Prepared for the Independent Hospital Pricing Authority

Development of a table of standard costs for conducting Clinical Trials in Australia 2015

Final Report

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Table of Contents

Section Page

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List of Abbreviations

ADA	Australia Dental Association
AMA	Australian Medical Association
ATO	Australian Taxation Office
CDA	Confidentiality disclosure agreement
CNC	Clinical Nurse Consultant
CNS	Clinical nurse specialist
COAG	Council of Australian Governments
CRF	Case Report Form
CRO	Contract Research Organisations
CT	Computed tomography
CTAG	Clinical Trials Action Group
CTC	Clinical Trials Coordinator
CTM	Clinical Trials Manager
CTN_x	Clinical Trial Notification
CTN	Clinical Trials Nurse
DVA	Department of Veterans' Affairs
ECG	Electrocardiogram
ED	Emergency Department
ERG	Expert Reference Group
FDG	Fluorodeoxyglucose
FLT	Fluorothymidine
GCP	Good Clinical Practice
GP	General Practitioner
HREC	Human research ethics committee
ICU	Intensive Care Unit
IHPA	Independent Hospital Pricing Authority
IWRS	Interactive Web Response System
MA	Medicines Australia
MBS	Medicare Benefits Schedule
MRI	Magnetic resonance imaging
MTAA	Medical Technology Association of Australia
NEP	National Efficient Price
NHCDC	National Hospital Costs Data Collection
NHMRC	National Health and Medical Research Council
NIHR	National Institute of Health Research
NSW	New South Wales
NUM	Nurse Unit Manager
PET	Positron emission tomography
PI	Principal Investigator
PICF	Participant information and consent form
RECIST	Response Evaluation Criteria In Solid Tumors
RGO	Research Governance Office
RN	Registered Nurse
ROHPG	Radiation Oncology Health Program Grant
SAC	Scientific advisory committee
SAE	Serious adverse event
SCOH	Standing Council on Health
SIV	Site initiation visit
SSA	Site Specific Assessment
UK	United Kingdom
VPN	Virtual private network
WA	Western Australia

Steering Committee membership

Name	Organisation representing
Dr Tony Sherbon	IHPA
Mr James Downie	IHPA
Dr Jenean Spencer	Commonwealth Department of Health
Ms Julia Herbele	NSW Ministry of Health
Ms Sue Hooper	Queensland Department of Health
Dr Suzanne Hasthorpe	Department of Health and Human Services, Victoria
Ms Genevieve Ryan	Department of Health and Human Services, Tasmania
Mr Winston Piddington	ACT Health
Ms Bernadette Swart	Department of Health, South Australia
Prof Peter Thompson AM	Department of Health, Western Australia
Ms Samantha Robertson	NHMRC
Prof Steve Webb	Australian Clinical Trials Alliance
Ms Sharon Charles	AusBiotech
Mr Mitch Kirkman	Medicines Australia
Mr Falko Thiele	Medical Technology Association Australia
Dr Gary Richards	Commonwealth Department of Industry and Science

Executive summary

THE STUDY CONTEXT

The Australian Government has pursued a number of initiatives designed to improve the processes of conducting clinical trials, and Australia's competitiveness as a destination for international clinical trials, starting with the formation of the Clinical Trials Action Group (CTAG) in October, 2009 through to the current 'Streamlining Clinical Trials' initiative. As part of these initiatives, the National Health and Medical Research Council (NHMRC) developed a standard list of activities associated with conducting clinical trials in Australia in 2012 (the 'List'). Subsequently, in late 2012, the Independent Hospital Pricing Authority (IHPA) was directed by the Commonwealth Minister of Health to develop a table of standard costs (the 'Table'), based on the initial List. An investigative report *Development of a table of standard costs for conducting Clinical Trials in Australia:* Final Report was produced in June 2013, and informed IHPA's *Determination of the Standard Table of Costs for Conducting Clinical Trials in Australia* (November, 2013).

In 2014, the NHMRC undertook a review of the initial List to address stakeholder feedback and produced a revised List in December 2014. On 19th December 2014, the Commonwealth Minister for Health issued Direction No.1, 2014 that IHPA, by 30th June 2015, must determine the costs of the revised List of items and any other items (above those cost required for standard care) as determined necessary by IHPA, associated with conducting clinical trials in Australia. The Ministerial Direction also required that IHPA must provide a report on the table of standard costs to the first meeting of the Standing Council on Health (SCOH) after 30th June 2015 (now the Council of Australian Governments (COAG) Health Council meeting scheduled for 7th August, 2015). It is important to clearly state that the Ministerial Direction requires IHPA **to determine cost not prices**. This report provides the information that will allow IHPA to comply with the Direction.

METHODOLOGY

HealthConsult was engaged by IHPA on 26th February, 2015, to undertake a project to *"provide 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 standard costs for the revised List of standard items associated with conducting clinical trials in Australia. The project methodology featured the development of a discussion paper as the basis of a call for public submissions; a broad stakeholder consultation process involving visits to nine public and three private hospitals to gather data to support activity based costing; discussions with trial sponsors (industry and research collaboratives) and other interested parties; detailed analysis of the information generated to calculate a standard cost for each of the 42 items on the revised List, and a three round Delphi process involving members of the Steering Committee acting as an Expert Reference Group (ERG) to reach consensus on the standard cost for each item.

BASIS OF CALCULATING 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 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 2014)*. These factors were carefully considered in developing the table of standard costs. In respect of clause 131(3) of the Act, a Steering Committee with relevant expertise was established; a process of inviting public submissions was undertaken (nine submissions were received, which influenced the final determination of the table of standard costs); actual costs were measured by gathering data from visits to nine different public and three private hospitals covering a range trial characteristics. In respect of the Ministerial Direction, the actual activities involved in each item were identified across all sites (except for one item which was deemed to be an overlap of other items); and the standard cost is based on the most representative cost incurred (determined through review of the spectrum of measured costs by the ERG).

For some items, the improvements in costing methodology have allowed the calculation of standard costs for activities within the item. This improvement will allow the table of standard costs to be used on an activity basis (e.g. for some items within the List, the frequency of occurrence of an activity can be used together with the standard cost for that activity to provide a more accurate measure of the trial specific cost). For example, item 1.1.1 'start-up meetings' includes the actual start-up meeting, as well as any additional online training undertaken by the Principal Investigator, Clinical Trial Coordinator and Supporting Department staff (so these amounts can be used, as applicable, in accordance with the requirements of the trial). This approach improves, the 2013 method, which involved the determination of one standard costs that represented both typical frequency and typical cost of activities within an item.

The suggested **standard cost for each item (or discrete activity within each item) includes the allocation of salary and organisational overheads** and reflects the nationally representative cost 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 (reflecting trial characteristics that make it more or less complex than the representative trial reflected by the standard cost). **However, publishing a nationally representative standard cost leaves potential trial host sites and trial sponsors free to use that 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.**

APPLICATION OF THE TABLE STANDARD COSTS

The production of the supporting Appendices to the table of standard costs (refer to Table 4.2) ensures that there is transparency in regards to the basis on which the standard cost was calculated. The Appendices provide details of the variation in cost that was observed for each item. This information facilitates the use of the table of standard costs as a reference point by funders/sponsors and clinical trials sites. Specifically, it is intended to **allow potential trial host sites and sponsors/funders to negotiate trial budgets with reference to the standard cost and the distribution of the measured costs, taking account of the specific features of the trial (target population, complexity, funds availability, applicable labour rates, etc.)**.

LIMITATIONS OF CALCULATING THE STANDARD COSTS OF THE REVISED LIST

The study has produced one or more standard costs for each item on the revised list except for item 2.6.7 'outpatient activity' which it is suggested be removed from the revised List as it duplicates other items. Each item has been costed on the basis of activities undertaken or with reference to external costs and/or fees (as per the 2013 method, Medicare Benefits Schedule (MBS) fees have been used as a reference point for clinical services). For one item, 3.2.1 (c) 'archiving of trial records – storage fee' where the predominant practice is for trial host sites to purchase the services from an external provider, the standard cost was calculated with reference to the typical charge. Even though the costing study has produced a more robust result than the 2013 study, as majority of items were costed on an activity basis, there are still limitations with the standard costs produced for each item (or discrete activities within items).

(a) Type of trial sponsor/funder

The study developed a standard cost for each item regardless of the sponsors/funder for the clinical trial. It is noted that, in general, investigator-initiated trials have limited external and/or internal funding, industry sponsored trials are adequately funded, and collaborative group trials have grant-funding, which is usually limited to an equal and small amount per site. The suggested standard is not differentiated on the type of clinical trials sponsor/funder, even though thematic analysis of the qualitative data suggests that funding source may impact on the costs for some (but not all) items in the revised List. For example, it was often argued that, due to their more limited resources, investigator-

initiated trials required more support to attain ethics and governance approvals. But, it is recognised that in other circumstances, investigator-initiated trials may have lower costs.

This discussion **is strictly about costs, not charges**. It is acknowledged, as per the NHMRC's principles published with the List, that trial host sites choose to absorb different amounts of trial cost with reference to the trial sponsor/funder. This practice, which effectively means that the trial host site becomes a part-funder of the trial, results in sponsors/funders being asked to meet different proportions of the actual cost of a trial with reference to expected funding availability. It is stressed that **this is a funding matter, not a costing matter, and that, as per the NHMRC's principles, publication of a standard cost is not intended to provide any incentives or disincentives to this practice**.

(b) Complexity of clinical trials

The gathered data did not support the calculation of differential standard costs based on phase of clinical trial (the sample size was not large enough to support robust calculations of the impact of cost drivers), however thematic analysis of the qualitative data suggests that there is little variation in terms of cost incurred for Phase 2 and 3 clinical trials (including non-pharmaceutical trial equivalents), but there is potential cost variation if the clinical trial is a Phase 1 or 4. Qualitative data suggest that the differences are mainly due to clinical trial sites taking longer to assess feasibility of the clinical trial (items 1.1.1-1.1.3), the patient population seeking to be included in the trial (i.e. increases the time spent on pre-screening (item 2.2.1) and recruitment activities (item 2.2.1)), and the amount of follow-up required of all participants included in the study. A larger study would be required to verify this theory empirically.

The study was unable to calculate differential standard costs based on trial target population due to the hospital sample included (i.e. only one paediatric hospital site). Again, if a larger study was undertaken, it would be possible to measure the impact of the trial target population as a cost driver. Once again, thematic analysis of the data gathered from the paediatric hospital site suggests that for some items on the List, the time taken (and hence costs incurred) to undertake the activities is greater.

(c) Variation in the input costs

In order to develop a standard cost for each item, which is largely driven by labour hours, an hourly rate for each type of personnel involved needed to be calculated. The site visits found that the variation in disciplines appointed to clinical trials positions and the Awards the individual professions are paid under are broad and vary across each State/Territory and setting (public, private etc.) in Australia. Although the calculated hourly rate (which represents a fully absorbed hourly rate) is based on reference to current Awards in numerous states/territories, the published standard cost may be too high or too low depending on the location of the trial host site (State/Territory) and what an individual institution pays.

DEFINING STANDARD CARE

It is important to note that, **consistent with the published NHMRC principles, in the context of negotiating a trial budget, the table of standard costs is intended to be applied only to those clinical services that are over and above standard care** (i.e. the table of standard costs is not intended to be applied to clinical services that patients would have received as part of standard care and treatment independent of their participation, or not, in a clinical trial).

As part of the study, stakeholders were asked how they differentiate between standard care versus non-standard care when working up clinical trials budgets. Stakeholders recognised the importance and complexity of the problem, and noted that a clinical service that is standard care in one clinical trial may not be standard care in a different trial context. The most often cited examples were pathology tests and/or imaging examinations that are required at higher frequency for clinical trial participants than

would otherwise be provided as standard care to non-clinical trial patients with the same condition. The additional tests are considered to be clinical trial specific. But, even in this relatively simple example, stakeholders noted that the test frequency was trial and context specific.

There was also discussion about whether standard care could/should be defined as part of the clinical trial protocol (by the sponsor), and this reference point can then become the basis for negotiation between the trial funder/sponsor and the trial host site. This practice seemed to vary across clinical trials, and stakeholders pointed out that in international trials what might be regarded as standard care in the country where the clinical trial was designed (typically not Australia) may not be standard care in Australia. So while, ideally, standard care would be defined in the trial protocol and act as the reference point for discussion, in practice this was found to be not always possible.

Another confounding issue raised by stakeholders was that standard care for a particular condition is not uniform within Australian hospitals, even for hospitals in the same jurisdiction, and sometimes even within a single hospital where clinicians have a different approach to practice. Again, for this reason it was not considered possible to provide specific (or generic) guidance on what constitutes standard care in the context of clinical trial. Rather, there has to be negotiation between the trial funder/sponsor and the trial host site to agree on standard care in the trial context.

In practice, some sites identify standard care versus non-standard care items on presentation of the detailed clinical trial protocol by the sponsor and show in their 'budget work up" what is considered by their site as "non-standard care" and therefore included in the requested budget for the clinical trial. Other sites believe that once a patient is on a clinical trial, whether the test is standard care is irrelevant as the additional requirements (including reporting) associated with that patient being on a clinical trial should be covered by the sponsor, and in some cases sponsors are happy to pay for it.

It is important to note that with the structure of the revised List, ensuring that the calculated standard cost is above those costs required for standard care, is not relevant for the items on two of the sub-lists. Basically, the activities included under the sub-lists of "site authorisation" or "site close-out" are always clinical trial specific. They do not include any clinical service items. Thus assessing whether the costs associated with these items is over and above standard care is not relevant.

Standard care is only relevant to items associated with the provision of clinical services to patients, i.e. "clinical services" (items 2.3.1 to 2.3.8), "biospecimen related" (items 2.5.1 -2.5.2) and "clinical resources" (items 2.6.1-2.6.7). The standard costs for these items is based on the actual cost of delivering these services irrespective of whether they are provided in the context of a clinical trial or not (as sometimes they will be standard care and other times they will not be). There will need to agreement between the trial host site and funder/sponsor on what constitutes standard care in the context of a specific trial, and the cost of these services will need to be excluded from the clinical trials budget.

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 means that change is always occurring and the relevance of items will also change. Also new input data (e.g. activity and/or cost) may become available which may provide additional transparency in relation to the costs. All or some of these developments may 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 or IHPA's annual indexation rate could be applied if no change to the items within the revised List has occurred. The costs in this Determination relate to the 2014-15 Financial Year. The standard cost for each item includes the allocation of all overheads.

1

Introduction

HealthConsult, was engaged on 26th February, 2015 by the Independent Hospital Pricing Authority (IHPA) to undertake a project to:

"provide 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 THE PROJECT CONTEXT

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; improving the efficiency and effectiveness of health care delivery; 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. Recognising these potential benefits, the Australian Government has pursued a number of initiatives designed to improve the processes of conducting clinical trials and Australia's competitiveness as a destination for international clinical trials, starting with the formation of the Clinical Trials Action Group (CTAG) in October, 2009 through to the current 'Streamlining Clinical Trials' initiative.

As part of these initiatives, the National Health and Medical Research Council (NHMRC) developed a standard list of activities associated with conducting clinical trials in Australia in 2012 (the 'List'). Subsequently, in late 2012, IHPA was directed by the Commonwealth Minister of Health to develop a table of standard costs (the 'Table'), based on the initial List. IHPA convened a Costing Study Steering Committee and engaged HealthConsult to assist with the development of the Table. The Report on this work*, Development of a table of standard costs for conducting Clinical Trials in Australia:* Final Report was produced in June 2013, and informed IHPA's *Determination of the Standard Table of Costs for Conducting Clinical Trials in Australia* that was published in November, 2013). Both the Report and the determination are available on IHPA's website.

As part of developing the first Table, IHPA and other stakeholders involved in the process, observed the need to refine the List due to a number of overlapping items. IHPA also identified other areas where the list would benefit from aggregating items. Thus, as part of the discussion of IHPA's Determination, the (then) Standing Council on Health (SCOH), in November 2013, agreed that the Commonwealth undertake further work to refine the List. As a result, in 2014, the NHMRC commissioned HealthConsult to undertake a review of the List, which was completed in September 2014 (the Report of this review is available on the NHMRC website). The draft revised List developed through this review with proposed definitions was then subject to a public consultation process undertaken by the NHMRC. The feedback obtained through this process resulted in a final revised List, which was completed in December 2014.

Most recently, on 19th December 2014, the then Commonwealth Minister for Health issued the Direction (Direction No.1 2014) that IHPA, by 30th June 2015, must determine the costs of the revised List of items and any other items (above those cost required for standard care) as determined necessary by IHPA, associated with conducting clinical trials in Australia. Additionally, the Ministerial Direction requires that IHPA must provide a report on the table of standard costs to the first meeting of the

SCOH after 30th June 2015 (now the COAG Health Council, meeting scheduled for 7th August, 2015). This report provides the information base that will allow IHPA to comply with the Direction.

1.2 PROJECT METHODOLOGY

Figure 1.1 presents the six stage methodology designed by HealthConsult to achieve the outcomes sought by 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 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 proposed approach to costing the 42 items on the revised standard list.

(3) **Stage 3:** Broad stakeholder consultation which included one to two day visits to nine public and three private hospitals involved in clinical trials, as well as discussions with representatives of industry trial sponsors and other key interested parties;

(4) **Stage 4:** Analysis of the gathered data (from written submissions; secondary data sources (e.g. Medicare Benefits Schedule (MBS), Awards), site visits, extracts from NHCDC etc.) to determine a standard cost for each item on the revised list of activities associated with clinical trials in Australia, including review by the Steering Committee (using a modified version of the Delphi process);

(5) **Stage 5:** The calculated standard cost of all items were refined through a three round Delphi process where members of the Steering Committee formed the Expert Reference Group (ERG). The first round consisted of the provision of the draft table of standard costs together with a questionnaire which asked all members to rate the reasonableness of the calculated standard cost for each item. Responses were received by 11 members representing one response from each representative organisation except the Commonwealth departments, ACT Health, NHMRC and IHPA. Where consensus was not reached on the reasonableness of the calculated standard costs the items were discussed at a face-to-face meeting of the ERG (second round). Again where consensus could not be reached the calculations were modified based on ERG input and the revised draft of standard costs for those items were provided again to the ERG members with the questionnaire. Responses were received by 10 of the 11 members which provided a response in round 1. After three rounds consensus was reached in regards to the reasonableness of the calculated standard cost for all items.

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

1.3 OVERVIEW OF THE NHMRC REVISED LIST OF STANDARD ITEMS

The revised List of 42 items is organised according to the three typical stages in the clinical trial lifecycle at a trial site (i.e. Site Authorisation, Site Implementation and Site Close-out). Table 1.1 summarises the features of the revised List, including the number of sub-lists; and the number of categories and items within each sub-list.

Table 1.1: Brief descriptive analysis of the NHMRC's revised List of items associated with clinical trials

Sub-list number	Sub-list label	Number of categories	Number of items	Comments
1	Site Authorisation	3	7	Represents the activities from feasibility assessment through to site authorisation. Includes the preparation of all the required ethics and research governance documentation and exchange of contracts including agreement on budget.
2	Site Implementation	9	31	Represents the activities associated with the implementation of the clinical trial at the site from study initiation through to accrual of participants and completion of follow-up. Includes all of the trial management activities as well as the clinical services provided to trial participants.
3	Site Close-out	4	4	Represents the activities associated with closing out the trial at a site from final trial data handover through to archiving of trial participant records.
Total		**16**	**42**	

1.4 PURPOSE OF THE HOSPITAL SITE VISITS

The evidence underpinning the development of the table of standard costs has been derived from a series of visits to 12 hospitals across Australia involved with the design and implementation of clinical trials. There was not sufficient time to conduct a prospective costing study to measure costs for each item on the standard List across hospital sites; so a protocol based costing methodology was used. In order to do this, site visit information was used to undertake activity based costing by developing process maps (where necessary), then identifying resource units required for each process step, then applying (externally sourced) standard unit costs, to derive an overall standard cost.

Table 1.2 shows that 33 of 42 items on the revised List were costed on an activity basis. The standard costs for the remaining nine items were derived by reference to published or otherwise available cost/fee schedules, as activity based costing was not possible (e.g. standard hourly rates). In addition to calculating a standard cost for each of the 42 items, where data was available/gathered, a standard cost for discrete activities within items was also calculated. This resulted in a standard cost calculated for 75 activities within the 41 items in the revised list. No standard cost for item 2.6.7 'outpatient time' has been calculated as HealthConsult are recommending this item be deleted from the list.

Table 1.2: Profile of items on the revised List that were costed on an activity basis

Use of Process Maps	Sub-list	Number of items	Discrete activities within items	Comment
Yes	Site Authorisation	7 out of 7	9	Items are based on activities that were well suited to process mapping.
	Site Implementation	13 out of 31	35	
	Close-out	4 out of 4	4	
No	Site Implementation	17 out of 31	27	Items did not consist of activities that could be process mapped (e.g. research nurse time, ward bed days etc.)
Total		**41**	**75**	

1.5 ORGANISATIONS SELECTED FOR SITE VISITS

Two members of the HealthConsult team visited the nominated 12 hospitals to gather information to be used to develop the table of standard costs. Table 1.3 shows the hospital sites included in the study that were nominated by State and Territory health departments and representatives of the private sector. Sites were considered by the Steering Committee to be reasonably representative of the settings in which clinical trials are conducted in Australia (i.e. provide coverage across trial and hospital characteristics including (type of intervention in clinical trial (e.g. drug, radiation oncology, surgical, diagnostic), jurisdiction, type of hospital (general, specialist); and sector of hospital (public, private).

Table 1.3: Organisations participating in the study site visits

State/Territory	Public Hospitals	Private Hospitals
New South Wales	Westmead Children's Hospital	Sydney Adventist Hospital
	Westmead Hospital	
	Gosford Hospital	
Victoria	Austin Hospital	Epworth
	Box Hill Hospital	
	Monash Health	
Queensland	Princess Alexandra Hospital	Wesley Private Hospital
Western Australia	Sir Charles Gardiner Hospital	
South Australia	Queen Elizabeth Hospital	
Total	**9**	**3**

Figure 1.1: Overview of the six stage methodology used

2

Revised list of standard items for clinical trials

This Chapter presents the revised List of standard items associated with the conduct of clinical trials in Australia. To put the List into context, it starts with a series of principles that should guide the use of the List and then the full set of items in the revised List with each item definition presented.

2.1 NHMRC PRINCIPLES DEVELOPED TO GUIDE THE USE OF THE STANDARD LIST

As part of the process of reviewing the initial List, the NHMRC has developed the following principles that should be noted by users of the List. Reference to these principles will enable the use of the List for the purpose that it was originally intended (i.e. 'to reduce uncertainty around clinical trial costs').

- The principal purpose of the List and the associated set of costs (once published by IHPA) is to provide a valuable reference point for the negotiation of a trial budget between a trial funder/sponsor and a health service that wishes to host a trial.
- The List has been developed principally with reference to hospitals (public or private) as the health service. It is acknowledged that many of the items on the List may also be applicable to other trial settings (e.g. community based health services and purpose-built Phase 1 Trial Centres).
- The List has been developed with reference to stakeholders from the commercial, collaborative research/trial group, and academic sector that are involved in funding/sponsoring trials. Although the principal point of reference for development of the initial List was commercial trials, it is acknowledged that the items on the List typically apply to all trials, it is the pricing practice that varies based on the trial funder/sponsor.
- The List is only intended to cover activities associated with clinical trials that are conducted at, or by, a health service that hosts a clinical trial. It is acknowledged that there are many other stakeholders (trial funders, trial sponsors, Contract Research Organisations (CROs), Clinical Trial Cooperative Groups or Networks and/or Third Party Trial Centres) that undertake activities that are necessary for the conduct of clinical trials in health services. Inclusion of these activities would not be consistent with the principal purpose of the List.
- The List is defined in terms of activities/services, not in terms of prevailing or usual practice fees that are associated with clinical trials. Each activity has an associated standard cost (once published by IHPA), which represents an independent determination of the typical cost of the activity/service covered by each item, but the setting of a price for a specific clinical trial remains a subject for negotiation between the trial funder/sponsor and the health service.
- The List is only intended to cover activities that are common to the conduct of clinical trials in health services (not all activities may apply to all trials). Activities that are less common (usually because they are specific to a narrow range of clinical trials) are not included and, in a clinical trial budget determination context, should be dealt with by negotiation between the trial funder/sponsor and the health service.

- Only those activities that represent a true cost to the site should be costed.
- Costs associated with activities should be inclusive of all charges such that additional overheads should not be applied.
- The appearance of an item with an associated cost on the List does not necessarily mean that it should attract a fee in the context of setting a trial budget. It is acknowledged that current practice is that many health services currently choose to support various investigator-initiated/academic clinical trials to a greater extent than industry sponsored trials by meeting a larger part of their costs by charging lower fees. Therefore for non-commercially sponsored or public good trials only the marginal costs of trial related activities or infrastructure should be used for budgeting purposes.
- The List is not intended to provide incentives or disincentives to this practice, merely to define the usual activities/services and their typical cost (once published by IHPA).
- Although a full suite of clinical services is included on the List, in determining trial budgets, it is intended that only those clinical services that are over and above the standard care that the patient would have received for his/her condition if he/she had not been enrolled in the clinical trial are used in the negotiations around setting trial budgets.

2.2 SITE AUTHORISATION ITEMS

The first sub-list itemises the activities from preliminary assessment through to site authorisation of a clinical trial. Table 2.1 shows that there are seven items on this sub-list in three different categories.

Table 2.1: The sub-list of standard items associated with clinical trials for Site Authorisation with definitions

Major category	Item	Reference number	Definitions
Feasibility Assessment	Preliminary assessment	1.1.1	• The activities associated with the exchange of the required reciprocal confidentiality agreements and preliminary review of the trial protocol by the potential Principal Investigator (and/or delegates) at the site. May also include initial discussions (by telephone or site visit) with the trial sponsor and/or representative.
	Protocol review	1.1.2	• The activities associated with the heads (or nominees) within the potential clinical trial host unit (e.g. oncology, respiratory, 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 for scientific merit and local interest/feasibility. The process may involve review by individuals or by a panel drawn from representatives of the above mentioned departments.
	Feasibility determination	1.1.3	• The activities associated with determining the feasibility and desirability of conducting the trial at a site (culminating with the completion of the feasibility assessment questionnaire) covering the assessment of: ➢ whether trial is consistent with institution's mission, research priorities and risk management profile; ➢ likelihood of being able to recruit suitable types and numbers of patients; ➢ availability of staff and other resources required to undertake the trial; ➢ the services that will be standard to care for patients on the trial and those that will be trial specific with reference to the trial protocol; ➢ acceptability of the proposed budget and contract; The activities may also include hosting a feasibility assessment visits by the trial sponsor and/or representative.

