clinical trials are stored in the pharmacy. The amount of medication/drug stock per clinical trial varies, and therefore the amount and type (e.g. shelf, fridge or freezer space) of required storage also varies. There are also different storage protocols to be followed depending on the type of drug. For example, Schedule 4, 8 or 11 drugs, which include drugs of dependence, must be stored in a locked facility (i.e. the storage facilities must be secured at all times other than during authorised transactions). For cytotoxic drugs, the storage area needs to be separate, include refrigeration, and be clearly marked.

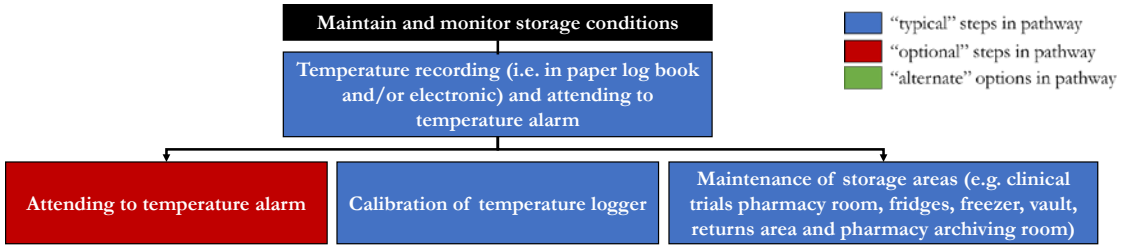
The process involved in temperature monitoring requires pharmacy staff, usually the technician, to daily check the temperature monitors, record the temperature in the log book (which may be online), and undertake any other electronic data entry that may be required. In addition, most drug storage facilities are required to have temperature alarm monitoring, therefore responding to any alarms (in or out of hours) is also part of the activities associated with temperature monitoring. Across sites, the reported time taken for temperature monitoring per week was consistent and minimal; and the times were reported for per week, rather than per trial (all pharmacy departments visited had multiple trials in progress).

It was noted that, whilst weekly time for temperature monitoring was an activity that covered all trials for which drugs were being stored, if a temperature excursion occurred, then it was necessary to contact and notify each trial sponsor. It was also noted that some sites set fees for storage, ranging from $228 ($57 per quarter) for room temperature storage to $350-$500 a year for refrigerated storage for bulky items. These latter fees include temperature monitoring. Also, many sites reported that activities/time associated with temperature monitoring are covered as a component of the dispensing fees.

Derived process map for "drug storage and temperature monitoring"

Figure B.7 presents the typical activities/processes involved in drug storage and temperature monitoring. The **blue** boxes represent the typical process. The **red** boxes represent the processes that may or may not occur in the pathway (e.g. dealing with a temperature alarm).

Figure B.7: Process map of the activities included under "drug storage and temperature monitoring"



Considerations for deriving the cost

Sites were asked to estimate the typical time spent on the various activities involved in drug storage and temperature monitoring, and they typically reported a total weekly time. This time covered all trials for which drugs temperature monitoring was occurring, not the time for one drug trial. Therefore, to calculate a cost per trial, adjustments needed to be made to reflect the fact that the temperature monitoring activity usually covered multiple trials (up to 100 at some sites), and also usually covered both trial and non-trial drugs.

It is important to note that "attending to the temperature alarm" was not costed, as it was not part of the typical pathway as part of drug storage and temperature monitoring. Also, clinical trial sites sometimes incur a cost (or charge a fee) associated with drug storage (i.e. bulk storage or in the refrigerator). These fees are also excluded as the figures provided were too variable and the fee was not typically charged (it was usually covered somewhere else (e.g. the dispensing fee).

So the typical time per week involved in a drug storage and temperature monitoring has been used as the basis for setting the standard cost. Again, the fully absorbed hourly rate for the pharmacy technician was based on a grade 1 pharmacist (using an average between NSW and Victoria again) and was calculated at $51/hour.

Table of standard costs for "drug storage and temperature monitoring"

Table B.18 presents the resource units, in hours, required for storage and temperature monitoring. The median cost is considered representative of the time per week across all trials. It represents $1,976 per annum. Given that this cost is typically spread across many trials as well as non-trial drugs, it is considered that a standard cost of $50 per annum per trial is reasonable.

Table B.18: Typical resources and unit cost involved in drug storage and temperature monitoring

Item	Personnel involved	Resource Unit (hours per week)					Unit cost	Standard cost (median)
		Min	25th percentile	Median	75th percentile	Max		
Drug storage and temperature monitoring	Pharmacy technician	0.2	0.25	0.75	1	1	$51	$38

It is suggested that that in any review of the NHMRC list of activities associated with clinical trials, the possibility of consolidating this item into the drug dispensing item (consistent with prevailing practice regarding fees) is explicitly considered.

Reference number	2.4.8
Item	Drug destruction
Sub-list	Clinical trial support services
Category	Pharmacy/Investigational Drug-related
Definition	Involves the destruction of drugs according to the institutions policy, sponsor requirements (if applicable), safe operating practices and the requirements of the trial.
Standard Cost	$77 per drug destruction service (excluding off-site destruction fees)

Related items

None.

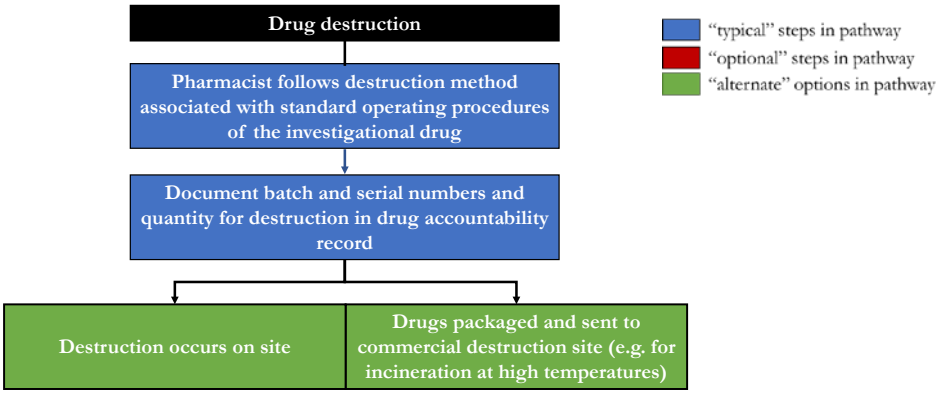
Learnings from site visits

Drug destruction processes vary depending on the type of drugs involved in the clinical trial (e.g. from emptying the vials down the sink to transferring drugs to commercial facilities for destruction (e.g. high temperature incinerators). Occasionally sites are also required to retain vials or outer packaging for dispensation reconciliation during the trial monitor visits.

Derived process map for "drug destruction"

Figure B.8 presents the typical activities/processes involved in drug destruction. The **blue** boxes represent the typical process. The **green** boxes represent the optional processes in the typical pathway that are dependent on the actual clinical trial (e.g. whether the pharmacy can undertake the drug destruction on site or requires sending the unused/expired clinical trials drugs to an offsite commercial drug destruction facility).

Figure B.8: Process map of the activities included under drug destruction



Considerations for deriving the cost

Sites were asked to estimate the typical time spent on the various activities involved in drug destruction. Again there was considerable variability which was dependent on the type of drug requiring destruction. Table B.19 presents various estimates on typical time per activity per drug destruction service, which are the basis for the standard cost. Again, the fully absorbed hourly rate for the pharmacy technician was based on a grade 1 pharmacist (using an average between NSW and Victoria) and was calculated at $51/hour.

It is important to note that the actual destruction cost, if off site, has not been costed due to the variable fees charged by different commercial facilities, and the fact that drug destruction is often done by the trial sponsor. In circumstances where off-site destruction is required, additional cost

would be incurred including drug transfer and the drug destruction fee. Fees for this service, if required would need to be negotiated on a case by case basis.

Table of standard costs for "drug destruction"

Table B.19 presents the resource units, in hours, required for drug destruction. As this activity most often relates to preparing the drugs for transfer to a destruction services (which may be the trial sponsor) and completing the appropriate documentation, the reported minimum was considered to be the most suitable basis for the standard cost of $77 per drug destruction service (excluding any off-site destruction charges).

Table B.19: Typical personnel, resources and unit cost involved in drug destruction

Activities	Personnel Involved	Resource Unit (hours)					Unit Cost	Standard cost (minimum)
		Min	25th percentile	Median	75th percentile	Max		
Pharmacist follows destruction method associated with standard operating procedures of the investigational drug	Pharmacy technician	1	1	1.5	2	2	$51	$51
Document batch and serial numbers and quantity for destruction in drug accountability record	Pharmacy technician	0.5	1	1	1	1	$51	$26
Total for drug destruction								**$77**

It is highlighted that there is potential duplication between the activities covered by the pharmacy related items on the NHMRC list, including, if used, a Department Establishment/Setup fee. Accordingly, it is suggested that in any review of the NHMRC list of activities, the opportunity to consolidate some of the pharmacy related items should be considered.

Reference number	2.5.1
Item	Biospecimen collection and processing (central and local)
Sub-list	Clinical trial support services
Category	Biospecimen-related
Definition	Includes the collection, processing and transport costs (e.g. quarantine permits, etc.) of clinical trial biospecimens. Examples of biospecimens include blood and other body fluids, tissues, nucleic acids, and other direct derivatives from human tissues. Processing of biospecimens includes those activities involved in preparing the biospecimen for analysis following collection and those activities involved in the arrangement of transfer of the biospecimen(s) to local or central laboratories.
Standard Cost	$30 per biospecimen collected for analysis by central laboratories (excludes transport costs (e.g. courier costs, any required quarantine permits, etc.) as these costs vary depending on the amount of biospecimens being transported, the delivery location (e.g. within Australia or overseas) as well as the temperature at which the biospecimens need to be transported at).

Related items

Table B.20 presents other items which are related to item 2.5.1 "biospecimen collection and processing".

Table B.20: Items related to biospecimen collection and processing (central and local)

Item	Reference Number	Comment
Laboratory Tests/Procedures	1.2.1	Item 1.2.1 includes the MBS fee and a loading that will cover the costs of collection and processing of biospecimens that will be tested and reported by the onsite pathology department. Item 2.5.1 should only reflect work done by trial staff (outside the pathology department) to collect and process biospecimens that will be tested and reported by central laboratories.
Other Clinical Tests or Procedures	1.5.1	Item 1.5.1 includes the MBS fee and a loading that will cover the costs of collection and processing of biospecimens that will be tested and reported by the onsite pathology department. Item 2.5.1 should only reflect work done by trial staff (outside the pathology department) to collect and process biospecimens that will be tested and reported by central laboratories.
Staff training	3.1.9	Activities related to personnel involved in obtaining and/or maintaining the required level of training/accreditation for biospecimen related activities (e.g. GCP, dangerous goods handling, safe transport etc.) should be captured under 3.1.9 and not 2.5.1.

Learnings from site visits

Biospecimen collection in clinical trials occurs at several points throughout the trial including: during the screening or baseline assessment visit; during the implementation of the trial; and/or at the completion of the trial. We found that the personnel involved in the collection and processing of biospecimens varied from the research nurse (who may collect the blood and centrifuge it ready for analysis by the local pathology provider and/or shipment to the central pathology laboratory) to the pathology department within the clinical trial site.

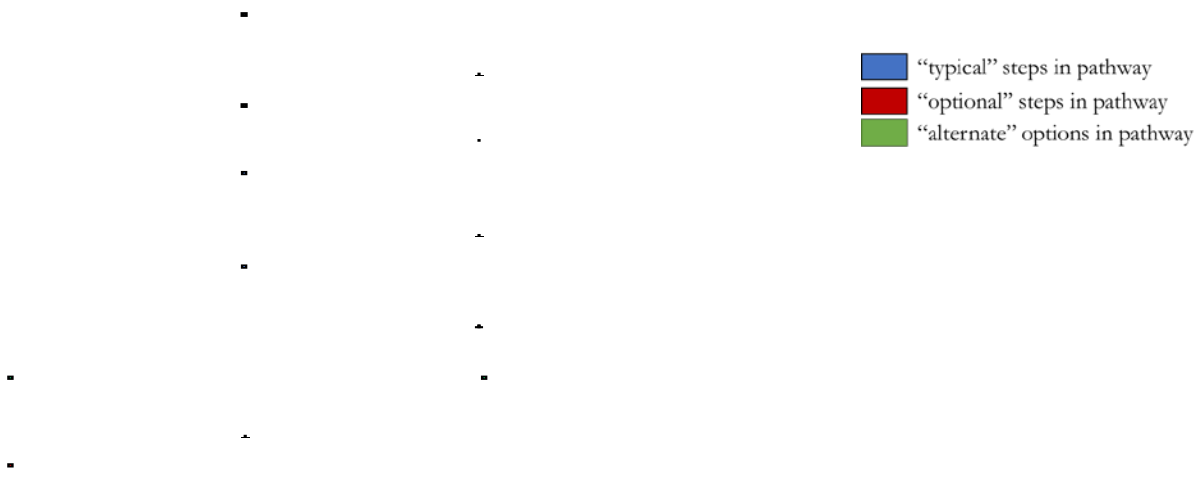
All sites had institutional standard operating procedures for the collection and processing of biospecimens. As well, there were often trial-specific procedures outlined in the trial protocol. The time taken for collection and processing varied depending on the whether analysis was being undertaken centrally or locally and whether the participant was an adult or child. We found that additional time was required in those trials where biospecimens were to be sent to a central laboratory (e.g. additional time required due to the extra documentation requirements).

The process map shows the activities involved in a single episode of biospecimen collection and processing, the total time required in a trial for biospecimen collection and processing will depend on the number of patients participating and the number of visits requiring biospecimen collection during the trial. We found that most sites make an estimate of the amount of time per participant per visit for visits where biospecimen collection and processing will occur.

Derived process map for "biospecimen collection and processing"

Figure B.9 presents the typical process involved in biospecimen collection and processing. Figure B.9 refers to those process occurring at the clinical trial site only (i.e. not the processes that are performed at the central laboratory).

Figure B.9: Process map of the activities included under "biospecimen collection and processing"



Considerations for deriving the cost

Clinical trial unit staff were asked to estimate the time it takes them to collect a single biospecimen (e.g. blood sample) and process it for a central or local laboratory (i.e. bloods are centrifuged). However, it is our view that when the analysis is done by local laboratories the cost incurred by the clinical trial site is covered by the MBS fee (particularly when the suggested 1.4 loading is applied). However, where clinical trial unit staff are collecting and pre-processing the biospecimen for testing and reporting by a central laboratory then no MBS fee (or equivalent) is charged by the clinical trial site and hence item 2.5.1 should be applicable.

It is also important to note that the determined standard cost does not include the transport costs (e.g. courier costs, any required quarantine permits, etc.) as these costs varied depending on the amount of biospecimens being transported, the delivery location (e.g. within Australia or overseas) as well as the temperature at which the biospecimens need to be transported.

Table of standard costs for "biospecimen collection and processing"

Table B.21 presents the resource units, in hours, required for biospecimen collection and processing. Consistent with the site visit experience it has been assumed that, if biospecimens are collected by the clinical trial staff, they are typically collected and prepared by the research nurse.

Table B.21: Typical personnel, resources and unit cost involved in biospecimen collection and processing

Item	Personnel involved	Resource unit (hours)					Unit cost	Standard cost (25th percentile)
		Min	25th percentile	Median	75th percentile	Max		
Biospecimens collection and processing (central)	Research Nurse	0.3	0.5	1.0	1.6	4.0	$60	$30

The typical cost is chosen at the 25th percentile for biospecimens prepared for sending to central laboratories, as it was considered that there was a respondent bias in answering the question (i.e. the times provided tended to relate to the more complicated instances of biospecimen collection and processing).

Reference number	2.5.2
Item	Biospecimen analysis (central and local)
Sub-list	Clinical-trial support services
Category	Biospecimen-related
Definition	Includes the analysis and reporting of biospecimens (including blood and other body fluids, tissues, nucleic acids, and other direct derivatives from human tissues) collected as part of the clinical trial where the test/procedure is not covered under the MBS.
Standard Cost	140% of the MBS fee for the nearest equivalent test listed on the MBS

Related items

Table B.22 presents other items which are related to item 2.5.2 "biospecimen analysis".

Table B.22: Items related to biospecimen analysis

Item	Reference Number	Comment
Laboratory Tests/Procedures	1.2.1	The MBS loading associated with item 1.2.1 already incorporates the additional time and hence costs associated with biospecimen analysis for tests covered under the MBS. Hence item 2.5.2 should include biospecimen analysis for only those tests not covered by an MBS item.
Other Clinical Tests or Procedures	1.5.1	The MBS loading associated with item 1.5.1 already incorporates the additional time and hence costs associated with biospecimen analysis for tests covered under the MBS. Hence item 2.5.2 should include biospecimen analysis for only those tests not included under the MBS.
Staff training	3.1.9	Activities related to personnel involved in obtaining and/or maintaining the required level of training/accreditation for biospecimen related activities (e.g. GCP, dangerous goods handling, safe transport etc.) should be captured under 3.1.9 and not 2.5.2.

Learnings from site visits

We found that majority of biospecimen analysis for industry sponsored trials occurs at central laboratories. Thus, when the analysis is undertaken at a central laboratory, the clinical trial site does not incur a cost. In some investigator led multi-site trials biospecimens were transported from satellite sites to the lead sites for analysis. Some pathology departments consulted stated that additional or different analysis is required for some clinical trial specimens, and the analysis is not standard and/or not covered under the MBS.

Derived process map for "biospecimen analysis (central and local)"

Not applicable.

Considerations for deriving the cost

In practice, it seemed that analysis of biospecimens undertaken by local laboratories not covered by the MBS did not occur often in practice. For those few biospecimens analysed locally where the test is not included in the MBS, in the absence of any other data, it has been determined that the best approach is to choose the nearest equivalent MBS item, as bottom up costing could not be attempted.

Table of standard costs for "biospecimen analysis (central and local)"

Table B.23 indicates that no relevant data were able to be obtained from sites, so best approach is to use the MBS fee for the nearest equivalent test. For consistency the same multiplier (1.4) used for the clinical tests and procedures in sub-list 1 is proposed. This arrangement is not entirely satisfactory, but based on the site visits this situation does not occur often in actual practice.

Table B.23: Typical personnel, resources and unit cost involved in biospecimen analysis

Item	Basis	Resource unit					Unit cost	Multiplier to derive standard cost
		Min	25th percentile	Median	75th percentile	Max		
Biospecimen analysis and reporting where test is not listed on MBS	MBS fee for nearest equivalent test with adjustment factor	N/A	N/A	N/A	N/A	N/A	N/A	1.4

Reference number	2.5.3
Item	Biospecimen storage (central and local)
Sub-list	Clinical-trial support services
Category	Biospecimen-related
Definition	Includes the storage and management of biospecimens (including blood and other body fluids, tissues, nucleic acids, and other direct derivatives from human tissues) collected as part of the clinical trial that are not covered under the MBS.
Standard Cost	Not determined, deemed to be included in 2.5.2

Related items

Table B.24 presents other items which are related to item 2.5.3 "biospecimen storage (central and local)".

Table B.24: Items related to biospecimen storage (central and local)

Item	Reference Number	Comment
Laboratory Tests/ Procedures	1.2.1	The MBS fee and loading associated with item 1.2.1 already incorporates the additional time and hence costs associated with biospecimen storage for tests covered under the MBS. Hence item 2.5.3 should include biospecimen storage for only those tests not covered by an MBS item.
Other Clinical Tests or Procedures	1.5.1	The MBS fee and loading associated with item 1.5.1 already incorporates the additional time and hence costs associated with biospecimen storage for other clinical tests and procedures covered under the MBS. Hence item 2.5.3 should include biospecimen storage for only those other clinical tests and procedures not covered under the MBS.
Biospecimen analysis (central and local)	2.5.2	The nearest equivalent MBS fee and loading associated with item 2.5.2 already incorporates the additional time and hence costs associated with biospecimen analysis for tests and procedures not covered under the MBS. Hence item 2.5.3 should include biospecimen storage for only biospecimens that are not tested and reported locally.
Staff training	3.1.9	Activities related to personnel involved in obtaining and/or maintaining the required level of training/accreditation for biospecimen related activities (e.g. GCP, dangerous goods handling, safe transport etc.) should be captured under 3.1.9 and not 2.5.3.

Learnings from site visits

For some industry sponsored trials, sites commented that there was significant time spent monitoring and reporting of temperature monitoring data relating to the storage of biospecimens to sponsors. In some trials (copies of) temperature monitoring reports/graphs were required to be printed out and sent to the sponsor or uploaded to the sponsor via the web. The intervals or frequency at which this monitoring was required was trial dependent. In a number of trials the temperature monitoring equipment and/or freezers were supplied by the sponsor.

Again, we found that the majority of biospecimens collected for industry sponsored trials are analysed and stored at central laboratories. For these trials, the only storage required by the trial sites is up until the time they are transported to the central laboratory. However for collaborative sponsored or other investigator-initiated trials, biospecimens are often stored on site or at an agreed central (i.e. lead site) location. But most (although not all) biospecimens collected as part of the non-industry sponsored clinical trials discussed were covered under the MBS.

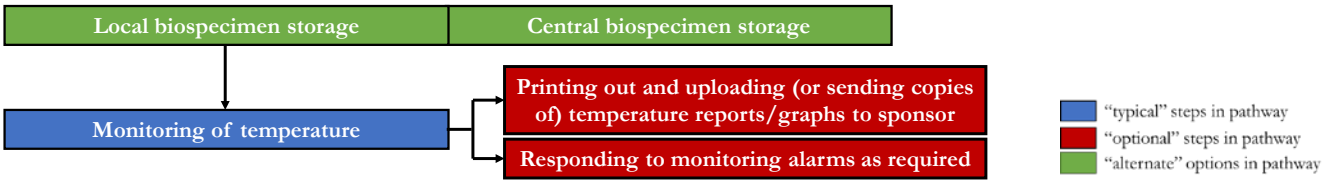
The standard MBS fee does include storage of the biospecimen and with the additional proposed loading of 1.4, the costs associated with additional storage or conditions required for clinical trial biospecimens should be covered under the MBS fee and loading. Even for industry sponsored

biospecimens stored at the clinical trial site, the MBS fee plus the loading should be sufficient to compensate for the storage and temperature monitoring activities.

Derived process map for "biospecimen storage (central and local)"

Figure B.10 presents the typical process involved in the biospecimen storage (central and local) process.

Figure B.10: Process map for activities included under biospecimen storage (central and local)"



Considerations for deriving the cost

The storage of biospecimens used to conduct tests that do not attract an MBS fee did not occur often, i.e. if testing and hence storage of the biospecimen was required locally, then the test is likely to be covered by the MBS. Otherwise, the biospecimen is likely to be tested and stored at a central laboratory and the trial sponsor would meet the cost of the testing and storage directly. No examples were found where biospecimens were stored locally, but not tested locally.

For those few biospecimens tested and stored locally, and where the test is not included in the MBS, in the absence of any other data, it has been determined that the best approach is to consider that the biospecimen storage costs are covered by the nearest equivalent MBS item (as determined in item 2.5.2), as bottom up costing could not be attempted. This determination means that the costs associated with item 2.5.3 (and also 2.5.4) would be covered by the MBS fee and associated loading for the nearest equivalent MBS test determined under item 2.5.2.

Table of standard costs for "biospecimen storage"

Table B.25 indicates that no relevant data were able to be obtained from sites, so best approach is to consider that the fee for local analysis (testing and reporting) of the biospecimen includes the cost of biospecimen storage. This fee would be charged under either items 1.2.1, 1.5.1 or 2.5.2. No separate standard cost for this item has been determined. This arrangement is not entirely satisfactory, but based on the site visits this situation does not occur often in actual practice.

Table B.25: Typical personnel, resources and unit cost involved in biospecimen storage

Item	Basis	Resource unit					Unit cost	Standard cost
		Min	25th percentile	Median	75th percentile	Max		
Local biospecimen storage	Included in MBS fee for nearest equivalent test with adjustment factor	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Reference number	2.5.4
Item	Biospecimen destruction (central and local)
Sub-list	Clinical-trial support services
Category	Biospecimen-related
Definition	Includes the destruction of biospecimens (including blood and other body fluids, tissues, nucleic acids, and other direct derivatives from human tissues) collected as part of the clinical trial that are not covered under the MBS.
Standard Cost	Not determined, deemed to be included in 2.5.2

Related items

Table B.26 presents other items which are related to item 2.5.4 "biospecimen destruction".