Major category	Item	Reference number	Definitions
Ethics Approval	Preparation of the HREC application	1.2.1	• The activities associated with the preparation and submission of the human research ethics committee (HREC) application form (or equivalent) and supporting documentation which includes the protocol, participant information and consent form (PICF), recruitment and advertising materials, etc. Also includes revisions to applications in response to ethics committee requests for additional information and forwarding copies of relevant approvals (once obtained) and associated documentation to the trial funder/sponsor.
	Ethics review	1.2.2	• The activities associated with the review of the ethics application by the HREC, including the preparation of any requests for additional information and subsequent consideration of the material provided.
Site-specific assessment	Preparation of the SSA application by the project team	1.3.1	• The activities associated with the preparation and submission of the Site Specific Assessment (SSA) form (or equivalent) by the PI or project team, which include completion of the form, obtaining authorising signatures, liaising with inter-institutional departments (e.g. radiology, pathology, pharmacy, etc.), adapting the Lead HREC approved master PICF(s) with site-specific letterhead and contact details; and liaison with sponsor including forwarding copies of relevant authorisations (once obtained) and associated documentation to the trial funder/sponsor. Also includes responding to Research Governance Office (RGO) queries and/or requests for additional information and forwarding copies of relevant authorisations (once obtained) and associated documentation to the trial funder/sponsor.
	Site processing and review	1.3.2	• The activities associated with the processing of country specific regulatory documents (e.g. the Clinical Trial Notification (CTN_x) Scheme form), insurance and indemnity documents, safety and/or biosafety reports, trial agreements, requesting, additional information and review of the SSA by the Site, including the preparation of any requests for additional information and subsequent consideration of the material provided.

2.3 SITE IMPLEMENTATION ITEMS

The second sub-list itemises the activities associated with the implementation of the clinical trial at the site from trial initiation through to accrual of participants and completion of follow-up. Table 2.2 shows that there are 31 items on this sub-list in nine different categories

Table 2.2: The NHMRC sub-list of standard items associated with clinical trials for Site Implementation with definitions

Major category	Item	Reference number	Definitions
Trial initiation	Start-up meetings	2.1.1	• The activities that occur at the start of the clinical trial with personnel involved in the trial. Includes any required handover of trial documentation, information sessions for principal or co-investigators and/or clinical trials manager/coordinators and representatives of the participating departments, and any training (e.g. detailed protocol, electronic case report form (eCRF), good clinical practice (GCP)) of staff directly involved in the clinical trial. This may include payment of travel and accommodation for participating staff, where appropriate.
	Departmental set-up	2.1.2	• The activities associated with each department involved in clinical trial getting ready for trial operation of the trial. Includes 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 any necessary preparation of medical records.
	Trial specific equipment set-up and maintenance	2.1.3	• The activities associated with the hire, purchase and/or receipt from the sponsor of any equipment (including IT infrastructure) required for the purposes of conducting the clinical trial. Includes the required set-up/customisation/commissioning of the equipment so that it is suitable for use in the clinical trial, as well as local maintenance of the equipment throughout the trial.
Patient accrual	Pre-screening activity	2.2.1	• 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 a 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).
	Recruitment activity	2.2.2	• The activities associated with involving potential and recruited clinical trials participants between the completion of pre-screening and the final determination of the assessment for suitability. Includes the provision of education and information to possible clinical trial participants, 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).
Clinical services	Screening and health assessment	2.3.1	• The 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.
	Laboratory tests and procedures	2.3.2	• Laboratory clinical services including pathology, histopathology, haematology, chemical, microbiology, immunology, tissue pathology, cytology, genetics, etc.

Major category	Item	Reference number	Definitions
	Imaging examinations and procedures	2.3.3	• Imaging clinical services including diagnostic radiology (e.g. plain radiography, computed tomography (CT), magnetic resonance imaging (MRI), ultrasound, nuclear medicine and positron emission tomography (PET) scans using the radiopharmaceuticals fluorodeoxyglucose (FDG) or non-FDG tracers' fluorothymidine (FLT)).
	Radiation therapy planning and treatment	2.3.4	• Radiation oncology treatment services including radiation therapy planning, external beam radiation therapy, brachytherapy, etc.
	Other clinical tests or procedures	2.3.5	• Surgical and non-surgical procedures (e.g. diagnostic and treatment related procedures) performed by clinically and/or scientifically qualified staff.
	Specialist medical consultations	2.3.6	• Clinical consultations services provided by medical specialists, General Practitioners (GPs), dentists and any other registered medical practitioner.
	Nursing services	2.3.7	• Clinical services provided by enrolled, registered and specialist nurses, midwifes and nurse practitioners.
	Allied health services	2.3.8	• Clinical services provided by registered allied health professionals (e.g. pharmacists, physiotherapists, dieticians, occupational therapists).
Pharmacy / Investigation Drug Related	Staff training (drug-specific)	2.4.1	• The activities associated with the 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.), doctors, nurses on the drug-specific aspects of the clinical trial protocol.
	Stock management	2.4.2	• The activities associated with the receiving of pharmacy stock for the clinical trial, completing an inventory check, downloading temperature log, 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.). Stock management also includes expiry management (e.g. labelling and re-labelling due to the extension of the expiry date of the product); recording and storing of used/unused products; any monitoring that is required to ensure the viability of the product, data entry associated with any expired or unused medicines; returning used or unused medicines to the sponsor; etc. during the implementation phase.
	Drug preparation and dispensing	2.4.3	• The activities associated with 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; the development and maintenance of special dosage forms (including the activities associated with the randomisation process if applicable). Includes the conduct of dispensing (including the provision of counselling to clinical trial participants), review of clinical trial participants' adherence to the trial protocol, costs related to on-call/call back and recording details of the clinical trial in the participant's medical record (paper based or electronic).
Biospecimen related	Biospecimen collection and processing (central labs)	2.5.1	• The activities associated with the collection, processing and transport (e.g. quarantine permits, etc.) of clinical trial biospecimens (e.g. 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 arranging transfer of the biospecimen(s) to central laboratories. For biospecimens tested on site, biospecimen collection and processing is covered by the appropriate test in the clinical services category.
	Biospecimen storage	2.5.2	• The activities associated with the local storage (if required) 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.

Major category	Item	Reference number	Definitions
Clinical resources	Investigator time	2.6.1	• The unit labour cost (fully absorbed hourly rate, i.e. inclusive of overheads) for any activities (clinical or non-clinical) that need to be carried out by an investigator, that are specific to the trial, and that are not covered by an item listed elsewhere on the standard List.
	Research nurse time	2.6.2	• The unit labour cost (fully absorbed hourly rate, i.e. inclusive of overheads) for any activities (clinical or non-clinical) that need to be carried out by a research nurse, are specific to the trial, and are not covered by an item listed elsewhere on the standard List.
	Clinical research coordinator (non-research nurse) time	2.6.3	• The unit labour cost (fully absorbed hourly rate, i.e. inclusive of overheads) for any activities (clinical or non-clinical) that need to be carried out by a clinical research coordinator, are specific to the trial, and are not covered by an item listed elsewhere on the standard List.
	Interpreter services	2.6.4	• The unit labour cost (fully absorbed hourly rate, i.e. inclusive of overheads) for any activities that need to be carried out by an interpreter that are specific to the trial.
	Ward bed days	2.6.5	• The unit cost (fully absorbed daily rate, i.e. inclusive of overheads) for a patient admitted to a ward to receive clinical services (including monitoring) that are specific to the trial (i.e. the services do not represent standard care).
	Clinic/theatre time	2.6.6	• The unit cost (fully absorbed hourly rate, i.e. inclusive of overheads) for a patient spending time in clinic and/or theatre to receive clinical services (including investigations) that are specific to the trial (i.e. the services do not represent standard care).
	Outpatient time	2.6.7	• The unit cost (fully absorbed daily rate, i.e. inclusive of overheads) for a patient receiving clinical services in an outpatient department.
Trial operation	Lead site coordination	2.7.1	• The activities conducted only at the lead site associated with the ongoing coordination and management of all the nominated sites participating in the clinical trial (i.e. excludes those activities conducted at the lead site that are specific to that site's participation in the clinical trial but includes activities associated with coordinating information flow to and from the Lead HREC, sponsor and other site).
	Administration, monitoring and reporting	2.7.2	• The activities associated with ongoing operation of the trial at the trial site that occur post initiation of the trial. Includes liaison with investigators and/or sponsor (including the monitors), preparing materials for, and involvement in, monitoring visits, CRF completion, data collection and entry, endpoint recording, accrual reporting, safety and adverse event reporting, review of SAE reports, managing clinical trial documentation, retrieving medical and/or clinical records, invoicing, and annual reporting including annual ethics report and final report.
Participant related	Participant time	2.8.1	• The unit cost for the time involved in participating in the clinical trial. This item is only intended to be used for Phase 1 healthy volunteer trials, where payment for participant time is the norm. Any provision for participant payment would be described in the Clinical Trial Agreement and in the Patient Information and Consent Form and will have been considered by the Lead HREC.
	Participant costs	2.8.2	• The costs that may be necessarily incurred by a trial participant due to participating in the trial. May include transport to and from the trial location, car parking, meal allowances (where extended time attendance is required), and overnight accommodation costs where participants need to travel significant distances to and from the trial locations and/or need to stay in close proximity to the trial site for an extended period. Any provision for reimbursement of participant costs would be described in the Clinical Trial Agreement and in the Patient Information and Consent Form and will have been considered by the Lead HREC.

Major category	Item	Reference number	Definitions
Amendment Processing	Amendment preparation and submission	2.9.1	• The activities associated with 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. Also includes responding to HREC and/or RGO queries and/or requests for additional information and forwarding copies of relevant authorisations (once obtained) and associated documentation to the trial funder/sponsor.
	Amendment review	2.9.2	• The activities associated with the review of the amendment documentation by the HREC and/or RGO, including the preparation of any requests for additional information and subsequent consideration of the material provided.

2.4 SITE CLOSE-OUT ITEMS

The third sub-list itemises the activities associated with closing out the trial at a site from final trial data handover through to archiving of trial participant records. Table 2.3 shows that there are four items on this sub-list in four different categories.

Table 2.3: The sub-list of standard items associated with clinical trials for Site close-out with definitions

Major category	Item	Reference number	Definitions
Site close-out visit	Site close-out visit	3.1.1	• The activities that occur at the end of a trial as part of the attendance by the sponsor (and/or representative) at the clinical trial site for a series of meetings with personnel that were involved in the trial. Includes verifying that the study procedures have been completed, all relevant data have been collected and transferred to the sponsor, preparing and implementing plans to un-blind/unmask and debrief site staff; and, if relevant, arranging for the study intervention to be returned to the responsible party or prepared for destruction, the activities undertaken to confirm that the site's clinical trial obligations have been met and post study obligations are understood. Covers the provision of assurances that the relevant data have been collected and transferred, and ensuring, where relevant, that the study intervention is returned to the sponsor and/or is destroyed in accordance with the sponsor's requirements.
Record archiving	Archiving of trial records	3.2.1	• The activities associated with archiving the trial records for the required period. Includes the boxing up of all trial material ready for archiving/storage as well as the secure storage of the material for up to the agreed number of years.
Drug return/destruction	Drug return/destruction	3.3.1	• The activities associated with the return of the trial drugs to the sponsor and/or the destruction of the trial drugs according to the institution's policy, sponsor requirements (if applicable), safe operating practices and the requirements of the trial.
Biospecimen transfer/destruction	Biospecimen return/destruction	3.4.1	• The activities associated with the transfer of biospecimens obtained throughout the trial to a tissue bank (if provided for by the trial protocol) and/or the destruction of biospecimens according to the institution's policy, sponsor requirements (if applicable), safe operating practices and the requirements of the trial.

3

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 revised 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.

3.1 PRINCIPLES USED IN COSTING THE REVISED LIST

The standard costs were derived using the following principles:

- **Activity based costing for each item on the list was used as the preferred method**. Where possible, items were costed on an activity basis. A protocol based approach was used that develops 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 used to derive an overall standard cost for each item on the revised List where activity based costing from first principles was used.
- **Unit costs will be externally derived.** Where items on the revised List were costed from first principles, the unit costs for the resource units were used to determine standard costs from secondary sources (e.g. the National Hospital Costs Data Collection held by the IHPA and other published costs schedules; various Awards, classifications and pay rates under which hospital staff are employed; and various charges levied by third parties (only where these charges became a cost to the health service that hosts the clinical trial).
- **Standard costs will be based on representative practice**. The timeframe available to the study were such that constructing a prospective data collection that attempted to measure actual costs for each item across a statistically significant number of trials and trial sites was not possible. The study calculated standard costs by investigating the actual processes used across a number of trial sites, but the standard costs are not based on the mean of a series of measurements. Rather, standard costs have been based on a synthesis of the process maps derived from the field work that identified the most representative practices through review by an Expert Reference Group (i.e. standard costs may be calculated at mean, median, 25th percentile, etc.).
- **Where activity based costing principles could not be used, standard costs/price schedules were used with adjustments as deemed appropriate.** For some items on the List (e.g. clinical services such as medical/nursing consultations or diagnostic tests), there was insufficient time available to the study to validate pre-existing cost/price schedules (i.e. activity based costing from first principles was not possible). In these circumstances, generally accepted standard cost/price schedules (e.g. MBS fees for diagnostic tests) were used. Consideration was however given, based on evidence, to applying adjustments for services provided in the context of a clinical trial. Where there were multiple cost/price schedules available for a given item, all cost/price schedules were examined and the most commonly accepted cost or price was used to determine the standard cost.

- **Actual practices were investigated in a number of clinical trial sites through fieldwork**. As, for items costed on an activity basis, the standard cost were not calculated as the mean of a series of measurements, purposeful random selection of field work sites was not required. However, the sampling strategy of the hospitals selected for field work were considered by the Steering Committee as reasonably representative of the settings in which clinical trials are conducted in Australia (i.e. provided reasonable coverage across trial and hospital characteristics including type of intervention in clinical trial (e.g. drug, surgical, diagnostic), jurisdiction (states/territories), type of hospital (general, specialist); and sector of hospital (public, private).
- **Standard costs were calculated on a fully absorbed basis[1].** The calculated standard costs include allocated health service overheads, so that the costs can be used without amendment, should trial funders/sponsors and clinical trial host sites choose to do so. It is not intended that the determined standard cost be loaded with further organisational overhead costs prior to their use in trial budget negotiations. However, consistent with the principles published by the NHMRC in association with the List, how, or if, the Table is used in the determination of the trial budget is ultimately a matter for the trial funder/sponsor and the health service that wishes to host a trial.
- **The costing process is transparent**. For each item on the revised List, potential users of the table of standard costs will 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 have been used to derive the standard cost of an item, they have been referenced.
- **Standard costs have been measured, not prices.** The study has produced a table of standard costs, and there are no mark-up on measured costs for pricing purposes (i.e. the cost for items associated with clinical trials, that IHPA is required to produce by Ministerial Direction, will equal the measured standard cost). Users are free to refer to the table of standard costs as they wish for the purposes of negotiating budgets for the establishment and operation of clinical trials.

The costs in this Determination relate to the 2014-15 Financial Year. The standard cost for each item includes the allocation of all overheads.

[1] 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 direct salary costs. 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 was considered to be reasonable.

3.2 COSTING THE SITE AUTHORISATION SUB-LIST

Table 3.1 provides details of the method used to determine the standard costs for the seven items on the site authorisation sub-list.

Table 3.1: The revised sub-list of standard items for site authorisation with associated costing method

Item number	Item	Costing method	Costing basis	Developed process map?	Method for determining resource units	Method for assigning unit costs to resource units
1.1.1	Preliminary assessment	Primary costing, protocol based	per potential clinical trial	Yes	• Identified the resource units (minutes of labour) required to complete each activity	• Used external source (e.g. relevant Award) to determine hourly rate (including provision for overhead) for each category of labour used
1.1.2	Protocol review	Primary costing, protocol based	per potential clinical trial	Yes	• Identified the resource units (minutes of labour) required to complete each activity	• Used external source (e.g. relevant Award) to determine hourly rate (including provision for overhead) for each category of labour used
1.1.3 (a)	Feasibility determination - completion of feasibility questionnaire	Primary costing, protocol based	per potential clinical trial	Yes	• Identified the resource units (minutes of labour) required to complete for three discrete activities (i.e. and)	• Used external source (e.g. relevant Award) to determine hourly rate (including provision for overhead) for each category of labour used
1.1.3 (b)	Feasibility determination - study site selection visit					
1.1.3 (c)	Feasibility determination - budget negotiation and contract review					
1.2.1	Preparation of the HREC application	Primary costing, protocol based	per HREC / clinical trial application	Yes	• Identified resource units (minutes of labour) required to complete each activity	• Used external source (e.g. relevant Award) to determine hourly rate (including provision for overhead) for each category of labour used
1.2.2	Ethics review	Primary costing, protocol based	per HREC / clinical trial application	Yes	• Identified resource units (minutes of labour) required to complete each activity	• Used external source (e.g. relevant Award) to determine hourly rate (including provision for overhead) for each category of labour used
1.3.1	Preparation of the SSA application by the project team	Primary costing, protocol based	per SSA application per clinical trial	Yes	• Identified resource units (minutes of labour) required to complete each activity	• Used external source (e.g. relevant Award) to determine hourly rate (including provision for overhead) for each category of labour used
1.3.2	Site processing and review	Primary costing, protocol based	per SSA application per clinical trial	Yes	• Identified resource units (minutes of labour) required to complete each activity	• Used external source (e.g. relevant Award) to determine hourly rate (including provision for overhead) for each category of labour used

Review of Table 3.1 shows that primary costing using a protocol based approach for deriving the standard costs was undertaken for all seven items on the site authorisation sub-list. For item 1.1.3 'feasibility determination' three separate standard costs for three discrete activities was calculated as there was considerable variability in regards to whether all three discrete activities occurred for every clinical trial (e.g. study site selection visit did not always occur).

3.3 COSTING THE SITE IMPLEMENTATION SUB-LIST

Table 3.2 provides details of the method used to determine the standard costs for the 31 items on the site implementation sub-list.

Table 3.2: The revised sub-list of standard items for site implementation with associated costing method

Item number	Item	Costing method	Costing basis	Developed process map?	Method for determining resource units	Method for assigning unit costs to resource units
2.1.1 (a)	Start-up meetings	Primary costing, protocol based	per clinical trial	Yes	• Identified resource units (minutes of labour) required to complete each activity	• Used external source (e.g. relevant Award) to determine hourly rate (including provision for overhead) for each category of labour used
2.1.1 (b-d)	Start-up meetings – online training		per personnel per trial			
2.1.2 (a)	Departmental set-up – host department	Primary costing, protocol based	per clinical trial per involved department	Yes	• Identified resource units (minutes of labour) required to complete each activity	• Used external source (e.g. relevant Award) to determine hourly rate (including provision for overhead) for each category of labour used
2.1.2 (b)	Departmental set-up – pharmacy department					
2.1.2 (c)	Departmental set-up – other supporting department					
2.1.3	Trial specific equipment set-up and maintenance	Primary costing, protocol based	per piece of clinical trial equipment	Yes	• Identified resource units (minutes of labour) required to complete each activity	• Used external source (e.g. relevant Award) to determine hourly rate (including provision for overhead) for each category of labour used
2.2.1	Pre-screening activity	Primary costing, protocol based	per potential clinical trial participant	Yes	• Identified resource units (minutes of labour) required to complete each activity	• Used external source (e.g. relevant Award) to determine hourly rate (including provision for overhead) for each category of labour used
2.2.2	Recruitment activity	Primary costing, protocol based	per potential clinical trial participant	Yes	• Identified resource units (minutes of labour) required to complete each activity	• Used external source (e.g. relevant Award) to determine hourly rate (including provision for overhead) for each category of labour used
2.3.1	Screening and health assessment	Reference to MBS fee schedules	per service	No	• Identified relevant items within the revised List that are applicable	• Used the relevant MBS fee and the multiplier to derive the standard cost

Item number	Item	Costing method	Costing basis	Developed process map?	Method for determining resource units	Method for assigning unit costs to resource units
2.3.2	Laboratory tests and procedures	Reference to MBS fee schedules	per service	No	• Identified applicable items on the MBS	• Used the relevant MBS fee and the multiplier to derive the standard cost
2.3.3	Imaging examinations and procedures	Reference to MBS fee schedules	per service	No	• Identified applicable items on the MBS	• Used the relevant MBS fee and the multiplier to derive the standard cost
2.3.4	Radiation therapy planning and treatment	Reference to MBS fee schedules	per service	No	• Identified applicable items on the MBS	• Used the relevant MBS fee and the multiplier to derive the standard cost
2.3.5	Other clinical tests or procedures	Reference to MBS fee schedules	per service	No	• Identified applicable items on the MBS	• Used the relevant MBS fee and the multiplier to derive the standard cost
2.3.6 (a and b)	Specialist medical consultations	Reference to MBS and ADA fee schedules	per service	No	• Identified applicable items on the MBS or ADA	• Used the relevant MBS and ADA fee and the multiplier to derive the standard cost
2.3.7	Nursing services	Reference to MBS fee schedules	per service	No	• Identified applicable items on the MBS	• Used the relevant MBS fee and the multiplier to derive the standard cost
2.3.8	Allied health services	Reference to MBS fee schedules	per service	No	• Identified applicable items on the MBS	• Used the relevant MBS fee and the multiplier to derive the standard cost
2.4.1	Staff training (drug-specific)	Primary costing, protocol based	per clinical trial per pharmacist	Yes	• Identified resource units (minutes of labour) required to complete each activity	• Used external source (e.g. relevant Award) to determine hourly rate (including provision for overhead) for each category of labour used
2.4.2 (a)	Stock management - drug stock received	Primary costing, protocol based	per drug stock received	Yes	• Identified resource units (minutes of labour) required to complete each activity	• Used external source (e.g. relevant Award) to determine hourly rate (including provision for overhead) for each category of labour used
2.4.2 (b)	Stock management - expiry management	Primary costing, protocol based	per week			
2.4.3 (a)	Drug preparation and dispensing – drug manufacturing	Primary costing, protocol based	per drug manufactured	Yes	• Identified resource units (minutes of labour) required to complete each activity	• Used external source (e.g. relevant Award) to determine hourly rate (including provision for overhead) for each category of labour used
2.4.3 (b)	Drug preparation and dispensing – simple		per *simple* preparation and dispensing			

Item number	Item	Costing method	Costing basis	Developed process map?	Method for determining resource units	Method for assigning unit costs to resource units
2.4.3 (c)	Drug preparation and dispensing – complex		per *complex* preparation and dispensing			
2.4.3 (d)	Drug preparation and dispensing – drug accountability		per participant per clinical trial drug preparation and dispensing			
2.4.3 (e)	Drug preparation and dispensing – provision of counselling		per provision of counselling to clinical trial participant			
2.5.1	Biospecimen collection and processing (central labs)	Primary costing, protocol based	per service (specimen collection and processing)	Yes	• Identified resource units (minutes of labour) required to complete each activity by different personnel	• Used external source (e.g. relevant Award) to determine hourly rate (including provision for overhead) for each category of labour used
2.5.2	Biospecimen storage	Reference to MBS fee schedules	per service	No	• Identified process for when items are on and not included in the MBS	• Use the relevant MBS fee and the multiplier to derive the standard cost or where item is not on MBS, biospecimen storage costs should be covered by the nearest equivalent MBS item
2.6.1	Investigator time	Reference to external labour cost schedules	rate per hour	No	• An hourly rate for an investigators time differentiated by Principal Investigator and co-investigator	• Used external source (e.g. relevant Award) to determine hourly rate (including provision for overhead) for each category of labour used
2.6.2	Research nurse time	Reference to external labour cost schedules	rate per hour	No	• An hourly rate for a research nurse's time	• Used external source (e.g. relevant Award) to determine hourly rate (including provision for overhead) for each category of labour used
2.6.3 (a –c)	Clinical research coordinator (non-research nurse) time	Reference to external labour cost schedules	rate per hour	No	• An hourly rate for a clinical research coordinator's time differentiated by Clinical Trials Coordinator (CTC), Clinical Trial Manager (CTM) or a combined (i.e. CTM/C) position	• Used external source (e.g. relevant Award) to determine hourly rate (including provision for overhead) for each category of labour used

Item number	Item	Costing method	Costing basis	Developed process map?	Method for determining resource units	Method for assigning unit costs to resource units
2.6.4	Interpreter services	Reference to external labour cost schedules	per hour	No	• An hourly rate for an interpreter's time	• Used external source (e.g. relevant Award) to determine hourly rate (including provision for overhead) for each category of labour used
2.6.5	Ward bed days	Reference to external cost/fee schedules	per bed-day	No	• Number of bed days	• Used external source (e.g. NHCDC) to determine bed-day cost (including provision for overhead) for each category of bed-day used
2.6.6	Clinic/theatre time	Reference to external cost/fee schedules	per hour	No	• An hourly rate for theatre time	• Used external source (e.g. NHCDC) to determine standard per minute theatre cost (including provision for overhead)
2.6.7	Outpatient time	N/A	N/A	N/A	• N/A	• N/A
2.7.1 (a and b)	Lead site coordination	Primary costing, protocol based	per clinical trial per annum	Yes	• Identified resource units (minutes of labour) required for each activity and differentiated for where there are four or less than, or more than four clinical trials sites involved	• Used external source (e.g. relevant Award) to determine hourly rate (including provision for overhead) for each category of labour used
2.7.2 (a)	Administration, monitoring and reporting – administration activities	Primary costing, protocol based	per clinical trial per annum	Yes	• Identify resource units (minutes of labour) required to complete for each activity in process map	• Use external source (e.g. relevant Award) to determine hourly rate (including provision for overhead) for each category of labour used
2.7.2 (b)	Administration, monitoring and reporting – other annual reporting		per clinical trial per annum			
2.7.2 (c)	Administration, monitoring and reporting – monitor visits		per visit			
2.7.2 (d)	Administration, monitoring and reporting – eCRF or CRF completion		per participant per visit			
2.7.2 (e)	Administration, monitoring and reporting – preparation of SAE and/or incident reports		per report reviewed			
2.7.2 (f)	Administration, monitoring and reporting – review of line items/SAE reports		per report prepared			
2.8.1	Participant time	Reference to external cost/fee schedules	per hour	No	• An hourly rate for participants time	• Used external source (e.g. relevant reimbursement schedule) to determine standard hourly rate

Item number	Item	Costing method	Costing basis	Developed process map?	Method for determining resource units	Method for assigning unit costs to resource units
2.8.2 (a to e)	Participant costs	Reference to external cost/fee schedules	per expense item	No	• Per night of accommodation • Per meal (breakfast, lunch or dinner) • Car travel per km per car type • Car parking at cost incurred	• Used external source (e.g. relevant reimbursement schedule to determine standard cost for each category of participant costs
2.9.1 (a)	Amendment preparation and submission – minor amendment	Primary costing, protocol based	per amendment	Yes	• Identified resource units (minutes of labour) required to complete each activity	• Used external source (e.g. relevant Award) to determine hourly rate (including provision for overhead) for each category of labour used
2.9.1 (b)	Amendment preparation and submission – major amendment		per amendment			
2.9.1 (c)	Amendment preparation and submission – if re-consenting required		per participant			
2.9.2 (a)	Amendment review – minor amendment by HREC office	Primary costing, protocol based	per amendment	Yes	• Identified resource units (minutes of labour) required to complete each activity	• Used external source (e.g. relevant Award) to determine hourly rate (including provision for overhead) for each category of labour used
2.9.2 (b)	Amendment review – major amendment by HREC office					
2.9.2 (c)	Amendment review – if re-consenting required by RGO office					

Table 3.2 shows that primary costing using a protocol based approach for deriving the standard costs was used for 13 out of the 31 items in the site implementation sub-list. For the remaining 17 items, reference to external costs or fee schedules was used. There was no standard cost calculated for item 2.6.7 'outpatient time' as we are suggesting it be deleted from the revised list as it overlaps with other items being items 2.3.6 'specialist medical consultations'; 2.3.7 'nursing services'; and 2.3.8 'allied health services'. The overlap is due to the reasons most clinical trial patients attend an outpatient clinic is to attend a medical specialist consultation (captured under item 2.3.6), a nurse clinic (captured under item 2.3.7) or an allied health clinic (captured under item 2.3.8)

Table 3.2 also shows that differential standard costs were calculated for 62 discrete activities within the 31 item in this sub-list. The reasons for calculating the differential costs was varied. Sometimes the differential cost was calculated due to:

- different personnel performing the same activity and hence different Awards were identified which varied the calculation of the standard cost (e.g. item 2.5.1 'Biospecimen collection and processing (central labs)" or item 2.6.1 'investigator time'; or item 2.6.3 'clinical research coordinator');
- the frequencies of occurrence of the discrete activities varied from annual (e.g. item 2.7.2 (a) administration or (b) other reporting activities) to per occurrence (e.g. item 2.7.2 (d) per review of a report or (e) per preparation of report;
- the complexity of the task (e.g. items 2.9.1 or 2.9.2 (a) minor amendment versus (b) major amendment; items 2.4.3 (b) drug preparation and dispensing – simple versus (c) Drug preparation and dispensing – complex);
- variability as to whether the discrete activity occur for a given trial (e.g. 2.4.3 (e) drug preparation and dispensing – provision of counselling); and
- estimated resources varied depending on which department of the hospital was involved (e.g. item 2.1.2 'departmental set-up').

3.4 COSTING THE SITE CLOSE-OUT SUB-LIST

Table 3.3 provides details of the method used to determine the standard costs for the four items on the site close-out sub-list.

Table 3.3: The revised sub-list of standard items for site close-out with associated costing method

Item number	Item	Costing method	Costing basis	Developed process map?	Method for determining resource units	Method for assigning unit costs to resource units
3.1.1	Site close-out visit	Primary costing, protocol based	per clinical trial	Yes	• Identified resource units (minutes of labour) required to complete each activity	• Used external source (e.g. relevant Award) to determine hourly rate (including provision for overhead) for each category of labour used
3.2.1 (a) and (b)	Archiving of trial records	Primary costing, protocol based	per clinical trial	Yes	• Identified resource units (minutes of labour) required to complete each activity differentiated by hospital department involved	• Used external source (e.g. relevant Award) to determine hourly rate (including provision for overhead) for each category of labour used
3.2.1 (c)	Archiving of trial records – storage fee	With reference to external cost/fee schedules	per clinical trial	No	• Identified typical fees charged by the private storage providers to archive the trial records and the number of boxes per clinical trial	• Choose median observation of years in storage and number of boxes
3.3.1	Drug return/destruction	Primary costing, protocol based	per drug return/destruction process	Yes	• Identified resource units (minutes of labour) required to complete each activity	• Used external source (e.g. relevant Award) to determine hourly rate (including provision for overhead) for each category of labour used

Item number	Item	Costing method	Costing basis	Developed process map?	Method for determining resource units	Method for assigning unit costs to resource units
3.4.1	Biospecimen return/destruction	Primary costing, protocol based	per biospecimen return/destruction process	Yes	• Identified resource units (minutes of labour) required to complete each activity	• Used external source (e.g. relevant Award) to determine hourly rate (including provision for overhead) for each category of labour used

Table 3.3 shows that primary costing using a protocol based approach for deriving the standard costs was used for all items in the site close-out sub-list however one discrete activity within item 3.2.1 'archiving of trial records' was calculated with reference to external fee schedules. A differential standard cost was calculated for item 3.2.1 (c) 'archiving of trial records – storage fee' as this varied by site as to whether they used off site storage and to the volume of boxes stored per clinical trial.

4

The table of standard costs

This Chapter presents 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 revised 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. IHPA will also issue a Determination, as directed by the Commonwealth Minister for Health, which should be considered in conjunction to this report.

4.1 BASIS OF CALCULATING 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 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 2014)*. These matters are set out in Table 4.1.

Table 4.1: 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 Act 2011*	Matters set out in the *Ministerial Direction to the Independent Hospital Pricing Authority on the Performance of its Functions (No. 1 of 2014)*
(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.*	*(i) 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 Steering Committee with relevant expertise was established; a process of inviting public submissions was undertaken; actual costs were measured and used to determine standard costs; and visits to nine different public and three private hospitals covering a range of characteristics were conducted. In respect of the Ministerial Direction, the actual activity of each item was considered and as activity was identified across all sites for all items (except for one item which was deemed to be an overlap

of other items); the standard cost is based on the typical cost incurred; and public submissions were invited, with the nine submissions received influencing the final determination of the table of standard costs.

In particular, there was a choice between calculating one standard cost (with no (or minimal) variation) or calculating a range for the standard cost for each item (i.e. lowest to highest) for each item on the revised List. Although the study was undertaken in a short time period, the improvements to the revised List has enabled differential costs to be calculated for some discrete activities within the revised list.

The standard cost for each item (or discrete activity within each item) is intended to be the national standard cost 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 4.3.

4.2 THE TABLE OF STANDARD COSTS

The costing information for all 42 items on the revised List of activities associated with clinical trials is presented in the same format, in Appendix A (site authorisation), B (site implementation) and C (site close-out) of this report. Within the relevant Appendix, there are between one and four pages for each revised List item, with the headings and content for each item being as shown in Table 4.2.

Table 4.2: 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 and the determined standard cost.
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 all 42 items (except the one suggested for deletion) on the revised List represents a mixture of services and activities for which costs can be derived using activity based costing, as well as a number of items that describe adjusted fee schedules. Table 4.3 presents the standard cost for each item (or discrete activities within the items) and a comments section to guide use of the standard cost.

Table 4.3: Table of standard costs for the revised 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 – Site Authorisation				
Feasibility Assessment	Preliminary assessment	1.1.1	• **$60.38** per *potential* clinical trial	• Based on the assumption that the PI and CTM/C are the only two involved in an preliminary assessment and that the hourly rate (fully absorbed) of the PI is $226.11/hour (as defined in item 2.6.1) and $90.78/hour for CTM/C (as defined in item 2.6.3). • Standard cost is calculated using the 25th percentile of the gathered data. • Potential outliers (i.e. data is suggestive although a large enough sample not available/gathered due to scope of project) were the paediatric clinical trials and Phase 1 clinical trials where the protocol is typically more detailed and requires more consideration (i.e. extra time) and hence the 25th percentile may be too low for these types of trials. • Although the costs are incurred by the clinical trial site the costs were not included in any clinical trial budget, as the activities occur before site selection, and are considered by sponsors to be part of the tendering process for site selection.
	Protocol review	1.1.2	• **$407.67** per *potential* clinical trial	• Based on the assumption that the PI and CTM/C are the only two involved in protocol review and that the hourly rate (fully absorbed) of the PI is $226.11/hour (as defined in item 2.6.1) and $90.78/hour for CTM/C (as defined in item 2.6.3). • Standard cost is calculated using the median of the gathered data. • Although the costs are incurred by the clinical trial site the costs were not included in any clinical trial budget, as the activities occur before site selection, and are considered by sponsors to be part of the tendering process for site selection.
	Feasibility determination – completion of feasibility questionnaire	1.1.3 (a)	• **$294.62** for completion of feasibility questionnaire required for a *potential* clinical trial	• Based on the assumption that the PI and CTM/C are the only two involved in protocol review and that the hourly rate (fully absorbed) of the PI is $226.11/hour (as defined in item 2.6.1) and $90.78/hour for CTM/C (as defined in item 2.6.3). • Standard cost is calculated using the median of the gathered data.
	Feasibility determination – study site visit	1.1.3 (b)	• **$675.95** for study site selection visit required by sponsor organisation for a *potential* clinical trial	• Based on the assumption that the PI, CTM/C and at least one supporting department (usually the pharmacy) are involved and that the hourly rate (fully absorbed) of the PI is $226.11/hour (as defined in item 2.6.1), $90.78/hour for CTM/C (as defined in item 2.6.3) and $86.72/hour (blended hourly rate, based on the assumption that the involved personnel from supporting departments is either a hospital scientist (i.e. Grade 3/4 hospital scientist) and/or pharmacist (i.e. Grade 3/5 pharmacist)). • Standard cost is calculated using the median of the gathered data.

Major category	Item	Reference number	Standard cost	Comments to guide use of the standard cost
	Feasibility determination – budget negotiation and contract review	1.1.3 (c)	• **$755.51** for budget negotiation and contract review for a *potential* clinical trial	• Based on the assumption that the PI, CTM/C, at least one supporting department (usually the pharmacy) and personnel from the RGO are involved and that the hourly rate (fully absorbed) of the PI is $226.11/hour (as defined in item 2.6.1), $90.78/hour for CTM/C (as defined in item 2.6.3), $86.72/hour (blended hourly rate, based on the assumption that the involved personnel from supporting departments is either a hospital scientist (i.e. Grade 3/4 hospital scientist) and/or pharmacist (i.e. Grade 3/5 pharmacist)) and $70.59/hour for RGO staff based on the average salary for a research and governance officer is $82,587 plus superannuation). • Standard cost is calculated using the median of the gathered data. • Assumes that the provided sponsors' contract is either the standard Medicines Australia (MA), or MTAA or other pre-approved agreement and includes the use of previously agreed or standard schedules (e.g. 4 and 7). If not, legal costs are incurred by the site (i.e. services either provided by internal or outsourced lawyer). This legal cost is not included in the standard cost.
Ethics Approval	Preparation of the HREC application	1.2.1	• **$2,607.83** per clinical trial (i.e. per HREC application)	• Based on the assumption that the PI and CTM/C are the only two involved in an preliminary assessment and that the hourly rate (fully absorbed) of the PI is $226.11/hour (as defined in item 2.6.1) and $90.78/hour for CTM/C (as defined in item 2.6.3). • Standard cost is calculated using the median of the gathered data. • As the data represents a mix of industry sponsored trials (where drafts of required documents are provided) as well as collaborative and investigator-initiated trials (where *de novo* applications are prepared) this accounts for the large variation from *min* to *75th percentile*. • The 'max' value was due to the data gathered from the one paediatric site included in the study. Setting a differential standard cost for paediatric clinical trials at the 75th percentile was considered. However as only one paediatric site was included in the sample, it was considered that there was insufficient evidence to set a differential standard cost for paediatric clinical trials at this stage, even though the gathered data suggests it would reflect a more realistic cost associated with the input time for such types of clinical trials.
	Ethics review	1.2.2	• **$2,099.42** per clinical trial application	• Based on the assumption that there are eight members on the HREC and the included skill mix are: 1 x chairperson, 1 x legal background; 2 x medical backgrounds, 2 x scientific and/or allied health discipline backgrounds, 1 x ethics officer; 1 x lay members. • Based on the assumption that each HREC application is reviewed in detail by a primary and secondary reviewer. • Standard cost is calculated using the median for all gathered data except for the data related to the ethics officer which is based on the 75th percentile. • It is recognised that although most members of HREC do not receive a sitting fee, a standard cost has been calculated on cost not fees incurred.

Major category	Item	Reference number	Standard cost	Comments to guide use of the standard cost
Site-specific assessment	Preparation of the SSA application by the project team	1.3.1	• **$398.69** per SSA application	• Based on the assumption that the PI and CTM/C are the only two involved in drafting the SSA application and that the hourly rate (fully absorbed) of the PI is $226.11/hour (as defined in item 2.6.1) and $90.78/hour for CTM/C (as defined in item 2.6.3). In addition, the most common process identified at least three supporting department who will review and sign the SSA, hence up to three supporting department involvement has been factored into the calculation for the standard cost. • Standard cost is calculated using the 25th percentile of the gathered data. • Although it is recognised that the RGO may be involved at this step, all activities (and hence time input) provided by RGO office are captured under item 1.3.2.
	Site processing and review	1.3.2	• **$264.71** per SSA application processed	• Based on the assumption that the RGO office is the only personnel/office involved and that the hourly rate (fully absorbed) blended across various positions in the RGO is on an average salary of $82,587 plus superannuation (or $70.59/hour). • Standard cost is calculated using the median of the gathered data. • Across items 1.1.3 and 1.3.2 the estimated RGO time is 5.25 hours per application. • Assumes that the provided sponsors' contract is either the standard Medicines Australia (MA), or MTAA or other pre-approved agreement and includes the use of previously agreed or standard schedules (e.g. 4 and 7). If not, legal costs are incurred by the site (i.e. services either provided by internal or outsourced lawyer). This legal cost is not included in the standard cost for this item or item 1.1.3 (c).
Sub-List 2 – Site Implementation				
Trial initiation	Start-up meetings	2.1.1 (a)	• **$1,879.69** per clinical trial start-up meeting (excluding online training)	• Based on the assumption that the mix of staff involved in the start-up meeting (involves organisaiton of the meeting, a group meeting and one-on-one meetings) includes one PI, two co-PIs, two CTM/C and four staff from supporting departments (e.g. pharmacy, pathology/imaging) attending the group meeting. Although additional staff do often attend (e.g. additional CTC, medical and/or nursing staff etc.) the standard cost reflects the core people identified through the case study visits. • Standard cost is calculated using the 25th percentile of the gathered data. • Excludes any training that needs to be undertaken outside the start-up meeting (e.g. online which is captured under item 2.1.1 (b), (c) and (d).
	Online training undertaken by PI	2.1.1 (b)	• **$282.64** per PI to undertake 1.25 hours of online training per clinical trial	• Based on the assumption that the PI fully absorbed hourly rate is $226.11/hour (as defined in item 2.6.1). • Standard cost is calculated using the 25th percentile of the gathered data.
	Online training undertaken by CTM/C	2.1.1 (c)	• **$295.04** per CTM/C to undertake 3.25 hours of online training per clinical trial	• Based on the assumption that the CTM/C fully absorbed hourly rate is $90.78/hour (as defined in item 2.6.3). • Standard cost is calculated using the 25th percentile of the gathered data.

Major category	Item	Reference number	Standard cost	Comments to guide use of the standard cost
	Online training undertaken by supporting department	2.1.1 (d)	• **$65.04** per supporting department personnel to undertake ¾ hours of online training per clinical trial	• Based on the assumption that the supporting department personnel fully absorbed hourly rate is $86.72/hour (blended hourly rate, based on the assumption that the involved personnel from supporting departments is either a hospital scientist (i.e. Grade 3/4 hospital scientist) and/or pharmacist (i.e. Grade 3/5 pharmacist)). • Standard cost is calculated using the 25th percentile of the gathered data. • Only online training undertaken by pharmacy staff that is not drug-specific (e.g. GCP etc.) is captured under this item. Drug-specific training (e.g. drug preparation, logging etc.) required for any clinical trial undertaken by pharmacy staff is included under item 2.4.1.
	Departmental set-up	2.1.2 (a)	• **$1,361.70** per host department per clinical trial	• Based on the assumption that the CTM/C fully absorbed hourly rate is $90.78/hour (as defined in item 2.6.3). • Standard cost is calculated using the 40th percentile of the gathered data as the ERG expressed that the median appeared too high and the 25th percentile too low.
	Departmental set-up	2.1.2 (b)	• **$530.40** per pharmacy department per clinical trial	• Based on the assumption that the pharmacist involved in departmental set-up has a fully absorbed hourly rate of $88.40/hour (i.e. Grade 3/5 pharmacist). • Standard cost is calculated using the 40th percentile of the gathered data as the ERG expressed that the median appeared too high and the 25th percentile too low.
	Departmental set-up	2.1.2 (c)	• **$346.88** per other supporting department per clinical trial	• Standard cost is calculated using the 40th percentile of the gathered data as the ERG expressed that the median appeared too high and the 25th percentile too low. • Based on the assumption that the supporting department personnel fully absorbed hourly rate is $86.72/hour (blended hourly rate, based on the assumption that the involved personnel from supporting departments is either a hospital scientist (i.e. Grade 3/4 hospital scientist) and/or pharmacist (i.e. Grade 3/5 pharmacist)).
	Trial specific equipment set-up and maintenance	2.1.3	• **$85.04** per piece of trial equipment	• Standard cost is calculated using the median of the gathered data. • Standard costs does not include equipment purchase and/or hire. • Standard costs does not include IT personnel time as their involvement was not always required.
Patient accrual	Pre-screening activity	2.2.1	• **$166.15** to screen each potential participant per clinical trial	• Based on the assumption that the PI and CTM/C are the main two involved in pre-screening and that the hourly rate (fully absorbed) of the PI is $226.11/hour (as defined in item 2.6.1) and $90.78/hour for CTM/C (as defined in item 2.6.3). • Standard cost is calculated using the median of the gathered data.
	Recruitment activity	2.2.2	• **$498.45** per potential participant per clinical trial	• Based on the assumption that the PI and CTM/C are the main two involved in recruitment and that the hourly rate (fully absorbed) of the PI is $226.11/hour (as defined in item 2.6.1) and $90.78/hour for CTM/C (as defined in item 2.6.3). • Standard cost is calculated using the median of the gathered data.

Major category	Item	Reference number	Standard cost	Comments to guide use of the standard cost
Clinical services	Screening and health assessment	2.3.1	• Calculated per service based on trial protocol using standard costs for items 2.3.2, 2.3.3, 2.3.4, 2.3.5, 2.3.6, 2.3.7 and 2.3.8	• 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 care or are in addition to standard care. • The screening visit and health assessment often includes a range of procedures and/or consultations under items 'clinical services'. All these activities should be costed according to their respective items.
	Laboratory tests and procedures	2.3.2	• 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 care laboratory tests and procedures.
	Imaging examinations and procedures	2.3.3	• 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 clinical trial participants. • There are a number of clinical 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. • Not all imaging examinations and/or procedures are included on the MBS (e.g. PET-FLT scans are not currently covered under any MBS item numbers). Where the imaging examinations and/or procedures are not on the MBS then the nearest equivalent imaging examination and/or procedure on the MBS should be used. In the absence of any other data this is considered to be the best approach. • Only for non-standard care imaging examinations and/or procedures.
	Radiation therapy planning and treatment	2.3.4	• 140% of the MBS fee including ROHPG component per service	• The MBS loading reflects the clinical trial specific activities (e.g. extra reporting, image transfer) associated with radiotherapy services provided to clinical trial participants. • Only for non-standard care radiation therapy planning and treatment.
	Other clinical tests or procedures	2.3.5	• 140% of the MBS fee per service	• The MBS loading reflects the clinical trial specific activities (e.g. extra reporting, image transfer) provided to clinical trial participants. • Only for non-standard care other clinical tests or procedures.
	Specialist medical consultations	2.3.6 (a)	• 140% of the MBS fee per specialist medical (including GP) service	• The MBS loading reflects the clinical trial specific activities (e.g. extra reporting, extra information) provided to clinical trial participants. • Only for non-standard care specialist medical consultations.
	Specialist medical consultations - dental	2.3.6 (b)	• 100% of ADA fee per specialist dental service	• The ADA Fee is unadjusted because it allows for a return on investment component in setting the fee. • Only for non-standard care specialist medical consultations.
	Nursing services	2.3.7	• **$81.90** per nurse consultation (based on 140% of the identified MBS fees)	• The MBS loading reflects the trial specific activities (e.g. extra reporting, extra information) provided to clinical trial participants. • Only for non-standard care nursing services.

Major category	Item	Reference number	Standard cost	Comments to guide use of the standard cost
	Allied health services	2.3.8	• **$98** per allied health consultation (based on 140% of the identified MBS fees)	• The MBS loading reflects the trial specific activities (e.g. extra reporting, extra information) provided to clinical trial participants. • Only for non-standard care allied health services.
Pharmacy / Investigation Drug Related	Staff training (drug-specific)	2.4.1	• **$176.80** per pharmacist to undertake two hours of drug-specific training per clinical trial	• Based on the assumption that the pharmacist involved has a fully absorbed hourly rate of $88.40/hour (i.e. Grade 3/5 pharmacist)) and that the training takes two hours per pharmacist. • Standard cost is calculated using the 25th percentile of the gathered data. • Charged by pharmacy department only and is for drug-specific training only. Other online training related to the clinical trial is captured under item 2.1.1 (d).
	Stock management – drug stock received	2.4.2 (a)	• **$72.85** per drug stock received	• Based on the assumption that stock management involves a pharmacy technician overseen by a pharmacist at a fully absorbed hourly rate of $88.40 (pharmacist) and $57.30 (for the pharmacy technician which is assumed to have a salary equivalent to a Grade 1 pharmacist). • Task is undertaken per stock delivery received. • Standard cost is calculated using the 25th percentile of the gathered data.
	Stock management – expiry management	2.4.2 (b)	• **$9.17** for expiry management per week	• Based on the assumption that expiry management is done weekly by a pharmacy technician at a fully absorbed hourly rate of $57.30 (assumed to have a salary equivalent to a Grade 1 pharmacist). • Standard cost is calculated using the 25th percentile of the gathered data.
	Drug preparation and dispensing – drug manufacturing	2.4.3 (a)	• **$169.43** for drug manufacturing (if required)	• Based on the assumption that two pharmacists are required to manufacture any clinical trials drugs at a fully absorbed hourly rate of $88.40 (i.e. Grade 3/5 pharmacist as defined under item 2.6.3). • Most of the drug manufacturing was found not to be done by clinical trial sites involved in the study. Where it was found to be done at participating sites, there was wide variation in time spent on manufacturing the required clinical trials drugs. • The cost associated with drug manufacturing may need to be negotiated on a per trial basis with some reference to this standard cost. • Standard cost is calculated using the median of the gathered data.
	Drug preparation and dispensing – simple	2.4.3 (b)	• **$43.32** for simple clinical trial drug preparation and dispensing	• Based on the assumption that two pharmacists are required to undertake simple (based on volume of items and complexity of process e.g. counting tablets, measuring liquids etc.) preparation and dispensing clinical trials drug activities at a fully absorbed hourly rate of $88.40 (i.e. Grade 3/5 pharmacist as defined under item 2.6.3). • Developing a standard cost for simple drug preparation and 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. • Standard cost is calculated using the median of the gathered data.

Major category	Item	Reference number	Standard cost	Comments to guide use of the standard cost
	Drug preparation and dispensing – complex	2.4.3 (c)	• **$110.21** for complex clinical trial drug preparation and dispensing	• Based on the assumption that two pharmacists are required to undertake complex (based on volume of items and complexity of process e.g. aseptic or cytotoxic) preparation and dispensing clinical trials drug activities at a fully absorbed hourly rate of $88.40 (i.e. Grade 3/5 pharmacist as defined under item 2.6.3). • Developing a standard cost for complex drug preparation and 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. • Standard cost is calculated using the median of the gathered data.
	Drug preparation and dispensing – drug accountability	2.4.3 (d)	• **$14.33** for clinical trial drug accountability activities per clinical trial participant	• Based on the assumption that drug accountability activities is largely undertaken by a pharmacy technician at a fully absorbed hourly rate of $57.30 (assumed to have a salary equivalent to a Grade 1 pharmacist). • Standard cost is calculated using the median of the gathered data.
	Drug preparation and dispensing – provision of counselling	2.4.3 (e)	• **$18.12** for provision of counselling services by a pharmacist at the time of dispensing the clinical trial drug(s) to a clinical trial participant	• It was found that counselling is not also performed by the pharmacy department (sometimes CTM/C takes on this role), however when it does this standard cost is based on the assumption that a pharmacist is required at a fully absorbed hourly rate of $88.40 (i.e. Grade 3/5 pharmacist as defined under item 2.6.3). • Standard cost is calculated using the median of the gathered data.
Biospecimen related	Biospecimen collection and processing (central labs) – performed by research nurse	2.5.1 (a)	• **$28.05** per clinical trial participant as per the occurrences described in the clinical trial protocol	• Based on the assumption that the biospecimen collection and processing is undertaken by a research nurse at a fully absorbed hourly rate of $74.79 as defined under item 2.6.2. • 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. • Standard cost is calculated using the median of the gathered data.
	Biospecimen collection and processing (central labs) – performed by research nurse	2.5.1 (b)	• **$34.04** per clinical trial participant as per the occurrences described in the clinical trial protocol	• Based on the assumption that the biospecimen collection and processing is undertaken by the CTM/C at a fully absorbed hourly rate of $90.78 as defined under item 2.6.3. • 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. • Standard cost is calculated using the median of the gathered data.
	Biospecimen collection and processing (central labs) – performed by pathology staff personnel	2.5.1 (c)	• **$31.89** per clinical trial participant as per the occurrences described in the clinical trial protocol	• Based on the assumption that the biospecimen collection and processing is undertaken by pathology department personnel (i.e. hospital scientist Grade 3/4) at a fully absorbed hourly rate of $85.04. • 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. • Standard cost is calculated using the median of the gathered data.

Major category	Item	Reference number	Standard cost	Comments to guide use of the standard cost
	Biospecimen storage	2.5.2	• Included under item 2.5.1 where the collection and processing of a biospecimen attracts an MBS fee; • Where the collection and processing of a biospecimen does not attract an MBS biospecimen storage costs should be covered by the nearest equivalent MBS item.	• Study found that the majority of biospecimens are not stored at local hospitals for prolonged periods of time. Generally they are regularly sent to the sponsor throughout the life of a trial, or at the end of the trial. Where specimens were found to be stored on site, they were generally small amounts and did not consume significant space.
Clinical resources	Investigator time – Principal Investigator	2.6.1 (a)	• **$226.11** per hour for Principal Investigator	• Based on the assumption that the PI is a senior specialist (i.e. average between years 8 and 9 on the AMA rates was used). • 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. items under clinical services).
	Investigator time – sub/co- investigator	2.6.1 (b)	• **$199.11** per hour for sub/co-investigator	• Based on the assumption that the Sub/Co-PI is less experienced than the PI but still a senior specialist (i.e. years 5 on the AMA rates was used). • This item should only be used where the clinician is acting in his/her capacity as an sub/co-investigator and should not include items costed on a per service basis (i.e. items under clinical services).
	Research nurse time	2.6.2	• **$74.79** per hour for research nurse	• Based on the assumption that the research nurse is a Clinical Nurse Specialist (CNS), taken at the average of a year 1 and 2 CNS. • This item should only be used where the clinician is acting in his/her capacity as an research nurse and should not include items costed on a per service basis (i.e. items under clinical services).
	Clinical research coordinator (non-research nurse) time – equivalent to Clinical Trials Coordinator (CTC)	2.6.3 (a)	• **$82.74** per hour for clinical research coordinator (equivalent to CTC)	• This role is more commonly known as a Clinical Trials Coordinator (CTC) and the discipline filling the positions varied between those qualified as Registered Nurses (RNs) or those with scientific qualifications (e.g. Grade 3/4 scientist) and/or allied health qualifications (e.g. pharmacist (e.g. Grade 3/5 pharmacist)). • Based on the assumption that the position of CTC is filled equally by a mix of the above identified disciplines. • This item should only be used where the position is acting in his/her capacity as a CTC and should not include items costed on a per service basis (i.e. items under clinical services).
	Clinical research coordinator (non-research nurse) time – equivalent to Clinical Trials Manager (CTM)	2.6.3 (b)	• **$93.16** per hour for clinical trials manager (CTM)	• The role of the CTM is to coordinate CTCs and is often heavily involved in the site authorisation process (more so than the CTC where the role of CTM exists). The CTM is usually a senior nurse, whose prior position was either a Nurse Unit Manager (NUM) or more commonly a CNC. • Based on the assumption that the position of CTM is filled equally by a CNC Grade 3. • This item should only be used where the position is acting in his/her capacity as a CTM and should not include items costed on a per service basis (i.e. items under clinical services).