Table B.26: Items related to biospecimen destruction

Item	Reference Number	Comment
Laboratory Tests/Procedures	1.2.1	The MBS loading associated with item 1.2.1 already incorporates destruction of biospecimens for those biospecimens covered under the MBS. Hence item 2.5.4 should include biospecimen destruction for only those biospecimens not included under the MBS.
Other Clinical Tests or Procedures	1.5.1	The MBS loading associated with item 1.5.1 already incorporates destruction of biospecimens for those biospecimens covered under the MBS. Hence item 2.5.4 should only include biospecimen destruction for those biospecimens not included under the MBS.
Biospecimen analysis (central and local)	2.5.2	The nearest equivalent MBS fee and loading associated with item 2.5.2 already incorporates the additional time and hence costs associated with biospecimen destruction for tests and procedures not covered under the MBS. Hence item 2.5.3 should include biospecimen destruction for only biospecimens that are not tested and reported locally.
Staff training	3.1.9	Activities related to personnel involved in obtaining and/or maintaining the required level of training/accreditation for biospecimen related activities (e.g. GCP, dangerous goods handling, safe transport etc.) should be captured under 3.1.9 and not 2.5.4.

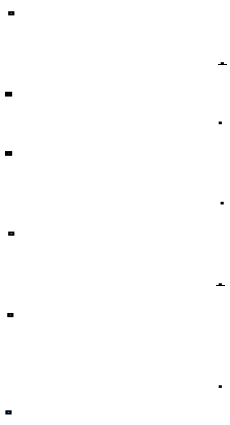
Learnings from site visits

For those biospecimen stored on site, we found that biospecimen destruction may be required for a number of reasons including biospecimen contamination, incorrect temperature storage (or variation) or for individuals for whom biospecimens were obtained at screening but who did not meet trial inclusion criteria. Again, we found that most biospecimens stored on site and requiring destruction are biospecimens taken for tests that attract an MBS fee. As with any biospecimen being destroyed there are similar procedures followed, therefore it was that if the MBS fee is charged and the suggested loading is applied, this fee would cover the reasonable cost of any required biospecimen destruction. The issue that concerned the sites was when the biospecimen did not attract and MBS fee how they would recover the cost.

Derived process map for "biospecimen destruction (central and local)"

Figure B.11 presents the typical process involved in the biospecimen destruction process.

Figure B.11: Process map for activities included under "biospecimen destruction"



Considerations for deriving the cost

The storage and subsequent destruction of biospecimens used to conduct tests that do not attract an MBS fee did not occur often, i.e. if testing, and hence storage and destruction of the biospecimen was required locally, then the test is likely to be covered by the MBS. Otherwise, the biospecimen is likely to be tested, stored and destroyed at a central laboratory and the trial sponsor would meet the cost of the testing and storage directly. No examples were found where biospecimens were stored and destroyed locally, but not tested locally.

For those few biospecimens tested, stored and destroyed locally, and where the test is not included in the MBS, in the absence of any other data, it has been determined that the best approach is to consider that the biospecimen destruction costs are covered by the nearest equivalent MBS item (as determined in item 2.5.2), as bottom up costing could not be attempted. This determination means that the costs associated with item 2.5.4 (and also 2.5.3) would be covered by the MBS fee and associated loading for the nearest equivalent MBS test determined under item 2.5.2.

Table of standard costs for "biospecimen destruction (central and local)"

Table B.27 indicates that no relevant data could be obtained from sites, so best approach is to consider that the fee for local analysis (testing and reporting) of the biospecimen includes the cost of biospecimen destruction. This fee would be charged under either items 1.2.1, 1.5.1 or 2.5.2. No separate standard cost for this item has been determined. This arrangement is not entirely satisfactory, but based on the site visits, this situation does not occur often in practice.

Table B.27: Typical personnel, resources and unit cost involved in biospecimen destruction

Item	Basis	Resource unit					Unit cost	Standard cost
		Min	25th percentile	Median	75th percentile	Max		
Local biospecimen destruction	Included in MBS fee for nearest equivalent test with adjustment factor	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Table B.27 indicates that no relevant data were able to be obtained from sites, so best approach is to use the MBS fee for the nearest equivalent test. For consistency the same multiplier used for the clinical tests and procedures in sub-list 1 is proposed. This arrangement is not entirely satisfactory, but based on the site visits this situation does not occur often in actual practice.

Reference number	2.5.5
Item	Tissue repository set-up and management
Sub-list	Clinical-trial support services
Category	Biospecimen-related
Definition	Includes the central project management set up, tracking and administration for establishing the tissue repository and ongoing management.
Standard Cost	Not determined as cost is typically not incurred at trial sites

Related items

None

Learnings from site visits

No clinical trial site that was visited was involved in the establishment or management of a tissue repository. We found examples where sites would collect biospecimens for the purpose of the clinical trial and send them to a central tissue bank, but we found no sites that had been involved in the set up or management of a tissue repository.

Derived process map for "tissue repository set-up and management"

Not possible using the study methodology.

Considerations for deriving the cost

Based on the learning that the set up or management of a tissue repository was not undertaken by any of the clinical trial sites visited throughout the project, and that it tends to be done by specialised tissue banking and repository services, no reasonable cost was determined. The lack of a determination is not considered a problem, as clinical trial sites typically do not incur this cost.

Table of standard costs for "tissue repository set-up and management"

Table B.28 indicates that no relevant data were able to be obtained from sites, so no separate standard cost for tissue repository, set up and management has been determined. The only cost incurred at a trial site is the biospecimen collection and processing (covered under 2.5.1) or biospecimen analysis covered under 2.5.2). If the biospecimen is to be sent to a tissue bank, it would be transported off-site, and transport cost would be met directly by the trial sponsor.

Table B.28: Typical resources and unit cost involved in tissue repository, set up and management

Item	Basis	Resource unit					Unit cost	Standard cost
		Min	25th percentile	Median	75th percentile	Max		
Tissue repository set up and management	No determination possible as cost typically not incurred by trial sites	N/A	N/A	N/A	N/A	N/A	N/A	N/A

The inclusion of this item in the list should be reviewed. If the intention is to capture or set reasonable costs to assist in the setting of budgets for sites involved in clinical trials, as no sites visited are involved in the set up or management of tissue repositories, inclusion of this item on the list does not seen warranted.

Reference number	2.6.1
Item	Coordinating principal investigator surcharge
Sub-list	Clinical-trial support services
Category	Clinical Staff/Resource Allocation
Definition	The stated additional time multiplied by unit labour cost (*hourly rate plus on-costs, overtime, overheads and CPI increases)* that the coordinating principal investigator is expected to spend on coordinating the clinical trial.
Standard Cost	$215 per hour

Related items

None.

Learnings from site visits

Most (multi-site) trials have a coordinating principal investigator. The principal investigator is almost always a senior medical doctor who is responsible for carrying out a clinical trial at a nominated trial site, and coordinating the trial across one or more other sites. The coordinating principal investigator would be nominated on the ethics application. We found that there is some additional work associated with being the coordinating principal investigator, although the number of hours required was very trial dependent. All the principal investigators involved in clinical trials were very senior medical doctors with reputations for being expert specialists in their field. The hourly rates typically charged by sites that we identified from fieldwork varied from about $200/hour to $350 per hour across both the public and private hospital settings visited.

Derived process map for "coordinating principal investigator surcharge"

Not applicable.

Considerations for deriving the cost of "coordinating principal investigator surcharge"

Notwithstanding the fact that there are a variety of hourly rates used in practice, the table of standard costs is developed, as far as possible, on a cost (not charge) basis. Accordingly, investigations into secondary sources of data on the cost of an hour of principal investigator time were undertaken. There were numerous choices, many of them were state-based awards. To obtain a figure that was nationally representative, we chose the AMA published full-time Specialists Minimum Remuneration levels as shown in Table B.29.

Consistent with the full-absorbed costing principle, it was important to identify a suitable source of salary on-costs and institutional overheads to apply to the direct salary cost presented in Table B.29. For this purpose a simple model of a human resources organisation was adopted which proposed that direct salary costs make up 60% of expenditure, salary on-costs make up 15% of expenditure and institutional overheads make up the other 25%. There is ample evidence to support the fact that salary on costs (paid leave, public holidays, superannuation, payroll tax, etc.) are typically around 15/60 = 25% of direct salary.

The proposition that institutional overheads are around 25/75 = 33% of salary costs has a weaker evidence base. It is clear that a series of costs will need to be incurred to make a person in an organisation productive (office space, furniture, equipment, internet and library resources, administrative support, light, power, insurances, etc.). Without incurring these costs, the employed person could not effectively discharge the role they occupy. It is acknowledged that these costs are very organisation dependent, but they are normally quoted in a range of 25% to

40% of salary costs. On this basis 33% of direct plus indirect salary costs is considered to be reasonable.

So using the AMA rates, (based on five days per week, 7.5 hours per day) calculated from the published weekly minimum, the hourly rate for a medical specialist was $94.75-$130.29 per hour. Applying the ratios needed to convert to fully absorbed costs, Table B.29 shows that the estimated cost per hour ranges from $157.92 to $217.14.

Table B.29: AMA rates for specialists in public hospitals

Specialist	AMA Minimum Weekly Rate	Hourly Rate	Salary Oncost	Institutional Overhead	Fully absorbed Hourly Rate
Specialist Year 1	$3,553.20	$94.75	$23.69	$39.48	$157.92
Specialist Year 2	$3,791.10	$101.10	$25.27	$42.12	$168.49
Specialist Year 3	$3,938.40	$105.02	$26.26	$43.76	$175.04
Specialist Year 4	$4,092.60	$109.14	$27.28	$45.47	$181.89
Specialist Year 5	$4,251.80	$113.38	$28.35	$47.24	$188.97
Specialist Year 6	$4,417.60	$117.80	$29.45	$49.08	$196.34
Specialist Year 7	$4,504.50	$120.12	$30.03	$50.05	$200.20
Specialist Year 8	$4,770.90	$127.22	$31.81	$53.01	$212.04
Specialist Year 9	$4,885.70	$130.29	$32.57	$54.29	$217.14

Table of standard costs for "coordinating principal investigator surcharge"

As most principal investigators are senior medical specialists, the choice of an hourly rate between AMA levels 8 and 9 is considered reasonable. On this basis the standard cost is set at $215 per hour (see Table B.30).

Table B.30: Determination of standard cost for coordinating principal investigator surcharge

Item	Basis	Resource unit (hourly rates)					Unit cost	Standard cost
		Min	25th percentile	Median	75th percentile	Max		
Coordinating principal investigator surcharge	Fully absorbed hourly rate	$158	N/A	N/A	N/A	$217	$215	$215

Reference number	2.6.2
Item	Investigator allocation
Sub-list	Clinical-trial support services
Category	Clinical Staff/Resource Allocation
Definition	The stated time allocation multiplied by unit labour cost (*hourly rate plus on-costs, overtime, overheads and CPI increases)* for each investigator (who is listed on the ethics approval) is expected to be involved in the clinical trial.
Standard Cost	$215 per hour

Related items

Table B.31 presents other items which are related (i.e. not necessarily mutually exclusive from) to item 2.6.2 "Investigator allocation".

Table B.31: Items related to Investigator allocation

Item	Reference Number	Comment
Laboratory Tests/Procedures	1.2.1	Depending on the clinical speciality of the investigator, he/she may be involved in providing laboratory tests and procedures.
Medical Imaging	1.3.1 and 1.3.2	Depending on the clinical speciality of the investigator, he/she may be involved in providing medical imaging services.
Radiation Therapy	1.4.1	Depending on the clinical speciality of the investigator, he/she may be involved in providing radiation therapy services.
Other Clinical Tests or Procedures	1.5.1	Depending on the clinical speciality of the investigator, he/she may be involved in providing other clinical tests or procedures.
Specialist Medical Consultations	1.6.1	Depending on the clinical speciality of the investigator, he/she may be involved in providing specialist medical consultations.
Nursing/Allied Health Consultations	1.7.1	Depending on the clinical speciality of the investigator, he/she may be involved in providing nursing/allied health consultations.

All these items have been costed on a per service basis (see sub-list 1), so it is important that item 2.6.2 is not used to cover clinical services that might be provided by a trial investigator as well. Item 2.6.2 should only be used where the clinician is acting in his/her capacity as an investigator.

In addition to clinical services, the trial investigators will be involved in the majority of the activities included in sub-lists 2 and 3. This item is therefore used to set the reasonable unit cost for investigator time, which is then used to calculate the costs of many of the other activities in sub-lists 2 and 3. If item 2.6.2 is used together with items such as site selection including feasibility and preparing ethics submissions care should be taken to avoid double counting.

Learnings from site visits

The investigators involved in clinical trials usually include a principal investigator and sub or co-investigators. The principal investigator is almost always a senior medical doctor who is responsible for carrying out a clinical trial at a nominated trial site. The sub or co-investigator(s) are also generally medical doctors who also participate (e.g. recruit participants etc.) in the clinical trial, but will not have the same authority over the clinical trial. All investigators would be included on the ethics application. We found that almost all the investigators involved in clinical trials were very senior medical doctors with reputations for being expert specialists in their field. The hourly rates typically charged by sites that we identified from fieldwork varied from about $200/hour to $350 per hour across both the public and private hospital settings visited.

Derived process map for "investigator allocation"

Not applicable.

Considerations for deriving the cost of "investigator allocation"

Notwithstanding the fact that there are a variety of hourly rates used in practice, the table of standard costs is developed, as far as possible, on a cost (not charge) basis. Accordingly, investigations into secondary sources of data on the cost of an hour of investigator time were undertaken. There were numerous choices, many of them were state-based awards. To obtain a figure that was nationally representative, we chose the AMA published full-time Specialists Minimum Remuneration levels as shown in Table B.32.

Consistent with the full-absorbed costing principle, it was important to identify a suitable source of salary on-costs and institutional overheads to apply to the direct salary cost presented in Table B.32. For this purpose a simple model of a human services organisation was adopted which proposed that direct salary costs make up 60% of expenditure, salary on-costs make up 15% of expenditure and institutional overheads make up the other 25%. There is ample evidence to support the fact that salary on costs (paid leave, public holidays, superannuation, payroll tax, etc.) are typically around 15/60 = 25% of direct salary.

The proposition that institutional overheads are around 25/75 = 33% of salary costs has a weaker evidence base. It is clear that a series of costs will need to be incurred to make a person in an organisation productive (office space, furniture, equipment, internet and library resources, administrative support, light, power, insurances, etc.). Without incurring these costs, the employed person could not effectively discharge the role they occupy. It is acknowledged that these costs are very organisation dependent, but they are normally quoted in a range of 25% to 40% of salary costs. On this basis 33% of direct plus indirect salary costs is considered to be reasonable.

So using the AMA rates, (based on five days per week, 7.5 hours per day) calculated from the published weekly minimum, the hourly rate for a medical specialist was $94.75-$130.29 per hour. Applying the ratios needed to convert to fully absorbed costs, Table B.32 shows that the estimated cost per hour ranges from $157.92 to $217.14.

Table B.32: AMA rates for specialists in public hospitals

Specialist	AMA Minimum Weekly Rate	Hourly Rate	Salary Oncost	Institutional Overhead	Fully absorbed Hourly Rate
Specialist Year 1	$3,553.20	$94.75	$23.69	$39.48	$157.92
Specialist Year 2	$3,791.10	$101.10	$25.27	$42.12	$168.49
Specialist Year 3	$3,938.40	$105.02	$26.26	$43.76	$175.04
Specialist Year 4	$4,092.60	$109.14	$27.28	$45.47	$181.89
Specialist Year 5	$4,251.80	$113.38	$28.35	$47.24	$188.97
Specialist Year 6	$4,417.60	$117.80	$29.45	$49.08	$196.34
Specialist Year 7	$4,504.50	$120.12	$30.03	$50.05	$200.20
Specialist Year 8	$4,770.90	$127.22	$31.81	$53.01	$212.04
Specialist Year 9	$4,885.70	$130.29	$32.57	$54.29	$217.14

Table of standard costs for "investigator allocation"

As most investigators are senior medical specialists, the choice of an hourly rate between AMA levels 8 and 9 is considered reasonable. On this basis the standard cost is set at $215 per hour.

Table B.33: Determination of standard cost for investigator allocation

Item	Basis	Resource unit (hourly rates)					Unit cost	Standard cost
		Min	25th percentile	Median	75th percentile	Max		
Investigator allocation	Fully absorbed hourly rate	$158	N/A	N/A	N/A	$217	$215	$215

Reference number	2.6.3
Item	Research nurse allocation
Sub-list	Clinical-trial support services
Category	Clinical Staff/Resource Allocation
Definition	The stated time allocation multiplied by unit labour cost (*hourly rate plus on-costs, overtime, overheads and CPI increases)* for the research nurses that are expected to be involved in the clinical trial.
Standard Cost	$60 per hour

Related items

Table B.34 presents other items which are related (i.e. not necessarily mutually exclusive from) to item 2.6.3 "Research nurse allocation".

Table B.34: Items related to research nurse allocation

Item	Reference Number	Comment
Nursing/Allied Health Consultations	1.7.1	Depending on the clinical speciality of the investigator, he/she may be involved in providing nursing/allied health consultations.

Nursing/allied health consultations have been costed on a per service basis (see sub-list 1), so it is important that item 2.6.3 is not used to cover clinical services that might be provided by a research nurse. Item 2.6.3 should only be used where the nurse is acting in his/her capacity as a researcher.

In addition to clinical services, the research nurses will be involved in the majority of the activities included in sub-lists 2 and 3. This item is therefore used to set the reasonable unit cost for investigator time, which is then used to calculate the costs of many of the other activities in sub-lists 2 and 3. If item 2.6.3 is used together with items such as site selection including feasibility and preparing ethics submissions care should be taken to avoid double counting.

Learnings from site visits

Clinical trials often involve a research nurse or clinical trials nurse (CTN) who may or may not also be the study coordinator. The role of the CTN varies and can include protocol development, ethics approval applications, recruitment and consenting of participants in trials, to administering or assisting with treatments within the bounds of their practice code and the evaluation of protocols. From the fieldwork, we found that the majority of CTNs recruited at each of the sites were registered nurses (RNs) between levels 4 to 8. The hourly rate quoted by most sites for their CTNs was between $80-$120/hour.

Derived process map for "research nurse allocation"

Not applicable.

Considerations for deriving the cost of "research nurse allocation"

Notwithstanding the fact that there are a variety of hourly rates used in practice, the table of standard costs is developed, as far as possible, on a cost (not charge) basis. Accordingly, investigations into secondary sources of data on the cost of an hour of research nurse time were undertaken. We found considerable variation between the nursing awards across States and Territories. There is, however, a national nurses award that was introduced on 1 January 2010. Although most States and Territories continue to use their own awards, to obtain a figure that was nationally representative, we chose to use the national award, as shown in Table B.35.

Consistent with the full-absorbed costing principle, it was important to identify a suitable source of salary on-costs and institutional overheads to apply to the direct salary cost presented in Table B.35. For this purpose a simple model of a human services organisation was adopted which proposed that direct salary costs make up 60% of expenditure, salary on-costs make up 15% of expenditure and institutional overheads make up the other 25%. There is ample evidence to support the fact that salary on costs (paid leave, public holidays, superannuation, payroll tax, etc.) are typically around 15/60 = 25% of direct salary.

The proposition that institutional overheads are around 25/75 = 33% of salary costs has a weaker evidence base. It is clear that a series of costs will need to be incurred to make a person in an organisation productive (office space, furniture, equipment, internet and library resources, administrative support, light, power, insurances, etc.). Without incurring these costs, the employed person could not effectively discharge the role they occupy. It is acknowledged that these costs are very organisation dependent, but they are normally quoted in a range of 25% to 40% of salary costs. On this basis 33% of direct plus indirect salary costs is considered to be reasonable.

So using the national nursing award, we found that there are five levels of RN with three to eight pay points within each level. As most CTNs consulted were level 5, we have used the pay rates for Level 5 to set the reasonable cost. For each point in the pay scale, we calculated the hourly rate (based on 38 hours per week) which worked out to be in the range of around $29 to $42 per hour. Applying the ratios needed to convert to fully absorbed costs, Table B.35 shows that the estimated cost per hour ranges from around $48 to $70.

Table B.35: Pay scales in national nursing award for registered nurse - level 5

RN Level 5	Annual Salary	Weekly Salary	Hourly rate	Salary Oncost	Institutional Overhead	Fully Absorbed Hourly Rate
Grade 1	$56,576	$1,088	$29.01	$7.25	$12.09	$48.36
Grade 2	$59,644	$1,147	$30.59	$7.65	$12.74	$50.98
Grade 3	$63,752	$1,226	$32.69	$8.17	$13.62	$54.49
Grade 4	$67,808	$1,304	$34.77	$8.69	$14.49	$57.96
Grade 5	$74,932	$1,441	$38.43	$9.61	$16.01	$64.04
Grade 6	$82,108	$1,579	$42.11	$10.53	$17.54	$70.18

Source: http://www.apna.asn.au/scripts/cgiip.exe/WService=APNA/ccms.r?PageId=11201

Table of standard costs for "research nurse allocation"

As most research nurses have achieved a fair degree of seniority in their award level, the choice of an hourly rate between grades 4 and 5 is considered reasonable. On this basis the standard cost is set at $60 per hour, as shown in Table B.36.

Table B.36: Determination of standard cost for research nurse allocation

Item	Basis	Resource unit (hourly rates)					Unit cost	Standard cost
		Min	25th percentile	Median	75th percentile	Max		
Research nurse allocation	Fully absorbed hourly rate	$48	N/A	N/A	N/A	$70	$60	$60

Reference number	2.6.4
Item	Clinical research coordinator (non-research nurse) allocation
Sub-list	Clinical-trial support services
Category	Clinical Staff/Resource Allocation
Definition	The stated time allocation multiplied by unit labour cost (*hourly rate plus on-costs, overtime, overheads and CPI increases)* for the clinical research coordinator (e.g. personnel with scientific qualification, etc.) that are expected to be involved in the clinical trial.
Standard Cost	$75 per hour

Related items

Clinical research coordinators will be involved in the majority of the activities included in sub-lists 2 and 3. This item is therefore used to set the reasonable unit cost for clinical research coordinator time, which is then used to calculate the costs of many of the other activities in sub-lists 2 and 3. If item 2.6.4 is used together with items such as site selection including feasibility and preparing ethics submissions care should be taken to avoid double counting.

Learnings from site visits

We found that the role of the clinical research coordinator varied between those qualified as registered nurses or those with scientific qualifications. On balance about 75% were RNs and 25% were scientists. As the reasonable costs of an RN was calculated for item 2.6.3, this item focuses on the reasonable cost for a non-research nurse as the clinical research coordinator.

Derived process map for "clinical research coordinator allocation"

Not applicable.

Considerations for deriving the cost of "clinical research coordinator allocation"

Consistent with the other labour rate based items, investigations into secondary sources of data on the cost of an hour of clinical research coordinator time were undertaken. Again, mostly state based awards were found. Several sources were interrogated to support the calculation including:

- Victorian Public Sector, Schedule B rates of pay and allowances for medical scientists, pharmacists and psychologists 2012-2016
- NSW Public Sector Part B monetary rates for Medical Scientists 2012-2016

The Victorian award had several levels including:

- Science trainee which consists of five pay points;
- Medical scientist level 1-5 which consists between five and seven pay points;
- Scientist Director which consists of one pay point; and
- Principal Scientist which consists of one pay point;

The NSW award which consisted of two levels including:

- Hospital Scientist/Scientific Officer which consists of eight pay points ;
- Senior or chief hospital scientists which also consisted of eight pay points.

There was no award for a scientific based research coordinator role that could be identified. The site visits confirmed that clinical research coordinators were paid based on their discipline (e.g. if

an RN then the RN award was used, if a scientist then the scientific award was used). Most study coordinators that were of the scientific background quoted being either level 3 or 4. None were classified as a director or principal scientist. Table B.37 shows the variation in salary range between Victoria and NSW. The annual average salary across grade 3 or 4 medical scientist in NSW is $73,260.20 and in Victoria its $92,890.20.

Table B.37: Medical Scientist salary range in NSW and Victoria for Grade 3 and 4

Medical Scientist	NSW			Victoria		
	Annual Salary	Weekly Salary	Hourly rate	Annual Salary	Weekly Salary	Hourly rate
Grade 3	$68,099.20	$1,309.60	$34.92	$87,094.80	$1,674.90	$44.66
Grade 4	$78,421.20	$1,508.10	$40.22	$98,685.60	$1,897.80	$50.61
Average	**$73,260.20**	**$1,408.85**	**$37.57**	**$92,890.20**	**$1,786.35**	**$47.64**

Consistent with the full-absorbed costing principle, it was important to identify a suitable source of salary on-costs and institutional overheads to apply to the direct salary cost presented in Table B.37. For this purpose a simple model of a human services organisation was adopted which proposed that direct salary costs make up 60% of expenditure, salary on-costs make up 15% of expenditure and institutional overheads make up the other 25%. There is ample evidence to support the fact that salary on costs (paid leave, public holidays, superannuation, payroll tax, etc.) are typically around 15/60 = 25% of direct salary.

The proposition that institutional overheads are around 25/75 = 33% of salary costs has a weaker evidence base. It is clear that a series of costs will need to be incurred to make a person in an organisation productive (office space, furniture, equipment, internet and library resources, administrative support, light, power, insurances, etc.). Without incurring these costs, the employed person could not effectively discharge the role they occupy. It is acknowledged that these costs are very organisation dependent, but they are normally quoted in a range of 25% to 40% of salary costs. On this basis 33% of direct plus indirect salary costs is considered to be reasonable.

So using the NSW and Victorian medical scientists awards, we calculated the hourly rate (based on five days per week, 7.5 hours per day), which worked out to be in the range of around $35 to $51 per hour. Applying the ratios needed to convert to fully absorbed costs, the estimated cost per hour ranges from around $58 to $85.

Table of standard costs for "clinical research coordinator allocation"

Given the variation, the choice of an hourly rate that takes the average between NSW and Victoria to estimate the costs of a medical scientist in the role of clinical research coordinator across Australia is considered reasonable. On this basis the standard cost is set at $75 per hour.

Table B.38: Determination of standard cost for clinical research coordinator allocation

Item	Basis	Resource unit (hourly rates)					Unit cost	Standard cost
		Min	25th percentile	Median	75th percentile	Max		
Clinical research coordinator	Fully absorbed hourly rate	$58	N/A	N/A	N/A	$85	$75	$75

Reference number	2.6.5
Item	Clinic/theatre usage
Sub-list	Clinical-trial support services
Category	Clinical Staff/Resource Allocation
Definition	The estimated amount of time (in hours) clinic and/or theatre usage is expected to be required to conduct the clinical trial
Standard Cost	Not determined, as there was no reasonable basis, and cost typically not charged by trial host sites, theatre use is usually for standard of care services

Related items

None.

Learnings from site visits

We found no site that had factored clinic/theatre usage charges, as a stand-alone item, into a clinical trial budget. For the clinical tests and procedure services in sub-list 1, clinic/theatre usage would be a component of a number of the services and has therefore been factored into the per-service cost (e.g. the IHPA published costs for nursing/allied health services clinics cover all costs including facilities and are published on a full absorbed costs basis).

There may be circumstances where clinic/theatre time is required, but no clinical service is delivered to a trial participant. However, we were not able to identify such occasions through the fieldwork, hence there is no real basis for setting a reasonable cost.

Derived process map for "clinic/theatre usage"

Not applicable.

Considerations for deriving the cost of "clinic/theatre usage"

Notwithstanding the problems, there was an attempt made to identify secondary sources of data for the costs of clinic/theatre time. The work of the National Procedure Banding Committee was investigated, but there was no information on the cost per theatre minute, only the allocation of MBS items into theatre bands based on the expected time in theatre. Reference was also made to DRG service weight studies for theatre that were done one to two decades ago, but due to information technology problems these data could not be accessed.

Table of standard costs for "clinic/theatre usage"

Table B.39 indicates that no relevant data were able to be obtained from sites, so no separate standard cost for clinic/theatre usage has been determined.

Table B.39: Determination of standard cost for clinic/theatre usage

Item	Basis	Resource unit (hourly rates)					Unit cost	Standard cost
		Min	25th percentile	Median	75th percentile	Max		
Clinic/Theatre usage	Fully absorbed hourly rate	N/A	N/A	N/A	N/A	N/A	N/A	N/A

The need for this item should be reviewed with regard to how the clinical tests and procedures items are handled and whether the clinic/theatre resources needed to provide those services should be an absorbed cost. If the item is retained to reflect clinic or theatre resources needed for clinical trials that do not also involve the provision of a clinical tests and procedure services, then a basis for costing basis needs to be identified. Direct measurement may be required.

Appendix C – Non-clinical services

Reference number	3.1.1
Item	Preparation of research proposal
Sub-list	Non-clinical services
Category	Project Development
Definition	Includes the preparation of the initial research synopsis, research proposal, grant application, the detailed clinical trial protocol and other material required for an ethics submission (e.g. Investigators Brochure, Patient Information and Consent Form (PICF), advertising and information materials, etc.).
Standard Cost	$80,858 per research proposal (for non-industry sponsored trials only)

Related items

None.

Learnings from site visits

Preparation of a research proposal for industry sponsored clinical trials is not undertaken by the trial site (it is done by the sponsor). However for investigator initiated trials, the development of a research, proposal, based on an investigator's idea, is always required in order to attract funding for the clinical trial. The funding source for investigator initiated trials varies and includes the NHMRC, pharmaceutical companies, trial collaboratives, etc.

Most investigators involved in initiating trials explained that the development of the research proposal was only the first aspect to getting a trial to the same stage as an industry sponsored trial (before site selection). So the process was costed by including all activities needed to get an investigator initiated trial to the same stage as first contact by an industry sponsored trial with a potential site. Hence the activities include preparation of the research proposal that is submitted to a funding body (usually the NH&MRC), the development of a detailed clinical trials protocol (which is not part of a grant application) and all supporting documentation required to make an ethics application (e.g. Investigator Brochure, PICF, information sheets, etc.).

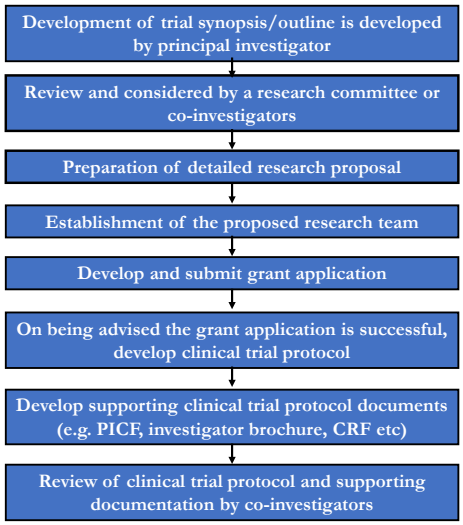
Principal and co-investigators found it difficult to estimate the time spent on all these activities as they usually involved many people and were undertaken in and around other activities (e.g. other research activities and/or delivering patient care). Nonetheless, most informants provided a rough estimate of their time and the time spent by others, which varied from four weeks full time to three months full time work depending on the complexity of the clinical trial, the number of investigators involved and the funding source. Most investigators also commented that the grant application process usually involved a number of repeat submissions for the one trial before a successful grant application was provided. For the basis of estimating the costing it was agreed this parameter would be excluded on the basis that it varies considerably.

It was often pointed out by researchers involved in investigator-initiated trials that the development of a research proposal into a clinical trial is largely an unfunded activity. Most stated that there is sometimes a budget provision for the development of a protocol, etc. if an NHMRC grant is awarded but often for collaborative-investigator initiated trials the work is undertaken by dedicated principal and co-investigators in and around their "day jobs".

Derived process map for "preparation of research proposal"

Figure C.1 presents the typical process involved in preparation of research proposal process. . The **blue** boxes represent the typical process.

Figure C.1: Process map of activities included under preparation of research proposal



Considerations for deriving the cost for "preparation of research proposal"

The number of personnel involved in the developing any research proposal varies depending on the type (e.g. drug vs. device, etc.) and size of the clinical trial (i.e. the bigger the trial the more investigators involved). In order to derive a reasonable cost associated with development of a research proposal, time (in hours) was chosen as the best resource unit.

As the process varied in terms of who was involved, costing for this activity was based on a simplified process which involved the principal investigator (and co-investigators), the clinical trials coordinator/manager (who was a registered nurse in 75% of cases and a medical scientist in 25% of site visits). The referenced unit cost for the principal investigator and co-investigators is the hourly rate determined in item 2.6.2; the reference cost for the clinical trials manager/coordinator is a combination of the hourly rate determined for items 2.6.3 Research Nurse (75% allocation) and 2.6.4 Clinical Research Coordinator (25% allocation).

Table of standard costs for "preparation of research proposal"

Table C.1 presents the resource units, in hours, required for each activity by specific personnel. Due to the variability in the type of clinical trial which was the subject of the research proposal, the median was considered the best basis for determining the standard cost of $80,858.

Table C.1: Typical personnel, resources and unit cost involved in preparation of research proposal

Activities	Personnel involved	Resource unit (hours)					Unit cost	Standard cost (median)
		Min	25th percentile	Median	75th percentile	Max		
Development of research proposal	Principal Investigator	20.0	42.5	175.5	229.1	500.0	$215.00	$37,733
	Co-investigators	10.0	50.0	100.0	122.5	720.0	$215.00	$21,500
Grant application	Principal Investigator	4.0	25.0	40.0	70.0	100.0	$215.00	$8,600
	Clinical Trials Manager/Coordinator	10.0	10.0	10.0	11.0	14.0	$63.75	$638
Development of detailed clinical trial protocol	Principal Investigator	5.0	5.0	7.5	17.5	40.0	$75.00	$563
	Clinical Trials Manager/Coordinator	15.0	20.0	25.0	60.0	100.0	$215.00	$5,375
Development of clinical trial supporting documentation	Principal Investigator	5.0	8.0	10.0	12.5	20.0	$215.00	$2,150
	Clinical Trials Manager/Coordinator	10.0	15.0	20.0	38.0	80.0	$215.00	$4,300
Total for preparation of research proposal								**$80,858**

Reference number	3.1.2
Item	Site selection including site feasibility assessment process
Sub-list	Non-clinical services
Category	Project Development
Definition	Includes the: • assessment of study feasibility at a site including the completion of feasibility questionnaire/s; • budget review and negotiation; • legal review and institutional sign off; and • the site selection/feasibility visit.
Standard Cost	$2,597 per site selection (including site feasibility assessment process)

Related items

Table C.2 presents other items which are related to item 3.1.2 "site selection including site feasibility assessment process".

Table C.2: Items related to site selection including site feasibility assessment process

Item	Reference Number	Comment
Departmental Establishment / Set Up Fee	2.2.1	Some sites include the activities associated with site selection, including site feasibility assessment process in the departmental establishment/set up fee. Care should be taken not to double count.

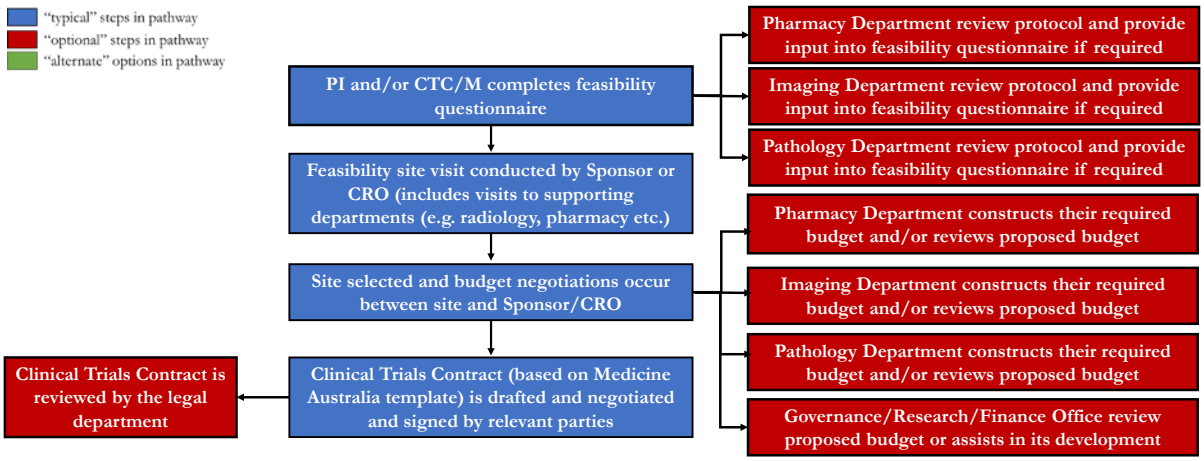
Learnings from site visits

Currently the costs associated with site selection including the site feasibility assessment process is not included in any budget negotiated with the sponsor (or their agent) as the activities occur before the clinical trial begins. However some clinical trial sites capture this work (i.e. associated cost) in their Departmental Establishment/Set Up fees. In the case of investigator initiated trials (including collaborative trials) site selection including the site feasibility assessment process is much more simplified or non-existent. For example, in single site investigator initiated trials, the principal investigator has designed a clinical trial for the sole purpose of conducting it at his/her site (regardless of the funding source). For collaborative trials, the process usually involves the collaborative or individual investigators nominating the sites, rather than going through a formal site selection feasibility process. For some industry sponsored trials, we found instances where a site will have a pre-established relationship with a sponsor and the site feasibility/selection visit is not required, or may take place over the phone or not at all.

Derived process map for "site selection including site feasibility assessment process"

Figure C.2 presents the typical process involved in site selection including the site feasibility assessment process. The **blue** boxes represent the typical process. The **red** boxes represent the optional processes in the typical pathway that are dependent on the actual clinical trial (e.g. drug trials involve pharmacy whereas device trials generally do not), and the process followed at each site in regards to which departments, if any, they get involved in budget setting and negotiation.

Figure C.2: Process map of activities included under site selection including the site feasibility assessment process



Considerations for deriving the cost for "site selection including site feasibility assessment process"

The number of personnel involved in site selection (including site feasibility assessment process) varies from site to site and even within sites across clinical trials units. The variability is around the involvement of the supporting service departments (e.g. pharmacy, pathology, etc.) and whether the legal department is involved in reviewing the contract. However using the estimates provided by site representatives, across the various trials examined, an estimate of each component of the activity involved was possible.

In order to derive a standard cost for the site selection process, professional time was chosen as the most suitable resource unit. The costing was based on the typical process which involved the principal investigator, the clinical trials coordinator/manager (who was a registered nurse in 75% of cases and a medical scientist in 25% of site visits); personnel from the various supporting departments (usually the department head), as well as the research governance officer.

The referenced unit cost for the Principal Investigator and heads of the other supporting departments is the hourly rate determined in item 2.6.2; the reference cost for the Clinical Trials Manager/Coordinator is a combination of the hourly rate determined for items 2.6.3 Research Nurse (75% allocation) and 2.6.4 Clinical Research Coordinator (25% allocation); and for the research governance officer, we assumed their qualifications being equivalent to someone with a generic qualification (i.e. like someone with a scientific qualification), so the standard cost determined for 2.6.4 Clinical Research Coordinator was used.

Table of standard costs for "site selection including site feasibility assessment process"

Table C.3 presents the resource units, in hours, required for each activity by specific personnel. Due to the variability in the resources required for the site selection process, the median was considered the best basis for setting the standard cost of $2,597 per site.

Table C.3: Typical personnel, resources and unit cost involved in site selection including site feasibility assessment process

Activities	Personnel Involved	Resource unit (hours)					Unit cost	Standard cost (median)
		Min	25th percentile	Median	75th percentile	Max		
PI and/or CTC/M completes feasibility questionnaire	Clinical Trials Manager/Coordinator	0.2	1.0	2.0	3.0	53.0	$63.75	$127.50
	Principal Investigator	0.2	0.3	0.5	1.0	7.5	$215.00	$107.50
	Supporting department personnel	0.2	0.5	2.0	2.3	6.0	$215.00	$430.00
Feasibility/site selection visit	Clinical Trials Manager/Coordinator	2.0	4.0	4.8	7.5	50.0	$63.75	$302.81
	Principal Investigator	0.3	1.0	1.0	1.4	3.0	$215.00	$215.00
	Supporting department personnel	0.5	1.0	1.0	2.0	4.0	$215.00	$215.00
Site selected and budget negotiations occur between site and Sponsor/CRO	Clinical Trials Manager/Coordinator	2.0	3.0	3.5	12.8	50.0	$63.75	$223.13
	Principal Investigator	0.5	0.8	1.0	1.5	4.0	$215.00	$215.00
	Research Governance/Finance Office	0.5	1.0	2.0	2.3	3.0	$75.00	$150.00
	Supporting department personnel	0.5	1.4	1.5	2.0	2.0	$215.00	$322.50
Review/negotiation Clinical Trials Contract	Clinical Trials Manager/Coordinator	0.5	0.5	1.0	1.0	22.5	$63.75	$63.75
	Research Governance Officer/Legal Officer	0.5	0.5	3.0	11.3	22.5	$75.00	$225.00
Total for site selection including site feasibility assessment process								**$2,597**

Reference number	3.1.3
Item	Preparation and submission of applications to HREC and institutions
Sub-list	Non-clinical services
Category	Project Development
Definition	**Preparation and submission of applications to HREC:** Includes the preparation and submission of the human research ethics committee (HREC) application form (or equivalent) and supporting documentation which includes the site specific participant information and consent form (PICF), processing of country specific regulatory documents (e.g. the Clinical Trial Notification (CTN) Scheme form), insurance and indemnity documents, trial agreements, recruitment and advertising materials, etc. Also includes revisions to applications according to ethics committee requests. **Preparation and submission of applications to institutions:** Includes the preparation and submission of the Site Specific Assessment (SSA) application forms which involves completion of the form, obtaining authorising signatures, liaising with inter-institutional Departments (e.g. radiology, pharmacy, etc.), adapting the Lead HREC approved master PICF(s) with site specific letterhead and contact details; submission of SSA to the research governance officer (RGO) for review; liaison with sponsor, responding to RGO queries, forwarding copies of relevant authorisations and associated correspondence/documentation to sponsor.
Standard Cost	HREC (non-lead) and SSA = $3,098 per application per clinical trial HREC (lead) and SSA $3,953 per application per clinical trial

Related items

Table C.4 presents other items which are related to item 3.1.3 "preparation and submission of applications to HREC and institutions".

Table C.4: Items related to preparation and submission of applications to HREC and institutions

Item	Reference Number	Comment
Departmental Establishment/Set Up Fees	2.2.1	Some sites include the activities associated with preparation and submission of applications to HREC and institution in the departmental establishment/set up fee. Care should be taken not to double count.
Lead HREC/Lead site fee	3.1.7	The additional time taken to prepare and submit the HREC application by the lead site should be captured under 3.1.3. However the additional time involved in managing the ongoing coordination of the clinical trial, due to be the lead site, should be captured under the Lead HREC/Lead site fee which is item 3.1.7.

Learnings from site visits

Due to the consistency in requirements for ethics submissions, the steps for preparation and submission of HREC application forms reported by sites were fairly standard. Time variation in completing a submission to a HREC was due to a number of factors including:

- whether a trial was industry sponsored or investigator initiated;
- whether a site was a lead-site or non-lead site in a multi-centre trial;
- the nature of the trial (e.g. whether multiple questionnaires were required or brochures to be developed); and
- nature of recruitment (e.g. if advertising material was required to be developed).

In industry sponsored clinical trials the detailed protocol, PICFs etc. were provided by the sponsor. However, even in these types of trials, most sites reported that additional time was required to adapt PICF to Australian wording (i.e. as most sponsors were overseas-based firms), incorporate into local ethic templates and include local site information (including the logo, letterheads, etc.).

Most sites commented on the recent process that involved NSW, Queensland and Victoria signing a Memorandum of Understanding (MOU) to introduce mutual acceptance of ethical and scientific review of multi-centre clinical trials. Under the interstate mutual acceptance initiative, each proposal for a multi-centre clinical trial is ethically and scientifically reviewed only once by a public health organisation HREC that has been certified by the NH&MRC. Most sites reported that mutual agreement had reduced ethics application time for clinical trials conducted across these three states however, the majority of multi-centre trials conducted in Australia were conducted in other states as well and therefore there was still significant burden. There were however some sites that felt the mutual agreement had not reduced any of their time dedicated to ethics applications and that the term "streamlined" approach was misleading. South Australia had only recently signed up to the mutual agreement and most clinical trials units were struggling with the new process.

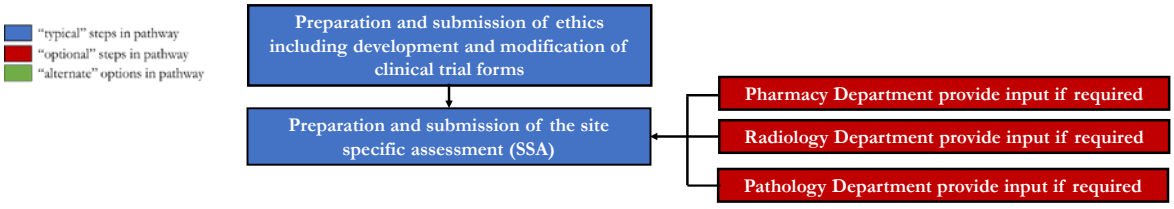
If the clinical trial unit was the lead site, most reported a number of additional tasks which added to the time required to complete the ethics submission including: set up communication links with appropriate people; initial preparation and submission of HREC documents (e.g. NEAF, PICF, patient questionnaires, investigator CVs, regulatory documents, drug safety information, radiation reports, etc.); electronic upload of all documents; collection of various signatures; resolution of queries raised by HREC; and then initiation of the SSA for all sites. Given the additional time taken to complete an ethics submission when a clinical trial site is the lead site, two standard costs for this item have been determined in Table C.5.

Most sites also reported completing a site specific assessment (SSA) or equivalent document. Most sites complete the SSA process in parallel with the ethics application process however, at most sites ethics approval was a component of the SSA. Therefore approval and completion of the SSA could not be finalised prior to obtaining ethics approval. The SSA process was similar across all sites however, the variation identified was more related to the nature of the trial (e.g. phase 1 vs. phase 2), as opposed to variations across sites.

Derived process map for "preparation and submission of applications to HREC and institutions"

Figure C.3 presents the typical process involved in preparation and submission of applications to HREC and institutions. The **blue** boxes represent the typical process. The **red** boxes represent the optional processes in the typical pathway that are dependent on the actual clinical trial (e.g. drug trials involve pharmacy whereas device trials generally do not).

Figure C.3: Process map of activities included under preparation and submission of applications to HREC and institutions



Considerations for deriving the cost for "preparation and submission of applications to HREC and institutions"

In order to derive a standard cost for the preparation and submission of applications to HREC and institutions professional time was chosen as the most suitable resource unit. The costing was based on the typical process which involved the principal investigator, the clinical trials coordinator /manager (who was a registered nurse in 75% of cases and a medical scientist in 25%

of site visits); and the research governance officer. Due to the variability in the input provided by the various supporting departments, and the fact that they were not routinely involved, the cost associated with their involvement has not been factored into the standard cost.

The referenced unit cost for the Principal Investigator is the hourly rate determined in item 2.6.2; the reference cost for the Clinical Trials Manager/Coordinator is a combination of the hourly rate determined for items 2.6.3 Research Nurse (75% allocation) and 2.6.4 Clinical Research Coordinator (25% allocation); and for the research governance officer, we assumed their qualifications being equivalent to someone with a generic qualification (i.e. like someone with a scientific qualification) so the standard cost determined for 2.6.4 Clinical Research Coordinator was used.

Table of standard costs for "preparation and submission of applications to HREC and institutions"

Table C.5 presents the resource units, in hours, required for each activity by specific personnel. The median was considered the best basis for setting the standard cost. Also as a number of the clinical trials units consulted provided information on the added time (in hours) required to be the lead site as opposed to a participating site, a separate standard cost was determined for a lead site plus the SSA process, and a participating site plus SSA process.