Major category	Item	Reference number	Standard cost	Comments to guide use of the standard cost
	Clinical research coordinator (non-research nurse) time – equivalent to Clinical Trials Manager (CTM)/Clinical Trials Coordinator (CTC)	2.6.3 (c)	• **$90.78** per hour for CTM/CTC	• A blended CTM/C hourly rate was calculated as the existence of either or both positions within hospital departments varies. • This item should only be used where the position is acting in his/her capacity as a CTM/C and should not include items costed on a per service basis (i.e. items under clinical services).
	Interpreter services	2.6.4	• **$53.91** per hour	• Found to be rarely used, although when used some sites use contracted interpreter services whereas other sites had interpreters (for at least the most common languages) available on site.
	Ward bed days	2.6.5	• **$1,130** per day	• A cost per ward bed days was calculated using NHCDC data from 2012-13. Excludes the cost components: allied health (as captured under item 2.3.8) imaging (as captured under item 2.3.3), pathology (as captured under item 2.3.2) and theatre costs (as captured under item 2.6.6). • The 2012-13 costs have been indexed as per the National Efficient Price Determination for 2013-14 indexation rate. • The costs calculated have been based on are the national costs, inclusive of all states/territories.
	Clinic/theatre time	2.6.6	• **$980** per theatre/clinic hour (excluding medical costs)	• The standard cost excludes medical costs (as these cost elements have been identified elsewhere (e.g. items 2.3.6 and 2.6.1). • Data were provided on hospitals in Queensland, South Australia and New South Wales. • Standard cost is calculated using the median of the gathered data.
	Outpatient time	2.6.7	• Not calculated	• Through both consultations with sites and through the public consultation process, majority view was that this item appeared to duplicate other items in the list (e.g. mainly items 2.3.6, 2.3.7 and 2.3.8). We are therefore suggesting that this item be deleted from the revised list.
Trial operation	Lead site coordination – four or less sites	2.7.1 (a)	• **$2,436.81** per clinical trial per annum	• Based on the assumption that the PI and CTM/C are the only two involved in lead site coordination and that the hourly rate (fully absorbed) of the PI is $226.11/hour (as defined in item 2.6.1) and $90.78/hour for CTM/C (as defined in item 2.6.3). • Standard cost is calculated using the 25th percentile of the gathered data.
	Lead site coordination – more than four sites	2.7.1 (b)	• **$5,100.08** per clinical trial per annum	• Based on the assumption that the PI and CTM/C are the only two involved in lead site coordination and that the hourly rate (fully absorbed) of the PI is $226.11/hour (as defined in item 2.6.1) and $90.78/hour for CTM/C (as defined in item 2.6.3). • Standard cost is calculated using the median of the gathered data.
	Administration, monitoring and reporting – administration activities	2.7.2 (a)	• **$1,073.32** per clinical trial per annum for administration activities	• Administration activities include tasks that occur post the establishment phase, including managing clinical trial documentation; retrieving medical and/or clinical records; invoicing; organising and maintaining virtual private network (VPN) access; and liaison with investigators and/or sponsor. • Standard cost is calculated using the median of the gathered data.

Major category	Item	Reference number	Standard cost	Comments to guide use of the standard cost
	Administration, monitoring and reporting – eCRF or CRF completion	2.7.2 (b)	• **$45.39** per eCRF or CRF per participant per visit	• Standard cost is calculated using the 25th percentile of the gathered data.
	Administration, monitoring and reporting – monitor visits	2.7.2 (c)	• **$234.03** per monitor visit (including remote monitoring visits)	• Standard cost is calculated using the 25th percentile of the gathered data.
	Administration, monitoring and reporting – review of line items/SAE reports	2.7.2 (d)	• **$77.23** per review of line listing/SAE reports	• Standard cost is calculated using the 25th percentile of the gathered data.
	Administration, monitoring and reporting – other annual reporting	2.7.2 (e)	• **$745.65** per clinical trial per annum for reporting activities – other annual reporting	• Other annual reporting includes tasks accrual reporting; annual governance reporting and annual ethics report but excludes safety and adverse/incident event reporting which is captured under item 2.7.2 (f). • Standard cost is calculated using the median of the gathered data.
	Administration, monitoring and reporting – preparation of SAE and/or incident reports	2.7.2 (f)	• **$251.69** per SAE and/or incident report prepared	• Standard cost is calculated using the 25th percentile of the gathered data.
Participant related	Participant time	2.8.1	• **$49** per hour	• Based on the average of a range of identified consumer hourly rates available in the public domain for similar activities.
	Participant costs - accommodation	2.8.2 (a)	• **$183** per night for accommodation	• Based on the average of the rate for overnight accommodation in the capital cities, as published on the ATO website, has been used to calculate the standard cost.
	Participant costs – breakfast	2.8.2 (b)	• **$25.35** per breakfast meal	• The calculated standard cost is based on the generic rate (i.e. no variation based on location) published on the ATO website, for those on an annual salary less than $112,610.
	Participant costs – lunch	2.8.2 (c)	• **$28.55** per lunch meal	• The calculated standard cost is based on the generic rate (i.e. no variation based on location) published on the ATO website, for those on an annual salary less than $112,610.
	Participant costs – dinner	2.8.2 (d)	• **$48.65** per dinner meal	• The calculated standard cost is based on the generic rate (i.e. no variation based on location) published on the ATO website, for those on an annual salary less than $112,610.
	Participant costs – car per km	2.8.2 (e)	• Car travel per km by car type	• The calculated standard cost is based on the rates per km by car type published on the ATO website.
	Participant costs – car parking	2.8.2 (f)	• Car parking – at cost incurred	• Car parking varies greatly dependent on location and the length of the clinical trial specific visit. As such it is suggested that car parking is reimbursed (by receipt) at the cost that has been incurred.

Major category	Item	Reference number	Standard cost	Comments to guide use of the standard cost
Amendment Processing	Amendment preparation and submission – minor amendment	2.9.1 (a)	• **$128.47** per minor amendment	• Based on the assumption that the PI and CTM/C are the only two involved in preparing minor amendments and that the hourly rate (fully absorbed) of the PI is $226.11/hour (as defined in item 2.6.1) and $90.78/hour for CTM/C (as defined in item 2.6.3). • Standard cost is calculated using the 25th percentile of the gathered data.
	Amendment preparation and submission – major amendment	2.9.1 (b)	• **$238.09** per major amendment	• Based on the assumption that the PI and CTM/C are the only two involved in preparing major amendments and that the hourly rate (fully absorbed) of the PI is $226.11/hour (as defined in item 2.6.1) and $90.78/hour for CTM/C (as defined in item 2.6.3). • Standard cost is calculated using the median of the gathered data.
	Amendment preparation and submission – if re-consenting required	2.9.1 (c)	• **$113.06** per participant if re-consenting is required as a result of the amendment.	• Based on the assumption that if re-consenting is required as a result of a major amendment then this will be undertaken by the PI at the hourly rate (fully absorbed) of $226.11/hour (as defined in item 2.6.1). • Standard cost is calculated using the median of the gathered data.
	Amendment review – minor amendment by HREC office	2.9.2 (a)	• **$35.30** per minor amendment/SAE review by HREC office	• Based on the assumption that review/processing of a minor amendment or minor SAE involves the HREC officer only at an assumed fully absorbed hourly rate of $70.59 based on an assumed average annual salary of $82,587 plus superannuation. • Standard cost is calculated using the median of the gathered data.
	Amendment review – major amendment by HREC office	2.9.2 (b)	• **$238.81** per major amendment/SAE review by HREC office (including it being tabled at HREC meeting)	• Based on the assumption that a major amendment/SAE will be prepared and presented at a HREC meeting involving the same eight people identified in item 1.2.2. • Standard cost is calculated using the median of the gathered data.
	Amendment review – if re-consenting required by RGO office	2.9.2 (c)	• **$35.30** per minor amendment/SAE review by RGO	• Based on the assumption that review/processing of a minor amendment or minor SAE submitted to the RGO involves the RGO officer only at an assumed fully absorbed hourly rate of $70.59 based on an assumed average annual salary of $82,587 plus superannuation. • Standard cost is calculated using the median of the gathered data.
Sub-List 3 – Site Close-out				
Site close-out visit	Site close-out visit	3.1.1	• **$821.26** per clinical trial	• Based on the site close-out visit activities including the CTM/C (fully absorbed hourly rate of $90.78 as defined under item 2.6.3), PI (fully absorbed hourly rate of $226.11 as defined under item 2.6.1) and personnel from involved supporting departments (fully absorbed hourly rate of $86.72 (i.e. blend of a hospital scientist (i.e. Grade 3/4 hospital scientist) and pharmacist (i.e. Grade 3/5 pharmacist). • Standard cost is calculated using the median of the gathered data.
Record archiving	Archiving of trial records – performed by host department	3.2.1 (a))	• **$272.34** per clinical trial	• Based on the assumption that the CTM/C is the only person involved in archiving of trial records of the host department at an hourly rate (fully absorbed) of $90.78/hour (as defined in item 2.6.3). • Standard cost is calculated using the median of the gathered data.
	Archiving of trial records – performed by supporting departments	3.2.1 (b)	• **$86.72** per clinical trial	• Based on the assumption that one person within each supporting department will be designated to perform the archiving of trial records in their department at a blended hourly rate (fully absorbed) of $86.72/hour (i.e. blend of a hospital scientist (i.e. Grade 3/4 hospital scientist) and pharmacist (i.e. Grade 3/5 pharmacist). • Standard cost is calculated using the median of the gathered data.

Major category	Item	Reference number	Standard cost	Comments to guide use of the standard cost
	Archiving of trial records – storage fee	3.2.1 (c)	• $1,575.00 per clinical trial	• Based on the assumption that the storage fee charged to the hospital department is $30.00 per box and that on average 3.5 boxes are stored for 15 years. • Standard cost is calculated using the median of the gathered data.
Drug return/destruction	Drug return/destruction	3.3.1	• **$72.24** per drug return/destruction process	• Based on the assumption that drug return/destruction activities is largely undertaken by a pharmacy technician at a fully absorbed hourly rate of $57.30 (assumed to have a salary equivalent to a Grade 1 pharmacist) but overseen by a pharmacist (average fully absorbed hourly rate of $88.40 for Grade 3/5 pharmacist (as defined in 2.6.3)). • Drug return/destruction occurs throughout the trial not just at close-out. • Standard cost assumes that the accountability, boxing up and returning excess stock to the sponsor is undertaken by hospital staff (i.e. pharmacy technician and/or pharmacist) and not the sponsor (during a monitoring visit). • Standard cost is calculated using the median of the gathered data.
Biospecimen transfer/destruction	Biospecimen return/destruction	3.4.1	• **$85.04** per biospecimen return/destruction process.	• The loading associated with item 2.3.2 already incorporates destruction of biospecimens for those biospecimens covered under the MBS. Hence item 3.4.1 is only relevant for biospecimen return and/or destruction not included under the MBS. • Standard cost is calculated using the median of the gathered data.

4.3 USING THE TABLE OF STANDARD COSTS

Review of the existing materials (including site discussions) has identified a range of discussion about the appropriateness or otherwise of adjusting standard costs that may be measured to take account of specific features of the trial. A list of possible factors for consideration is:

- **Target population of trial.** Some trials target populations that may be expected to have different costs experiences to the typical adult population. For example, in Australia, there may be additional costs associated in conducting a trial in some population subgroups such as children, Aboriginal and Torres Strait Islander Peoples and people from culturally and linguistically diverse backgrounds. There may be a need to consider adjustments to the standard costs for trials involving a high proportion of participants from these population subgroups.
- **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).
- **Standard care services, and services over and above standard care**. In most clinical trials, many of the clinical services provided would have been provided if the patient had not been enrolled in the clinical trial (i.e. they represent standard care). It is acknowledged that general principles that allow standard care services to be distinguished from non-standard care services are difficult to define. Ultimately, the determination of standard care for a trial is likely to be best made by the trial funder/sponsor working with all the sites participating in the trial. However, unlike the first table of standard costs, the costing methodology used for the revised Table acknowledges the need to consider adjustments to the standard costs for clinical services based on whether the service is agreed to be standard care or not. For example, whether it is planned to have two standard costs for diagnostic tests, one for when the test is not standard care, and another, lower cost, for when the test is standard care, which will reflect the additional work associated with data collection and reporting the test for patients on clinical trials, but not the cost of the test itself.

Although a differential standard cost has not be calculated based on any of the above factors, as there was insufficient data gathered to support it, variations noted in the gathered data based on phase and/or target population is mentioned on some items in both Table 4.2 and in the supporting Appendices.

5 Conclusion

The study gathered a very considerable evidence base relating to the activities on the revised List and the costs of conducting clinical trials in Australia. This Chapter summarises a number of identified issues and/or opportunities with/for the table of standard costs.

5.1 DEVELOPING THE TABLE OF STANDARD COSTS

The study has produced one or more standard costs for each item on the revised list except for item 2.6.7 'outpatient activity' which it is suggested be removed from the revised List as it duplicates other items. Each item has been costed on the basis of activities undertaken or with reference to external costs and/or fees (as per the 2013 method, MBS fees have been used as a reference point for clinical services). For one item, 3.2.1 (c) 'archiving of trial records – storage fee' where the predominant practice is for trial host sites to purchase the services from an external provider, the standard cost was calculated with reference to the typical charge. Even though the costing study has produced a more robust result than the 2013 study, as majority of items were costed on an activity basis, there are still limitations with the standard costs produced for each item (or discrete activities within items).

Firstly, the study developed a standard cost for each item regardless of the sponsors/funder for the clinical trial. It is noted that, in general, investigator-initiated trials have limited external and/or internal funding, industry sponsored trials are adequately funded, and collaborative group trials have grant-funding, which is usually limited to an equal and small amount per site. The suggested standard is not differentiated on the type of clinical trials sponsor/funder, even though thematic analysis of the qualitative data suggests that funding source may impact on the costs for some (but not all) items in the revised List. For example, it was often argued that, due to their more limited resources, investigator-initiated trials required more support to attain ethics and governance approvals. But, it is recognised that in other circumstances, investigator-initiated trials may have lower costs.

This discussion **is strictly about costs, not charges**. It is acknowledged, as per the NHMRC's principles published with the List, that trial host sites choose to absorb different amounts of trial cost with reference to the trial sponsor/funder. This practice, which effectively means that the trial host site becomes a part-funder of the trial, results in sponsors/funders being asked to meet different proportions of the actual cost of a trial with reference to expected funding availability. It is stressed that **this is a funding matter, not a costing matter, and that, as per the NHMRC's principles, publication of a standard cost is not intended to provide any incentives or disincentives to this practice**.

Secondly, the gathered data did not support the calculation of differential standard costs based on phase of clinical trial (the sample size was not large enough to support robust calculations of the impact of cost drivers), however thematic analysis of the qualitative data suggests that there is little variation in terms of cost incurred for Phase 2 and 3 clinical trials (including non-pharmaceutical trial equivalents), but there is potential cost variation if the clinical trial is a Phase 1 or 4. Qualitative data suggest that the differences are mainly due to clinical trial sites taking longer to assess feasibility of the clinical trial (items 1.1.1-1.1.3), the patient population seeking to be included in the trial (i.e. increases the time spent on pre-screening (item 2.2.1) and recruitment activities (item 2.2.1)), and the amount of follow-up required of all participants included in the study. A larger study would be required to verify this theory empirically.

Thirdly, in order to develop a standard cost for each item, which is largely driven by labour hours, an hourly rate for each type of personnel involved needed to be calculated. The site visits found that the variation in disciplines appointed to clinical trials positions and the Awards the individual professions are paid under are broad and vary across each State/Territory and setting (public, private etc.) in Australia. Although the calculated hourly rate (which represents a fully absorbed hourly rate) is based on reference to current Awards in numerous states/territories, the published standard cost may be too high or too low depending on the location of the trial host site (State/Territory) and what an individual institution pays.

Fourth, the study was unable to calculate differential standard costs based on trial target population due to the hospital sample included (i.e. only one paediatric hospital site). Again, if a larger study was undertaken, it would be possible to measure the impact of the trial target population as a cost driver. Once again, thematic analysis of the data gathered from the paediatric hospital site suggests that for some items on the List, the time taken (and hence costs incurred) to undertake the activities is greater. For example:

- preparation of the ethics documentation (item 1.3.1) requires additional documentation in relation to the PICF (e.g. one for child if 12 or above, one for parent etc.);
- consent process usually takes additional visits educating and answering parents questions and concerns in relation to their child being involved on a clinical trial (e.g. item 2.2.2);
- laboratory tests in paediatric trials are generally more costly;
- imaging examinations in paediatric trials generally take longer and hence are more costly;
- radiotherapy services in paediatric trials generally take longer and hence are more costly;

The production of the supporting Appendices to the table of standard costs (refer to Table 4.2) ensures that there is transparency in regards to the basis on which the standard cost was calculated. The Appendices provide details of the variation in cost that was observed for each item. This information facilitates the use of the table of standard costs as a reference point by funders/sponsors and clinical trials sites. Specifically, it is intended to **allow potential trial host sites and sponsors/funders to negotiate trial budgets with reference to the standard cost and the distribution of the measured costs, taking account of the specific features of the trial (target population, complexity, funds availability, applicable labour rates, etc.)**.

5.2 DEFINING STANDARD CARE

It is important to note that, **consistent with the published NHMRC principles, in the context of negotiating a trial budget, the table of standard costs is intended to be applied only to those clinical services that are over and above standard care** (i.e. the table of standard costs is not intended to be applied to clinical services that patients would have received as part of standard care and treatment independent of their participation, or not, in a clinical trial).

As part of the study, stakeholders were asked how they differentiate between standard care versus non-standard care when working up clinical trials budgets. Stakeholders recognised the importance and complexity of the problem, and noted that a clinical service that is standard care in one clinical trial may not be standard care in a different trial context. The most often cited examples were pathology tests and/or imaging examinations that are required at higher frequency for clinical trial participants than would otherwise be provided as standard care to non-clinical trial patients with the same condition. The additional tests are considered to be clinical trial specific. But, even in this relatively simple example, stakeholders noted that the test frequency was trial and context specific.

There was also discussion about whether standard care could/should be defined as part of the clinical trial protocol (by the sponsor), and this reference point can then become the basis for negotiation between the trial funder/sponsor and the trial host site. This practice seemed to vary across clinical

trials, and stakeholders pointed out that in international trials what might be regarded as standard care in the country where the clinical trial was designed (typically not Australia) may not be standard care in Australia. So while, ideally, standard care would be defined in the trial protocol and act as the reference point for discussion, in practice this was found to be not always possible.

Another confounding issue raised by stakeholders was that standard care for a particular condition is not uniform within Australian hospitals, even for hospitals in the same jurisdiction, and sometimes even within a single hospital where clinicians have a different approach to practice. Again, for this reason it was not considered possible to provide specific (or generic) guidance on what constitutes standard care in the context of clinical trial. Rather, there has to be negotiation between the trial funder/sponsor and the trial host site to agree on standard care in the trial context.

In practice, some sites identify standard care versus non-standard care items on presentation of the detailed clinical trial protocol by the sponsor and show in their 'budget work up" what is considered by their site as "non-standard care" and therefore included in the requested budget for the clinical trial. Other sites believe that once a patient is on a clinical trial, whether the test is standard care is irrelevant as the additional requirements (including reporting) associated with that patient being on a clinical trial should be covered by the sponsor, and in some cases sponsors are happy to pay for it.

It is important to note that with the structure of the revised List, ensuring that the calculated standard cost is above those costs required for standard care, is not relevant for the items on two of the sub-lists. Basically, the activities included under the sub-lists of "site authorisation" or "site close-out" are always clinical trial specific. They do not include any clinical service items. Thus assessing whether the costs associated with these items is over and above standard care is not relevant.

Standard care is only relevant to items associated with the provision of clinical services to patients, i.e. "clinical services" (items 2.3.1 to 2.3.8), "biospecimen related" (items 2.5.1 -2.5.2) and "clinical resources" (items 2.6.1-2.6.7). The standard costs for these items is based on the actual cost of delivering these services irrespective of whether they are provided in the context of a clinical trial or not (as sometimes they will be standard care and other times they will not be). There will need to agreement between the trial host site and funder/sponsor on what constitutes standard care in the context of a specific trial, and the cost of these services will need to be excluded from the clinical trials budget.

5.3 DEVELOPMENT OF A SUPPORTING BUDGETTING TEMPLATE

The United Kingdom (UK) embarked on a similar process in understanding the costs of running clinical trials with the aim of increasing the number of clinical trials in the UK. This work was done by the National Institute of Health Research (NIHR). One part of this work was the production of a budgeting template (in Excel) that can be used by clinical trial funders/sponsors and potential clinical trial host sites to work up and negotiate a trial budget. The existence of this tool was raised with some stakeholders, who advised that the template could be a valuable tool in both educating sites on how to develop clinical trials budget and also in standardising the approach to determining clinical trial budgets.

Over the course of our work from 2013 to 2015 in clinical trials in Australia we are aware that some pharmaceutical companies already have developed their own budgeting templates. A few of these templates have been provided on a commercial in confidence basis to the consulting team. A quick review of them revealed that they were all a bit different and that they did not incorporate use of the standard List or table of standard costs. Stakeholders also pointed out that there are proprietary products such as "GrantPlan" that can be used to work up a clinical trial budget, which include a fees benchmarking facility based on international data.

Notwithstanding the availability of these products, it is considered that the development of a budgeting template, which makes it simple to use the standard List and the associated table of standard costs would be a catalyst for the wider adoption of the revised List. The template, which would most likely take the form of an Excel spreadsheet and be made available free of charge, as in the UK, would contain the standard List of items and associated table of standard costs. The intent would be for the template to be used to develop a trial budget as the starting point for negotiations between the trial funders/sponsors and potential trial host sites. It is important to note that the UK has developed four different budgeting templates, one each for drugs and devices, for both the primary and secondary care sectors. It is suggested that the development of such a template for use in Australia be considered, however we would suggest that only one template be developed for hospital based trials as a starting point, and not distinguish between device and drug trials. If that template proved to be useful, then subsequent work could develop templates that are more tailored to the intervention and/or the trial setting, as in the UK.

5.4 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 means that change is always occurring and the relevance of items will also change. Also new input data (e.g. activity and/or cost) may become available which may provide additional transparency in relation to the costs. For example, some stakeholders:

- felt that the outcomes of the IHPA Teaching, Training and Research costing study may provide additional insight as to the costs incurred by clinical trials sites;
- noted that there are impending changes to the CTN_x[2] moving from a paper based to an electronic process (i.e. $eCTN_x$). No site included in the study hospital was yet using the $eCTN_x$ process so it was not be possible to cost these impending changes in the study. Although some sites felt this would result in an increase in their time, sponsors felt that this would decrease clinical trial site time;
- felt that the breakdown of the mutual acceptance for ethics approval when Victorian sites are involved may change the way ethics approval is being sought by non-Victorian sites;
- increasing use of clinical research organisations and/or associates by pharmaceutical companies is increasing time spent by sites in budget negotiation, monitoring visits etc.

All or some of these developments may 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 or IHPA's annual indexation rate could be applied if no change to the items within the revised List has occurred.

5.5 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.

[2]CTN is required for any product not entered on the Australian Register of Therapeutic Goods; or use of a registered or listed product in a clinical trial beyond the conditions of its marketing approval

5.6 DELIVERY OF CLINICAL TRIALS IN THE HOSPITAL SETTING

HealthConsult has now undertaken two rounds of this costing study, once in 2013 and again in 2015. HealthConsult also consulted widely in developing the revised List for the NHMRC. Through these projects we have developed a detailed understanding of clinical trials in Australia and it is our view that the costs incurred by sites is also impacted by a number of factors, outside those activities included in the revised List, although the costs reflected in the table of standard costs are impacted by these factors. For example:

- the capability of personnel within hospitals is widely varied. No such training for CTM/C exist, except for on the job training, therefore there are huge learning curves incurred (and hence inefficiencies) especially when departments are undertaking clinical trials for the first time and/or in small volumes;
- the capability of departments within hospitals is widely varied. Clinical trials are usually isolated to specific departments within a hospital (e.g. respiratory, haematology, oncology etc.) with little (if any) sharing of processes. Some departments such as oncology have a long history in running clinical trials and usually have a pool of staff dedicated to clinical trials. The long standing history means they have become efficient at processes involved in establishing, running and closing down a clinical trial. There is no forum where these learnings can be shared and in fact within hospitals these "super clinical trials" departments are either unknown or untapped resources;
- generally a lack of support from hospital support department such as finance and human resources to assist clinical trials staff to manage the clinical trial so that they can track their costs, issue timely invoices, recruit required personnel. This means that clinical trial staff that are not trained in finance and/or recruitment are spending consider time doing administrative tasks better suited to be done by others in the hospital; and each department undertaking a clinical trial is replicating the same tasks which if pooled would be more efficient;
- lack of computer access and/or speed of internet also impacts on the efficiency (and cost) of undertaking clinical trials at hospitals. Slow internet speeds means that time spent on online training, eCRF data entry etc. is greatly increased due to issues with IT infrastructure at sites.

Some hospitals are recognising the lack of capability and inefficiencies involved in running clinical trials within and across hospital departments and have developed positions known as "start-up specialists" which are experienced CTM/C who are the first port of call when a department is assessing whether or not to be a site for a clinical trial. However these positions are rare and will only solve some of the inefficiency issues in hospital departments that are running clinical trials. It is our view that a state approach, or better still, national approach to addressing some of these issues would assist in Australia being a more competitive destination for running clinical trials.

Appendix A – Site Authorisation

Item 1.1.1 - Preliminary assessment

Reference number	1.1.1
Item	Preliminary assessment
Sub-list	Site authorisation
Category	Feasibility assessment
Definition	The activities associated with the exchange of the required reciprocal confidentiality agreements and preliminary review of the trial protocol by the potential Principal Investigator (and/or delegates) at the site. May also include initial discussions (by telephone or site visit) with the trial sponsor and/or representative.
Standard cost	**$60.38** per *potential* clinical trial

LEARNINGS FROM SITE VISITS

For the majority of sites, the initial contact (which is usually via email) made by the sponsor organisation is with the Principal Investigator (PI) and/or Clinical Trial Manager/Coordinator (CTM/C). The email usually contains a brief description of the potential clinical trial and rarely a brief synopsis of the clinical trial protocol. If the contact person is the CTM/C then they will have a discussion with a potential PI. If the PI is interested then they would sign a confidentiality disclosure agreement (CDA, either in their own right or seek an authorised signature from personnel within the hospital) and return the signed CDA to the sponsor organisation.

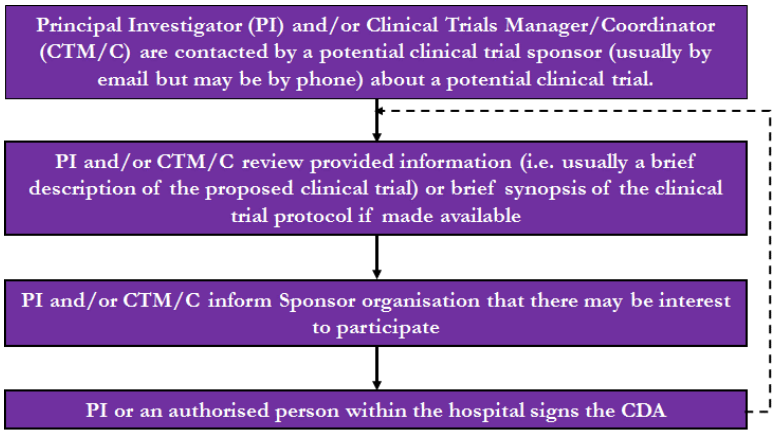
Some variations were noted to the above process. For example, at one site the hospital is actively seeking and approaching sponsor companies on behalf of their organisation to express an interest in being included in a clinical trial. At another site, a third party organisation was the first point of contact for a sponsor organisation, and these opportunities were then circulated to members for consideration.

It was also observed that some hospitals are now investing in different roles to support clinical trials (e.g. study start-up specialists, business development managers and/or clinical trials/research operations managers). These roles are involved in supporting hospital departments in either establishing themselves in clinical trials and/or improving efficiency of managing and running clinical trials. In the initial phase of the clinical trials process these positions are often used as substitutes for the Clinical Trial Coordinator/Manager and/or Principal Investigators.

DERIVED PROCESS MAP FOR "PRELIMINARY ASSESSMENT"

Figure A.1 presents the typical process for preliminary assessment process.

Figure A.1: Process map of activities included under "preliminary assessment"



CONSIDERATIONS FOR DERIVING THE COST OF "PRELIMINARY ASSESSMENT"

The most typical process identified for the preliminary assessment involved a PI and/or the CTM/C. As such in order to derive a standard cost for the preliminary assessment process, professional time was chosen as the most suitable resource unit. The PI was generally found to be an experienced medical specialist whereas the CTM/C was either a Clinical Nurse Specialist (CNS), Clinical Nurse Consultant (CNC), Registered Nurse (RN), a scientist or pharmacist. The hourly rate calculated for the CTM/C role was calculated as a blended rate of CNS (mid-point for the identified nursing positions), a scientist and a pharmacist. While only at a few sites did we find that staff participated in this process, this was atypical, so the standard cost is based on PI and CTM/C involvement only.

TABLE OF STANDARD COSTS FOR "PRELIMINARY ASSESSMENT"

Table A.1 presents the basis for calculating the standard cost for the preliminary assessment process involved in a clinical trial.

Table A.1: Typical personnel, resources and unit costs for "preliminary assessment"

Item	Basis	Resource unit (hours)					Unit cost (per labour hour)	Standard cost (25th percentile)
		Min	25th percentile	Median	75th percentile	Max		
Preliminary assessment	Principal Investigator	0.08	0.17	0.38	0.75	1.50	$226.11	$37.69
	Clinical Trials Manager/Coordinator	0.08	0.25	0.25	0.50	1.50	$90.78	$22.70
Total								**$60.38**

Note: The calculated (fully absorbed) hourly rate for a PI is presented in item 2.6.1 and for the CTM/C in item 2.6.3. Totals may not be exactly additive due to rounding errors.

Table A.1 presents the resource units, in hours, required for each activity by specific personnel. Due to the prevailing view that PIs were more often than not the only person involved in the preliminary assessment process and it was a "5-10 minute job", the 25th percentile was considered the best basis for setting the standard cost of $60.38 per potential clinical trial.

It is important to note that 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.) prior to moving to item 1.1.2 or item 1.1.3 and the other was a metropolitan hospital reviewing a Phase 1 trial protocol which are typically more detailed and need more consideration.

Item 1.1.2 – Protocol review

Reference number	1.1.2
Item	Protocol review
Sub-list	Site authorisation
Category	Feasibility assessment
Definition	The activities associated with the heads (or nominees) within the potential clinical trial host unit (e.g. oncology, respiratory, 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 for scientific merit and local interest/feasibility. The process may involve review by individuals or by a panel drawn from representatives of the above mentioned departments.
Standard cost	**$407.67** per *potential* clinical trial

LEARNINGS FROM SITE VISITS

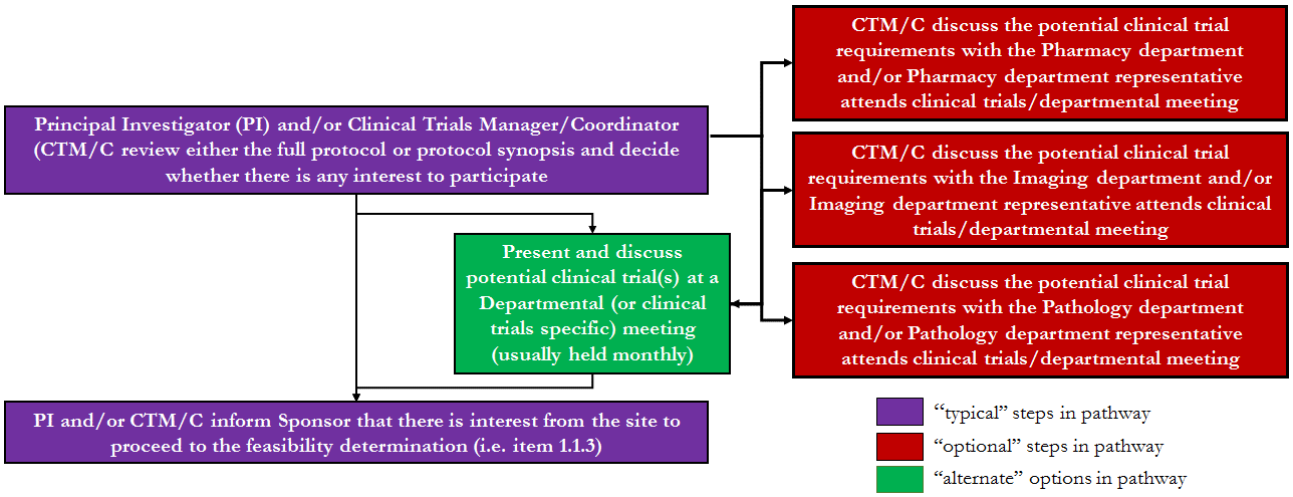
The protocol review process was mostly completed by the PI and CTM/C. For some departments within hospitals, some input was required at this point from supporting departments (e.g. pharmacy, imaging and/or pathology) to ensure ability and/or capacity to meet the requirements of the proposed trial, but in general this information was sought during the feasibility determination process (i.e. item 1.1.3). If sites had not completed a CDA during the preliminary assessment (i.e. item 1.1.1), then this would be completed at this point in the process.

Within some departments, the decision to assess site feasibility was discussed at a departmental meeting. This usually involved the potential PI to make a presentation about the potential clinical trial in order to gauge interest from their colleagues. We found large variation in regards to whether this meeting occurred and if so the number and range of people that would attend.

DERIVED PROCESS MAP FOR "PROTOCOL REVIEW"

Figure A.2 shows the typical process involved in protocol review activities in the **purple** boxes. Optional steps are shown in the **red** boxes and the alternative steps are shown in **green** boxes.

Figure A.2: Process map of activities included under protocol review



CONSIDERATIONS FOR DERIVING THE COST OF "PROTOCOL REVIEW"

The most typical process identified was for the protocol review to be undertaken by the PI and/or CTM/C. As such in order to derive a standard cost for the protocol review process, professional time was chosen as the most suitable resource unit.

While a number of hospital departments reported that their typical process involved other hospital personnel, this was not the most common process identified across all the department/sites.

TABLE OF STANDARD COSTS FOR "PROTOCOL REVIEW"

Table A.2 presents the basis for calculating the standard cost for the protocol review process involved in a clinical trial.

Table A.2: Typical personnel, resources and unit costs for "protocol review"

Item	Basis	Resource unit (hours)					Unit cost (per labour hour)	Standard cost (median)
		Min	25th percentile	Median	75th percentile	Max		
Protocol review	Principal Investigator	0.17	0.50	1.00	2.00	5.00	$226.11	$226.11
	Clinical Trials Manager/Coordinator	0.33	1.00	2.00	3.00	15.00	$90.78	$181.56
Total								**$407.67**

Note: The calculated hourly rate for a PI is presented in item 2.6.1 and for the CTM/C in item 2.6.3. Totals may not be exactly additive due to rounding errors.

Table A.2 presents the resource units, in hours, required for each activity by specific personnel. Due to the variability in the resources required for the protocol review process, the median was considered the best basis for setting the standard cost of **$407.67** per potential clinical trial.

Item 1.1.3 – Feasibility determination

Reference number	1.1.3
Item	Feasibility determination
Sub-list	Site authorisation
Category	Feasibility assessment
Definition	The activities associated with determining the feasibility and desirability of conducting the trial at a site (culminating with the completion of the feasibility assessment questionnaire) covering the assessment of: • whether trial is consistent with institution's mission, research priorities and risk management profile; • likelihood of being able to recruit suitable types and numbers of patients; • availability of staff and other resources required to undertake the trial; • the services that will be standard to care for patients on the trial and those that will be trial specific with reference to the trial protocol; and • acceptability of the proposed budget and contract. The activities may also include hosting a feasibility assessment visit by the trial sponsor and/or representative.
Standard cost	**$294.62** for completion of feasibility questionnaire required for a *potential* clinical trial; **$675.95** for study site selection visit required by sponsor organisation for a *potential* clinical trial; **$755.51** for budget negotiation and contract review for a *potential* clinical trial.

LEARNINGS FROM SITE VISITS

Feasibility determination encapsulate a number of discrete activities including the completion of the feasibility questionnaire, study site selection visit, budget and contract negotiations. Development of the standard cost involved identifying the time associated with personnel undertaking each discrete activity.

Budget negotiations, at almost all sites, commenced during this phase, but not all sites completed the budget negotiation during the, as defined, feasibility determination process. The approach to budget negotiations also varied. Some departments simply accept the budget proposed by the sponsor, while other departments reported being asked by sponsors to produce a 'bottom up' budget for the trial and then commenced a negotiation with the sponsor or CRO. Often even if budgets were accepted by the hospital department it was generally after they had spent some time to ensure that the budget would cover their perceived costs. In some circumstances we found that the budget negotiations were undertaken by a third party, after input was provided by the relevant hospital department(s). Most departments also reported that when budget negotiations were carried out with a CRO, rather than directly with the sponsor, the time spent by hospital staff was considerably lengthened.

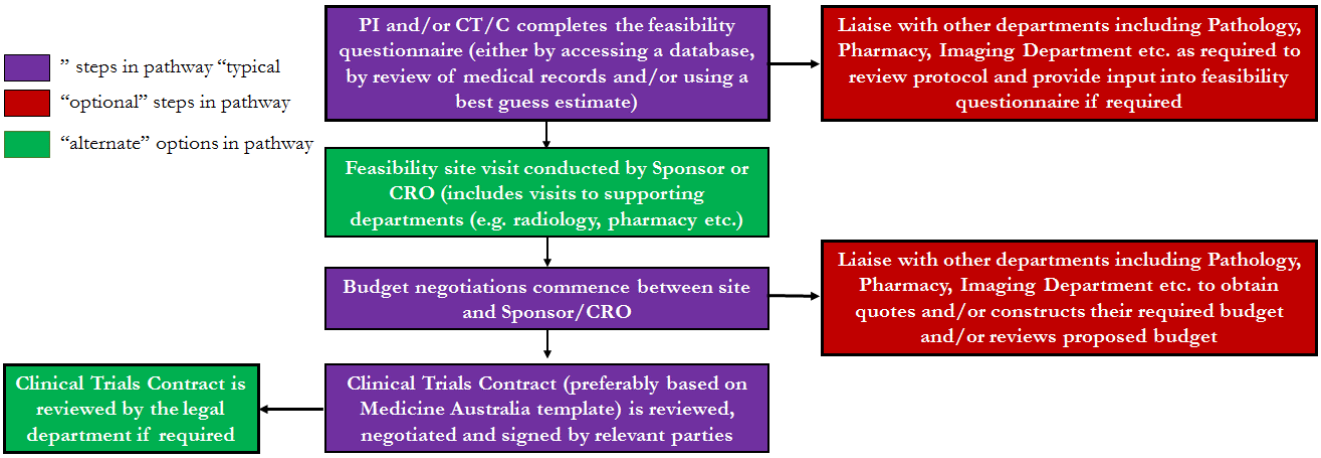
Whether a study site selection visit occurred in the feasibility determination process depended on the sponsors familiarity with the hospital department (and/or their facilities) and who the sponsor was (e.g. this is not a relevant activity for investigator-initiated trials and did not often occur when collaborative groups were a sponsor).

Most hospitals departments either expressed a preference to receive contracts (or would only accept) in the Medicines Australia (MA) template format. Where the format of the provided contract varied from the MA template, including the associated schedules, this required additional resources and would often involve seeking (either internal or external) legal review.

PROCESS MAP FOR "FEASIBILITY DETERMINATION"

Figure A.3 below shows the typical process involved in the feasibility determination process in the **purple** boxes. Optional steps are shown in the **red** boxes and the alternative steps are shown in **green** boxes.

Figure A.3: Process map of activities included under feasibility determination



CONSIDERATIONS FOR DERIVING THE COST OF "FEASIBILITY DETERMINATION"

The typical process involved in feasibility determination includes at least three discrete activities. Therefore a standard cost for each discrete activity has been calculated. The standard cost for each discrete activity has been based on the most common personnel involved in each discrete activity that was identified through the site visits. For completion of the feasibility questionnaire it includes the PI and CTM/C. If a study site selection visit was undertaken the most common personnel involved were the PI, CTM/C and personnel from supporting departments. For budget negotiations and contract review it most commonly involved the PI, CTM/C, personnel from the supporting department (e.g. research and governance officer, pharmacy, imaging, pathology etc.). When the contract provided varied from the standard MA agreement (included varying previously agreed schedule 7) then sites sought legal advice either from an internal lawyer or externally. However this was not considered typical and therefore has not been included in the standard cost. However it is important to note that when the standard contract is varied legal costs are being borne by the sites. We also found that supporting department (e.g. pathology, pharmacy, medical records, finance etc.) involvement varied depending on the type of clinical trial, as do the professions involved. Hence a blended rate of hospital scientists and pharmacy staff was calculated for the hourly rate attributed to supporting department personnel.

TABLE OF STANDARD COSTS FOR "FEASIBILITY DETERMINATION"

Table A.3 presents the basis for calculating the standard cost for three discrete activities involved in the feasibility determination for a clinical trial.

Table A.3: Typical personnel, resources and unit costs for feasibility determination

Item	Basis	Resource unit (hours)					Unit cost (per labour hour)	Standard cost (median)
		Min	25th percentile	Median	75th percentile	Max		
Completion of feasibility questionnaire	Principal Investigator	0.08	0.29	0.50	1.00	2.00	$226.11	$113.06
	Clinical Trials Manager/Coordinator	0.25	0.50	2.00	7.50	76.00	$90.78	$181.56
Total								**$294.62**
Study site selection visit	Principal Investigator	0.25	0.50	1.00	1.00	2.00	$226.11	$226.11
	Clinical Trials Manager/Coordinator	0.25	2.00	4.00	5.00	20.00	$90.78	$363.12
	Supporting Departments	0.17	0.50	1.00	1.63	4.00	$86.72	$86.72
Total								**$675.95**
Budget negotiations and contract review	Principal Investigator	0.50	0.50	0.50	1.25	2.00	$226.11	$113.06
	Clinical Trials Manager/Coordinator	0.30	2.00	4.00	15.75	114.00	$90.78	$363.12
	Supporting Departments	0.50	1.00	2.00	4.00	38.00	$86.72	$173.44
	RGO staff	0.25	0.50	1.50	2.00	4.00	$70.59	$105.89
Total								**$755.51**

Note: The calculated hourly rate (fully absorbed) for a PI is presented in item 2.6.1 and for the CTM/C in item 2.6.3. The hourly rate (fully absorbed) for personnel from supporting departments is based on a blended hourly rate of a hospital scientist (i.e. Grade 3/4 hospital scientist) and pharmacist (i.e. Grade 3/5 pharmacist). The hourly rate (fully absorbed) for personnel from the research and governance office is based on an average salary of $82,587 plus superannuation sourced from averaging four current advertisement for research ethics office and/or governance office in NSW and Qld. Totals may not be exactly additive due to rounding errors.

Table A.3 presents the resource units, in hours, required for each discrete activity by specific personnel. Due to the variability in the resources required for the discrete activities involved in feasibility determination, the median was considered the best basis for setting the standard cost of **$294.62** for completion of feasibility questionnaire required for a potential clinical trial; **$675.95** for study site selection visit required by sponsor organisation; and **$755.51** for budget negotiation and contract review for a potential clinical trial.

Item 1.2.1 – Preparation of the HREC application

Reference number	1.2.1
Item	Preparation of the HREC application
Sub-list	Site authorisation
Category	Ethics approval
Definition	The activities associated with the preparation and submission of the human research ethics committee (HREC) application form (or equivalent) and supporting documentation which includes the protocol, participant information and consent form (PICF), recruitment and advertising materials, etc. Also includes revisions to applications in response to ethics committee requests for additional information and forwarding copies of relevant approvals (once obtained) and associated documentation to the trial funder/sponsor.
Standard cost	**$2,607.83** per clinical trial (i.e. per HREC application)

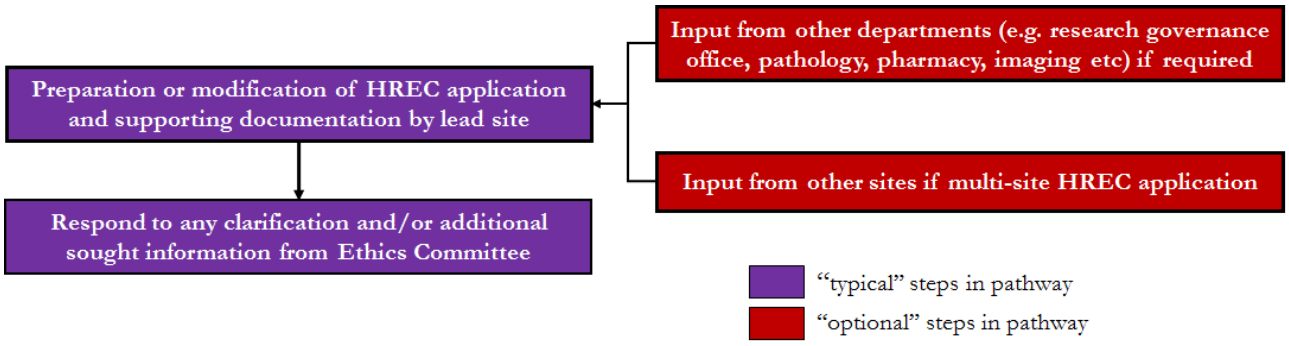
LEARNINGS FROM SITE VISITS

There was vast variability in the amount of time sites reported was involved in a HREC application. The variation was due to numerous factors including (1) whether the sponsor organisation provided a good quality draft HREC application and supporting documentation that meant the lead site had minimal changes to make; (2) whether the sponsor organisation provided a poor quality draft HREC application and supporting documentation that meant the lead site had to spend considerable time in getting the documentation to the required standard; (3) investigator-initiated and collaborative sponsored trials usually meant the lead site had to draft the HREC application and supporting documentation de novo; or (4) if a Victorian site was involved in the clinical trial. We found that mutual acceptance does not seem to be working if a Victorian clinical trial site is included in a HREC application where the Lead is a non-Victorian site due to the varied requirements of HREC in Victoria. This has meant that non-Victorian clinical trial sites are starting to ask if a Victorian site is going to be included in the clinical trial, they either refuse to be the lead site or ask the sponsor organisation to contract them as a single site. This finding was corroborated by Victorian sites stating that when multi-site ethic applications are developed, there are additional sections specifically relating to Victoria that are required to be completed.

DERIVED PROCESS MAP FOR "PREPARATION OF THE HREC APPLICATION"

Figure A.4 shows the typical process involved in the preparation of the HREC application in the **purple** boxes. Optional steps have been provided in the **red** boxes

Figure A.4: Process map of activities included under preparation of the HREC application



CONSIDERATIONS FOR DERIVING THE COST OF "PREPARATION OF THE HREC APPLICATION"

The personnel involved in preparing the HREC application varied depending on who the sponsor organisation was for the clinical trial. For investigator-initiated and/or collaborative clinical trials, the principal author was the proposed PI and/or their Fellow. For drug or device clinical trials, the

principal author was usually the CTM/C. As such in order to derive a standard cost for the preparation of the HREC application process, professional time was chosen as the most suitable resource unit. It was not common for the supporting departments (e.g. pathology, imaging, pharmacy) to be involved except to sign the application. It was also variable as to whether the RGO was involved. This varied by site and capability of the author of the HREC application and supporting documentation.

TABLE OF STANDARD COSTS FOR "PREPARATION OF THE HREC APPLICATION"

Table A.4 presents the basis for calculating the standard cost for the preparation of HREC application.

Table A.4: Typical personnel, resources and unit costs for "preparation of HREC application"

Item	Basis	Resource unit (hours)					Unit cost (per labour hour)	Standard cost (median)
		Min	25th percentile	Median	75th percentile	Max		
Preparation of HREC application	Principal Investigator	0.25	0.46	2.50	9.75	76.00	$226.11	$565.28
	Clinical Trials Manager/Coordinator	0.75	15.00	22.50	38.00	114.00	$90.78	$2,042.55
Total								**$2,607.83**

Note: The calculated hourly rate (fully absorbed) for a PI is presented in item 2.6.1 and for the CTM/C in item 2.6.3. Totals may not be exactly additive due to rounding errors.

Table A.4 presents the resource units, in hours, required for each activity by specific personnel. It is important to note that where the sponsor does the majority of the preparation of the HREC application that the 25th percentile is more reflective of the standard cost, whereas for investigator-initiated and/or collaborative trials the 75th percentile is more reflective of the standard cost. Due to this variability in the resources required for the preparation of HREC application process, the median was considered the best basis for setting the standard cost of **$2,607.83** per clinical trial. In particular the 'max' value presented was driven by data gathered from the one paediatric site included in the study. Note a differential standard cost for paediatric clinical trials set at the 75th percentile was considered. However as only one paediatric site was included in the sample, we felt there was insufficient evidence to set a differential standard cost for paediatric clinical trials at this stage, even though the gathered data suggests it would reflect a more realistic cost associated with the input time for such types of clinical trials.

Item 1.2.2 – Ethics review

Reference number	1.2.2
Item	Ethics review
Sub-list	Site authorisation
Category	Ethics approval
Definition	The activities associated with the review of the ethics application by the HREC, including the preparation of any requests for additional information and subsequent consideration of the material provided.
Standard cost	**$2,099.42** per clinical trial application.

LEARNINGS FROM SITE VISITS

Before an application is submitted to a HREC, we found that most sites require the HREC application to be reviewed first by a 'gateway' committee(s) (e.g. drug committee (if a drug was involved in the proposed clinical trial) and/or scientific advisory committee (SAC)). Typically when a drug is involved in the clinical trial, most sites required the HREC application to be submitted to both the Drug Committee and SAC prior to submission to HREC. Both the skill mix and use of these gateway committees vary. For these reasons a standard cost of reviewing the HREC application by a gateway Committee has not been calculated.

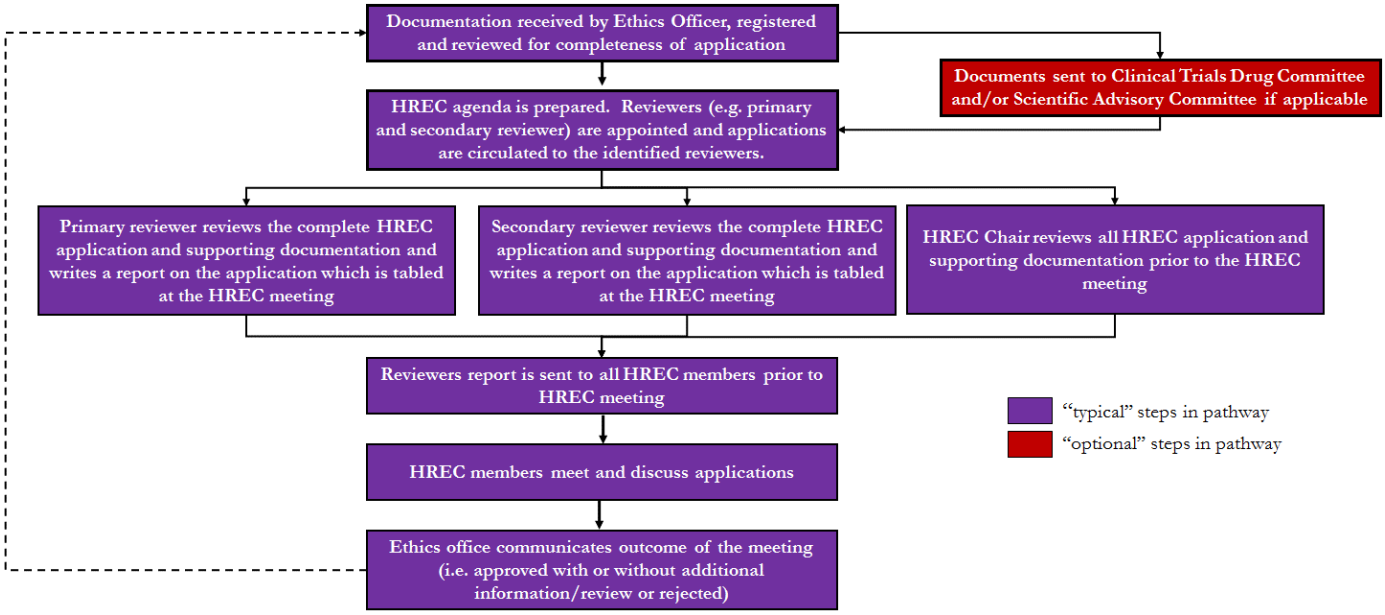
The study found that typically there were 8-10 members on the HREC and the skill mix of the members included one with a legal background, two or three with medical backgrounds, two or three with scientific and or allied health discipline backgrounds, an ethics officer and up to two lay members. The most common approach was for applications to be reviewed by a primary and secondary reviewer, a brief report would be prepared by each reviewer, the brief report would be distributed to all HREC members prior to the meeting, the primary reviewer would present the application at the HREC meeting and then all members would discuss the proposed clinical trial. In addition all applications were typically reviewed in full by the chairperson. It was only identified at one site that all HREC members would review the applications prior to the HREC the meeting. Usually the PI would only attend if requested to.

Besides the HREC committee, most sites often had a low risk committees. However, most clinical trials are not usually considered as low risk. Some sites also reported not having a separate ethics and governance process and that the two were a combined function within their organisations. For these sites the timing allocated for the combined function was split across item 1.2.2 and 1.3.2.

DERIVED PROCESS MAP FOR "ETHICS REVIEW"

Figure A.5 shows the typical process involved in completing the ethics review in the **purple** boxes. Optional steps are shown in the **red** boxes.

Figure A.5: Process map of activities included under ethics review



CONSIDERATIONS FOR DERIVING THE COST OF "ETHICS REVIEW"

The ethics review process is a combination of processing and review work completed by the ethics department, combined with review by the committee members prior to an ethics meeting and then the time spent assessing each of the ethics applications within the meeting. The most typical process identified variable mix of staffing in the completion of the ethics review. As such in order to derive a standard cost for the preparation of the HREC application process, professional time was chosen as the most suitable resource unit. The ethics staff were generally found to be administrative type staff. For the members of the committee, an estimate was based on the mix of member including clinicians, lawyers and lay people. The chairperson was most commonly found to have a scientific background. While most of the members of the committee are voluntary, the project requires a standard cost irrespective of any payments that may or may not be made.

TABLE OF STANDARD COSTS FOR "ETHICS REVIEW"

Table A.5 presents the basis for calculating the standard cost for ethics review per clinical trial.