Table C.5: Typical personnel, resources and unit cost involved in preparation and submission of applications to HREC and institutions

Activities	Personnel Involved	Resource units					Unit cost	Standard costs (median)
		Min	25th percentile	Median	75th percentile	Max		
Non-lead site ethics submission								
Completion of NEAF including development and modification of trial forms	Principal Investigator	0.1	0.5	1.0	1.0	49.5	$215.00	$215.00
	Clinical Trials Manager/Coordinator	2.0	12.0	30.0	40.0	988.0	$63.75	$1,912.50
	Research/Governance Officer	1.0	1.0	1.0	4.0	12.0	$75.00	$75.00
Lead ethics submission (add on to non-lead site ethics submission)								
Additional tasks required as part of being Lead site	Principal Investigator	0.5	0.9	1.5	2.0	2.0	$215.00	$322.50
	Clinical Trials Manager/Coordinator	3.0	4.0	6.0	11.0	37.5	$63.75	$382.50
	Research/Governance Officer	1.0	1.4	2.0	2.3	4.0	$75.00	$150.00
Governance approval								
Governance /completion of site specific assessment (SSA)	Principal Investigator	0.1	0.1	0.5	1.0	37.5	$215.00	$107.50
	Clinical Trials Manager/Coordinator	2.5	5.8	10.0	19.3	57.0	$63.75	$637.50
	Research/Governance Officer	1.0	1.0	2.0	3.3	7.5	$75.00	$150.00
Total - HREC (non-lead) and SSA								**$3,098**
Total - HREC (lead) and SSA								**$3,953**

Note: totals may not be exactly additive due to rounding errors

Reference number	3.1.4
Item	Radiation safety and/or biosafety reports
Sub-list	Non-clinical services
Category	Project Development
Definition	Includes the preparation and submission of the safety and/or biosafety reports
Standard Cost	$99 per radiation safety and/or biosafety report

Related items

None.

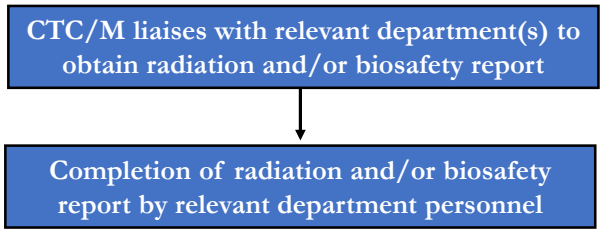
Learnings from site visits

Radiation safety and/or biosafety reports are required to be completed for any clinical trial involving the use of human blood, tissues or other biological materials; recombinant DNA; ionising radiation sources; or other activities with significant biosafety hazard. The activities involved in this process were consistent across all sites and involved only two people, the clinical trials coordinator working with the radiation/biosafety officer.

Derived process map for "radiation safety and/or biosafety reports"

Figure C.4 presents the typical process involved in site selection including the site feasibility assessment process.

Figure C.4: Process map for item 3.1.4 "radiation safety and/or biosafety reports"



Considerations for deriving the cost for "radiation safety and/or biosafety reports"

In order to derive a reasonable cost associated with the preparation and submission of the safety and/or biosafety reports, professional time was chosen as the most suitable basis due to the activities involved and the various personnel. The personnel involved was common across all sites and included the clinical trials coordinator/manager; and the radiation/biosafety officer (who was almost always a qualified medical scientist).

The referenced unit cost for the Clinical Trials Manager/Coordinator is a combination of the hourly rate determined for items 2.6.3 Research Nurse (75% allocation) and 2.6.4 Clinical Research Coordinator (25% allocation); and for the radiation/biosafety officer, we assumed their qualifications being equivalent to someone with a medical science degree, so the reasonable cost determined for 2.6.4 Clinical Research Coordinator was used.

Table of standard costs for "radiation safety and/or biosafety reports"

Table C.6 presents the resource units, in hours, required for each activity by specific personnel. The median was considered the best basis for setting the standard cost of $99.

Table C.6: Typical personnel, resources and unit cost involved in radiation safety and/or biosafety reports

Activities	Personnel Involved	Resource unit (hours)					Unit cost	Standard costs (median)
		Min	25th percentile	Median	75th percentile	Max		
Liaise with relevant department to undertake report	Clinical Trials Manager/Coordinator	0.3	0.3	0.4	0.5	0.5	$63.75	$24.23
Complete report	Radiation/Biosafety Personnel	0.5	1.0	1.0	1.0	4.0	$75.00	$75.00
Total for radiation safety and/or biosafety reports								**$99**

Reference number	3.1.5
Item	HREC (ethical) review fee
Sub-list	Non-clinical services
Category	Project Development
Definition	Is the fee charged by the Ethics Committee for the review of the HREC application
Standard Cost	$3,000 per HREC (ethics) application

Related items

Table C.7 presents other items which are related to item 3.1.5 "HREC (ethical) review fee".

Table C.7: Items related to HREC (ethical) review fee

Item	Reference Number	Comment
Preparation and submission of applications to HREC and institutions	3.1.3	The cost associated with the personnel time required for the preparation and submission of the applications to HREC and institutions should be captured under item 3.1.3 and not 3.1.5.
Institutional (site assessment) review fee	3.1.6	The fee associated with the review of the site assessment application fee should be captured under 3.1.6 and not 3.1.5.
Lead HREC/Lead site fee	3.1.7	The additional fee associated with the review of a lead HREC application should be captured under 3.1.7 and not 3.1.5.

Learnings from site visits

Most sites consulted had an onsite NHMRC approved HREC. The fees charged for industry sponsored trials were always higher than for investigator-initiated trials. For investigator-initiated trials, fees were often minimal (e.g. $150 per application) or waived completely. At some sites differentiation was made on the basis of whether a trial was fully or partially funded by an industry sponsor or whether the trial was a multi-site trial. Differentiation was also made if the ethics application had already been approved through another (NHMRC certified) ethics committee prior to submission at the current site.

Although the mix of membership of each ethics committees was similar the number of members that attend each meeting varied from six to 20. The frequency of the meetings varied from fortnightly to every two months. The process for reviewing the applications varied from all attending members undertaking detailed review to only two members undertaking detailed review and one being nominated to present (i.e. the spokesperson) the clinical trial to the committee. The length of the meetings also varied from one hour to four hours, which was largely dependent on the number of applications and the frequency of the meetings.

Most ethics/research officers would review all applications prior to sending it to the committee and would send back any applications that did not meet certain minimum requirements with the aim to minimise wasting the time of the ethics committee members. No ethics committee members were paid for their time (i.e. all membership was on honorary basis).

Derived process map for "HREC (ethical review fee)"

Not applicable

Considerations for deriving the cost

As this item was a fees item Table C.8 represents the fees charged by the sites rather than the cost associated with activities captured under item 3.1.5. There was noticeable variability in the fee charged by ethics committees that was largely dependent on the sponsor of the clinical trial.

Table of standard costs for "HREC (ethical review fee)"

Table C.8 presents the fee range charged by various clinical trials sites around Australia. Due to the variation in fees charged, the median was assessed to be the most reasonable basis for setting the standard cost, which is actually a fee of $3,000.

Table C.8: Typical fees associated with HREC (ethical review fee)

Activities	Basis	Resource unit (fee)					Unit cost	Standard cost (median)
		Min	25th percentile	Median	75th percentile	Max		
HREC (ethical review fee)	Typical fees	$0	$1,131	$3,000	$3,350	$8,800	n/a	$3,000

Reference number	3.1.6
Item	Institutional (site assessment) fee
Sub-list	Non-clinical services
Category	Project Development
Definition	Is the fee charged by the research governance office for the review of the site specific assessment (or equivalent) application
Standard Cost	$750 per institutional (site assessment) application

Related items

Table C.9 presents other items which are related to item 3.1.6 "institutional (site assessment) fee".

Table C.9: Items related to institutional (site assessment) fee

Item	Reference Number	Comment
Preparation and submission of applications to HREC and institutions	3.1.3	The cost associated with the personnel time required for the preparation and submission of the applications to HREC and institutions should be captured under item 3.1.3 and not 3.1.6.
HREC (ethical) review fee	3.1.5	The fee associated with the review of the HREC (ethical) application fee should be captured under 3.1.4 and not 3.1.6.

Learnings from site visits

All clinical trial sites visited has their own research governance office (RGO), which was supported by one to four full time staff. The fees for submission of an SSA through RGOs were variable across sites, partly due to a number of sites now changing their fee structure due to the impact of the interstate mutual ethics acceptance initiative. Previously most sites had quite modest fees (e.g. $800 or less per application) for SSA applications, although these too varied depending on whether it was an industry sponsored trial or an investigator initiated trial. Now with the modification to the ethics process (at least in Qld, NSW, Vic and most recently SA), the governance fees have increased to incorporate a brief review of an ethics application that has already been approved through a HREC at the lead site.

Derived process map for "institutional (site assessment) review"

Not applicable

Considerations for deriving the cost for "institutional (site assessment) review"

As this item was defined as fee based, Table C.10 represents the fees charged by the sites rather than the cost associated with activities captured under item 3.1.5. However, costs were discussed at the site visits. The advice received was that a governance review, including the review of the SSA may take anywhere between a few hours to a maximum of two days. Usually the governance review involved only one person within the research governance office, and the variation in time was generally due to whether the submitted SSA was complete on the first submission (i.e. all documentation was provided and the forms were correctly filled in) or whether it took the research governance officer several interactions with the applicant to gather or the required information.

It is acknowledged that the institutional (site assessment) review fee is set lower than the HREC fee. The reasons for this choice include:

- Under item 3.1.2 – five hours of RGO time is already included to cover off the time associated with budget negotiations between site and sponsor/CRO (i.e. two hours) and

review/negotiation of clinical trials contract (i.e. three hours) which equates to an additional $375;

- Under item 3.1.3 – five hours of RGO time is included to cover off the time for completing the NEAF including development and modification of the trial forms (i.e. one hour) and additional tasks required as being part of the lead site (i.e. two hours) and completion of SSA (i.e. two hours) which equates to an additional $375.
- Under item 3.2.10 – is the fee associated with the RGO (or HREC) charging for amendment review $275

All this information has been taken into account in selecting the most suitable basis for the standard costs (which is actually an institutional (site) assessment fee).

Table of standard costs for "institutional (site assessment) review"

Table C.10 presents the fee range charged by various clinical trials sites around Australia. Due to the fact that some sites are now capturing the ethics review within the SSA fee, and due to the quoted time of research governance office personnel involvement, the 25th percentile was assessed to be the most reasonable basis for setting the standard cost, which is actually a fee of $750 for institutional (site assessment) review.

Table C.10: Typical fees associated with institutional (site assessment) review fee

Activities	Basis	Resource unit (fee)					Unit cost	Standard cost (25th percentile)
		Min	25th percentile	Median	75th percentile	Max		
Institutional (site assessment) review fee	Typical fees	$0	$750	$3,000	$3,805	$6,050	n/a	$750

In selecting the 25th percentile, it is noted that an hourly rate of $75, the chosen fee level represents about 10 hours of research governance office time. This number is towards the upper end of the quoted range of time required (two hours to two days), and is therefore considered to be a suitable basis for setting the standard cost.

Reference number	3.1.7
Item	Lead HREC/Lead site fee
Sub-list	Non-clinical services
Category	Project Development
Definition	Is the fee charged by the lead site for the ongoing coordination and management of all the nominated sites participating in the clinical trial
Standard Cost	$400 per additional site per annum

Related items

Table C.11 presents other items which are related to item 3.1.7 "lead HREC/lead site fee".

Table C.11: Items related to lead HREC/lead site fee

Item	Reference Number	Comment
Preparation and submission of applications to HREC and institutions	3.1.3	The additional personnel time required for the preparation and submission of the lead HREC application to the HREC and institutions should be captured under item 3.1.3 and not 3.1.7. The fee charged by the lead site for the ongoing coordination and management of the participating sites involved the clinical trial should be captured under item 3.1.7 and not 3.1.3.
HREC (ethical) review fee	3.1.5	The fee associated with the review of the lead HREC (ethical) application should be captured under 3.1.5 and not 3.1.7.

Learnings from site visits

Most clinical trials units that were the lead site for a clinical trial discussed the additional work required in the ongoing coordination and management of the clinical trial. A number of sites commented they try not to be the lead because they do not feel any fee they could charge would justify the additional work. Most sites that are happy to be the lead sites have recently introduced a fee which covers the additional work, which is charged on a per additional site basis (e.g. for every additional site they charge a set fee which is generally annual).

Derived process map for "lead HREC/lead site fee"

Not applicable

Considerations for deriving the cost for "lead HREC/lead site fee"

As this item was a fees item, Table C.12 represents the fees charged by the sites rather than the cost associated with activities captured under item 3.1.7. The costs of the additional work required by the lead site in the ethics application process is covered under item 3.1.3.

Table of standard costs for "lead HREC/lead site fee"

Table C.12 presents the fee range charged by various clinical trials sites around Australia. Due to the variation in fees charged, the median was assessed to be the most reasonable basis for setting the standard cost, which is actually a fee of $400 per additional site per annum.

Table C.12: Typical fees associated with the lead HREC/lead site fee

Activities	Basis	Resource unit (fee per additional site per annum)					Unit cost	Standard cost (median)
		Min	25th percentile	Median	75th percentile	Max		
Lead HREC/Lead site fee	Typical Fee	$0	$150	$400	$605	$2,000	n/a	$400

Reference number	3.1.8
Item	Investigator meetings
Sub-list	Non-clinical services
Category	Project Development
Definition	Includes the organisation and the attendance of principal or co-investigators and/or Clinical Trials Manager/Coordinator at meetings about the clinical trial
Standard Cost	$1,020 per Clinical Trials Manager/Coordinator attending an international investigator meeting (excluding travel time and travel expenses) $3,440 per Principal Investigator attending an international investigator meeting (excluding travel time and travel expenses) OR $287 per Clinical Trials Manager/Coordinator attending a domestic investigator meeting (excluding travel time and travel expenses) $882 per Principal Investigator attending an domestic investigator meeting (excluding travel time and travel expenses)

Related items

None.

Learnings from site visits

The investigator meeting was generally held before any sites began recruiting, and involved detailed review of the protocol as well as training in various aspects of the clinical trial. As a minimum the principal investigator would attend, and commonly also the study coordinator. Principal investigators and study coordinators highlighted the value of attending such meetings, particularly to network and share learnings with national and international colleagues. As a result there was usually no charge made for attendance, and one instance of site staff taking annual leave to attend the meetings (so no charge needed to be made) was identified.

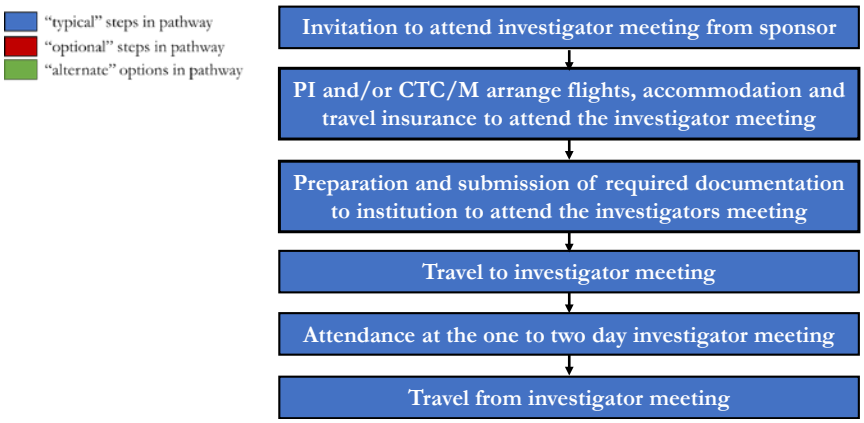
The location of the investigator meetings seemed to vary depending on the trial sponsor and the number of sites participating in the trial. Investigator meetings for international multi-site trials were sometimes held in Europe or America. The length of the meetings was generally one to two days, however it requires at least two to three days on either side of the meeting to travel to and from the location. When investigator meetings were held in Asia, again they were likely to be one to two days in length but the travel time either side of the meetings was more like one to two days. However a number of sites commented that there is an increasing trend to have the investigator meetings in major Australian airports (e.g. Sydney or Melbourne Qantas lounges), where the normal duration is about one half day.

The most common practice is that invited attendees are reimbursed for their travel and accommodation (excluding travel insurance). As already indicated, the time of the investigators or study coordinators to attend the meeting was most often not charged, however a few sites reported requesting a per diem fee for attending. This fee ranged from $250 per day for non-medical personnel to $1,000 per day for medical specialists.

Derived process map for "investigator meetings"

Figure C.5 presents the typical process involved in investigator meetings.

Figure C.5: Process map of activities included under "investigator meetings"



Considerations for deriving the cost

The number of personnel involved in the organisation and attendance at the investigator meeting varied from either the PI only, the study coordinator only, or both attending. The other variation was the location of the meeting. As the location was variable, the time taken to travel to and from the location was excluded from the standard cost determination, although the information gathered is presented in Table C.13. As there was a high degree of variability in time and cost separate determinations have been made for domestic and international meetings.

In order to derive a reasonable cost associated with attendance at investigator meetings, professional time was chosen as the most suitable resource unit. The referenced unit cost for the Principal Investigator is the hourly rate determined in item 2.6.2; and the reference cost for the Clinical Trials Manager/Coordinator is a combination of the hourly rate determined for items 2.6.3 Research Nurse (75% allocation) and 2.6.4 Clinical Research Coordinator (25% allocation).

Table of standard costs for "investigator meetings"

Table C.13 presents the resource units, in hours, required for attendance at investigator meetings (domestic and overseas) by specific personnel. Only professional time is included, as it is assumed that travel expenses, i.e. flights, ground transport, accommodation, meals, etc. would be met directly by the trial sponsor.

Table C.13: Typical personnel, resources and unit cost involved in investigator meetings

Activities	Personnel involved	Resource unit (hours)					Unit Cost	Standard costs domestic (minimum)	Standard costs overseas (median)
		Min	25th percentile	Median	75th percentile	Max			
Arranging flights, accommodation and insurance	Clinical Trials Manager/Coordinator	0.5	0.5	0.5	0.6	1.5	$63.75	$31.88	$31.88
	Principal Investigator	0.1	0.3	0.5	0.5	1.5	$215.00	$21.50	$107.50
Preparation and submission of institution documentation for attendance	Clinical Trials Manager/Coordinator	0.0	0.5	0.5	0.5	1.0	$63.75	$0.00	$31.88
	Principal Investigator	0.0	0.5	0.5	0.5	1.0	$215.00	$0.00	$107.50
Travel (to and from, overseas only)	Clinical Trials Manager/Coordinator	15.0	48.0	48.0	72.0	72.0	$63.75	N/A	$3,060.00
	Principal Investigator	15.0	48.0	48.0	72.0	72.0	$215.00	N/A	$10,320.00
Attendance at meeting	Clinical Trials Manager/Coordinator	4.0	14.1	15.0	54.0	72.0	$63.75	$255.00	$956.25
	Principal Investigator	4.0	13.1	15.0	60.0	72.0	$215.00	$860.00	$3,225.00
Total - Clinical Trials Manager/Coordinator to attend the investigator meeting (excluding travel time)								**$287**	**$1,020**
Total - Principal Investigator to attend the investigator meeting (excluding travel time)								**$882**	**$3,440**

As can be seen in Table C.13, due to the increasing number of investigator meetings being held in Australia, the costs were split into those for domestic versus overseas investigator meetings. Most of the times reported by sites related to international investigator meetings, so the median was considered the best basis for determining the standard cost of $3,440 for attendance by the principal investigator, and $1,020 for attendance by the clinical trials manager/coordinator at an overseas meeting. For domestic investigator meetings the observed minimum time (four hours) was considered to be the best basis for determining the standard cost of $882 for attendance by the principal investigator, and $287 for attendance by the clinical trials manager/coordinator.

Reference number	3.1.9
Item	Staff training
Sub-list	Non-clinical services
Category	Project Development
Definition	Includes any training (e.g. detailed protocol, eCRF, GCP) of staff directly involved in the clinical trial (excluding staff training that occurs during the start-up meeting).
Standard Cost	$638 per Clinical Trials Manager/Coordinator required to undertake staff training per clinical trial (based on 10 hours of training per clinical trial). $430 per Principal Investigator required to undertake staff training per clinical trial (based on two hours of training per clinical trial).

Related items

Table C.14 presents other items which are related to item 3.1.9 "staff training".

Table C.14: Items related to staff training

Item	Reference Number	Comment
Departmental Establishment/Set Up Fees	2.2.1	The Departmental Establishment/Set Up Fees should not include any activities associated with staff training. All staff training, excluding pharmacy staff specific training and training associated with the start-up meeting, should be captured under 3.1.9.
Departmental Ongoing Administration fees	2.3.1	The Departmental Ongoing Administration fees should not include any activities associated with staff training. All staff training, excluding pharmacy staff specific training and training associated with the start-up meeting, should be captured under 3.1.9
Staff training (drug specific)	2.4.1	Activities associated with pharmacy staff undertaking training specific to pharmacy work involved in clinical trials should be captured under 2.4.1 and not 3.1.9.
Start Up meeting	3.2.1	Staff training that occurs on the day of the start-up meeting should be captured under item 3.2.1 and not 3.1.9.

Learnings from site visits

Most sites consulted commented that the amount of training required as a result of participating in clinical trials was increasing, and more and more of it needed to be done online, by at least two people involved in the clinical trial, before the start up meeting.

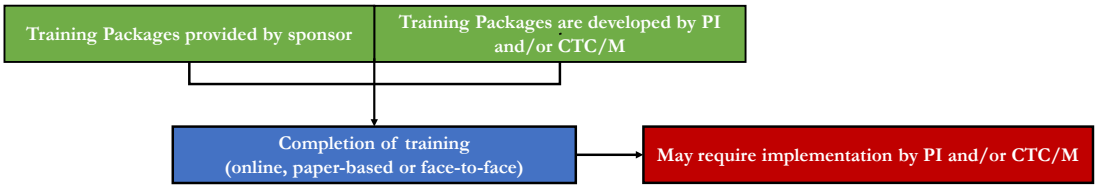
In general, industry sponsored trials training was provided usually in an online/web-based format, or on CD-ROM. Some sites reported difficulty accessing online/web-based training packages due to hospital firewalls. They were either prevented from accessing the material from hospital network computers or access was extremely slow, thereby increasing the time required to complete the training. Good Clinical Practice (GCP) training is mandated in clinical trials. Some sites accredit their staff in GCP and require refreshers every couple of years; and therefore do not need GCP training with every trial. Other sites are required to complete GCP training with each new trial. Unfortunately some sites stated that sponsors do not recognise all GCP training courses so they are required to undertake the training repeatedly for each clinical trial in which they are involved.

For investigator initiated trials, the amount of training required varied, but as a minimum it generally included two staff undertaking eCRF and GCP training. Typically, eCRF training (regardless of the sponsor) varies from 30 minutes to four hours; and GCP training is between an hour and two days. Other training about the protocol can vary from an hour to a day.

Derived process map for "staff training"

Figure C.6 presents the typical process involved in staff training.

Figure C.6: Process map of activities involved under staff training



Considerations for deriving the cost for "staff training"

The number of staff having to undertake the training for sites to be able to begin recruitment varied from two to four personnel. Usually these staff included the Principal Investigator and at least one Clinical Trials Manager/Coordinator.

The referenced unit cost for the Principal Investigator is the hourly rate determined in item 2.6.2; and the referenced unit cost for the Clinical Trials Manager/Coordinator is a combination of the hourly rate determined for items 2.6.3 Research Nurse (75% allocation) and 2.6.4 Clinical Research Coordinator (25% allocation). A reasonable cost has been determined based on each individual undertaking the minimum training.

Table of standard costs for "staff training"

Table C.15 presents the resource units, in hours, required for each activity by specific personnel. Due to the variability in the amount of training hours required for any given clinical trial, the median was considered the best basis for determining the standard cost, which was an estimated 10 hours training for Clinical Trials Managers/Coordinators and two hours for Principal Investigators.

Table C.15: Typical personnel, resources and unit cost involved in staff training

Activities	Basis	Resource unit (hours)					Unit cost	Standard cost (median)
		Min	25th percentile	Median	75th percentile	Max		
Staff training	Clinical Trials Manager/Coordinator	2	6	10	16	120	$63.75	$638
	Principal Investigator	1	1	2	5	16	$215.00	$430

Reference number	3.1.10
Item	Trial-specific equipment hire/purchase
Sub-list	Non-clinical services
Category	Project Development
Definition	Includes the hire and/or purchase of any equipment (excluding IT infrastructure) required for the purposes of conducting the clinical trial.
Standard Cost	$75 per trial-specific equipment hire/purchase for a biomedical engineering check

Related items

Table C.16 presents other items which are related to item 3.1.10 "Trial-specific equipment hire/purchase".

Table C.16: Items related to trial-specific equipment hire/purchase

Item	Reference Number	Comment
Staff training	3.1.9	Staff training related to any aspect of the clinical trial, including the use of trial specific equipment, should be captured under item 3.1.9 and not item 3.1.10.
Ongoing administration, monitoring and reporting	3.2.6	The time required to maintain trial-specific equipment for the duration of the trial, either by the study coordinator/manager or for regular testing and calibrating by other staff, should be captured under item 3.2.6 not 3.1.10.
Study close-out activity including preparation for audit	3.2.11	The time required to pack up and return trial-specific equipment that has been "loaned" to the site for the duration of the trial, should be captured under item 3.2.11 not 3.1.10.

Learnings from site visits

For industry sponsored trials, trial-specific equipment is supplied "on loan" by the sponsor. In most trials this equipment was required to be returned to the sponsor at the completion of the trial with the sponsor paying for the transport of the equipment. Some sites/trials reported that at the completion of the trial they were offered the opportunity to purchase the trial-specific equipment at a reduced price. In some instances, equipment was able to be kept by the trial site at no cost. For investigator-initiated trials where purchase of equipment was beyond the budget of the trial, companies were approached to donate equipment for use for the duration of the trial.

Although we did not find any site that incurred a direct cost for the purchase and/or hire of any trial specific equipment, the local biomedical engineering department was generally required to commission the equipment on site, and to conduct regular checks post installation to ensure it complied with local safety and quality procedures. Often, the relevant staff also needed to be trained on the use of the equipment for the purposes of the trial.

Derived process map for "trial-specific equipment hire/purchase"

Not applicable.

Considerations for deriving the cost "trial-specific equipment hire/purchase"

We found no evidence that any clinical trial site incurred the direct cost for the hire or purchase of any trial specific equipment. The cost incurred by the sites in undertaking training related to the trial specific equipment was factored in under item 3.1.9, and the costs incurred to maintain the trial specific equipment was factored into item 3.2.6.

In order to derive a standard cost associated with commissioning any trial specific equipment, the professional time spent by the biomedical engineer was chosen as the most suitable resource unit. The referenced unit cost for the biomedical engineer was item 2.6.4, as we assumed the biomedical engineer's qualifications and pay rates were directly comparable to medical scientists, so the fully absorbed unit costs was $75/hour.

Table of standard costs for "trial-specific equipment hire/purchase"

Table C.17 presents the resource units, in hours, required for each activity by specific personnel. The median was considered the best basis for determining the standard cost of $75 per item of trial-specific equipment.

Table C.17: Typical personnel, resources and unit cost for trial-specific equipment hire/purchase

Activities	Personnel Involved	Resource unit (hours per equipment item)					Unit cost	Standard costs (median)
		Min	25th percentile	Median	75th percentile	Max		
Biomedical engineer safety and quality check	Biomedical engineer	0.5	1.0	1.0	1.5	2.0	$75	$75
Total for trial specific equipment hire/purchase								**$75**

Reference number	3.1.11
Item	IT set-up, equipment and maintenance
Sub-list	Non-clinical services
Category	Project Development
Definition	Includes the purchasing and/or hiring of the IT equipment required for the clinical trial as well as the required set-up/customisation of the IT infrastructure so that it is suitable for use in the clinical trial.
Standard Cost	$37.50 per trial-specific IT equipment item for set-up

Related items

Table C.18 presents other items which are related to item 3.1.11 "IT set-up, equipment and maintenance".

Table C.18: Items related to IT set up, equipment and maintenance

Item	Reference Number	Comment
Staff training	3.1.9	Staff training related to any aspect of the clinical trial, including the use of IT equipment, should be captured under item 3.1.9 and not item 3.1.11.
Ongoing administration, monitoring and reporting	3.2.6	The time required to maintain trial-specific IT equipment for the duration of the trial should be captured under item 3.2.6 not 3.1.10.
Study close-out activity including preparation for audit	3.2.11	The time required to pack up and return trial-specific IT equipment that has been "loaned" to the site for the duration of the trial, should be captured under item 3.2.11 not 3.1.11.

Learnings from site visits

For industry sponsored trials, we found that any required IT equipment is supplied "on loan" by the sponsor. In the majority of trials this equipment was required to be returned to the sponsor at the completion of the trial with the sponsor paying for the transport of the equipment. Some sites reported that at the completion of the trial they were offered the opportunity to purchase the trial-specific IT equipment at a reduced price, or to keep it at no cost. At the majority of sites, any IT equipment supplied by an external source (e.g. pharmaceutical company/sponsor) was required to be tested and approved by site IT departments. In some cases, this required changing power connections to Australian compatible versions.

Derived process map for "IT set-up, equipment and maintenance"

Not applicable.

Considerations for deriving the cost for "IT set-up, equipment and maintenance"

We found no evidence that any clinical trial site incurred the direct cost for the hire or purchase of any trial specific IT equipment. The cost incurred by the sites in undertaking training related to the trial specific IT equipment (often the associated software) was factored in under item 3.1.9, and the costs incurred to maintain the trial specific IT equipment was factored into item 3.2.6.

In order to derive a standard cost associated with certifying any trial specific equipment, the professional time spent by the IT Department's computer scientist was chosen as the most suitable resource unit. The referenced unit cost for the computer scientist was item 2.6.4, as we assumed the computer scientist's qualifications and pay rates were directly comparable to medical scientists, so the fully absorbed unit cost was $75/hour.

Table of standard costs for "IT set-up, equipment and maintenance"

Table C.19 presents the resource units, in hours, required for each activity by specific personnel. The median was considered the best basis for determining the standard cost of $37.50 per item of trial-specific IT equipment that needed to be set up.

Table C.19: Typical personnel, resources and unit cost for IT set-up, equipment and maintenance

Activities	Personnel Involved	Resource Unit (hours per IT equipment item)					Unit cost	Standard costs (median)
		Min	25th percentile	Median	75th percentile	Max		
Computer scientist to set-up the IT equipment	Computer scientist	0.2	0.2	0.5	1.0	1.0	$75	$37.50
Total for IT set up, equipment and maintenance								**$37.50**

Reference number	3.1.12
Item	Trial centre set-up and development
Sub-list	Non-clinical services
Category	Project Development
Definition	Including the central (i.e. across all trial sites) set up and development of all clinical trial support materials including grants, budgets, Case Report Forms (CRFs), databases, randomisation procedures, statistical plan, quality assurance, etc.
Standard Cost	Not determined, as cost typically not incurred by trial sites

Related items

None.

Learnings from site visits

It is acknowledged that investigator-initiated and industry sponsored trials require significant time and multiple diverse activities for trial centre set up and development. But, the trial sites visited were typically not engaged in trial centre set up and development. Representatives of the trial sites advised that this work is typically not done by staff at the trial site, but it is done by the sponsor (some industry trials) or the sponsor's agent (most industry sponsored trials and collaborative trials). Some occasions of single investigator trials at single sites were found were the investigator acting in the role of trial sponsor (i.e. the trial is funded by a research grant that he/she obtained) hired staff on-site to undertake the trial centre set up and development work. This variation was rare, and most investigator initiated trials used trial collaborative organisations to do this work.

One site visited had a unit that has the capability to undertake trial centre set up and development work. This unit was not set up on a commercial basis, such as other trial centre data units (e.g. the NHMRC Clinical Trails Centres at the University of Sydney and the Centre for Biostatistics and Clinical Trials (BACT) that operates out of the Peter MacCallum Cancer Institute). The experience is that the depth of skill and expertise that is required for trial centre work is difficult to maintain at one trial site (no economies of scale) and consequently a shared services model operating on a commercial (Contracted Research Organisations) or semi commercial (NHMRC CTC and BACT) was the norm. At the visited site where there was in-house expertise, the process for putting the service onto a semi-commercial basis so that it was sustainable was a key focus of the discussions.

Based on this advice from trial sites, the CTAG report and the associated NHMRC list were revisited. The CTAG report states that "the purpose of the list is to reduce uncertainty around clinical trial costs in the public health system". Taking this intent into account, it was considered that the focus of the costing study should be on those costs incurred in the public health system (although consistent with other parts of the CTAG report, private hospitals were included in the fieldwork). Consistent with these principles, the study design did not provide for investigation of costs incurred outside the public health system (and private hospitals), and hence there is no real basis on which to determine a cost for trial centre set up and development.

Derived process map for "trial centre set-up and development"

Not possible.

Considerations for deriving the cost for "trial centre set-up and development"

In the course of the project, representatives of trial centres made contact with the study team and also made submissions to clarify whether the project was focussed on the costs necessarily and

typically incurred by a trial site to participate in a trial, or whether it included, more broadly, all costs incurred by a trial sponsor. It was pointed out that many sponsor costs (e.g. trial monitors, quality assurance audits) that are not in trial site budgets do not fit neatly into items on the NHMRC list (as it seems that this list was designed primarily to categorise costs incurred by trial sites).

On this basis, and given the study design did not include fieldwork that would enable analysis of all costs incurred by trial sponsors (including trial centre set up and development costs where the work is usually done by a contracted research organisation, a semi-commercial expert organisation operating out of a University or major hospital or a trial collaborative organisation), it was decided to not make any determination with respect to costs that are not typically incurred at a trial site. It is considered, particularly for industry sponsored trials, disclosure of information to enable analysis of such costs is unlikely for reasons of commercial confidentiality.

Table of standard costs for "trial centre set-up and development"

Table C.20 indicates that no relevant data were able to be obtained from sites, so no separate standard cost for trial centre set up and development, has been determined.

Table C.20: Typical resources and unit cost involved in trial centre set-up and development

Item	Basis	Resource unit					Unit cost	Standard cost
		Min	25th percentile	Median	75th percentile	Max		
Trial centre set up and development	No determination possible as cost typically not incurred by trial sites	N/A	N/A	N/A	N/A	N/A	N/A	N/A

The inclusion of this item in the list should be reviewed. If the intention is to capture or set reasonable costs to assist in the setting of budgets for sites involved in clinical trials, then the item is not required as trial sites are typically not involved in the set up or management of a trial centre. However, if it is intended to capture all costs associated with conducting a clinical trial including all sponsor costs (whether the sponsor is industry or not) then this item should be retained, and it is likely that other items will need to be added.

Reference number	3.2.1
Item	Start-up meeting
Sub-list	Non-clinical services
Category	Project Implementation
Definition	The meeting that occurs at the start of the clinical trial, where the sponsor representative attends the clinical trial site for a series of meetings with personnel to be involved in the trial.
Standard Cost	$1,815 per start-up meeting

Related items

Table C.21 presents other items which are related to item 3.2.1 "start-up meeting".

Table C.21: Items related to start-up meeting

Item	Reference Number	Comment
Staff training	3.1.9	Some staff training does occur at the site start up meeting. Any staff training that occurs on the day of the site start up meeting should be captured under item 3.2.1 and not 3.1.9.

Learnings from site visits

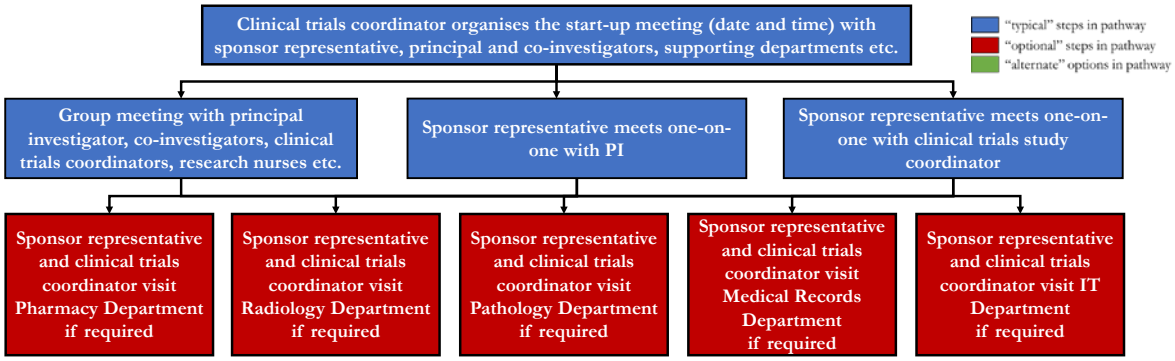
The majority of industry sponsored trials held start-up meetings with each site participating in the clinical trial. The start-up meeting usually involved the sponsor's representative being on site for up to a full day, with about half of the time spent solely with the relevant clinical trials coordinator, an hour one on one with the principal investigator, a one hour meeting (focus group style) with all staff who are interested or will be involved in the clinical trial (i.e. typically 8-10 clinicians attend, with about half of them being medical doctors and the remainder a mix of nurses and medical scientists). The remainder of the day is spent meeting with supporting departments (e.g. radiology, pathology, pharmacy, etc.) if they will be involved in the clinical trial (e.g. if a drug trial, the pharmacy will typically be visited).

Some sites stated that with investigator initiated trials, there was also a start-up meeting, however usually only one would be held in each state requiring the clinical trials coordinator and the principal investigator to travel to another site within the State/Territory. In contrast, other clinical trials units informed us that start up meetings are rarely held with investigator initiated trials. A site reported that for one collaborative trial, a start-up meeting by telephone was held.

Derived process map for "start-up meeting"

Figure C.7 presents the typical process involved in the site start-up meeting.

Figure C.7: Process map for the activities included under "start-up meeting"



Considerations for deriving the cost for "start-up meeting"

The number of personnel involved in the start-up meeting was fairly standard for each clinical trial (the main variation was in the focus group style meeting, where more clinicians would be involved for the larger trials, but the focus group would still typically run for one hour). The variability was mainly in the length of time the sponsor representative would be on site from one half to a full day. Using the estimates provided by site representatives, across the various trials examined, an estimate of each component of the start-up meeting activity involved was possible.

In order to derive a reasonable cost associated with the start-up meeting, time (in hours) was chosen as the best resource unit, for each of the staff types normally involved. The costing for the start-up meeting included the following personnel: the principal investigator (and co-investigators), the clinical trials coordinator/manager; up to four staff specialists/co-investigators; two research nurses and two medical scientists. The referenced unit cost for the principal investigator and co-investigators is the hourly rate determined in item 2.6.2; the reference cost for the clinical trials manager/coordinator is a combination of the hourly rate determined for items 2.6.3 Research Nurse (75% allocation) and 2.6.4 Clinical Research Coordinator (25% allocation); the reference cost for the research nurses is the hourly rate determined for items 2.6.3 Research Nurse; and the reference cost for the medical scientists is 2.6.4 Clinical Research Coordinator.

Table of standard costs for "start-up meeting"

Table C.22 presents the resource units, in hours, required for each activity by specific personnel. Due to the variability in the length of time of a usual start-up meeting, and the fact that up to nine staff, as well as the principal investigator and clinical trials coordinator, the 25th percentile was considered the best basis for setting the standard cost of $1,815 per start-up meeting.

Table C.22: Typical personnel, resources and unit cost involved in start-up meeting

Activities	Personnel Involved	Resource unit (hours)					Unit cost	Standard cost (25th percentile)
		Min	25th percentile	Median	75th percentile	Max		
Involvement in the start-up meeting	Clinical Trials Coordinator/Manager	2.0	4.0	6.0	7.5	9.0	$63.75	$255.00
	Principal Investigator	0.3	1.0	1.0	1.8	2.0	$215.00	$215.00
	Staff Specialists/Co-Investigators x 4	1.0	1.0	1.0	1.0	1.0	$215.00	$860.00
	Research Nurse x 2	1.0	1.0	1.0	1.0	1.0	$60.00	$120.00
	Medical Scientists x 2	1.0	1.0	1.0	1.0	1.0	$75.00	$150.00
	Supporting department personnel	0.5	1.0	1.5	2.0	3.0	$215.00	$215.00
Total for start-up meeting								**$1,815**

Potential trials sites and trial sponsors should use this cost as a guideline when setting a trial budget. There will be trials for which not as may staff are involved in the start-up meeting (because of the smaller scope of the trial), where a lower cost may be representative. There may also be trials for which a larger number of staff need to be involved in the start-up meeting, where a higher cost may be more reasonable.

Reference number	3.2.2
Item	Pre-screening activity
Sub-list	Non-clinical services
Category	Project Implementation
Definition	Involves the activities directly linked with clinical trial cohort identification which includes: • database and medical records review; • the development of recruitment plans including suggested strategies, timelines and costs; • the development and execution of consultation plan to support study recruitment as well as provide opportunities to increase awareness about clinical research and opportunities to participate; • interviewing potential participants which includes asking questions to address the specific inclusion/exclusion criteria for the study and other issues of suitability (either by telephone or face-to-face); and • documenting pre-screening trial activity (irrespective of eligibility).
Standard Cost	$4,003 per clinical trial

Related items

Table C.23 presents other items which are related to item 3.2.2 "pre-screening activity"

Table C.23: Items related to pre-screening activity

Item	Reference Number	Comment
Screening Visit and Health Assessment	1.1.1	At some sites there was overlap between pre-screening, recruitment and the clinical tests and procedures conducted as part of the screening/health assessment visit. Any clinical tests and procedures undertaken as part of screening (i.e. the "screening visit and health assessment") should be captured under 1.1.1. Time spent on the initial cohort identification of potential clinical trial participants should be captured under item 3.2.2. Time spent on screening activities that include and occur post obtaining informed consent should be captured under item 3.2.3.
Departmental Protocol Review	2.1.1	Some sites reported that screening of patient records was undertaken when reviewing the protocol to determine if they had eligible patients and/or the number of eligible patients. These activities should be captured under 2.1.1 and not 3.2.2.
Site selection including site feasibility assessment process	3.1.2	Some sites reported that screening of patient records was undertaken during the feasibility assessment process to determine if they had eligible patients and/or the number of eligible patients as sponsors required estimates of the number of patients the site could recruit. These activities are considered part of completing the feasibility questionnaire and should be captured under 3.1.2 and not 3.2.2.
Recruitment Activity	3.2.3	In some trials patients are required to attend the site for further pre-screening assessment which may involve the completion of questionnaires. These types of activities are still considered part of pre-screening and should be captured under item 3.2.2 and not 3.2.3.

Learnings from site visits

There was considerable trial-dependent variation in time required for pre-screening activity. In some trials, patients were recruited mainly from an existing relatively small patient group that was already attending the site regularly for treatment. In these instances, time to pre-screen was minimal, as principal investigators (and/or study coordinators/managers) were familiar with their patient cohort. In other instances, time for pre-screening was longer due to the need to review a large number of patient records and the fact that, often, there had been considerable time elapsed since the patients had last attended the clinic.

Trials recruiting for healthy volunteers required the longest time for pre-screening activities. As an example, trials requiring healthy volunteers included Phase I and immunisation/vaccination trials. These trials used multiple methods for recruiting patients from a broad base therefore requiring more time on pre-screening. Methods such as advertising on radio or newspaper generated high numbers of potential participants requiring pre-screening however a large proportion of the potential participants were ineligible. These types of recruitment methods (mainly implemented in trials requiring health volunteers) were also associated with increased costs for advertisements in newspapers and targeted mail outs (e.g. to the GP population).

Patients identified through existing medical records (and/or databases) were pre-screened through telephone contact. In this phone call assessment against exclusion and inclusion criteria was made for those items not requiring onsite assessment. The length of the pre-screening phone call varied, however irrespective of the length of the call, sites reported a significant amount of time in contact attempts and call backs whilst trying to reach potential participants to undertake the 'pre-screening' telephone call. In some trials, participants were required to attend the clinic for further pre-screening assessment which generally included the completion of a questionnaire. As consent was generally not yet obtained, most considered this activity as part of pre-screening.

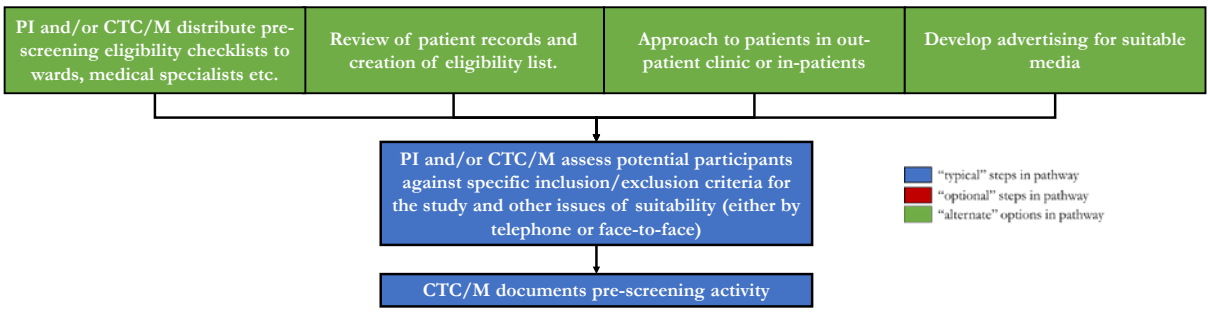
Some pre-screening was undertaken face-to-face when patients attended outpatient clinics or were admitted to hospital. The principal investigator would mainly be involved in pre-screening the potential participant against the selection criteria, however the clinical trials coordinator/nurse may have already identified the patient as a potential participant and left a flag attached to the patient's medical record to alert the doctor to discuss the clinical trial with them on their next visit.

In general there was a mix of experiences in terms of the time pre-screening activities took, as it was dependent on the phase of trial, the type of trial participant (i.e. healthy volunteer). Most clinical trials sites felt that pre-screening activities were not-costed well into trial budgets.

Derived process map for "pre-screening activity"

Figure C.8 presents the typical process involved in the pre-screening activity process.

Figure C.8: Process map for the activities included under "pre-screening activity"



Considerations for deriving the cost for "pre-screening activity"

The number of personnel involved in the pre-screening activities was fairly standard for each clinical trial. The variability was mainly due to the time spent on pre-screening activities which was largely dependent on the type and phase of the clinical trial. However using the estimates provided by site representatives, across the various trials examined, an estimate of both the principal investigator and clinical trials coordinator/manager time was possible.

In order to derive a reasonable cost associated with the pre-screening activities, time (in hours) was chosen as the best resource unit, for each of the typical staff involved. Hence costing for the pre-screening activities included time of the principal investigator and the clinical trials coordinator/manager. The referenced unit cost for the principal investigator is the hourly rate determined in item 2.6.2; and the reference unit cost for the clinical trials manager/coordinator is a combination of the hourly rate determined for items 2.6.3 Research Nurse (75% allocation) and 2.6.4 Clinical Research Coordinator (25% allocation).

Table of standard costs for "pre-screening activity"

Table C.24 presents the resource units, in hours, required for each activity by specific personnel. Due to the variability in the amount of time required for pre-screening activities (largely due to the phase and type of trial), the median was considered the best basis for setting the reasonable cost of $4,003 for pre-screening activities.

Table C.24: Typical personnel, resources and unit cost involved in pre-screening activity

Activities	Personnel Involved	Resource unit (hours)					Unit cost	Standard costs (median)
		Min	25th percentile	Median	75th percentile	Max		
Pre-screening activities	Clinical Trials Manager/Coordinator	1.5	18.8	37.5	67.5	337.5	$63.75	$2,390.63
	Principal Investigator	1.9	7.5	7.5	15.0	75.0	$215.00	$1,612.50
Total for pre-screening activity								**$4,003**

Reference number	3.2.3
Item	Recruitment activity
Sub-list	Non-clinical services
Category	Project Implementation
Definition	Includes all activities involving potential and recruited clinical trials participants between the completion of pre-screening and the final determination of the assessment for suitability. Such activities include the provision of education and information to possible clinical trial participants, the informed consent process, organising the screening visit (which includes any required assessments and/or tests), and documenting all the recruitment activity (irrespective of the number of potentially eligible participants that fail the screening assessment).
Standard Cost	$349 per potential clinical trial participant screened and assessed

Related items

Table C.25 presents other items which are related to item 3.2.3 "recruitment activity"

Table C.25: Items related to recruitment activity

Item	Reference Number	Comment
Screening Visit and Health Assessment	1.1.1	At some sites there was overlap between pre-screening, recruitment and the clinical tests and procedures conducted as part of the screening/health assessment visit. Any clinical tests and procedures undertaken as part of screening (i.e. the "screening visit and health assessment") should be captured under 1.1.1. Time spent on the initial cohort identification of potential clinical trial participants should be captured under item 3.2.2. Time spent on screening activities that include and occur post obtaining informed consent should be captured under item 3.2.3.
Departmental Protocol Review	2.1.1	Some sites reported that screening of patient records was undertaken when reviewing the protocol to determine if they had eligible patients and/or the number of eligible patients. These activities should be captured under 2.1.1 and not 3.2.3.
Site selection including site feasibility assessment process	3.1.2	Some sites reported that screening of patient records was undertaken during the feasibility assessment process to determine if they had eligible patients and/or the number of eligible patients as sponsors required estimates of the number of patients the site could recruit. These activities are considered part of completing the feasibility questionnaire and should be captured under 3.1.2 and not 3.2.3.
Pre-screening activity	3.2.2	The line between pre-screening and recruitment is blurred. However for the purposes of trying to achieve mutual exclusivity between 3.2.2 and 3.2.3, activities that occur before the process of gaining informed consent (which includes a consultation with the PI and/or CTC/M prior to informed consent being obtained) should be captured under item 3.2.2.