Table A.5: Typical personnel, resources and unit costs for "ethics review"

Activity	Basis	Resource unit (hours)					Unit cost (per labour hour)	Standard cost (median or 75th percentile)
		Min	25th percentile	Median	75th percentile	Max		
Initial process and review	Ethics officer*	0.50	2.00	3.25	7.69	13.00	$70.59	$542.66
Detailed review of application	Primary reviewer	1.00	2.00	3.00	3.00	4.00	$142.08	$426.24
	Secondary reviewer	1.00	2.00	3.00	3.00	4.00	$142.08	$426.24
	Chairperson	1.00	1.00	1.00	1.88	3.00	$142.08	$142.08
Presentation and discussion of HREC application at meeting	Legal officer	0.13	0.27	0.33	0.43	0.75	$199.11	$66.37
	Medical clinician (x2)	0.13	0.27	0.33	0.43	0.75	$199.11	$132.74
	Scientific/Allied Health (x2)	0.13	0.27	0.33	0.43	0.75	$85.40	$56.93
	Ethics officer	0.13	0.27	0.33	0.43	0.75	$70.59	$23.53
	Lay person	0.13	0.27	0.33	0.43	0.75	$70.59	$23.53
	Chairperson	0.13	0.27	0.33	0.43	0.75	$142.08	$47.36
Post meeting activities	Ethics officer*	0.25	0.81	1.50	3.00	4.00	$70.59	$211.77
Total								**$2,099.45**

Note: The calculated hourly rate (fully absorbed) for a medical clinician is presented in item 2.6.1 (co-investigator). The hourly rate (fully absorbed) for reviewers and chair person is based on the median of the co-investigator (see item 2.6.1) and scientist. The calculated hourly rate (fully absorbed) for a scientific/allied health is based on the average hourly rate of a hospital scientist (i.e. Grade 3/4 hospital scientist). The hourly rate (fully absorbed) for personnel from the research and governance office is based on an average salary of $82,587 plus superannuation sourced from averaging four current advertisement for research ethics office and/or governance office in NSW and Qld. It is also assumed that the legal representative will be as senior as a co-investigator. It was assumed that the lay person would be at least equivalent in salary terms to the ethics officer. * Standard cost calculated at the 75th percentile. Totals may not be exactly additive due to rounding errors.

Table A.5 presents the resource units, in hours, required for each activity by specific personnel. Due to the variability in the resources required for ethics review, the median was considered the best basis for setting the standard cost for all activities except those that involved the ethics officer where the 75th percentile was considered to be the best basis, meaning that the standard cost is set at **$2,099.42** per clinical trial application.

Item 1.3.1 - Preparation of the SSA application by the project team

Reference number	1.3.1
Item	Preparation of the SSA application by the project team
Sub-list	Site authorisation
Category	Site-specific assessment
Definition	The activities associated with the preparation and submission of the Site Specific Assessment (SSA) form (or equivalent) by the PI or project team, which include completion of the form, obtaining authorising signatures, liaising with inter-institutional departments (e.g. radiology, pathology, pharmacy, etc.), adapting the Lead HREC approved master PICF(s) with site-specific letterhead and contact details; and liaison with sponsor including forwarding copies of relevant authorisations (once obtained) and associated documentation to the trial funder/sponsor. Also includes responding to RGO queries and/or requests for additional information and forwarding copies of relevant authorisations (once obtained) and associated documentation to the trial funder/sponsor.
Standard cost	**$398.69** per SSA application

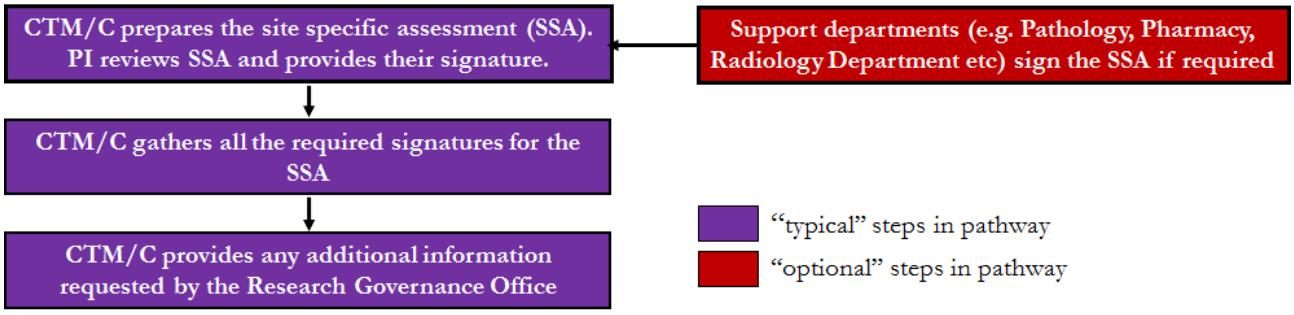
LEARNINGS FROM SITE VISITS

Generally the completion of the SSA application was considered a straight forward step at most sites. The challenge that emerged was the elapsed time involved in chasing up the required signatures from all those involved in the clinical trial. As mentioned in 1.2.1 some sites reported not having a separate ethics and governance process and that the two were a combined function within their organisations. For these sites the timing allocated for the combined function was split across item 1.2.2 and 1.3.2.

DERIVED PROCESS MAP FOR "PREPARATION OF THE SSA APPLICATION BY THE PROJECT TEAM"

Figure A.6 shows the typical process involved in the preparation of the SSA application by the project team in the **purple** boxes. Optional steps are shown in the **red** boxes.

Figure A.6: Process map of activities included under preparation of the SSA application by project team



CONSIDERATIONS FOR DERIVING THE COST OF "PREPARATION OF THE SSA APPLICATION BY THE PROJECT TEAM"

The most typical process identified in the preparation of the SSA involved the CTM/C drafting the SSA and seeking the signatures and review of the SSA documentation from all involved supporting departments (at least three was the most common supporting department involvement per clinical trial). In addition, the PI would often do a quick review of the SSA and sign the application. It is important to note the RGO time is factored in under item 1.3.2 'site processing and review'. Although legal review time has not been factored into this item (or under item 1.1.3) it is important to note that where the contract is not a standard Medicines Australia or Medical Technology Association of Australia (MTAA) agreement (or another pre-approved agreement) with pre-approved schedules sites will have the contract reviewed by legal personnel (either sourced internally or externally) and this cost will be site specific depending on their how they seek legal advice.

TABLE OF STANDARD COSTS FOR "PREPARATION OF THE SSA APPLICATION BY THE PROJECT TEAM"

Table A.6 presents the basis for calculating the standard cost for 'preparation of the SSA application by the project team' for a clinical trial.

Table A.6: Typical personnel, resources and unit costs for "preparation of the SSA application by the project team"

Item	Basis	Resource unit (hours)					Unit cost (per labour hour)	Standard cost (25th percentile)
		Min	25th percentile	Median	75th percentile	Max		
Preparation of the SSA application by the project team	Principal Investigator	0.50	0.50	0.50	0.75	1.00	$226.11	$113.06
	Clinical Trials Manager/Coordinator	0.25	2.00	4.00	10.00	38.00	$90.78	$181.56
	Supporting Departments – 1	0.10	0.40	0.60	6.50	15.00	$86.72	$34.69
	Supporting Departments – 2	0.10	0.40	0.60	6.50	15.00	$86.72	$34.69
	Supporting Departments – 3	0.10	0.40	0.60	6.50	15.00	$86.72	$34.69
Total								**$398.69**

Note: The calculated hourly rate (fully absorbed) for a PI is presented in item 2.6.1 and for the CTM/C in item 2.6.3. The hourly rate (fully absorbed) for personnel from supporting departments is based on a blended hourly rate of a hospital scientist (i.e. Grade 3/4 hospital scientist) and pharmacist (i.e. Grade 3/5 pharmacist). Totals may not be exactly additive due to rounding errors.

Table A.6 presents the resource units, in hours, required for each activity by specific personnel. Due to the variability in the resources, and the perceived over estimate provided by some sites (i.e. as a number found it difficult to distinguish between elapsed time and total time spent undertaking the activity) required for the preparation of the SSA application by the project team process, the 25th percentile was considered the best basis for setting the standard cost of **$398.69** per clinical trial.

Item 1.3.2 - Site processing and review

Reference number	1.3.2
Item	Site processing and review
Sub-list	Site authorisation
Category	Site-specific assessment
Definition	The activities associated with the processing of country specific regulatory documents (e.g. the Clinical Trial Notification (CTN_x) Scheme form), insurance and indemnity documents, safety and/or biosafety reports, trial agreements, requesting, additional information and review of the SSA by the site, including the preparation of any requests for additional information and subsequent consideration of the material provided.
Standard cost	**$264.71** per SSA application processed

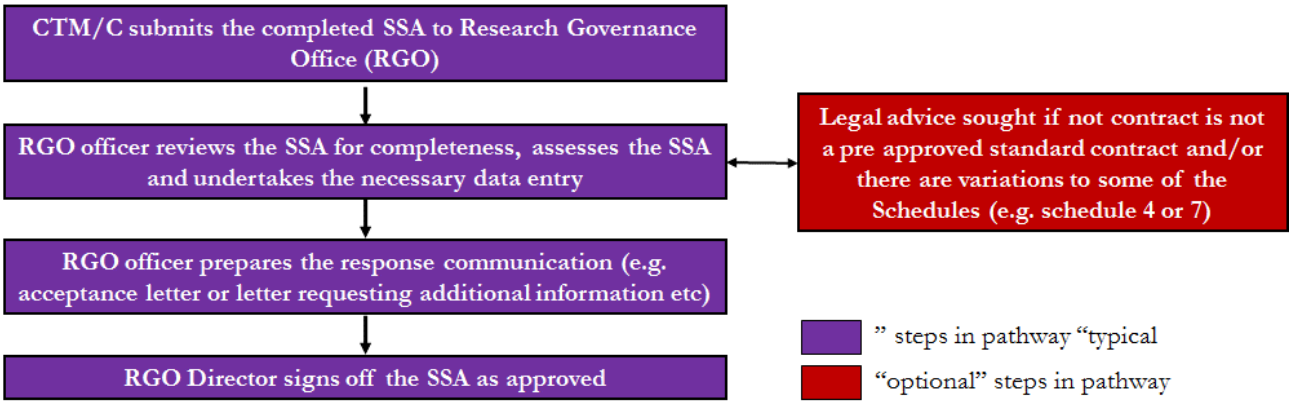
LEARNINGS FROM SITE VISITS

The process of reviewing the governance submission at sites varied greatly based on the quality of the documentation that was presented. Documentation that was compliment with site requirements and in a standard format, were easily able to be reviewed and processed for site governance approval. Again where the documents, in particular legal documents and schedules did not comply with the preferred or pre-approved standard templates, then this increased the time and the length of the process, which is reflected in the varying times in the Table A.7.

DERIVED PROCESS MAP FOR "SITE PROCESSING AND REVIEW"

Figure A.7 shows the typical process involved in site processing and review in the **purple** boxes. Optional steps are shown in the **red** boxes.

Figure A.7: Process map of activities included under preparation of site processing and review



CONSIDERATIONS FOR DERIVING THE COST OF "SITE PROCESSING AND REVIEW"

The typical personnel that were identified to be involved in site processing and review were research governance officer and the Director for final sign off. It is also important to note that it is recognised that the RGO becomes involved under item 1.1.3 and between this item (i.e. median is 3.75) and 1.1.3 (i.e. median is 1.5 hours) it is estimated that RGO time is 5.25 hours per application.

Although legal review time has not been factored into this item (or under item 1.1.3) it is important to note that where the contract is not a standard Medicines Australia or MTAA agreement (or another pre-approved agreement) with pre-approved schedules sites will have the contract reviewed by legal personnel (either sourced internally or externally) and this cost will be site specific depending on their how they seek legal advice.

TABLE OF STANDARD COSTS FOR "SITE PROCESSING AND REVIEW"

Table A.7 presents the basis for calculating the standard cost for 'site processing and review' per clinical trial.

Table A.7: Typical personnel, resources and unit costs for "site processing and review"

Item	Basis	Resource unit (hours)					Unit cost (per labour hour)	Standard cost (median)
		Min	25th percentile	Median	75th percentile	Max		
Site processing and review	RGO Staff	1.00	2.00	3.75	8.00	37.83	$70.59	$264.71
Total								**$264.71**

Note: The hourly rate (fully absorbed) for personnel from the research and governance office is based on an average salary of $82,587 plus superannuation sourced from averaging four current advertisement for research ethics office and/or governance office in NSW and Qld. Totals may not be exactly additive due to rounding errors.

Table A.7 presents the resource units, in hours, required for each activity by specific personnel. Due to the variability in the resources required for site processing and review process, the median was considered the best basis for setting the standard cost of **$264.71** per application/clinical trial.

Appendix B – Site Implementation

Item 2.1.1 - Start-up meetings

Reference number	2.1.1
Item	Start-up meetings
Sub-list	Site implementation
Category	Trial initiation
Definition	The activities that occur at the start of the clinical trial with personnel involved in the trial. Includes any required handover of trial documentation, information sessions for principal or co-investigators and/or clinical trials manager/coordinators and representatives of the participating departments, and any training (e.g. detailed protocol, eCRF, GCP) of staff directly involved in the clinical trial. This may include payment of travel and accommodation for participating staff, where appropriate.
Standard cost	**$1,879.69** per clinical trial start-up meeting (excluding online training) **$282.64** per PI to undertake 1.25 hours of online training per clinical trial **$295.04** per CTM/C to undertake 3.25 hours of online training per clinical trial **$65.04** per supporting department personnel to undertake ¾ hours of online training per clinical trial

LEARNINGS FROM SITE VISITS

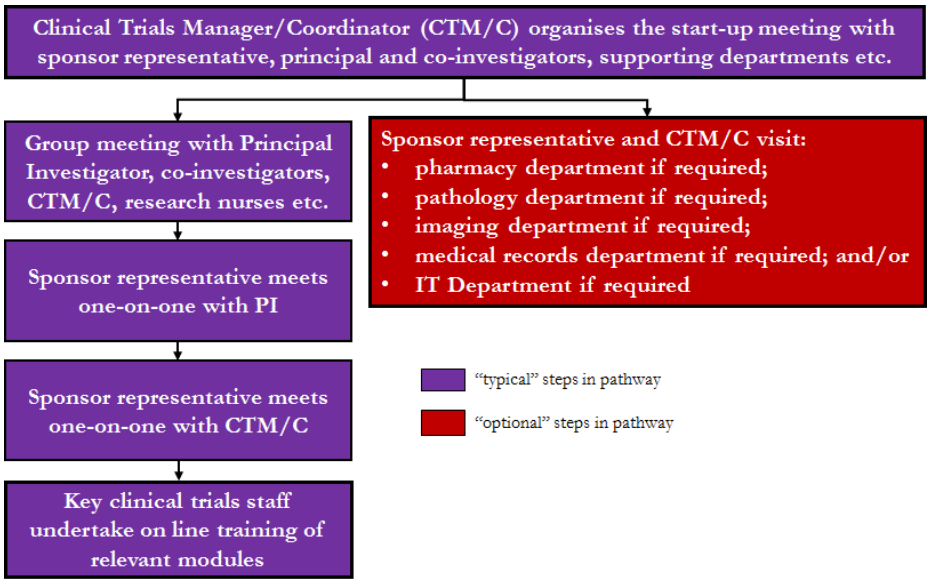
For the majority of sites there is a start-up meeting held on site as part of a site initiation visit (SIV). The SIV typically consisted of a group meeting held for key clinical trial staff to attend, the sponsor representative would also have one-on-one meetings with the PI, CTM/C, as well as tour other key departments to be involved in the clinical trial (e.g. pharmacy, pathology and/or imaging etc.). For some clinical trials the SIV is replaced with a teleconference, rather than a face-to-face in person visit.

In addition to the SIV, online training needs to be completed by key personnel involved in the clinical trial. Sites reported that undertaking online training is increasing and less training is being provided at the SIV. The time required by staff to complete the online training was not insignificant, and was noted as an additional demand on the limited time of clinical trials staff including the PIs.

DERIVED PROCESS MAP FOR "START-UP MEETINGS"

Figure B.1 shows the typical process involved in start-up meetings in the **purple** boxes. Optional steps are shown in the **red** boxes.

Figure B.1: Process map of the activities involved under "start-up meetings"



CONSIDERATIONS FOR DERIVING THE COST

Professional time was chosen as the most suitable resource unit for calculating the stat up meeting standard cost. Although there is a range of staff involved in any start-up meeting process, the standard cost has been based on one PI, two co-PIs, two CTM/C, four staff from supporting departments (e.g. pharmacy, pathology/imaging) attending the group meeting. Although additional staff do often attend (e.g. additional CTC, medical and/or nursing staff etc.) the standard cost reflects the core people identified through the case study visits. In addition, a standard cost for online training has also been calculated on a per personnel rate on the 25th percentile of hours. Only online training undertaken by pharmacy staff that is not drug-specific (e.g. GCP etc.) is captured under this item. Drug-specific training (e.g. drug preparation, logging etc.) required for any clinical trial undertaken by pharmacy staff is included under item 2.4.1.

TABLE OF STANDARD COSTS FOR "START-UP MEETINGS"

Table B.1 presents the basis for calculating the standard cost for 'start-up meeting' per clinical trial.

Table B.1: Typical personnel, resources and unit costs for the start-up meeting

Item	Personnel involved	Resource unit (hours)					Unit cost (per labour hour)	Standard cost (25th percentile)
		Min	25th percentile	Median	75th percentile	Max		
Preparation for a site initiation visit	Clinical Trials Manager/Coordinator	0.25	0.75	1.00	2.00	15.00	$90.78	$68.09
	Principal Investigator	0.17	0.50	0.88	1.38	4.00	$226.11	$113.06
	Other supporting departments (x2)	0.50	0.50	0.50	1.00	1.00	$86.72	$86.72
Group Meeting	Principal Investigator	0.50	1.00	1.00	3.00	21.00	$226.11	$226.11
	Sub-investigators (x2)	0.50	1.00	1.00	2.00	3.00	$226.11	$452.22
	Clinical Trials Manager/Coordinator (x2)	0.25	1.00	2.00	6.88	59.00	$90.78	$181.56
	Other supporting departments (x4)	0.25	1.00	1.00	2.00	25.00	$86.72	$346.88
One-on-one meetings	Principal Investigator	0.50	0.50	1.00	3.38	21.00	$226.11	$113.06
	Clinical Trials Manager/Coordinator	1.00	2.50	4.00	7.75	59.00	$90.78	$226.95
	Other supporting departments (x2)	0.17	0.38	0.58	1.00	1.67	$86.72	$65.04
Total								**$1,879.69**
Online training	Principal Investigator	1.00	1.25	2.00	3.75	8.00	$226.11	$282.64
	Clinical Trials Manager/Coordinator	1.00	3.25	4.00	8.00	22.50	$90.78	$295.04
	Other supporting departments	0.33	0.75	2.00	4.00	32.00	$86.72	$65.04

Note: The calculated hourly rate (fully absorbed) for a PI is presented in item 2.6.1 and for the CTM/C in item 2.6.3. The hourly rate (fully absorbed) for personnel from supporting departments is based on a blended hourly rate of a hospital scientist (i.e. Grade 3/4 hospital scientist) and pharmacist (i.e. Grade 3/5 pharmacist). Totals may not be exactly additive due to rounding errors.

Table B.1 presents the resource units, in hours, required for each activity by specific personnel. Due to the variability in the resources required for the start-up meeting process, the 25th percentile was considered the best basis for setting the standard cost of **$1,879.69** per clinical trial (excluding online training).

Item 2.1.2 - Departmental set-up

Reference number	2.1.2
Item	Departmental set-up
Sub-list	Site implementation
Category	Trial initiation
Definition	The activities associated with each department involved in clinical trial getting ready for trial operation of the trial. Includes 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 any necessary preparation of medical records.
Standard cost	**$1,361.70** per host department per clinical trial; **$530.40** per pharmacy department per clinical trial; and **$346.88** per other supporting department per clinical trial.

LEARNINGS FROM SITE VISITS

Most hospital departments advises that there were set-up activities required to get the departments ready to start the clinical trial. For the host department (e.g. renal, oncology etc.) this involved preparing the necessary procedure sheets, protocol guidelines, supporting documentation, templates and forms to ensure the adequate capture of information and clinical care provided to a trial patient aligned with the trial protocol. These tasks were found to be largely the responsibility of the CTM/C.

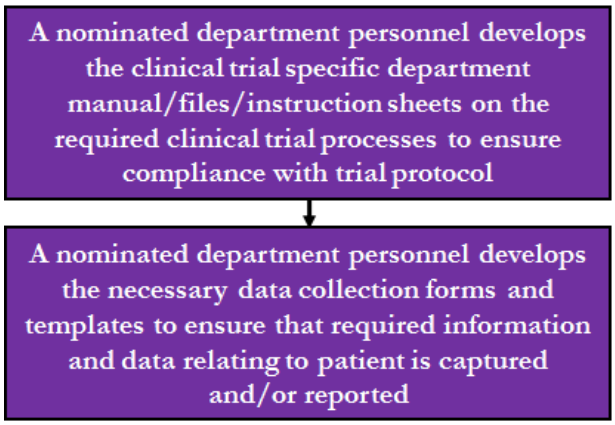
In the support departments (e.g. pharmacy, pathology, imaging, medical records etc.) the department set-up activities related to setting up clinical trial folders that clearly and plainly describes the processes required for processing requests for trial patients. The clinical trial specific folder often contains information about how the clinical trial protocol varies from 'standard preparations, tests or reporting of results'. This set-up process also involves the key clinical trial personnel from the department educating other department staff about the clinical trial protocol and the procedures that need to be followed for the specific clinical trial.

A number of the CTM/C reported that the level and standard of source documentation that is being provided by sponsors is deteriorating. This is creating additional work for the sites to generate and develop the templates and documentation required during the department set-up phase, which in turn requires additional time resources to be applied to these activities.

DERIVED PROCESS MAP FOR "DEPARTMENTAL SET-UP"

Figure B.2 presents the typical process involved in undertaking 'departmental set-up' in the **purple** boxes.

Figure B.2: Process map of the activities involved under "departmental set-up"



CONSIDERATIONS FOR DERIVING THE COST

The most typical process identified for the department set-up involved the CTM/C and a key person from each of the supporting departments. As such in order to derive a standard cost for the department set-up process, professional time was chosen as the most suitable resource unit.

TABLE OF STANDARD COSTS FOR "DEPARTMENTAL SET-UP"

Table B.2 presents the basis for calculating the standard cost for departmental set-up per clinical trial.

Table B.2: Typical personnel, resources and unit costs for "departmental set-up"

Item	Personnel involved	Resource unit (hours)						Unit cost (per labour hour)	Standard cost (40th percentile)
		Min	25th percentile	40th percentile	Median	75th percentile	Max		
Departmental set-up	Clinical Trials Manager/Coordinator	0.50	5.00	15.00	20.00	37.50	75.00	$90.78	$1,361.70
	Pharmacy department	2.00	5.50	6.00	7.50	8.50	20.00	$88.40	$530.40
	Other supporting departments	1.00	2.00	4.00	4.00	5.00	15.00	$86.72	$346.88

Note: The calculated hourly rate (fully absorbed) for a CTM/C in item 2.6.3. The hourly rate (fully absorbed) for personnel from pharmacy department is based on the average hourly rate for pharmacist (i.e. Grade 3/5 pharmacist). The hourly rate for personnel from other supporting departments is based on the average for a hospital scientist (i.e. Grade 3/4 hospital scientist). Totals may not be exactly additive due to rounding errors.

Table B.2 presents the resource units, in hours, required for each activity by specific personnel. Due to the variability in the resources required (particularly for a host department between the 25th percentile and the median) for the departmental set-up process, the 40th percentile was considered the best basis for setting the standard cost for the host department of **$1,361.70** per clinical trial, **$530.40** per pharmacy department per clinical trial and **$346.88** per other supporting department per clinical trial.

Item 2.1.3 - Trial specific equipment set-up and maintenance

Reference number	2.1.3
Item	Trial specific equipment set-up and maintenance
Sub-list	Site implementation
Category	Trial initiation
Definition	The activities associated with the hire, purchase and/or receipt from the sponsor of any equipment (including IT infrastructure) required for the purposes of conducting the clinical trial. Includes the required set-up/customisation/commissioning of the equipment so that it is suitable for use in the clinical trial, as well as local maintenance of the equipment throughout the trial.
Standard cost	**$85.04** per piece of trial equipment

LEARNINGS FROM SITE VISITS

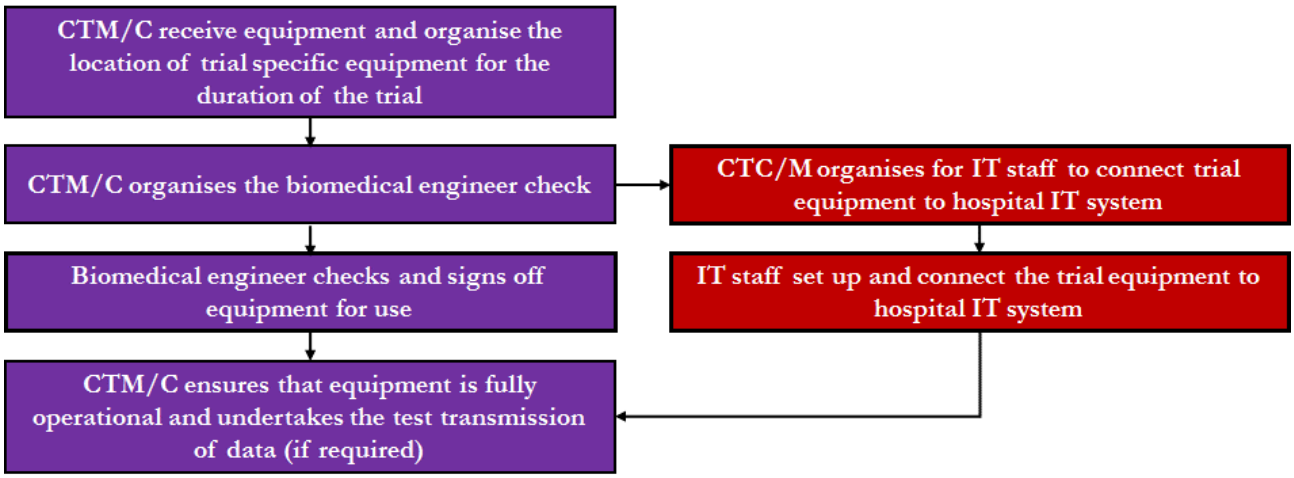
Sites hosting clinical trials often have equipment that is provided by the sponsor for use during the trial. A few examples of the type of equipment that is provided by sponsors included centrifuges and electrocardiogram (ECG) machines. While sites were required to find space or a location in which the equipment could be set up or stored, the maintenance costs of the equipment were usually met by the sponsor organisation.

Depending on local hospital policy, equipment usually needed to be checked by biomedical staff prior to the machine being able to be used. A number of sites voiced frustration with the process of setting up some of the equipment, mainly the ECG machine. While using the machine was not the issue, it was the time it took to complete the test transfer of data to the host site. The variability in time it took to perform initial set-up, which was dependent on the connection speed and quality of the provided guidance information, is not reflected in Table B.3 as it was highly variable and was undertaken usually by the CTM/C and is therefore captured under 2.6.3. Depending on the equipment, IT staff may sometimes be required to connect the equipment to the hospital network.