Learnings from site visits

In general, recruitment activities were undertaken by a variety of staff including the principal investigator, the study coordinator/manager and/or other medical staff specialists (i.e. colleagues of the principal investigator) who were aware or involved in the clinical trial (i.e. co or sub-investigators). In general, the initial approach regarding the trial was made to a potential participant by a principal investigator (PI) or the clinical trial coordinator/manager (CTC/M) and generally involved a consultation with both or either, post the initial pre-screening activity had occurred (i.e. item 3.2.2).

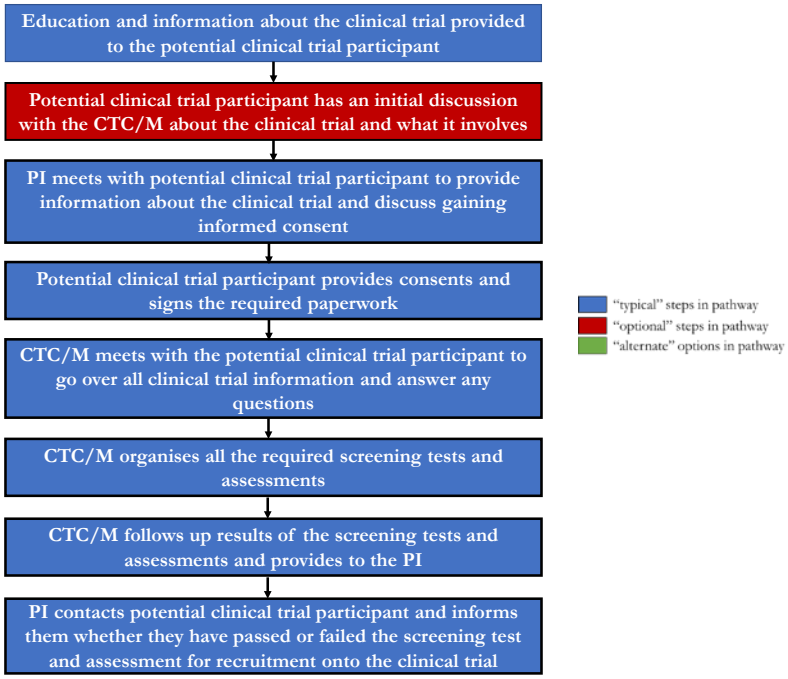
Across all trials, obtaining informed consent was undertaken by the PI and generally involved a 30 minute to 1.5 hour conversation with the patient (i.e. was very dependent on the complexity of the trial, the phase of trial, and diagnosis cohort). Most times gaining informed consent took two consultations, allowing the patient at least 24 hours to take away the information regarding the clinical trial to consider. For trials in paediatric populations, consent was given via the parents or guardians, those aged 13-18 were able to give 'assent' however full consent was required to be obtained if the subject turned 18 years of age during the trial. Investigators undertaking trials in paediatric populations reported that screening took twice or three times as long as with adults due to additional time required to explain the trial and its implications to parents/guardians and also undertaking screening assessments, tests and procedures took longer in children.

Once informed consent was obtained, the CTC/M would generally spend time with the potential clinical trial participant to further explain the clinical trial, and the process of screening. Once the potential clinical trial participant was satisfied all their questions had been answered, the CTC/M would organise all the screening tests and assessments. The time required to organise the screening tests and a subsequent visit (i.e. to obtain the results) varied depending on the number of tests and assessments required and whether all tests and/or assessment could be undertaken at the one site. Once all the tests and assessments were completed (which are covered under item 1.1.1), the CTC/M would follow up the results, provide to the PI, and the PI would then contact the potential clinical trial participant to inform them of the outcome of the screening tests.

Derived process map for "recruitment activity"

Figure C.9 presents the typical process involved in the recruitment activity process.

Figure C.9: Process map for the activities included under "recruitment activity"



Considerations for deriving the cost for "recruitment activity"

The number of personnel involved in the recruitment activities was fairly standard for each clinical trial. The variability was mainly due to the time spent by each personnel with each

potential clinical trial participant which was largely dependent on the type and phase of the clinical trial and the population cohort (i.e. paediatric clinical trials required more recruitment activity time compared to most adult clinical trials, unless they were healthy volunteer trials). However using the estimates provided by site representatives, across the various trials examined, an estimate of both the PI and CTC/M time was possible.

It is important to note that the activities included under "recruitment" (item 3.2.3) relate only to the time (in hours) dedicated by the PI and CTC/M in explaining the clinical trial, gaining informed consent and organising the tests and procedures and providing the potential clinical trial participant with the results. The reasonable cost does not include the costs of any clinical tests and procedures (as these are covered under items in sub-list 1).

In order to derive a reasonable cost associated with the recruitment activities, time (in hours) was chosen as the best resource unit, for each of the typical staff involved. Hence costing for the recruitment activities included time of the PI and the CTC/M. The referenced unit cost for the principal investigator is the hourly rate determined in item 2.6.2; and the reference cost for the clinical trials manager/coordinator is a combination of the hourly rate determined for items 2.6.3 Research Nurse (75% allocation) and 2.6.4 Clinical Research Coordinator (25% allocation).

Table of standard costs for "recruitment activity"

Table C.26 presents the resource units, in hours, required for each activity by specific personnel. Due to the over-representation of paediatric trials in the study sites, the 25th percentile was considered the best basis for setting the standard cost of $349 for each recruitment activity per potential clinical trial participant (it is acknowledges that the cost for paediatric trials will typically be higher, a fact that should be taken into account in negotiations between trial sites and sponsors.

Table C.26: Typical personnel, resources and unit cost involved in recruitment activity

Activities	Personnel Involved	Resource unit (hours)					Unit cost	Standard costs (25th percentile)
		Min	25th percentile	Median	75th percentile	Max		
Recruitment activities	Clinical Trials Manager/Coordinator	0.5	2.1	3.5	5.1	20.0	$63.75	$133.88
	Principal Investigator	0.3	1.0	1.3	1.8	3.0	$215.00	$215.00
Total for recruitment activity per potential clinical trial participant								**$349**

In practice, it was found that a number of trial sponsors put a cap on the number of 'screen-fails' that they would fund, as a proportion of the number of participants recruited ('screen successes'). This is not a cost issue, so no comment is offered in terms of standard cost, expect to say that the costs are incurred irrespective of whether the patient is eventually recruited to the trial or not (the effectiveness of pre-screening activities that lead to patients being more or less likely to meet the trial criteria on detailed screening and assessment is a separate matter).

Reference number	3.2.4
Item	Medical records set-up, access and storage
Sub-list	Non-clinical services
Category	Project Implementation
Definition	Includes the work undertaken by the medical records departments to access the medical record, for the purposes of the clinical trial only, and provide to the clinical trial host unit for clinical trial monitoring requirements.
Standard Cost	$10 per medical record accessed (for clinical trial visits only i.e. excluding standard of care visits)

Related items

Table C.27 presents other items which are related to item 3.2.4 "medical records set-up, access and storage"

Table C.27: Items related to medical records set-up and storage

Item	Reference Number	Comment
Departmental Establishment/Set up Fees	2.2.1	Some sites cover the establishment of the medical and/or clinical trial record, as well as accessing and storing the medical record under item 2.2.1 "Departmental Establishment/Set up Fees". To prevent double counting it is suggested that the setup of the medical and/or clinical trial record is covered under the establishment fee/set up fee under item 2.2.1.
Ongoing administration, monitoring and reporting	3.2.6	The time taken for the clinical trials unit to make a request that the medical records department retrieve the medical record, should be covered under the ongoing administration, monitoring and reporting item i.e. 3.2.6 and not under item 3.2.4.
Archiving of trial records	3.2.12	The long term storage of the clinical trial record (i.e. archiving) post study close out should be covered under item 3.2.12 and not item 3.2.4.

In order to reflect the derived definition of this item number, it is suggested that the item be re-titled "medical records access and storage".

Learnings from site visits

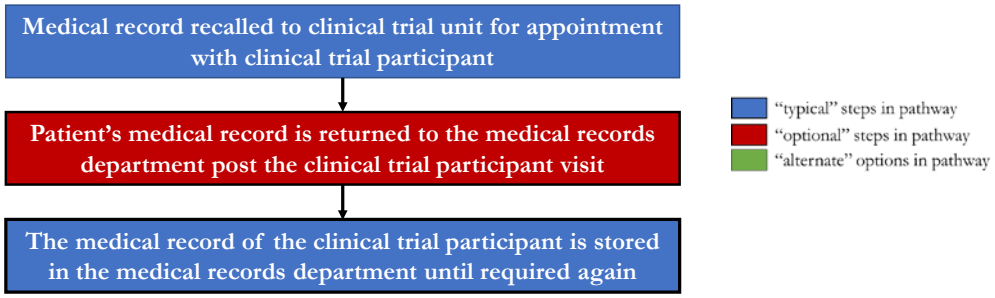
Most clinical trials units create a clinical trial medical record which is separate to the medical record held by the hospital (note that the cost of creating such records should be covered under the Departmental Establishment/Set up Fee (see item 2.2.1)). However in order for the clinical trial participants medical record to be kept up to date, every time a clinical trial participant attends for a clinical trial appointment, the medical record will need to be retrieved by the medical records department so that the notes can be updated to reflect the clinical trial visit. We found that some medical records departments are now charging clinical trials units a fee that varies from about $200 per trial per year to $10-$30/medical record, for medical records accessed for the sole purpose of a clinical trial, where there was an industry sponsor involved.

Some of the private hospital clinical trials units commented that accessing the medical record was a little more complex due to the billing systems (i.e. clinical trials participants were not billed (or their private health insurer) for clinical trial visits, however for standard of care visits, time needed to be taken to ensure the appropriate bill was sent). This was not so much of an issue for the public hospitals involved in clinical trials. However there were a few clinical trials units that were quite proactive in tracking which visits were standard of care and which were part of the clinical trial, so the appropriate documentation could be made and the bill sent to the sponsor.

Derived process map for "medical records set-up, access and storage"

Figure C.10 presents the typical process involved in medical records access and storage process.

Figure C.10: Process map for the activities included under "medical records set-up, access and storage"



Considerations for deriving the cost

There are several components to the setup, access and storage of a medical record during a clinical trial. Due to the structure of the clinical trials activity list, we have excluded from the reasonable cost the following:

- the establishment of the medical and/or clinical trial record (this should be covered under item 2.2.1 "Departmental Establishment/Set up Fees);
- the time taken for the clinical trials unit to make a request to the medical records department to retrieve the medical record of a clinical trial participant (this should be covered under item 3.2.6 "ongoing administration, monitoring and reporting").
- the long term storage of the clinical trial record (i.e. archiving) post study close (this should be covered under item 3.2.12).

The only cost left with this item is reflected by the fee being charged by some medical records department to access medical records of clinical trials participants. As this item is considered a fees item Table C.28 represents the fees charged by the sites rather than the cost associated with activities captured under item 3.2.4.

Table of standard costs for "medical records access and storage"

Table C.28 presents the fee range charged by various clinical trials sites around Australia. Due to the variation in fees, and the fact that only four sites visited had a fee associated with medical records retrieval for the purposes of a clinical trial, the 25th percentile was assessed to be the most reasonable basis for setting the standard cost, which is actually a fee of $10/medical record.

Table C.28: Typical fees associated with medical records access and storage

Activities	Basis	Resource unit (fee)					Unit cost	Standard cost (25th percentile)
		Min	25th percentile	Median	75th percentile	Max		
Medical records retrieval and storage fee	Typical fees	$0	$10	$20	$20	$25	n/a	$10

Reference number	3.2.5
Item	Interpreter services
Sub-list	Non-clinical services
Category	Project Implementation
Definition	Includes the fees associated with using interpreter services for the purposes of the clinical trial.
Standard Cost	$52 per hour

Related items

None.

Learnings from site visits

Only very few instances of the use of interpreters in clinical trials were reported at the site visits. Most trial site representatives reported that interpreter services were generally not needed. Where interpreter services were used, some sites used contracted interpreter services whereas other sites interpreters (for at least the most common languages) available on site. Those sites that used contracted interpreter services were no able to provide advice on the typical fees paid.

Derived process map for "interpreter services"

Not applicable.

Considerations for deriving the cost of "interpreter services"

Notwithstanding the fact that they are rarely used, there are circumstances in which interpreters are required for the purposes of a clinical trial. For the purpose of determining the standard cost, we chose to take an employed staff approach (a prevailing charge approach could also be taken). As a representative point, we took the rates of pay for employees in the NSW health system covered by the Health Employee's Interpreters State Award that apply from 1st July, 2012.

Consistent with the full-absorbed costing principle, it was important to identify a suitable source of salary on-costs and institutional overheads to apply to the direct salary cost presented in Table B.35. For this purpose a simple model of a human services organisation was adopted which proposed that direct salary costs make up 60% of expenditure, salary on-costs make up 15% of expenditure and institutional overheads make up the other 25%. There is ample evidence to support the fact that salary on costs (paid leave, public holidays, superannuation, payroll tax, etc.) are typically around 15/60 = 25% of direct salary.

The proposition that institutional overheads are around 25/75 = 33% of salary costs has a weaker evidence base. It is clear that a series of costs will need to be incurred to make a person in an organisation productive (office space, furniture, equipment, internet and library resources, administrative support, light, power, insurances, etc.). Without incurring these costs, the employed person could not effectively discharge the role they occupy. It is acknowledged that these costs are very organisation dependent, but they are normally quoted in a range of 25% to 40% of salary costs. On this basis 33% of direct plus indirect salary costs is considered to be reasonable.

So using the NSW Health Employee's Interpreters State Award, we found that there are four levels of interpreter from Grade 1 through to Coordinators of Interpreter Services, with four to five pay points within each level. Given the relative complexity and sensitivity of the material that may need to be translated for clinical trial participants, we have used the pay rates for Interpreters Grade 3 to set the standard cost. For each point in the pay scale, we calculated the

hourly rate (based on 37.5 hours per week) which worked out to be in the range of around $29 to $32 per hour. Applying the ratios needed to convert to fully absorbed costs, Table C.29 shows that the estimated cost per hour ranges from around $49 to $53.

Table C.29: Pay scales in NSW Health Employee's Interpreters State Award for Interpreter Grade 3

Interpreter Grade 3	Annual Salary	Weekly Salary	Hourly rate	Salary Oncost	Institutional Overhead	Fully Absorbed Hourly Rate
First year	$56,938	$1,094.96	$29.20	$7.30	$12.17	$48.66
Second year	$58,409	$1,123.25	$29.95	$7.49	$12.48	$49.92
Third year	$60,301	$1,159.63	$30.92	$7.73	$12.88	$51.54
Fourth year	$61,832	$1,189.08	$31.71	$7.93	$13.21	$52.85

Source: http://www0.health.nsw.gov.au/policies/ib/2012/pdf/IB2012_023.pdf

Table of standard costs for "interpreter services"

Without any further information, the choice of an hourly rate for a Grade 3 Interpreter at third year level is considered reasonable. On this basis the standard cost is set at $52 per hour, as shown in Table C.30.

Table C.30: Determination of standard cost for interpreter services

Item	Basis	Resource unit (hourly rates)					Unit cost	Standard cost
		Min	25th percentile	Median	75th percentile	Max		
Interpreter services	Fully absorbed hourly rate	N/A	N/A	N/A	N/A	N/A	$52	$52

Reference number	3.2.6
Item	Ongoing administration, monitoring and reporting
Sub-list	Non-clinical services
Category	Project Implementation
Definition	**Ongoing administration** activities include administration tasks that occur post the establishment phase and includes managing clinical trial documentation, retrieving medical and/or clinical records, invoicing, preparing materials for monitoring visit, VPN access etc.; **Ongoing monitoring** activities include liaison with investigators and/or sponsor (including the monitors), CRF completion, data entry, endpoint recording, involvement in monitor visits, review of SAE reports, etc.; and **Ongoing reporting** activities include: accrual reporting, safety and adverse event reporting, annual reporting, annual ethics report, etc.
Standard Cost	$470 per participant per annum

Related items

Table C.31 presents other items which are related to item 3.2.6 "ongoing administration, monitoring and reporting"

Table C.31: Items related to ongoing administration, monitoring and reporting

Item	Reference Number	Comment
Departmental Establishment/Set up Fees	2.2.1	Some sites capture the first year's administration work under item 2.2.1. If an establishment fee is charged, then the ongoing administration, monitoring and reporting fee should not be charged until year two (or be significantly reduced to remove the administration aspect of item 3.2.6).
Departmental ongoing administration fees	2.3.1	The fee captured under item 2.3.1 is similar to the fee listed in item 3.2.6, except that item 3.2.6 includes ongoing monitoring and reporting. Care should be taken not to double count administration activities.

Learnings from site visits

There was variation in regards to whether sites charged an ongoing administration, monitoring and reporting fee or whether it was included and/or covered by their Departmental Establishment/Set up Fees and/or Departmental ongoing administration fees. In fact, the number of items dedicated to administration was confusing to most sites consulted. However, most sites reported that there is extensive administration work that occurs at the beginning of the trial and then there is ongoing administration, monitoring and reporting that is variable depending on the number of clinical trial participants, the sponsor, the phase of the trial, and the complexity of the trial. Most sites were able to report on average the time they spent per patient for activities per year that they considered should be included under ongoing administration, monitoring and reporting.

Derived process map for "ongoing administration, monitoring and reporting"

Figure C.11 presents the typical process involved in ongoing administration, monitoring and reporting.

Figure C.11: Process map for the activities included under "ongoing administration, monitoring and reporting"

Considerations for deriving the cost

In order to derive a reasonable cost associated with ongoing administration, monitoring and reporting, professional time by staff type was chosen as the most suitable resource unit. The personnel involved was common across majority of sites visited and typically involved the clinical trials coordinator/manager with some input from the principal investigator. The activities involved in ongoing administration, monitoring and reporting are driven on a per participant per annum basis. The referenced unit cost for the principal investigator is the hourly rate determined in item 2.6.2; and the reference cost for the clinical trials manager/coordinator is a combination of the hourly rate determined for items 2.6.3 Research Nurse (75% allocation) and 2.6.4 Clinical Research Coordinator (25% allocation).

Table of standard costs for "ongoing administration, monitoring and reporting"

Table C.32 presents the resource units, in hours, required for each activity by specific personnel. Due to the variability in the amount of time estimated per participant per annum for ongoing administration, monitoring and reporting and the observed overlap (i.e. double counting) between this item and related items on the list (i.e. items 2.2.1 and 2.3.1), the 25th percentile was considered the best basis for setting the reasonable cost of $470 per participant per annum for ongoing administration, monitoring and reporting activities.

Table C.32: Typical personnel, resources and unit cost associated with ongoing administration, monitoring and reporting

Activities	personnel	Resource unit (hours)					Unit cost	Standard cost (25th percentile)
		Min	25th percentile	Median	75th percentile	Max		
Ongoing administration, monitoring and reporting	Clinical Trials Manager /Coordinator	1.0	4.0	8.0	12.0	24.0	$63.75	$255.00
	Principal Investigator	1.0	1.0	1.0	1.0	16.0	$215.00	$215.00
Total (per participant per annum)								**$470**

It is suggested that any review of the NHMRC list that may be commissioned specifically consider whether it is necessary to continue to have both items 2.3.1 and 3.2.6. There may be an opportunity to consolidate these items and hence reduce the difficulties associated with interpreting them due to the high potential for overlap.

Reference number	3.2.7
Item	Data analysis (+/- study report)
Sub-list	Non-clinical services
Category	Project Implementation
Definition	Includes the time spent in undertaking the clinical trial data analysis and/or producing the study report.
Standard Cost	Not determined, as cost typically not incurred by trial sites

Related items

Table C.33 presents other items which are related to item 3.2.7 "data analysis (+/- study report)".

Table C.33: Items related to pre-screening activity

Item	Reference Number	Comment
Ongoing administration, monitoring and reporting	3.2.6	Data reporting that is done by the trial site to the sponsor (e.g. accrual reporting, CRF completion, data entry, serious adverse event reporting, etc.) should be captured under item 3.2.6, not 3.2.7.

Learnings from site visits

It is acknowledged that investigator-initiated and industry sponsored trials require significant time for data analysis and the preparation of the study report. But, none of the trial sites visited was engaged in data analysis (simply data reporting) or preparation of the study report. Representatives of the trial sites advised that this work is typically not done by staff at the trial site, but it is done by the sponsor (some industry trials) or the sponsor's agent (most industry sponsored trials and collaborative trials). Some occasions of single investigator trials at single sites were found where the investigator acting in the role of trial sponsor (i.e. the trial is funded by a research grant that he/she obtained) hired (or utilised) staff on-site (or at the university where they held a joint appointment) to do the data analysis and assist with the study report and/or publications. This variation was common to NHMRC sponsored clinical trials, however the time and personnel involved in this process varied considerably. For most collaborative-investigator initiated trials, a collaborative organisation would do this work.

One site visited had a unit that has the capability to undertake data analysis and prepare the study report. This unit was not set up on a commercial basis, such as other trial centre data units (e.g. the NHMRC Clinical Trails Centres at the University of Sydney and the Centre for Biostatistics and Clinical Trials (BaCT) that operates out of the Peter MacCallum Cancer Institute). The experience is that the depth of skill and expertise that is required for trial centre work is difficult to maintain at one trial site (no economies of scale) and consequently a shared services model operating on a commercial (Contracted Research Organisations) or semi commercial (NHMRC CTC and BaCT) was the norm. At the visited site where there was in-house expertise, the process for putting the service onto a semi-commercial basis so that it was sustainable was a key focus of the discussions.

Based on this advice from trial sites, the CTAG report and the associated NHMRC list were revisited. The CTAG report states that "the purpose of the list is to reduce uncertainty around clinical trial costs in the public health system". Taking this intent into account, it was considered that the focus of the costing study should be on those costs incurred in the public health system (although consistent with other parts of the CTAG report, private hospitals were included in the

fieldwork). Consistent with these principles, the study design did not provide for investigation of costs incurred outside the public health system (and private hospitals), and hence there is no real basis on which to determine a cost for data analysis and preparation of the study report.

Derived process map for "data analysis (+/- study report)"

Not possible.

Considerations for deriving the cost for "data analysis (+/- study report)"

In the course of the project, representatives of trial centres made contact with the study team and also made submissions to clarify whether the project was focussed on the costs necessarily and typically incurred by a trial site to participate in a trial, or whether it included, more broadly, all costs incurred by a trial sponsor. It was pointed out that many sponsor costs (e.g. trial monitors, quality assurance audits) that are not in trial site budgets do not fit neatly into items on the NHMRC list (as it seems that this list was designed primarily to categorise costs incurred by trial sites).

On this basis, and given the study design did not include fieldwork that would enable analysis of all costs incurred by trial sponsors (including data analysis +/- study report costs where the work is usually done by a contracted research organisation, a semi-commercial expert organisation operating out of a University or major hospital or a trial collaborative organisation), it was decided to not make any determination with respect to costs that are not typically incurred at a trial site. It is considered, particularly for industry sponsored trials, disclosure of information to enable analysis of such costs is unlikely for reasons of commercial confidentiality.

Table of standard costs for "data analysis (+/- study report)"

Table C.34 indicates that no relevant data were able to be obtained from sites, so no separate standard cost for data analysis (+/- study report) has been determined.

Table C.34: Typical resources and unit cost involved in data analysis (+/- study report)

Item	Basis	Resource unit					Unit cost	Standard cost
		Min	25th percentile	Median	75th percentile	Max		
Data analysis (+/- study report)	No determination possible as cost typically not incurred by trial sites	N/A	N/A	N/A	N/A	N/A	N/A	N/A

The inclusion of this item in the list should be reviewed. If the intention is to capture or set reasonable costs to assist in the setting of budgets for sites involved in clinical trials, then the item is not required as trial sites are typically not involved in data analysis and/or preparation of the study report. However, if it is intended to capture all costs associated with conducting a clinical trial including all sponsor costs (whether the sponsor is industry or not) then this item should be retained, and it is likely that other items will need to be added.

Reference number	3.2.8
Item	Trial centre data management, data analysis and ongoing administration, monitoring and reporting
Sub-list	Non-clinical services
Category	Project Implementation
Definition	Includes the CRF design, CRF annotation, database designing, data-entry, data validation, discrepancy management, medical coding, data extraction, and database locking in compliance with regulatory standards. It also includes the continual monitoring and reporting of the data in the trial centre database.
Standard Cost	Not determined, as cost typically not incurred by trial sites

Related items

Table C.35 presents other items which are related to item 3.2.7 "Trial centre data management, data analysis and ongoing administration, monitoring and reporting".

Table C.35: Items related to pre-screening activity

Item	Reference Number	Comment
Ongoing administration, monitoring and reporting	3.2.6	Data reporting that is done by the trial site to the sponsor (e.g. accrual reporting, CRF completion, data entry, serious adverse event reporting, etc.) should be captured under item 3.2.6, not 3.2.8.

Learnings from site visits

It is acknowledged that investigator-initiated and industry sponsored trials require significant time for trial centre data management, data analysis and ongoing administration, monitoring and reporting. But, the trial sites visited were typically not engaged in the activities covered by trial centre data management. Representatives of the trial sites advised that this work is typically not done by staff at the trial site, but it is done by the sponsor (some industry trials) or the sponsor's agent (most industry sponsored trials and collaborative trials). Some occasions of single investigator trials at single sites were found were the investigator acting in the role of trial sponsor (i.e. the trial is funded by a research grant that he/she obtained) hired staff on-site to do the trial centre data management activities. This variation was rare, and most investigator initiated trials used trial collaborative organisations to do this work.

One site visited had a unit that has the capability to undertake the activities covered by trial centre data management. This unit was not set up on a commercial basis, such as other trial centre data units (e.g. the NHMRC Clinical Trails Centres at the University of Sydney and the Centre for Biostatistics and Clinical Trials (BaCT) that operates out of the Peter MacCallum Cancer Institute). The experience is that the depth of skill and expertise that is required for trial centre work is difficult to maintain at one trial site (no economies of scale) and consequently a shared services model operating on a commercial (Contracted Research Organisations) or semi commercial (NHMRC CTC and BaCT) was the norm. At the visited site where there was in-house expertise, the process for putting the service onto a semi-commercial basis so that it was sustainable was a key focus of the discussions.

Based on this advice from trial sites, the CTAG report and the associated NHMRC list were revisited. The CTAG report states that "the purpose of the list is to reduce uncertainty around clinical trial costs in the public health system". Taking this intent into account, it was considered that the focus of the costing study should be on those costs incurred in the public health system (although consistent with other parts of the CTAG report, private hospitals were included in the

fieldwork). Consistent with these principles, the study design did not provide for investigation of costs incurred outside the public health system (and private hospitals), and hence there is no real basis on which to determine a cost for the activities covered by trial centre data management.

Derived process map for "Trial centre data management, data analysis and ongoing administration, monitoring and reporting"

Not possible.

Considerations for deriving the cost for "Trial centre data management, data analysis and ongoing administration, monitoring and reporting"

In the course of the project, representatives of trial centres made contact with the study team and also made submissions to clarify whether the project was focussed on the costs necessarily and typically incurred by a trial site to participate in a trial, or whether it included, more broadly, all costs incurred by a trial sponsor. It was pointed out that many sponsor costs (e.g. trial monitors, quality assurance audits) that are not in trial site budgets do not fit neatly into items on the NHMRC list (as it seems that this list was designed primarily to categorise costs incurred by trial sites).

On this basis, and given the study design did not include fieldwork that would enable analysis of all costs incurred by trial sponsors (including trial centre data management, data analysis and ongoing administration, monitoring and reporting, where the work is usually done by a contracted research organisation, a semi-commercial expert organisation operating out of a University or major hospital or a trial collaborative organisation), it was decided to not make any determination with respect to costs that are not typically incurred at a trial site. It is considered, particularly for industry sponsored trials, disclosure of information to enable analysis of such costs is unlikely for reasons of commercial confidentiality.

Table of standard costs for "Trial centre data management, data analysis and ongoing administration, monitoring and reporting"

Table C.36 indicates that no relevant data were able to be obtained from sites, so no separate standard cost for trial centre data management, data analysis and ongoing administration, monitoring and reporting has been determined.

Table C.36: Typical resources and unit cost involved in trial centre data management, data analysis and ongoing administration, monitoring and reporting

Item	Basis	Resource unit					Unit cost	Standard cost
		Min	25th percentile	Median	75th percentile	Max		
Trial centre data management, data analysis and ongoing administration, monitoring and reporting	No determination possible as cost typically not incurred by trial sites	N/A	N/A	N/A	N/A	N/A	N/A	N/A

The inclusion of this item in the list should be reviewed. If the intention is to capture or set reasonable costs to assist in the setting of budgets for sites involved in clinical trials, then the item is not required as trial sites are typically not involved in the activities covered by trial centre data management. However, if it is intended to capture all costs associated with conducting a clinical trial including all sponsor costs (whether the sponsor is industry or not) then this item should be retained, and it is likely that other items will need to be added.

Reference number	3.2.9
Item	Amendment preparation and submission
Sub-list	Non-clinical services
Category	Project Implementation
Definition	Includes the preparation and submission of protocol amendments to the HREC and RGO including amendments to the PICFs, investigator brochures and any other trial information which has been updated/amended
Standard Cost	$343 per amendment (excluding fee charged by the RGO and/or HREC for review)

Related items

Table C.37 presents items related to item 3.2.9 "amendment preparation and submission"

Table C.37: Items related to amendment preparation and submission

Item	Reference Number	Comment
Amendment review	3.2.10	This item refers to the fee charged by sites per amendment whereas 3.2.9 refers to the time spent preparing and submitting clinical trial amendments to the HREC.

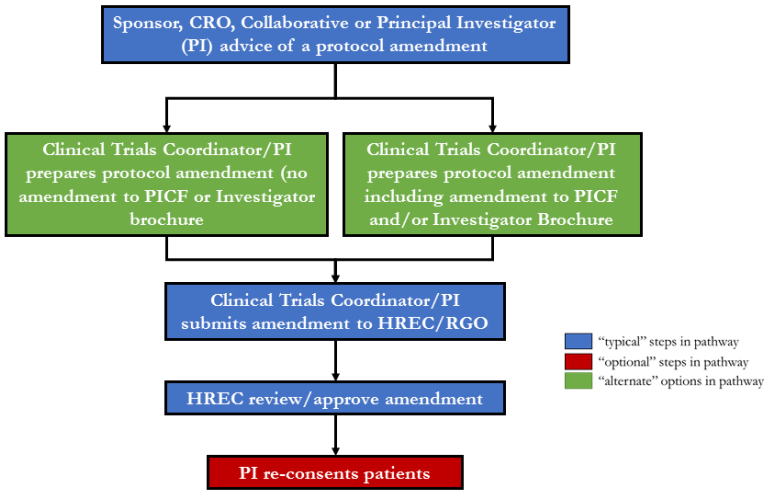
Learnings from site visits

The work required to deal with amendment to the trial protocols varies. A small change to the protocol i.e. minor wording change, might only require a short letter to the HREC identifying the update, which could take thirty minutes to prepare and submit. However, in many cases there are amendments which require significant updates to the protocol i.e. changing how something is done, or there are changes to the patient information consent form, or Investigator Brochure. In these cases it can take anywhere between one to two days to prepare and submit and an amendment to the HREC. The clinical trials coordinator / manager is generally tasked with preparing amendments which are sometimes reviewed and signed off by the principal investigator. For each amendment to the Patient Information Consent Form the patient has to be re-consented. Amendments to protocols occur multiple times during a clinical trial and some sites report completing four to five amendments to protocol before the trial has started.

Derived process map for "amendment preparation and submission"

Figure C.12 presents the typical process involved in amendment preparation and submission.

Figure C.12: Process map for the activities included under "amendment preparation and submission"



Considerations for deriving the cost for "amendment preparation and submission"

The amendment preparation and submission activities were generally undertaken by the principal investigator and/or the clinical trials coordinator/ manager across the sites visited. The variability in the resources required was mainly due to the size and complexity of the amendment. Major amendments such as changing the method of administering a drug take considerably more time to prepare compared to minor wording changes in the trial protocol. Using the estimates provided by site representatives, across the various trials examined, an estimate of both the typical principal investigator and clinical trials manager/coordinator typical time was possible.

In order to derive a standard cost associated with the amendment preparation and submission activities, time (in hours) was chosen as the best resource unit, for each of the staff types involved. Hence costing for the amendment preparation and submission activities included time of the principal investigator and the clinical trials coordinator/manager. The referenced unit cost for the principal investigator is the hourly rate determined in item 2.6.2; and the reference cost for the clinical trials manager/coordinator is a combination of the hourly rate determined for items 2.6.3 Research Nurse (75% allocation) and 2.6.4 Clinical Research Coordinator (25% allocation).

Table of standard costs for "amendment preparation and submission"

Table C.38 presents the resource units, in hours, required for each activity by specific personnel. Due to the fact that the time required for amendment preparation and submission reported at the site visits related largely to the more complex amendments, the 25th percentile was considered the best basis for setting the standard cost of $343 per amendment.

Table C.38: Typical personnel, resources and unit cost involved in amendment preparation and submission

Activities	Personnel	Resource unit (hours per amendment)					Unit cost	Standard cost (25th percentile)
		Min	25th percentile	Median	75th percentile	Max		
Preparation of an amendment to the protocol	Clinical Trials Manager/Coordinator	0.5	2.0	3.3	7.5	15.0	$63.75	$127.50
	Principal Investigator	1.0	1.0	1.1	1.2	1.5	$215.00	$215.00
Total for amendment preparation and submission (per amendment)								**$343**

Reference number	3.2.10
Item	Amendment review
Sub-list	Non-clinical services
Category	Project Implementation
Definition	This includes the fee charged by the RGO and/or HREC to review an amendment. The time spent by the clinical trials unit to prepare and submit the amendment to the RGO and/or HREC is included under item 3.2.9.
Standard Cost	$275 per amendment reviewed

Related items

Table C.39 presents other items which are related to item 3.2.10 "amendment review".

Table C.39: Items related to amendment preparation and submission

Item	Reference Number	Comment
Amendment preparation and submission	3.2.9	Item 3.2.10 focuses only on the fee charged for the HRCEC and RGO to consider the amendment, whereas item 3.2.9 captures the costs of preparing and submitting the amendment to the HREC and RGO.

It is our view that the item title should be retitled to "amendment review fee".

Learnings from site visits

Amendment review fees vary across sites, some sites do not charge and others charge an amount per amendment, which varies depending on the amendment requirements. The fee is usually divided between major amendments (i.e. amendment modifies PICF) and minor amendments (i.e. amendment does not modify PICF). If a major amendment to the trial protocol is required (e.g. change to drug administration), then the process of reviewing this amendment might require a submission to the full ethics committee whereas other smaller amendments might only require sign off from the Chair of the Ethics Committee. Fees are usually waived for investigator driven trials and collaborative Group trials. Trial sites are now more commonly charging for dealing with amendments for industry sponsored trials as they feel that there has been an increase in the number of amendments per trial due to the haste with which sponsors get trials into the field.

Derived process map for "amendment review"

Not applicable.

Considerations for deriving the cost for "amendment review"

As this item was a fees item, Table C.40 reports the range of fees charged by the visited sites, rather than the cost associated with the HREC or RGO considering the amendment (the cost of preparing the amendment is reflected in item 3.2.9). There was noticeable variability in the fee charged by the HREC and RGO, which was largely dependent on the sponsor of the clinical trial.

Table of standard costs for "amendment review"

Table C.40 presents the fee range charged by various clinical trials sites around Australia. Due to the variation in fees charged, the median was assessed to be the most reasonable basis for setting the standard cost, which is actually a fee of $275 per amendment.

Table C.40: Typical fees associated with the "amendment review"

Activities	Basis	Resource unit (fee)					Unit cost	Standard cost (median)
		Min	25th percentile	Median	75th percentile	Max		
Amendment review	Typical fee	$0	$100	$275	$550	$1,000	n/a	$275

Reference number	3.2.11
Item	Study close-out activity including preparation for audit
Sub-list	Non-clinical services
Category	Project Implementation
Definition	Includes the activities undertaken to confirm that each site's clinical trial obligations have been met and post study obligations are understood. The closeout activities include verifying that the study procedures have been completed, data is collected, and, if relevant, study intervention is returned to the responsible party or prepared for destruction. For example, if the clinical trial is a randomised, double-blind clinical trial, the close-out should include plans to unblind/unmask and debrief site staff and subjects upon trial completion. The boxing up of all trial material ready for archiving/storage is also included under this item.
Standard Cost	$693 for study close out per clinical trial

Related items

Table C.41 presents other items which are related to item 3.2.11 "study close out".

Table C.41: Items related to study close out

Item	Reference Number	Comment
Archiving of trial records	3.2.12	The hours to undertake archiving are included in item 3.2.11. The fees for archiving trial records is included under item 3.2.12

Learnings from site visits

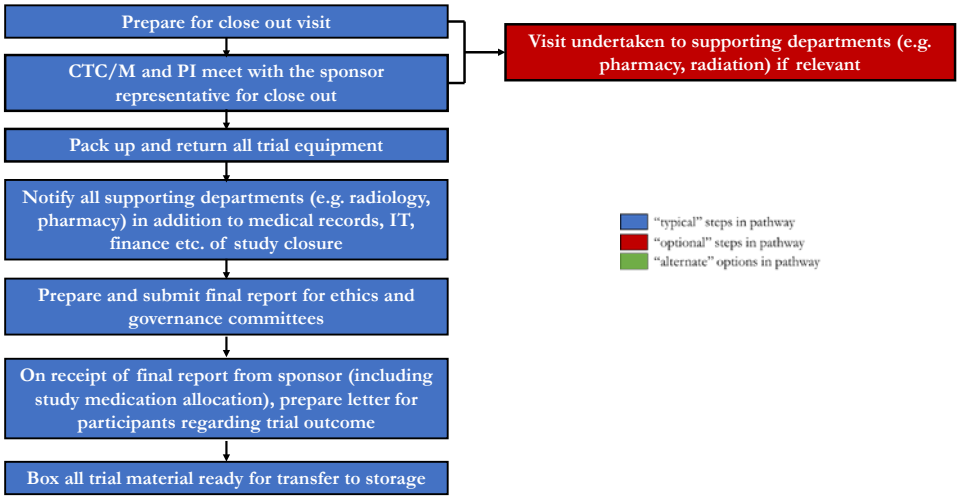
Close out activities include preparation for close-out by arranging the date for the final visit by the sponsor (or sponsor's agent) with the clinical trials coordinator, principal investigator, and representatives of any other relevant departments. Close out also includes completing all trial documentation, attending/participating in the close-out visit (generally 1-2 days), preparing trial records for archiving, repacking/returning all "on loan" or hired trial equipment, notification to medical records, IT and finance departments to close study accounts, as well as preparing and submitting final reports to ethics and governance, and the preparation and mailing of letter to participants regarding study outcome and study medication allocation during the blinded phase of the study (upon receipt of final study report).

Some of the visited trial sites incorporated a close out fee into budgets negotiated with sponsors, which ranged from $300 to $1,500. In some trials, pharmacy also had a close out fee included in the trial budget ranging from $300 to $450. At some sites, close out is incorporated into an administration fee/levy. Archiving costs are separate to these fees and are itemised in Item 3.2.12. If a full audit was undertaken at close-out, the time required was extended. It was generally found that Phase I trials reported the longest times for close out activities.

Derived process map for "study close out"

Figure C.13 presents the typical process involved in study close out.

Figure C.13: Process map for the activities included under "study close out"



Considerations for deriving the cost for "study close out"

In order to derive a reasonable cost associated with study close-out, professional time was chosen as the most suitable resource unit. The personnel involved was common across majority of sites and typically involved the clinical trials coordinator/manager with some input from the principal investigator. If supporting departments were also involved (e.g. pharmacy) then they would also have to participate in close out activities. Due to the involvement of the supporting departments being variable dependent on the type of trial (i.e. sometimes there were no other involved departments and other times there was more than one), it was decided to not include data for other departments in determining the cost for closeout (it was considered that any close out costs incurred by these departments should be covered by the department specific fees).

The referenced unit cost for the principal investigator is the hourly rate determined in item 2.6.2; and the reference cost for the clinical trials manager/coordinator is a combination of the hourly rate determined for items 2.6.3 Research Nurse (75% allocation) and 2.6.4 Clinical Research Coordinator (25% allocation).

Table of standard costs for "study close out"

Table C.42 presents the resource units, in hours, required for each activity by specific personnel. Due to the variability in the amount of time required for close-out activities, the median observation was considered to be the best basis for setting the standard cost of $693.

Table C.42: Typical personnel, resources and unit cost involved in study close out

Activities	Personnel	Resource unit (hours for study close out)					Unit cost	Standard cost (median)
		Min	25th percentile	Median	75th percentile	Max		
Study close-out activities	Clinical Trials Manager/Coordinator	4.0	7.5	7.5	23.0	45.0	$63.75	$478
	Principal Investigator	0.3	1.0	1.0	1.0	2.0	$215.00	$215
Total for study close out								**$693**

Reference number	3.2.12
Item	Archiving of trial records
Sub-list	Non-clinical services
Category	Project Implementation
Definition	Includes the storage fee charged for archiving of clinical trial related documents for up to the agreed number of years of storage.
Standard Cost	$750 per clinical trial

Related items

Table C.43 presents other items which are related to item 3.2.12 "archiving of trial records".

Table C.43: Items related to archiving of trial records

Item	Reference Number	Comment
Study close-out activity including preparation for audit	3.2.11	Activities associated with the preparation of trial records for archiving should be included under item 3.2.11 and not 3.2.12.

Learnings from site visits

All trial records must be archived at the completion of the study. For trials in adult populations trial records were required to be archived for 15 years. For trials in paediatric populations (<18 years) trial records were required to be kept for 25 years. At some sites, an additional fee associated with record retrieval post-archiving (e.g. $10 per record) was also included in a trial budget. The majority of sites, however, did not report a fee for retrieval of medical records post archiving. Trial records were typically archived offsite. Fees for archiving were either incorporated into the initial trial budget or were funded by the sponsor at the time of archiving as a separate cost.

Derived process map for "archiving of trial records"

Not applicable.

Considerations for deriving the cost for "archiving of trial records"

As this item was a fees item Table C.44 represents the fees charged by the sites rather than the cost associated with activities captured under item 3.2.12. There was some variability in the fee charged due to whether the sites were paediatric or adult.

Table of standard costs for "archiving of trial records"

Table C.44 presents the fee range reported by various clinical trials sites around Australia. Due to the fact that paediatric trials were over-represented in the site visited, the 25th percentile was assessed to be the most reasonable basis for setting the standard cost, which is actually a fee of $750 per clinical trial (it is acknowledged that the cost is likely to be higher for paediatric trials).

Table C.44: Typical fees associated with the "archiving of trial records"

Activities	Basis	Resource unit (fees)					Unit cost	Standard cost (25th percentile)
		Min	25th percentile	Median	75th percentile	Max		
Archiving of trial records fee	Typical fee	$500	$750	$1,500	$1,800	$2,000	n/a	$750

Reference number	3.3.1
Item	Participant payment
Sub-list	Non-clinical services
Category	Participant-related
Definition	Includes a payment made to clinical trial participants to join in the clinical trial. Such payments are generally described in the Clinical Trial Agreement and in the Patient Information and Consent Form (PICF) and may be paid in a lump sum at the beginning of the trial or the conclusion of the trial or in instalments at each visit.
Standard Cost	Not determined, any payments made at discretion of the trial sponsor

Related items

Table C.45 presents other items which are related to item 3.3.1 "participant payment"

Table C.45: Items related to participant payment

Item	Reference Number	Comment
Ongoing administration, monitoring and reporting	3.2.6	Any invoicing associated with participant payments should be captured under item 3.2.6 and not 3.3.1.

Learnings from site visits

In general, participants in clinical trials do not receive payments for joining in a clinical trial. The only exceptions identified through the hospital site visits was for some Phase 1 trials involving healthy volunteers. The payment for trial participation is not always necessarily cash (although sometimes it is) but could include vouchers for goods or services of various kinds. The incentive to participate is dependent on the trial target population (i.e. young adults generally get cash, whereas teenage participants get movie vouchers) and the funder of the clinical trial.

Many hospital sites reported that making participant payments adds administrative burden. Often, working with the finance department, clinical trials participants are paid for attendance and then the funder (e.g. industry) is billed per trial participant to keep the identity of the participant confidential from the funder.

Derived process map for "participant payment"

Not applicable.

Considerations for deriving the cost

No specific schedules were identified that could be used to establish a reasonable payment for participants in clinical trials. On the assumption that such payments are only applicable for Phase 1 trials, it is suggested that the payment be based on factors such as:

- whether the participant remains in isolation (i.e. a closed environment) and is therefore unable to continue with many normal duties;
- the extent of travel required;
- the time required to record any necessary study data; and
- the duration of the trial.

Based on discussions with participating hospitals (there were few involved in these types of trials), payments ranged from a nominal amount to cover travel and incidental expenses (see items 3.3.3 to 3.3.5) through to payments of $100 per attendance where the participant was healthy or was required to remain within a secure environment for observation.

Table of standard costs for "participant payment"

Table C.46 indicates that no standard cost has been determined for participant payment. This item is not considered to be cost based, it is discretionary to the trial sponsor, and it is argued that it is only appropriate to make payments to participants who are healthy volunteers (paying patients to obtain a particular type of treatment would not be ethical). The relevant cost to the trial site is the administration of the payment process, these costs should be determined as part of item 3.2.6.

Table C.46: Determination of standard cost for participant payment

Item	Basis	Resource unit					Unit cost	Standard cost
		Min	25th percentile	Median	75th percentile	Max		
Participant payment	Not determined	N/A	N/A	N/A	N/A	N/A	N/A	N/A

The need for this item should be reviewed (in fact the need for all participant payment related items should be reviewed). The only costs that are relevant to trial sites are the costs of administering the participant payment process. The amount of participant payments, where they are considered ethical, is discretionary, and should quite properly be determined by the trial sponsor.

In any review of the NHMRC list, it is suggested that consideration be given to replacing all of the participant payment items (3.3.1 to 3.3.8) with one item termed 'administration of participant payments'. A standard cost could then be determined for this item, based on an analysis of the payment processes. Pending such a review the cost associated with administering participant payments should be reflected in item 3.2.6 'ongoing administration, monitoring and reporting'.

Reference number	3.3.2
Item	Participant/carer time and inconvenience reimbursement
Sub-list	Non-clinical services
Category	Participant-related
Definition	Includes a payment, provided to a clinical trial participant, which is linked to the time involved in participating in the clinical trial and inconvenience created. Such payments are generally described in the Clinical Trial Agreement and in the Patient Information and Consent Form and may be paid in a lump sum at the beginning of the trial or the conclusion of the trial or in instalments at each visit.
Standard Cost	Not determined, any payments made at discretion of the trial sponsor

Related items

Table C.47 presents other items which are related to item 3.3.2 "participant/carer time and inconvenience reimbursement"

Table C.47: Items related to participant/carer time and inconvenience reimbursement

Item	Reference Number	Comment
Ongoing administration, monitoring and reporting	3.2.6	Any invoicing associated with participant/carer time and inconvenience reimbursement should be captured under item 3.2.6 and not 3.3.2.

Learnings from site visits

In general, participants in clinical trials and/or their carers are not reimbursed for any inconvenience caused by their joining in a clinical trial. Again, the only exception identified through the hospital site visits was for some Phase 1 trials involving healthy volunteers. The payment for trial participation is not always necessarily cash (although sometimes it is) but could include vouchers for goods or services of various kinds. The incentive to participate is dependent on the trial target population (i.e. young adults generally get cash, whereas teenage participants get movie vouchers) and the funder of the clinical trial.