DERIVED PROCESS MAP FOR "TRIAL SPECIFIC EQUIPMENT SET-UP AND MAINTENANCE"

Figure B.3 shows the typical process involved in 'trial specific equipment set-up and maintenance' in the **purple** boxes. Optional steps are shown in the **red** boxes.

Figure B.3: Process map of the activities involved in "trial specific equipment set-up and maintenance"



CONSIDERATIONS FOR DERIVING THE COST

The most typical process identified for the trial specific equipment set-up and maintenance' involved the biomedical engineer assessing the provided trial equipment as such in order to derive a standard cost, professional time was chosen as the most suitable resource unit. The assumption was that biomedical engineer was included within the hospital scientist rates. The time spent by the CTM/C coordinating the biomedical engineer check and or setting up the equipment is not included in this item rather under 2.2.1 'departmental set-up'. As IT personnel were not always required this has not been factored in when calculating the standard cost. It is important to note that maintenance cost has also not been factored into the standard cost as all sites consulted reported that the sponsor usually meets all maintenance costs.

TABLE OF STANDARD COSTS FOR "TRIAL SPECIFIC EQUIPMENT SET-UP AND MAINTENANCE"

Table B.3 presents the basis for calculating the standard cost for 'trial specific equipment set-up and maintenance' per piece of trial equipment.

Table B.3: Typical personnel, resources and unit costs for "trial specific equipment set-up and maintenance"

Item	Personnel involved	Resource unit (hours)					Unit cost (per labour hour)	Standard cost (median)
		Min	25th percentile	Median	75th percentile	Max		
Trial specific equipment set-up and maintenance	Biomedical engineer	0.25	0.63	1.00	1.75	30.00	$85.04	$85.04
Total								**$85.04**

Note: The calculated hourly rate (fully absorbed) for personnel from biomedical engineering is based on an average hourly rate of a hospital scientist (i.e. Grade 3/4 hospital scientist). Totals may not be exactly additive due to rounding errors.

Table B.3 presents the resource units, in hours, required for each activity by specific personnel. Due to the variability in the resources required for the trial specific equipment set-up process, the median was considered the best basis for setting the standard cost of **$85.04** per piece of trial equipment.

Item 2.2.1 – Pre-screening activity

Reference number	2.2.1
Item	Pre-screening activity
Sub-list	Site implementation
Category	Patient accrual
Definition	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 a 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	**$166.15** to screen each potential participant per clinical trial

LEARNINGS FROM SITE VISITS

There was considerable variation in the time and approaches that were adopted by the sites for pre-screening activities. There was also trial-dependent variability (e.g. type of trial, phase of trial etc.) within sites as well. The types of activities included:

- review of patient databases (if they exist);
- review of patients during outpatient clinic attendances;
- review of admitted patients during their stay;
- review of patients at Emergency Department (ED) attendances;
- at departmental meetings;
- by approaching colleagues for patients that may meet the trial criteria; and/or
- use of a broad range of advertising materials including posters, recruitments stands at local shopping centres, newspaper and radio advertisements.

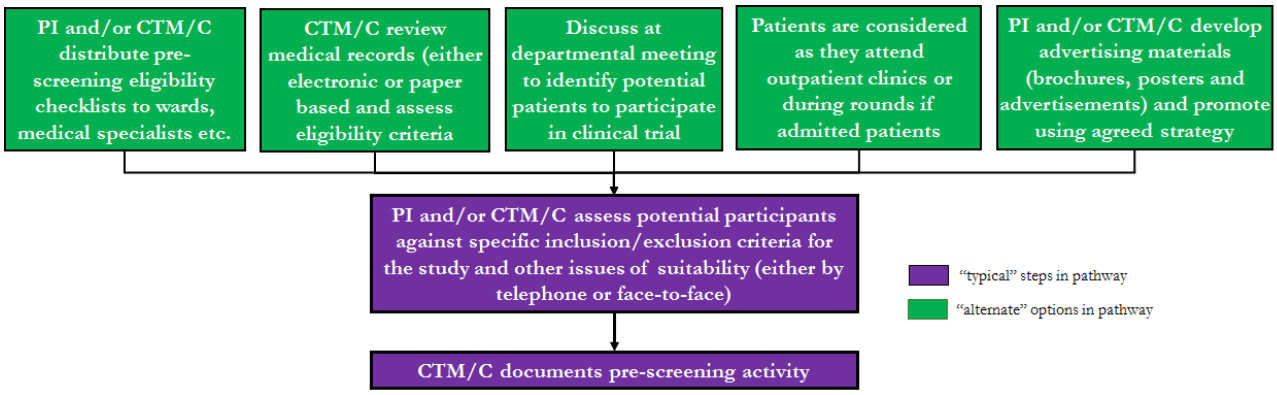
Identified potential participants are then usually contacted and an interview (usually via the telephone unless they are in the hospital) is conducted to further review the specific inclusion and exclusion criteria and assess potential participant suitability.

Sites reported an increasing level of specificity in the inclusion/exclusion criteria of more recent trials. This has resulted in increased difficulty to identify potential trial participants, thus not allowing some sites to achieve the level of patient recruitment indicated during feasibility. Most felt this was an issue, especially for a country like Australia that has a relatively proportionally smaller population size. The other compounding effect of increased specificity in the selection criteria is an increase in the time that is required to be dedicated to pre-screening activities.

DERIVED PROCESS MAP FOR "PRE-SCREENING ACTIVITY"

Figure B.4 shows the typical process involved in pre-screening activity in the **purple** boxes. Alternative steps that were found have been provided in the **green** boxes.

Figure B.4: Process map of activities included under pre-screening activity"



CONSIDERATIONS FOR DERIVING THE COST

The most typical process identified for undertaking pre-screening activity involved the PI and/or CTM/C, as such in order to derive a standard cost, professional time was chosen as the most suitable resource unit. We did find that at some sites assistance in this activity was provided by support departments. However as this was not typical it has not been factored into the calculated standard cost.

TABLE OF STANDARD COSTS FOR "PRE-SCREENING ACTIVITY"

Table B.4 presents the basis for calculating the standard costs for pre-screening activity per potential participant for a clinical trial.

Table B.4: Typical personnel, resources and unit cost involved pre-screening activity

Activities	Personnel involved	Resource unit (hours)					Unit cost	Standard cost (median)
		Min	25th percentile	Median	75th percentile	Max		
Pre-screening activity	Principal Investigator	0.10	0.16	0.33	0.58	1.00	$226.11	$75.37
	Clinical Trials Manager/Coordinator	0.17	0.50	1.00	2.67	37.5	$90.78	$90.78
Total								**$166.15**

Note: The calculated hourly rate (fully absorbed) for a PI is presented in item 2.6.1 and for the CTM/C in item 2.6.3. Totals may not be exactly additive due to rounding errors.

Table B.3 presents the resource units, in hours, required for each activity by specific personnel. Due to the variability in the resources required for the pre-screening activity, the median was considered the best basis for setting the standard cost of **$166.15** per potential participant per clinical trial.

Item 2.2.2 – Recruitment activity

Reference number	2.2.2
Item	Recruitment activity
Sub-list	Site implementation
Category	Patient accrual
Definition	The activities associated with involving potential and recruited clinical trials participants between the completion of pre-screening and the final determination of the assessment for suitability. Includes the provision of education and information to possible clinical trial participants, 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	**$498.45** per potential participant per clinical trial

LEARNINGS FROM SITE VISITS

The first process that was identified within recruitment activities was to gain the consent of the patient. The consent process usually occurred over a number of interactions with the patient and/or family by either the PI and/or the CTM/C providing answers to their questions. Final consent was always undertaken by the PI and/or Co-PIs. In the majority of instances there was an initial contact with the patient to describe the trial and associated risks and potential benefits, followed by a period of time for the patient to consider their decision. During this time the patient is actively encouraged to discuss their decision with family members, as well as their GPs and other relevant parties. Once the patient has made their decision they meet with the PI and sign the informed consent form. If the patient was an emergency admission, for a device trial for example, the consent process was dramatically reduced due to the clinical need of the patient.

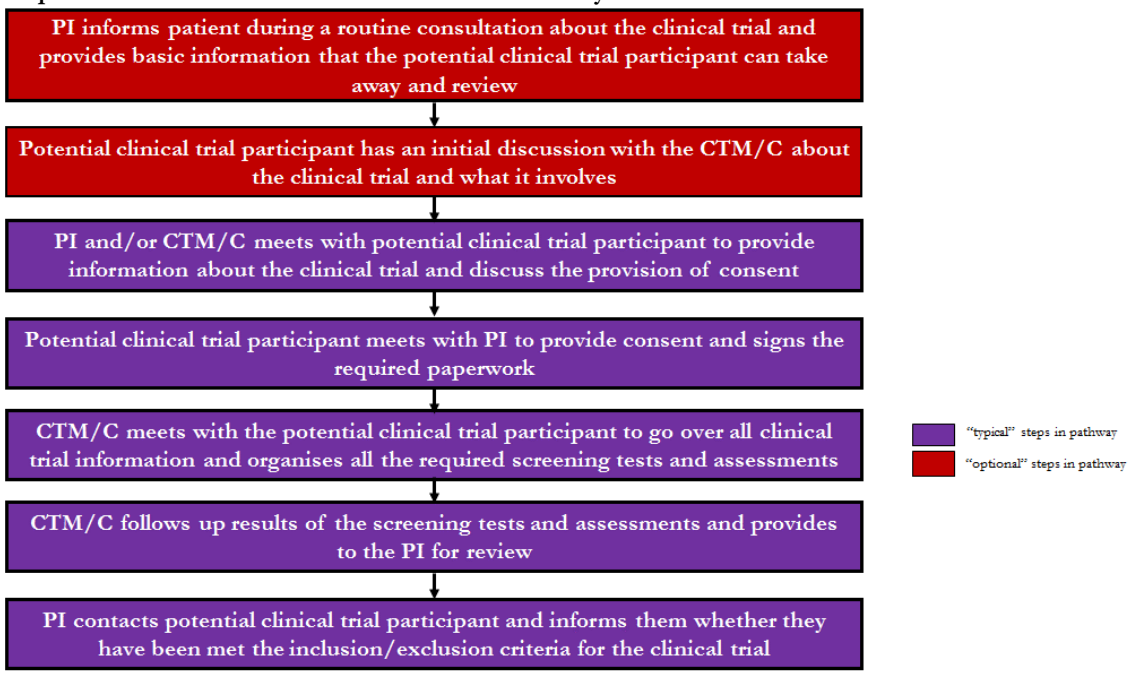
Once consent has been given, generally the CTM/C then arranges the required assessments and tests to further ascertain if the patient is suitable for inclusion in the clinical trial. Once the assessment and tests results have been collated and reviewed by the PI, the patient is informed of their suitability for inclusion in the trial or not.

Where the patient is unable to provide consent themselves, for example if the patient is unconscious, an Intensive Care Unit (ICU) patient, or a child under the legal age of consent, then additional processes are required. In these circumstances consent needs to be provided by the relevant next of kin or legal guardian. It was found that this generally increases the length of time required to gain consent.

DERIVED PROCESS MAP FOR "RECRUITMENT ACTIVITY"

Figure B.5 shows the typical process involved in recruitment activity in the **purple** boxes. Optional steps are shown in the **red** boxes.

Figure B.5: Process map of activities included under "recruitment activity"



CONSIDERATIONS FOR DERIVING THE COST

The most typical process identified for recruitment activity involved the PI and/or CTM/C, as such in order to derive a standard cost, professional time was chosen as the most suitable resource unit.

TABLE OF STANDARD COSTS FOR "RECRUITMENT ACTIVITY"

Table B.5 presents the basis for calculating the standard costs for recruitment activity per potential participant per clinical trial.

Table B.5: Typical personnel, resources and unit cost involved recruitment activity

Activities	Personnel involved	Resource unit (hours)					Unit cost	Standard cost (median)
		Min	25th percentile	Median	75th percentile	Max		
Provision of information and education	Principal Investigator	0.03	0.33	0.63	1.00	4.00	$226.11	$141.32
	Clinical Trials Manager/Coordinator	0.25	0.50	1.00	2.00	15.00	$90.78	$90.78
Coordination of screening activities	Clinical Trials Manager/Coordinator	0.50	1.00	2.00	5.25	15.00	$90.78	$181.56
Review of results	Principal Investigator	0.25	0.31	0.38	0.44	0.50	$226.11	$84.79
Total								**$498.45**

Note: The calculated hourly rate (fully absorbed) for a PI is presented in item 2.6.1 and for the CTM/C in item 2.6.3.

Table B.5 presents the resource units, in hours, required for each activity by specific personnel. Due to the variability in the resources required for the recruitment activity process, the median was considered the best basis for setting the standard cost of **$498.45** per potential participant per clinical trial.

Item 2.3.1 - Screening and health assessment

Reference number	2.3.1
Item	Screening and health assessment
Sub-list	Site implementation
Category	Clinical services
Definition	The 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 2.3.2, 2.3.3, 2.3.4, 2.3.5, 2.3.6, 2.3.7 and 2.3.8

LEARNINGS FROM SITE VISITS

Screening visits are often the longest visit in the trial and often 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. about 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 CTM/C was the person who arranged participant attendance and the booking of appropriate tests and consultations/assessments. 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 PI in addition to the CTM/C. These latter activities are captured under item 2.2.2.

It is important to note that the screening visit is used to determine or confirm a participant's eligibility to participate in the clinical 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'. Once the results of tests and assessments are ready, they are collated by the CTM/C, reviewed by the PI and then the potential clinical trial participant is informed of their results and whether they meet the clinical trial inclusion/exclusion criteria or not. Again these latter activities are captured under item 2.2.2.

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, procedures and assessments undertaken. It will also vary according to whether components of the screening visits and health assessment are considered standard care or are in addition to standard care. Thus cost of the 'screening visit and health assessment' will be made up of the costs of other items within the site implementation items including those items listed in Table B.6 as appropriate to each clinical trial.

TABLE OF STANDARD COSTS FOR "SCREENING VISIT AND HEALTH ASSESSMENT"

Table B.6 presents the basis for calculating the standard cost for the screening and health assessment services per participant per clinical trial.

Table B.6: Typical personnel, resources and unit costs for "screening visit and health assessment"

Reference Number	Item	Service volume	Unit cost	Standard cost
2.3.2	Laboratory tests and procedures	No. of services	as per 2.3.2	volume * unit cost
2.3.3	Imaging examinations and procedures	No. of services	as per 2.3.3	volume * unit cost
2.3.4	Radiation therapy planning and treatment	No. of services	as per 2.3.4	volume * unit cost
2.3.5	Other clinical tests or procedures	No. of services	as per 2.3.5	volume * unit cost
2.3.6	Specialist medical consultations*	No. of services	as per 2.3.6	volume * unit cost
2.3.7	Nursing services*	No. of hours	as per 2.3.7	hours * unit cost
2.3.8	Allied health services*	No. hours	as per 2.3.8	hours * unit cost
2.3.1	**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

Table B.6 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.

Item 2.3.2 - Laboratory tests and procedures

Reference number	2.3.2
Item	Laboratory tests and procedures
Sub-list	Site implementation
Category	Clinical services
Definition	Laboratory clinical services including pathology, histopathology, haematology, chemical, microbiology, immunology, tissue pathology, cytology, genetics, etc.
Standard cost	140% of the MBS fee per laboratory test and/or procedure

LEARNINGS FROM SITE VISITS

Most clinical trials will involve pathology testing of biospecimens (e.g. blood, urine etc.) from clinical trial participants at multiple points during the clinical trial. The required pathology tests and required testing time points are detailed in each 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. The most common process involved the CTM/C or the pathology department collecting and sending samples to central laboratories for processing (usually in Asia) rather than the local pathology departments to analyse the samples themselves.

Most consulted sites invest time in identifying pathology tests that are considered part of standard care and those that are considered clinical trial specific. Those laboratory tests and procedures considered as part of standard 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 standard care or not. Some of these sites argued that although the test may be considered part of standard 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 (and some were referencing the 2013 clinical trials Table of standard costs). However, this practice was not widespread, and it was not possible to verify the locally derived costs (task too complex within the time and resources available). Accordingly, research was undertaken to ascertain either alternative secondary sources for the cost of pathology tests that could be used for the process of costing a clinical trial or identify the differential time involved in analysing and reporting pathology results as part of a clinical trial as opposed to standard care.

Most sites consulted stated that the budget derived for pathology testing often referred to the MBS (or Australian Medical Association, AMA) but included a loading on the MBS (usually not on the AMA) to reflect the additional reporting requirements required for the clinical trial and/or different procedures (e.g. non-standard parameters for paediatric trials although undertaking these different procedures is becoming less likely to be done by a local pathology department) that need to be followed to meet the protocol requirements. Most pathology departments consulted reported that if there were additional reporting requirements, that the additional reporting time, once any change to the reporting template was made (as part of 'departmental set-up' item 2.1.2), was in the range of 5-15 minutes. Taking the median of 10 minutes, and assuming the pathology test reporting is done by a senior medical

specialist/pathologist (i.e. assume year 6) at a fully absorbed hourly rate of $206.87 (see Table B.25) this equates to $34.48 per report. However using this approach assumes that the MBS fee associated with the test equates to the cost, and although the MBS has regard to cost it is not based on costs. Therefore if sites charge an additional fee (e.g. $34.48) on top of the MBS fee this would not be reflective of the actual cost incurred by the hospital. For this reason, we have decided not to change the standard cost for "Laboratory tests and procedures" from that proposed in the 2013 report (i.e. a loading factor applied to the MBS for each laboratory test and procedure). Data gathered from the loading factors used by sites in this 2015 study is presented in Table B.7.

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 also 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.

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 was not possible within the provided timeframe, and most sites negotiate trial budgets based on an MBS (or AMA) multiplier. Table B.7 presents a number of reference points for the MBS multipliers applied by the visited sites.

Table B.7: 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 and procedures	MBS fee with adjustment factor	0.8	1.2	1.4	1.8	2.2	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.

Item 2.3.3 – Imaging examinations and procedures

Reference number	2.3.3
Item	Imaging examinations and procedures
Sub-list	Site implementation
Category	Clinical services
Definition	Imaging clinical services including diagnostic radiology (e.g. plain radiography, computed tomography (CT), magnetic resonance imaging (MRI), ultrasound, nuclear medicine and positron emission tomography (PET) scans using the radiopharmaceuticals fluorodeoxyglucose (FDG) or non-FDG tracers' fluorothymidine (FLT)).
Standard cost	140% of the MBS fee per imaging examination and/or procedure

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 care) and payment for additional services/activities beyond those normally included in the imaging procedure (such as additional reporting and uploading of images to central repositories).

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.

PROCESS MAP FOR "IMAGING EXAMINATIONS AND PROCEDURES"

Not applicable.

CONSIDERATIONS FOR DERIVING THE COST OF "IMAGING EXAMINATIONS AND PROCEDURES"

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-$150 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 associated with performing the imaging examinations including:

- additional reporting such as Response Evaluation Criteria In Solid Tumors (RECIST) reporting, which is usually charged based on time;
- production of CD containing images;
- organising data extracts and/or uploading images to central repositories.

Currently, some sites cover the "additional costs" in their fixed establishment/set-up fee or the ongoing administration fees. For the same reasons as described under item 2.3.2, we have decided not to change the standard cost for "imaging examinations and procedures" from that proposed in the 2013 report.

In regards to the use of PET and MRI in clinical trials 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. The principal difference in the cost of PET-FDG and PET-FLT is 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 "IMAGING EXAMINATIONS 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 was not possible within the provided timeframe, and most sites negotiate trial budgets based on an MBS multiplier. Table B.8 presents a number of reference points for the MBS multipliers applied by the visited sites.

Table B.8: 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	1.0	1.4	1.6	1.8	2.2	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, uploading of images to central repositories etc.) 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. Although the median is showing a multiplier of 1.6, it would be preferable to set the multiple for MBS the same regardless of the item number. Hence 1.4 reflects the same multiplier as item 2.3.2 'laboratory tests and procedures'.

Where the imaging examinations and/or procedures are not on the MBS then the nearest equivalent imaging examinations and/or procedure on the MBS should be used. In the absence of any other data this is considered to be the best approach.

Item 2.3.4 - Radiation therapy planning and treatment

Reference number	2.3.4
Item	Radiation therapy planning and treatment
Sub-list	Site implementation
Category	Clinical services
Definition	Radiation oncology treatment services including radiation therapy planning, external beam radiation therapy, brachytherapy, etc.
Standard cost	140% of the MBS fee including ROHPG component per service

LEARNINGS FROM SITE VISITS

Radiation therapy procedures are often a component of oncology clinical trials. Although the majority of procedures are standard 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). It was found that investigator-initiated and/or collaborative sponsored trials were the predominant sponsor of radiation oncology trials rather than industry.

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 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 was not possible in the time available, and most sites negotiate trial budgets based on an MBS multiplier. Table B.9 indicates that insufficient data on the multipliers applied in the visited sites was able to be obtained.

Table B.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.

Item 2.3.5 - Other clinical tests or procedures

Reference number	2.3.5
Item	Other clinical tests or procedures
Sub-list	Site implementation
Category	Clinical services
Definition	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

LEARNINGS FROM SITE VISITS

Majority of clinical trials discussed at the site visits required tests or procedures that fit into this category of 'other clinical tests or procedures' (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.) and/or CTM/C. Similar arrangements to the other diagnostic services (i.e. laboratory tests, imaging examinations, etc.) that might be used for participants in a clinical trial generally applied.

DERIVED PROCESS MAP FOR "OTHER CLINICAL TESTS OR PROCEDURES"

Not applicable.

CONSIDERATIONS FOR DERIVING THE COST OF "OTHER CLINICAL TESTS OR PROCEDURES"

The MBS was the only source for information relating to the costs of "other clinical tests or procedures" 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, uploading data to a central repository, and billings).

It is also important to note, however, that in some instances there are 'other clinical tests or procedures' undertaken for the purposes of a clinical trial that 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.

TABLE OF STANDARD COSTS FOR "OTHER CLINICAL TESTS OR 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 was not possible in the time available, and most sites negotiate trial budgets based on an MBS multiplier. Table B.10 indicates that insufficient data on the multipliers applied in the visited sites was able to be obtained.

Table B.10: MBS multipliers for other clinical tests or procedures

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	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, data/test results transfer) associated with "other clinical tests or procedures" 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" services required by the trial.

Item 2.3.6 - Specialist medical consultations

Reference number	2.3.6
Item	Specialist medical consultations
Sub-list	Site implementation
Category	Clinical services
Definition	Clinical consultations services provided by medical specialists, General Practitioners (GPs), dentists and any other registered medical practitioner.
Standard cost	140% of the MBS fee per specialist medical (including GP) service 100% of ADA fee per specialist dental service

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 care;
- a clinical trial participant attends a consultation considered for the most part as standard 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 care the trial budget usually includes the full cost of the specialist medical consultation. In the case where additional activities and time is added to a consultation that is part of standard care the proportional cost (or usually time) is usually 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"

Table B.11 shows the response by medical specialists who were asked to estimate the additional time they spent with a patient due to the fact that they are on a clinical trial. The responses were varied and were dependent on the patient population (i.e. max is driven by paediatric clinical trials responses) and the minimum driven was oncologists with well organised CTM/C that ensure the patient file has a list of additional items the specialist needs to ask the clinical trial participant. Due to this variability the additional time was considered too variable to be the basis for calculating the standard cost.

Table B.11: Typical personnel, resources and unit cost involved in specialist medical consultations

Item	Personnel involved	Resource unit (hours)					Unit cost	Standard cost (median)
		Min	25th percentile	Median	75th percentile	Max		
Specialist medical consultations	Medical Specialist (year 6)	0.083	0.25	0.5	1	4	$206.87	$103.44

Note: Assumed medical Specialist (year 6) at a fully absorbed hourly rate of $206.87 (see Table B.25)

The further investigation into a basis for setting the standard cost of specialist medical services identified a number of options. The MBS, the AMA Fee Schedule, and the Department of Veterans' Affairs (DVA) Fee Schedule all represent approaches that are consistent with common billing practices. Table B.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 B.12: Comparison of Fee Schedules (amounts rounded)

Item	MBS	AMA	DVA
Item 36 GP Attendance Level C (20-39 minutes)	$72	$126	$83
Item 104 Specialist Consultation Initial	$86	$150	$118
Item 105 Specialist Consultation Follow-up	$43	$80	$59

Note: MBS rates; http://www9.health.gov.au/mbs/search.cfm?q=15215&sopt=S; AMA rates are current as at 2013 as rates are no longer publically accessible; DVA from http://www.dva.gov.au/sites/default/files/files/providers/fee_schedules.pdf.

Through the site visits, examples of sites using the MBS fee with an add-on percentage to recognise that additional data collection time and 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 none of the site visits undertaken in 2015 were currently undertaking any dentistry clinical trials, 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 services sub-list, MBS is also used as the basis for classifying and setting the standard costs for specialist medical consultations (except dental services). Use of the MBS fee as a reference point is appropriate, as bottom up costing could not be attempted in the project timeframe, and most sites negotiate trial budgets based on an MBS multiplier. Table B.13 indicates that insufficient data on the multipliers applied in the visited sites (not all sites used MBS) was able to be obtained.

Table B.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 data collection and 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 consultations required by the clinical trial.

The same approach cannot be used for dental services as there are no MBS items for most services. Therefore, 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). 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.

Item 2.3.7 – Nursing services

Reference number	2.3.7
Item	Nursing services
Sub-list	Site implementation
Category	Clinical services
Definition	Clinical services provided by enrolled, registered and specialist nurses, midwifes and nurse practitioners.
Standard cost	**$81.90** per nurse consultation (based on 140% of the identified MBS fees)

LEARNINGS FROM SITE VISITS

The use of nursing consultations vary as part of a clinical trial depending on the discipline of the CTM/C. If the CTM/C is a nurse then they often also provide nursing services in addition to CTM/C services. However where the CTM/C is a non-nurse then accessing nursing services is more common. Regardless nursing services are a necessity of the vast majority of clinical trials. Either the participant is seen for trial activities as part of a standard 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 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 service is often included in the trial budget.

DERIVED PROCESS MAP FOR "NURSING SERVICES"

Not applicable.

CONSIDERATIONS FOR DERIVING THE COST OF "NURSING SERVICES"

The investigation into a basis for setting the standard cost of nursing services identified a number of options. The MBS and the AMA Fee Schedule represent approaches that are consistent with common billing practices. Table B.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 B.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

Source: MBS rates; http://www9.health.gov.au/mbs/search.cfm?q=15215&sopt=S; AMA rates are current as at 2013 as rates are no longer publically accessible.

Assuming the median of the MBS fee is more appropriate than the AMA fee (to align with other clinical services items), Table B.15 presents an option for calculating the standard cost of nursing services as $81.90 per nursing consultation.

Table B.15: Typical personnel, resources and unit cost involved in nurse consultations

Item	Basis	Resource Unit					Unit cost	Multiplier to derive standard cost
		Min	25th percentile	Median	75th percentile	Max		
Nursing services	MBS fee with adjustment factor	$58	N/A	N/A	N/A	$59	$58.50	$81.90

Another possible source of data is the national efficient price determined by 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 (NHCDC), which covers a very large proportion of public hospital services provided in Australia. Table B.16 sets out the prices published by IHPA for 2013/14 for a range of predominately nursing clinics.