Many hospital sites reported that making participant/carer payments adds administrative burden. Often, working with the finance department, clinical trials participants/carers are paid for attendance and then the funder (e.g. industry) is billed per trial participant/carer to keep the identity of the participant/carer confidential from the funder.

Derived process map for "participant/carer time and inconvenience reimbursement"

Not applicable.

Considerations for deriving the cost

No specific schedules were identified that could be used to establish a reasonable payment for participant/carer time and inconvenience caused by joining in clinical trials. On the assumption that such payments are only applicable for Phase 1 trials, it is suggested that the payment be based on factors such as:

- whether the participant remains in isolation (i.e. a closed environment) and is therefore unable to continue with many normal duties;
- the extent of travel required;
- the extent of carer support required during the trial period;
- the time required to record any necessary study data; and
- the duration of the trial.

No instances of payment for participant/carer time and inconvenience caused by joining in clinical trials were found in the site visits. Any payments made were probably more appropriately classified under item 3.3.1.

Table of standard costs for "participant/carer time and inconvenience reimbursement"

Table C.48 indicates that no standard cost has been determined for participant/carer time and inconvenience reimbursement. This item is not considered to be cost based, it is discretionary to the trial sponsor, and it is argued that it is only appropriate to make payments to participants who are healthy volunteers (paying patients to obtain a particular type of treatment (or their carers to facilitate that treatment) would not be ethical). The relevant cost to the trial site is the administration of the payment process, these costs should be determined as part of item 3.2.6.

Table C.48: Determination of standard cost for participant/carer time and inconvenience reimbursement

Item	Basis	Resource unit					Unit cost	Standard cost
		Min	25th percentile	Median	75th percentile	Max		
Participant/carer time and inconvenience reimbursement	Not determined	N/A	N/A	N/A	N/A	N/A	N/A	N/A

The need for this item should be reviewed (in fact the need for all participant payment related items should be reviewed). The only costs that are relevant to trial sites are the costs of administering the participant payment process. The amount of participant/carer time and inconvenience reimbursements, where they are considered ethical, is discretionary, and should quite properly be determined by the trial sponsor.

In any review of the NHMRC list, it is suggested that consideration be given to replacing all of the participant payment items (3.3.1 to 3.3.8) with one item termed 'administration of participant payments'. A standard cost could then be determined for this item, based on an analysis of the payment processes. Pending such a review the cost associated with administering participant/carer time and inconvenience reimbursement should be reflected in item 3.2.6 'ongoing administration, monitoring and reporting'.

Reference number	3.3.3
Item	Participant/carer travel
Sub-list	Non-clinical services
Category	Participant-related
Definition	Includes participant/carer out-of-pocket travel costs as described in the Clinical Trial Agreement and in the Patient Information and Consent Form.
Standard Cost	Not determined, any payments made at discretion of the trial sponsor

Related items

Table C.49 presents other items which are related (i.e. not necessarily mutually exclusive from) to item 3.3.3 "participant/carer travel".

Table C.49: Items related to participant/carer travel

Item	Reference Number	Comment
Ongoing administration, monitoring and reporting	3.2.6	Any invoicing associated with participant/carer travel reimbursements should be captured under 3.2.6 and not 3.3.3.
Participant/carer parking	3.3.4	Sites often include the participant/carer parking allowance under participant/carer travel. Care should be taken to not double count.
Participant/carer meals	3.3.5	Sites often include the participant/carer meals allowance under participant/carer travel. Care should be taken to not double count.

Learnings from site visits

Most clinical trial sites include some allowance for participant travel expenses in the trial budget. The amount allowed varies by site, but is largely determined on a per participant per visit basis. The allowance may cover travel expenses such as petrol, taxi (usually in the form of vouchers) and public transport costs. If participants recruited to the clinical trial are from regional/rural areas where flights are required to access services, most sites individually negotiate with the trial sponsor to cover these travel expenses.

Although travel expenses are often included in the budget of clinical trials, they are not always paid to each participant per visit. Expenses are generally paid on a participant request basis and receipts are required, often bulked up and paid monthly or quarterly. Most sites stated that some participants do not require the allowed amount (e.g. they live in walking distance or use public transport) whereas others exceed the allowed amount (e.g. those living considerable distances away and/or those that use taxis).

Many hospital sites reported that making participant payments adds administrative burden. Often, working with the finance department, clinical trials participants are paid for attendance and then the funder (e.g. industry) is billed per trial participant to keep the identity of the participant confidential from the funder.

Derived process map for "participant/carer travel"

Not applicable.

Considerations for deriving the cost for "participant/carer travel"

Each of the potential participant (and carer as appropriate) travel related expense components were examined as follows:

- **Air travel.** Travel by air was generally separately negotiated with the sponsor in advance and paid for on a reimbursement basis. Where necessary (and agreed with the sponsor) the travel of a carer may also be reimbursed.
- **Taxi travel.** Travel by taxi was sometimes paid on a reimbursement basis after submission of receipts, and other times taxi vouchers were provided. The cost is highly variable.
- **Car travel.** Practices for reimbursing the reasonable costs of travel by private car were examined and there were two primary methods for establishing a base these costs. Each state/territory has established a travel assistance scheme (for isolated patients usually travelling more than 100 km to access a service) to assist people to attend health appointments. Travel is reimbursed on a kilometre basis in the range of $0.16 to $0.30 depending on the jurisdiction. An alternative source of standardised costs is the Australian Taxation Office kilometre rates, which relate to tax deductibility. For 2011/12 the ATO rates varied from $0.63 to $0.75 depending on engine size.
- **Accommodation.** In some instances trial participants are required to stay away from home overnight either for clinical reasons or due limitation on travel options. Under the state/territory travel assistance schemes, accommodation is subsidised on a daily basis within the range of $30 to $60 per night (depending on the jurisdiction). The ATO also set rates representing reasonable travel expenses, which relate to tax deductibility. These rates depend on the location (city) and for 2012/13 vary from $132 to $233 per night.

Table of standard costs for "participant/carer travel"

Table C.50 indicates that no standard cost has been determined for participant/carer travel. This item is not thought to be cost based (to the trial site), it is discretionary to the trial sponsor. The relevant cost to the trial site is the administration of the payment process, these costs should be included as part of item 3.2.6. Although a standard cost is not determined, Table C.50 provides some guidance on car travel and overnight accommodation allowances used in other contexts, to assist trial sites and sponsors to determine a reasonable budget for participant/carer travel.

Table C.50: Determination of standard cost for participant/carer travel

Item	Basis	Resource unit					Unit cost	Standard cost
		Min	25th percentile	Median	75th percentile	Max		
Air Travel	Reimbursement	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Taxi	Reimbursement	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Car Travel	Per kilometre	$0.16	$0.30	$0.63	$0.64	$0.75	N/A	N/A
Accommodation	Per night	$30	$35	$60	$132	$233	N/A	N/A

The need for this item should be reviewed (in fact the need for all participant payment related items should be reviewed). The only costs that are relevant to trial sites are the costs of administering the claims for participant/carer travel. The amount of paid to participants/carers, is discretionary, and should quite properly be determined by the trial sponsor.

In any review of the NHMRC list, it is suggested that consideration be given to replacing all of the participant payment items (3.3.1 to 3.3.8) with one item termed 'administration of participant payments'. A standard cost could then be determined for this item, based on an analysis of the payment processes. Pending such a review the cost associated with administering participant payments should be reflected in item 3.2.6 'ongoing administration, monitoring and reporting'.

Reference number	3.3.4
Item	Participant/carer parking
Sub-list	Non-clinical services
Category	Participant-related
Definition	Includes participant/carer out-of-pocket parking costs as described in the Clinical Trial Agreement and in the Patient Information and Consent Form.
Standard Cost	Not determined, any payments made at discretion of the trial sponsor

Related items

Table C.51 presents other items which are related (i.e. not necessarily mutually exclusive from) to item 3.3.4 "participant/carer parking".

Table C.51: Items related to participant/carer parking

Item	Reference Number	Comment
Ongoing administration, monitoring and reporting	3.2.6	Any invoicing associated with participant/carer travel reimbursements should be captured under 3.2.6 and not 3.3.4.
Participant/carer travel	3.3.3	Sites often include the participant/carer parking allowance under participant/carer travel. Care should be taken to not double count.

Learnings from site visits

A number of clinical trial sites include some allowance for participant parking expenses in the trial budget, under the heading 'participant/carer travel expenses' (i.e. there is not usually a separate line in the budget for travel as opposed to parking). The amount allowed varies by site, but is largely determined on a per participant per visit basis. The allowance for parking is usually equivalent to the onsite parking costs for either a half day or full day, depending on the expected length of the visit, as dictated by the trial specific protocol.

Although parking is often included in the budget of clinical trials, it is not always paid to each participant per visit. Parking expenses are generally paid on a participant request basis and receipts are required (or for on-site parking, the ticket issued by the machine is swapped for a pre-paid ticket). If paid on a receipt basis, then the site usually processes parking reimbursement monthly or quarterly. Most sites stated that some participants do not require the allowed amount; it depends on whether they drive and trial site location. Also, if clinical trials visits coincide with standard of care treatments, then parking reimbursement is not provided to the clinical trial participant.
Many hospital sites reported that making participant payments adds administrative burden. Often, working with the finance department, clinical trials participants are paid for attendance and then the funder (e.g. industry) is billed per trial participant to keep the identity of the participant confidential from the funder.

Derived process map for "participant/carer parking"

Not applicable.

Considerations for deriving the cost of "participant/carer parking"

Participants who are able to access the trial site using their own or their carer's car, will generally incur parking expenses. These expenses vary considerably based on the location of the hospital in a range from zero to as much as $20 to $30 per visit.

Table of standard costs for "participant/carer parking"

Table C.52 indicates that no standard cost has been determined for participant/carer parking. This item is not considered to be cost based (to the trial host site), it is discretionary to the trial sponsor. The relevant cost to the trial site is the administration of the payment process, these costs should be determined as part of item 3.2.6.

Table C.52: Determination of standard cost for participant/carer parking

Item	Basis	Resource unit					Unit cost	Standard cost
		Min	25th percentile	Median	75th percentile	Max		
Participant/carer parking	Reimbursement	N/A	N/A	N/A	N/A	N/A	N/A	N/A

The need for this item should be reviewed (in fact the need for all participant payment related items should be reviewed). The only costs that are relevant to trial sites are the costs of administering the claims for participant/carer parking. The amount paid to participants/carers, is discretionary, and should quite properly be determined by the trial sponsor.

In any review of the NHMRC list, it is suggested that consideration be given to replacing all of the participant payment items (3.3.1 to 3.3.8) with one item termed 'administration of participant payments'. A standard cost could then be determined for this item, based on an analysis of the payment processes. Pending such a review the cost associated with administering participant payments should be reflected in item 3.2.6 'ongoing administration, monitoring and reporting'.

Reference number	3.3.5
Item	Participant/carer meals
Sub-list	Non-clinical services
Category	Participant-related
Definition	Includes participant/carer out-of-pocket meal costs as described in the Clinical Trial Agreement and in the Patient Information and Consent Form.
Standard Cost	Not determined, any payments made at discretion of the trial sponsor

Related items

Table C.53 presents other items which are related (i.e. not necessarily mutually exclusive from) to item 3.3.5 "participant/carer meals".

Table C.53: Items related to participant/carer meals

Item	Reference Number	Comment
Ongoing administration, monitoring and reporting	3.2.6	Any invoicing associated with participant/carer travel reimbursements should be captured under 3.2.6 and not 3.3.5.
Participant/carer travel	3.3.3	Sites often include the participant/carer meals allowance under participant/carer travel. Care should be taken to not double count.

Learnings from site visits

A number of clinical trial sites include some allowance for participant/carer meals in the trial budget under the heading 'participant/carer travel expenses' (i.e. there is not usually a separate line in the budget for meals as opposed to travel). The amount allowed varies by site, but is largely determined on a per participant per visit basis. The allowance for meals is usually equivalent to the cost of a sandwich and a drink from the on-site café and is only provided if it is expected that participants/carers will be required on site for a full day or sometimes a half day when fasting is required. Sites usually provide meal vouchers rather than 'cash' to participants.

Derived process map for "participant/carer meals"

Not applicable

Considerations for deriving the cost of "participant/carer meals"

Where an allowance for participant/carer meals was provided, it was generally quite modest, with an indicative range being $10 to $20 per visit.

Table of standard costs for "participant/carer meals"

Table C.54 indicates that no standard cost has been determined for participant/carer meals. This item is not considered to be cost based (to the trial host site), it is discretionary to the trial sponsor. The relevant cost to the trial host site is the administration of the payment process, these costs should be determined as part of item 3.2.6.

Table C.54: Determination of standard cost for participant/carer meals

Item	Basis	Resource unit					Unit cost	Standard cost
		Min	25th percentile	Median	75th percentile	Max		
Participant/carer meals	Reimbursement	N/A	N/A	N/A	N/A	N/A	N/A	N/A

The need for this item should be reviewed (in fact the need for all participant payment related items should be reviewed). The only costs that are relevant to trial sites are the costs of administering the claims for participant/carer meals. The amount paid to participants/carers, is discretionary, and should quite properly be determined by the trial sponsor.

In any review of the NHMRC list, it is suggested that consideration be given to replacing all of the participant payment items (3.3.1 to 3.3.8) with one item termed 'administration of participant payments'. A standard cost could then be determined for this item, based on an analysis of the payment processes. Pending such a review the cost associated with administering participant payments should be reflected in item 3.2.6 'ongoing administration, monitoring and reporting'.

Reference number	3.3.6
Item	Participant/carer accommodation
Sub-list	Non-clinical services
Category	Participant-related
Definition	Includes participant/carer out-of-pocket accommodation costs as described in the Clinical Trial Agreement and in the Patient Information and Consent Form.
Standard Cost	Not determined, any payments made at discretion of the trial sponsor

Related items

None

Learnings from site visits

In general, clinical trial sites do not include an allowance for "participant/carer accommodation" in the trials budget. If there are some participants, like those travelling from regional/rural areas to metropolitan hospitals where the clinical trial is being undertaken who require overnight accommodation, clinical trial sites normally negotiate with the sponsor (usually industry sponsors) to cover accommodation expenses (i.e. agree a rate per night). Sometimes, they agree to use some of the budget allocated to "participant/carer travel" for this purpose. This process is managed on a per participant basis depending on circumstances.

Derived process map for "participant/carer accommodation"

Not applicable

Considerations for deriving the cost for "participant/carer accommodation"

Typical allowances to cover accommodation costs were investigated as part of the consideration of the participant/carer travel item. It was found that, under the state/territory travel assistance schemes (usually for isolated patients who need to travel more than 100 km to access a service), accommodation is subsidised on a daily basis within the range of $30 to $60 per night (depending on the jurisdiction). The ATO also sets reasonable allowances for accommodation for the purposes of determining tax deductibility. These rates depend on the location (city) and for 2012/13 vary from $132 to $233 per night.

Table of standard costs for "participant/carer accommodation"

Table C.55 indicates that no standard cost has been determined for participant/carer accommodation. This item is not thought to be cost based (to the trial site), it is discretionary to the trial sponsor. The relevant cost to the trial site is the administration of the payment process, these costs should be determined as part of item 3.2.6. Although a standard cost is not determined, Table C.55 provides some guidance on accommodation allowances used in other contexts, to assist trial sites and sponsors to set a reasonable budget for participant/carer accommodation.

Table C.55: Determination of standard cost for participant/carer accommodation

Item	Basis	Resource unit					Unit cost	Standard cost
		Min	25th percentile	Median	75th percentile	Max		
Participant/carer accommodation	Per night	$30	$35	$60	$132	$233	N/A	N/A

The need for this item should be reviewed (in fact the need for all participant payment related items should be reviewed). The only costs that are relevant to trial sites are the costs of administering the claims for participant/carer accommodation. The amount of paid to participants/carers, is discretionary, and should quite properly be determined by the trial sponsor.

In any review of the NHMRC list, it is suggested that consideration be given to replacing all of the participant payment items (3.3.1 to 3.3.8) with one item termed 'administration of participant payments'. A standard cost could then be determined for this item, based on an analysis of the payment processes. Pending such a review the cost associated with administering participant payments should be reflected in item 3.2.6 'ongoing administration, monitoring and reporting'.

Reference number	3.3.7
Item	Participant/carer overnight stay
Sub-list	Non-clinical services
Category	Participant-related
Definition	Includes any out-of-pocket costs incurred by clinical trial participants for an overnight stay in a participating clinical trial institution.
Standard Cost	Not determined, as no evidence of participants being charged in practice was found.

Related items

None.

Learnings from site visits

Dependent on the trial protocol, there were instances where participants and/or their carers are required to stay overnight at the clinical trial site. In some trials (e.g. haematology), where overnight infusions were part of the clinical trial, for example, the participant was often admitted to hospital under standard of care, and therefore no cost was attributed to the clinical trial budget. However there were some clinical trials, where the clinical trials participant was admitted to hospital for the sole reason of being in the clinical trial, and clinical trials sites stated that sponsors often would not cover the cost of the overnight stay.

Private hospitals felt this issue was problematic as private health insurers only cover their members for services that represent standard of care, but do not cover hospital stays if the member is, for example, on the experimental arm of an infusion study with a drug that is not TGA approved. The hospital either negotiates with the sponsor for the cost of the overnight stay to be covered, or the cost is borne by the private hospital involved in the clinical trial. Representatives of private hospitals felt this situation made their site less competitive for hosting clinical trials requiring overnight stays as they are not able to subside the cost of the overnight stay, whereas, they argued that public hospitals have more flexibility to subsidise these costs.

Derived process map for "participant/carer overnight stay"

Not applicable.

Considerations for deriving the costs for "participant/carer overnight stay"

Through the site visits, no instance of participants having to meet costs associated with overnight stay, as a result of adhering to the clinical trial protocol was found in practice. So no participant related standard cost has been determined for this item.

Table of standard costs for "participant/carer overnight stay"

Table C.56 indicates that no standard cost has been determined for participant/carer overnight stay, as it was not identified in practice. Participants are typically not charged in circumstances where the trial protocol dictates an overnight stay and, as a consequence, there is no cost to the trial site associated with the administration of participant payments. The need for this item should be reviewed (in fact the need for all participant payment related items should be reviewed).

Table C.56: Determination of standard cost for participant/carer overnight stay

Item	Basis	Resource unit					Unit cost	Standard cost
		Min	25th percentile	Median	75th percentile	Max		
Participant/carer overnight stay	Reimbursement	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Consideration of this item raises a much broader issue though, that is where a clinical trial protocol explicitly requires a service that involves overnight stay, how does the cost of the service get reflected in the trial budget. Given the structure of the NHMRC list, this issue needs to be dealt with as part of sub-list 1 (i.e. it is a clinical service). Currently, there are no items on sub-list 1 that obviously relate to the non-health professional costs associated with overnight stays, as there is a reliance on the MBS for almost all the clinical tests and procedures items.

So there is no place to deal with the hospital accommodation cost, if the clinical tests and procedures service requires hospital admission. The trial site can cover the cost of the professional service (medical, nursing or allied health time) but not the institution cost (the MBS multiplier recommended for most of the items on sub-list 1 is intended to cover the additional costs associated with providing the service in a clinical trial context, not the costs associated with intermediate hospital services (e.g. ward accommodation). This issue should be dealt with as part of a review of the NHMRC list, to eliminate redundancy in the categories and to ensure that all necessary clinical services are exhausted by the categories.

Reference number	3.3.8
Item	Participant/carer outpatient/day stay
Sub-list	Non-clinical services
Category	Participant-related
Definition	Includes any out-of-pocket costs incurred by clinical trial participants for an outpatient visit or day stay in a participating clinical trial institution.
Standard Cost	Not determined, as no evidence of participants being charged in practice was found.

Related items

None.

Learnings from site visits

Through the site visits, we found that most clinical trials participant and/or their carers are not required for outpatient/day stays (the item was interpreted to mean admission as a day patient, or provision of a service on an outpatient basis that might otherwise be provided on a day patient basis). However, in the case of paediatric trials, if a general anaesthetic was required (e.g. for certain investigations such as blood tests, imaging, etc. as the process would be too traumatic for the participant to remain awake) then the admission policy of the clinical trials site was to admit the participant to the institution. Most representatives of paediatric clinical trials reported was the costs associated with this circumstance was either not budgeted for or not covered by sponsors.

Derived process map for "participant/carer outpatient/day stay"

Not applicable.

Considerations for deriving the cost

Through the site visits, no instance of participants having to meet costs associated with outpatient/day stay, as a result of adhering to the clinical trial protocol was found in practice. So no participant related standard cost has been determined for this item.

Table of standard costs for "participant/carer outpatient/day stay"

Table C.57 indicates that no standard cost has been determined for participant/carer outpatient/day stay, as it was not identified in practice. Participants are typically not charged in circumstances where the trial protocol dictates an outpatient/day stay and, as a consequence, there is no cost to the trial site associated with the administration of participant payments. The need for this item should be reviewed (in fact the need for all participant payment related items should be reviewed).

Table C.57: Determination of standard cost for participant/carer outpatient/day stay

Item	Basis	Resource unit					Unit cost	Standard cost
		Min	25th percentile	Median	75th percentile	Max		
Participant/carer outpatient/day stay	Reimbursement	N/A	N/A	N/A	N/A	N/A	N/A	N/A

As with participant/carer overnight stay, consideration of this item raises a much broader issue though, that is where a clinical trial protocol explicitly requires a service that involves an outpatient/day stay, how does the cost of the service get reflected in the trial budget. Given the structure of the NHMRC list, this issue needs to be dealt with as part of sub-list 1 (i.e. it is a

clinical service). Currently, there are no items on sub-list 1 that obviously relate to the non-health professional costs associated with outpatient/day stays, as there is a reliance on the MBS for almost all the clinical tests and procedures items.

So there is no place to deal with the day procedure suite cost, if the clinical tests and procedures service requires admission as a day patient. The trial site can cover the cost of the professional service (medical, nursing or allied health time) but not the institution cost (the MBS multiplier recommended for most of the items on sub-list 1 is intended to cover the additional costs associated with providing the service in a clinical trial context, not the costs associated with intermediate hospital services (e.g. accommodation in the day procedure suite). This issue should be dealt with as part of a review of the NHMRC list, to eliminate redundancy in the categories and to ensure that all necessary clinical services are exhausted by the categories.

Appendix D – List of submissions received

Number	Date received	Submission from
1	30/04/2013	St Vincent's Hospital Melbourne
2	1/05/2013	Society of Hospital Pharmacists
3	1/05/2013	University of Western Australia
4	6/05/2013	Amgen Australia Pty Limited
5	6/05/2013	Barwon Health
6	6/05/2013	Consumer Health Forum of Australia
7	6/05/2013	Centre for Biostatistics and Clinical Trials
8	6/05/2013	Confidential
9	6/05/2013	Roche Products Pty Ltd
10	6/05/2013	Victorian Paediatric Integrated Cancer Services
11	6/05/2013	Cancer Trials Australia
12	6/05/2013	Victorian Comprehensive Cancer Council
13	6/05/2013	Department of Health Victoria
14	6/05/2013	GlaxoSmithKline Australia
15	6/05/2013	Clinical Network Clinical Research Professionals Committee
16	6/05/2013	Children's Hospital Westmead
17	6/05/2013	Medical Technology Association of Australia (MTAA)
18	6/05/2013	Epworth HealthCare
19	6/05/2013	St Vincent's Hospital Sydney Research Community
20	6/05/2013	St Johns of God Health Care
21	7/05/2013	Pharmaceutical Industry Council
22	7/05/2012	South Australia Department of Health
23	9/05/2013	Confidential
24	10/05/2013	Australia Clinical Trials Alliance
25	10/05/2013	Clinical Oncological Society of Australia (COSA) and Cancer Cooperative Trials Groups (CCTG)

Appendix E - Other stakeholders consulted

- National Health and Medical Research Council
- Pharmaceutical Industry Council – Research and Development Taskforce
- Roche Products Pty Ltd
- Novartis Pharmaceuticals Australia Pty Ltd
- Medical Technology Association of Australia (MTAA)
- Amgen Australia Pty Ltd
- Victorian Comprehensive Cancer Centre
- Cancer Trials Australia
- Centre for Biostatistics and Clinical Trials