Table B.16: Nursing outpatient clinic costs, as published by IHPA for 2013/14

Tier 2 Clinic Code	Item	Price weight*	Price (based on NEP of $5,007)
40.07	Pre-admission and pre-anaesthesia	0.1051	$526
40.13	Wound management	0.0575	$288
40.22	Stomal therapy	0.0906	$454
40.28	Midwifery	0.0485	$243
40.32	Continence	0.0323	$162

* price weight based on non-indigenous patient and funding source = 1

TABLE OF STANDARD COSTS FOR "NURSING SERVICES"

There are wide variations in cost/prices of nursing services derived from the potential sources investigated. While the 2013 study concluded that there was insufficient information in the MBS to cover all nursing services, and recommended the use of the 'pre-admission and pre-anaesthesia clinic' as an indicator of nursing services, the variation in the price weights since means the cost of $526 does not align this item to other standard cost suggested in the 2015 study. In addition the use of the MBS loading would mean that the standard cost would be $81.90 per nursing service compared to $74.79 per hour calculated for a research nurse in item 2.6.2 'research nurse time'. In order to align with the other clinical services the suggested option is presented in Table B.15 which shows a standard cost of **$81.90** per nursing service.

Item 2.3.8 – Allied health services

Reference number	2.3.8
Item	Allied health services
Sub-list	Site implementation
Category	Clinical services
Definition	Clinical services provided by registered allied health professionals (e.g. pharmacists, physiotherapists, dieticians, occupational therapists).
Standard cost	**$98** per allied health consultation (based on 140% of the identified MBS fees)

LEARNINGS FROM SITE VISITS

Allied health consultations feature to a lesser degree in the clinical trials from the sites visited. Either the participant is seen for trial activities as part of a standard care visit or as a separate clinical trial specific visit. In the latter case, the trial budgets typically include the cost of 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 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.

DERIVED PROCESS MAP FOR "ALLIED HEALTH CONSULTATIONS"

Not applicable.

CONSIDERATIONS FOR DERIVING THE COST OF "ALLIED HEALTH CONSULTATIONS"

The investigation into a basis for setting the standard cost of allied health services identified a number of options. 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 B.17. 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 B.17: 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	$55.84	$135.80	n.a
	Standard consultation < 30 minutes	n.a	$44.94	$54.90	n.a
Physiotherapy	Initial consult	$88.40	$96.79	$80.25	n.a
	Standard consult	$74.90	$50.33	$64.45	n.a

Source: http://www.comcare.gov.au/claims_and_benefits/benefits_and_entitlements/rates_and_reimbursements/allied_health_rates. n.a = not available

The calculated average of all the data points in Table B.17 is $79 and the median is $70 per allied health consultation (unbound by time).

Another possible source of data is the national efficient price determined by IHPA for the purpose of activity based funding in public hospitals. These prices are determined based on the average costs

derived NHCDC, which covers a very large proportion of public hospital services provided in Australia. Table B.18 sets out the prices published by IHPA for 2013/14 for allied health clinics.

Table B.18: Allied health outpatient clinic costs, as published by IHPA for 2013/14

Tier 2 Clinic v3.0	Tier 2 Clinic descriptor	Price weight*	Price (based on NEP of $5,007)
40.04	Clinical Pharmacy	0.1771	$887
40.05	Hydrotherapy	0.0495	$248
40.06	Occupational Therapy	0.0271	$136
40.09	Physiotherapy	0.0390	$195
40.11	Social Work	0.0506	$253
40.14	Neuropsychology	0.1505	$754
40.15	Optometry	0.0111	$56
40.16	Orthoptics	0.0133	$67
40.17	Audiology	0.0515	$258
40.18	Speech Pathology	0.0465	$233
40.23	Nutrition/Dietetics	0.0525	$263
40.24	Orthotics	0.0486	$243
40.25	Podiatry	0.0503	$252
40.29	Psychology	0.0302	$151
Average			**$285**
Median			**$248**

* price weight based on non-indigenous patient and funding source = 1

In comparing Table B.17 to B.18 there is considerable difference between the two averages and means of allied health consultations. In addition, a fully absorbed hourly rate calculated for pharmacists (see Table B.29) was $88.40 per hour.

TABLE OF STANDARD COSTS FOR "ALLIED HEALTH CONSULTATIONS"

Like nursing services, there are wide variations in cost/prices of allied health services derived from the potential sources investigated. While the 2013 study concluded that there was insufficient information in the MBS to cover all nursing services, and recommended the use of the IHPA price with no adjustment for allied health services/clinics, the variation in the price weights since means the median cost of $248 does not align this item to other standard cost suggested in the 2015 study. In addition the use of the MBS loading would mean that the standard cost would be $70 (median) per allied health service compared to $88.40 per hour calculated for a pharmacist under item 2.6.3. In order to align with the other clinical services the suggested option presented in Table B.19 shows a standard cost of **$98** per allied health service which is based on applying a loading of 1.4 to the median of $70.

Table B.19: Typical personnel, resources and unit cost involved in allied health services

Item	Basis	Resource Unit					Unit cost	Multiplier to derive standard cost
		Min	25th percentile	Median	75th percentile	Max		
Allied health services	MBS fee with adjustment factor	$45	N/A	N/A	N/A	$136	N/A	**$98**

Item 2.4.1 - Staff training (drug-specific)

Reference number	2.4.1
Item	Staff training (drug-specific)
Sub-list	Site implementation
Category	Pharmacy/investigation drug related
Definition	The activities associated with the 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.), doctors, nurses on the drug-specific aspects of the clinical trial protocol.
Standard cost	**$176.80** per pharmacist to undertake two hours of drug-specific training per clinical trial

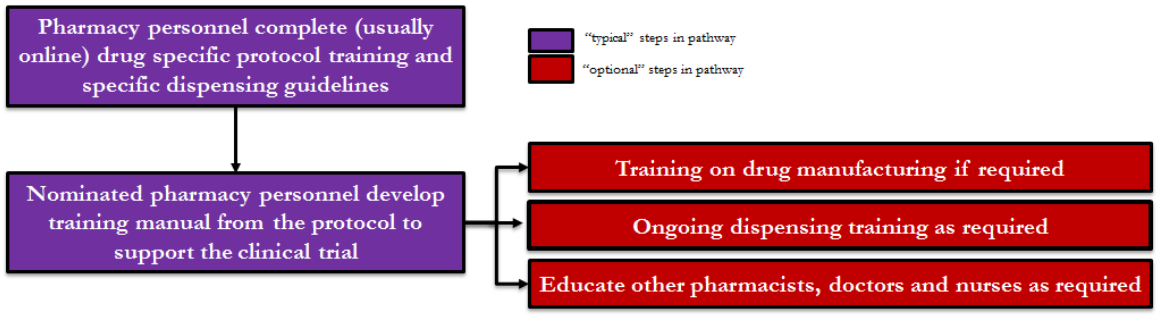
LEARNINGS FROM SITE VISITS

Pharmacy staff reported that majority of the drug-specific training is now undertaken online. Pharmacy staff reported that there are usually numerous modules they need to complete prior to the commencement on the trial (e.g. related to the protocol, temperature monitoring, drug logging etc.). At least one pharmacist must undertake the training; however for most clinical trials at least two undertake the training to ensure there is backup personnel available. The main pharmacist assigned to the clinical trial then takes on the role to educate others (e.g. other pharmacists, doctors, nurses etc.) in relation to their learnings.

DERIVED PROCESS MAP FOR "STAFF TRAINING (DRUG-SPECIFIC)"

Figure B.6 presents the typical process involved in staff training (drug-specific) in the **purple** boxes. Optional steps are shown in the **red** boxes.

Figure B.6: Process map for activities included under staff training (drug-specific)"



CONSIDERATIONS FOR DERIVING THE COST

The most typical process identified involved at least one key pharmacy personnel undertaking the drug-specific training related to a clinical trial, as such in order to derive a standard cost for the staff training (drug-specific), professional time was chosen as the most suitable resource unit. As drug-specific training is undertaken by pharmacy staff, this has been reflected in the rate that has been applied to derive the standard cost. It is important to note that the development of the training manual which supports the clinical trial is not included in the standard cost for this item, rather it is included under item 2.2.1 'departmental set-up'.

TABLE OF STANDARD COSTS FOR "STAFF TRAINING (DRUG-SPECIFIC)"

Table B.20 presents the basis for calculating the standard cost for staff training (drug-specific) per clinical trial.

Table B.20: Typical personnel, resources and unit cost involved in 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	0.50	2.00	2.50	4.00	6.00	$88.40	$176.80
Total								**$176.80**

Note: The calculated hourly rate (fully absorbed) for pharmacist is based on the average hourly rates for Grade 3/5 pharmacist, (as defined in 2.6.3) see Table B.30. Totals may not be exactly additive due to rounding errors.

Table B.20 presents the resource units, in hours, required for each activity by specific personnel. Due to the variability in the resources required for the staff training (drug-specific), the 25th percentile was considered the best basis for setting the standard cost of **$176.80** per pharmacist to undertake two hours of drug-specific training per clinical trial.

Item 2.4.2 – Stock management

Reference number	2.4.2
Item	Stock management
Sub-list	Site implementation
Category	Pharmacy/investigation drug related
Definition	The activities associated with the receiving of pharmacy stock for the clinical trial, completing an inventory check, downloading temperature log, 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.). Stock management also includes expiry management (e.g. labelling and re-labelling due to the extension of the expiry date of the product); recording and storing of used/unused products; any monitoring that is required to ensure the viability of the product, data entry associated with any expired or unused medicines; returning used or unused medicines to the sponsor; etc. during the implementation phase.
Standard cost	**$72.85** per drug stock received **$9.17** for expiry management per week.

LEARNINGS FROM SITE VISITS

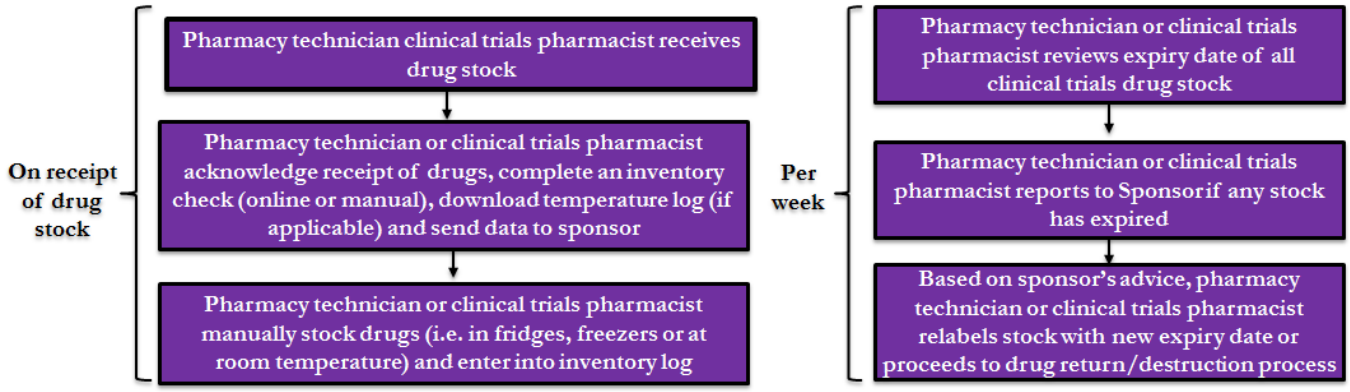
From the site visits we found that the amount of time required for stock management processes varied based on the volume of goods that were received and level of stock required to be managed. Stock was processed when received and this involved several tasks including validating the items, checking the quantity received, ensuring the stock is recorded in the inventory management system, undertaking a temperature check (if required), ensuring stock is stored compliant with specifications, updating trial logs and advising the sponsor that stock has been received. The time required to complete these tasks directly correlated with volume of stock received within the shipment. Expired stock was managed through regular checks of stock to identify items nearing the expiry date. Some sites reported that the monitor undertakes expiry stock management as part of their regular visits.

Recording and data entry of returned drugs was completed on an as needs basis (the basis for calculating the standard cost is shown under item 3.3.1). Most sites reported that sometimes a simple task took an extra ordinary amount of time due to IT connection issues.

DERIVED PROCESS MAP FOR "STOCK MANAGEMENT"

Figure B.7 presents the typical process involved in stock management process in the **purple** boxes. Note the process of drug stock return/destruction is shown under item 3.3.1. Where expiry management is undertaken by the monitor then the standard cost for expiry management is not relevant.

Figure B.7: Process map for activities included under "stock management"



CONSIDERATIONS FOR DERIVING THE COST

The most typical process identified usually involved time of a technician and the clinical trials pharmacist to oversee stock management, as such in order to derive a standard cost for the stock management process, professional time was chosen as the most suitable resource unit.

TABLE OF STANDARD COSTS FOR "STOCK MANAGEMENT"

Table B.21 presents the basis for calculating the standard cost for stock management (excluding expiry management of drug stock) per stock delivery received and expiry management per week.

Table B.21: Typical personnel, resources and unit cost involved in stock management

Activities	Personnel involved	Resource unit (hours)					Unit cost	Standard cost (25th percentile)
		Min	25th percentile	Median	75th percentile	Max		
Stock management (excluding expiry management)	Pharmacist	0.25	0.50	1.00	1.88	4.00	$57.30	$28.65
	Pharmacy technician	0.25	0.50	0.83	1.17	4.33	$88.40	$44.20
Total								**$72.85**
Expiry management of drug stock	Pharmacy technician	0.08	0.16	0.21	0.25	0.50	$57.30	$9.17

Note: The calculated hourly rate (fully absorbed) for pharmacist is average hourly rates for Grade 3/5 pharmacist (as defined in 2.6.3). The calculated hourly rate (fully absorbed) for pharmacy technician is average hourly rates for Grade 1 pharmacist. Totals may not be exactly additive due to rounding errors.

Table B.21 presents the resource units, in hours, required for each activity by specific personnel. Due to the variability in the resources required for the stock management process, the 25th percentile was considered the best basis for setting the standard cost of **$72.85** per drug stock received and the standard cost of **$9.17** for expiry management per week.

Item 2.4.3 – Drug preparation and dispensing

Reference number	2.4.3
Item	Drug preparation and dispensing
Sub-list	Site implementation
Category	Pharmacy/investigation drug related
Definition	The activities associated with 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; the development and maintenance of special dosage forms (including the activities associated with the randomisation process if applicable). Includes the conduct of dispensing (including the provision of counselling to clinical trial participants), review of clinical trial participants' adherence to the trial protocol, costs related to on-call/call back and recording details of the clinical trial in the participant's medical record (paper based or electronic).
Standard cost	**$169.43** for drug manufacturing (if required); **$43.32** for simple clinical trial drug preparation and dispensing; **$110.21** for complex clinical trial drug preparation and dispensing; **$14.33** for clinical trial drug accountability activities per clinical trial participant; **$18.12** for provision of counselling services by a pharmacist at the time of dispensing the clinical trial drug(s) to a clinical trial participant.

LEARNINGS FROM SITE VISITS

The majority of sites visited perceived drug preparation and dispensing to be integrated tasks based on the drug request/prescriptions received. The process of distinguishing between a simple versus complex dispensing was based on the number of items that were required per request, as well as the preparation requirements for a particular drug. Where drug preparation was required to be in an aseptic environment, including cytotoxic compounds, usually two staff are required to wear appropriate safety clothing items and equipment. Manufacturing drugs on site was not found to be commonly undertaken by the pharmacy staff although there were six individuals that provided estimates when such activities are undertaken.

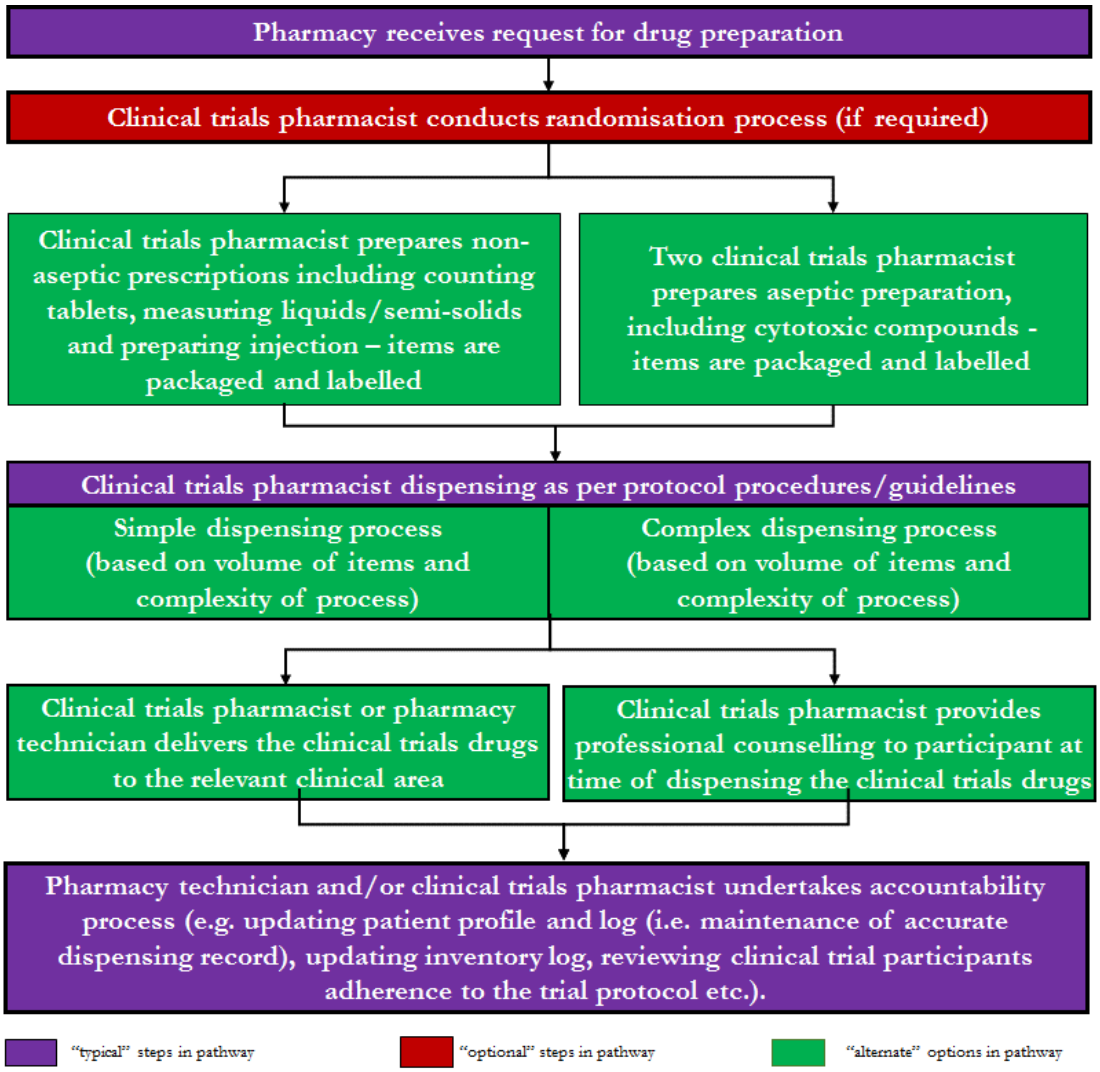
Randomisation was completed if required by pharmacy staff although sometimes it was found that randomisation was undertaken by CTM/C. For clinical trials drugs collected directly from the pharmacy by the trial participant, pharmacy staff require time to speak with and counsel the patient at the time of collection (i.e. provision of counselling). For clinical trials drugs that are delivered to the host clinical trial department, counselling time is not required but it still requires someone usually the pharmacy technician to deliver the drugs to the relevant clinical area.

The accountability processes and ensuring that records were kept updated for trial drugs was flagged as a time consuming process required to be completed by pharmacy staff. It was often undertaken by the pharmacy technician and review/oversight provided by a pharmacist.

DERIVED PROCESS MAP FOR "DRUG PREPARATION AND DISPENSING"

Figure B.8 presents the typical process involved in drug preparation and dispensing in the **purple** boxes. Optional steps are shown in the **red** boxes and alternative pathways in the **green** boxes.

Figure B.8: Process map for activities included under "drug preparation and dispensing"



CONSIDERATIONS FOR DERIVING THE COST

The most typical process identified that two pharmacists were involved in most drug preparation and dispensing process or the pharmacy technician (for the accountability process), as such in order to derive a standard cost professional time was chosen as the most suitable resource unit. As either a pharmacist or pharmacy technician are involved in drug preparation and dispensing, this has been reflected in the rate that has been applied to derive the standard cost.

TABLE OF STANDARD COSTS FOR "DRUG PREPARATION AND DISPENSING"

Table B.22 presents the basis for calculating the standard costs for drug preparation and dispensing activities. Given the differences in resources used, separate standard costs have been set for manufacturing, simple and complex preparation and dispensing, accountability and counselling activities at the median of the observations.

Table B.22: Typical personnel, resources and unit cost involved in drug preparation and dispensing

Activities	Personnel involved	Resource unit (hours)					Unit cost	Standard cost (median)
		Min	25th percentile	Median	75th percentile	Max		
Manufacturing	Two Pharmacist	0.50	0.56	0.96	1.23	2.00	$88.40	$169.43
Simple preparation and dispensing	Two Pharmacists	0.03	0.14	0.25	0.29	0.68	$88.40	$43.32
Complex preparation and dispensing	Two Pharmacist	0.05	0.36	0.62	1.02	2.33	$88.40	$110.21
Accountability	Pharmacy technician	0.08	0.16	0.25	0.50	0.50	$57.30	$14.33
Counselling	Pharmacist	0.08	0.08	0.21	0.50	1.00	$88.40	$18.12

Note: The calculated hourly rate (fully absorbed) for pharmacist is average hourly rates for Grade 3/5 pharmacist (as defined in 2.6.3). The calculated hourly rate (fully absorbed) for pharmacy technician is the average hourly rate for Grade 1 pharmacist. Totals may not be exactly additive due to rounding errors.

Table B.22 presents the resource units, in hours, required for each activity by specific personnel. Due to the variability in the resources required for the drug preparation and dispensing activities, the median was considered the best basis for setting the standard cost of **$169.43** for drug manufacturing (which includes two pharmacists), **$43.32** for simple clinical trial drug preparation and dispensing (which includes two pharmacists), **$110.21** for complex clinical trial drug preparation and dispensing (which includes two pharmacists), **$14.33** for clinical trial drug accountability activities (undertaken largely by a pharmacy technician) and **$18.12** for provision of counselling services by a pharmacist at the time of dispensing the clinical trial drug to a clinical trial participant.

Item 2.5.1 - Biospecimen collection and processing (central labs)

Reference number	2.5.1
Item	Biospecimen collection and processing (central labs)
Sub-list	Site implementation
Category	Biospecimen related
Definition	The activities associated with the collection, processing and transport (e.g. quarantine permits, etc.) of clinical trial biospecimens (e.g. 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 arranging transfer of the biospecimen(s) to central laboratories. For biospecimens tested on site, biospecimen collection and processing is covered by the appropriate test in the clinical services category.
Standard cost	**$28.05** if undertaken by a research nurse per clinical trial participant as per the occurrences described in the clinical trial protocol; **$34.04** if undertaken by a CTM/C per clinical trial participant as per the occurrences described in the clinical trial protocol; **$31.89** if undertaken by pathology personnel per clinical trial participant as per the occurrences described in the clinical trial protocol.

LEARNINGS FROM SITE VISITS

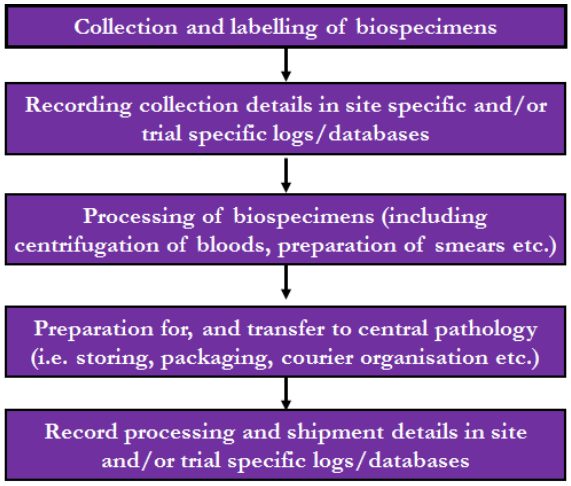
Generally it was found that pathology specimens are taken, labelled, spun and prepared for transfer to a central laboratory. The determination was generally based on the preference of the sponsor organisation and the capacity of the local pathology department. Pathology specimens were taken or organised by either the research nurse, CTM/C or by the local pathology department staff. All service delivery processes are reflected in the costing table below.

There are instances where the tests are processed and analysed by the clinical trials site pathology department or their outsourced pathology provider. However, 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 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.

DERIVED PROCESS MAP FOR "BIOSPECIMEN COLLECTION AND PROCESSING (CENTRAL LABS)"

Figure B.9 presents the typical process involved in biospecimen collection and processing (central labs) in the purple boxes.

Figure B.9: Process map for activities included under "biospecimen collection and processing (central labs)"



CONSIDERATIONS FOR DERIVING THE COST OF "BIOSPECIMEN COLLECTION AND PROCESSING (CENTRAL LABS)"

Clinical trial unit staff were asked to estimate the time it takes them to collect a single biospecimen (e.g. usually a blood sample) and process it for a central or local laboratory (i.e. bloods are centrifuged). The site visits identified that it was site dependent in regards to who was involved in biospecimen collection and processing (central labs). As such in order to derive a standard cost for the biospecimen collection and processing (central lab), professional time was chosen as the most suitable resource unit. Biospecimen collection and processing was found to be generally undertaken by either the CTM/C, research nurse or pathology staff. Hence a different standard cost based on the same time variables has been calculated.

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 (CENTRAL LABS)"

Table B.23 presents the basis for calculating the standard costs for biospecimen collection and processing (central labs) per trial participant based on the clinical trial protocol.

Table B.23: Typical personnel, resources and unit cost involved in biospecimen collection and processing (central labs)

Activities	Personnel involved	Resource unit (hours)					Unit cost	Standard cost (median)
		Min	25th percentile	Median	75th percentile	Max		
Biospecimen collection and processing (central labs)	Research Nurse	0.16	0.25	0.38	0.50	1.50	$74.79	$28.05
	Clinical Trials Manager/Coordinator	0.16	0.25	0.38	0.50	1.50	90.78	$34.04
	Pathology staff	0.16	0.25	0.38	0.50	1.50	$85.04	$31.89

Note: The calculated hourly rate (fully absorbed) for a research nurse is presented in item 2.6.2 and for a CTM/C is presented in item 2.6.3. The hourly rate (fully absorbed) for pathology staff is based on an average hourly rate of a hospital scientist Grade 3/4. Totals may not be exactly additive due to rounding errors.

Table B.23 presents the resource units, in hours, required for each activity by specific personnel. Due to the variability in the resources required for biospecimen collection and processing (central labs), the median was considered the best basis for setting the standard cost of **$28.05** if undertaken by a research nurse, **$34.04** if undertaken by a CTM/C or **$31.89** if undertaken by pathology personnel per trial participant based on the clinical trial protocol.

Item 2.5.2 – Biospecimen storage

Reference number	2.5.2
Item	Biospecimen storage
Sub-list	Site implementation
Category	Biospecimen related
Definition	The activities associated with the local storage (if required) 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.
Standard cost	• Included under item 2.5.1 where the collection and processing of a biospecimen attracts an MBS fee; • Where the collection and processing of a biospecimen does not attract an MBS biospecimen storage costs should be covered by the nearest equivalent MBS item.

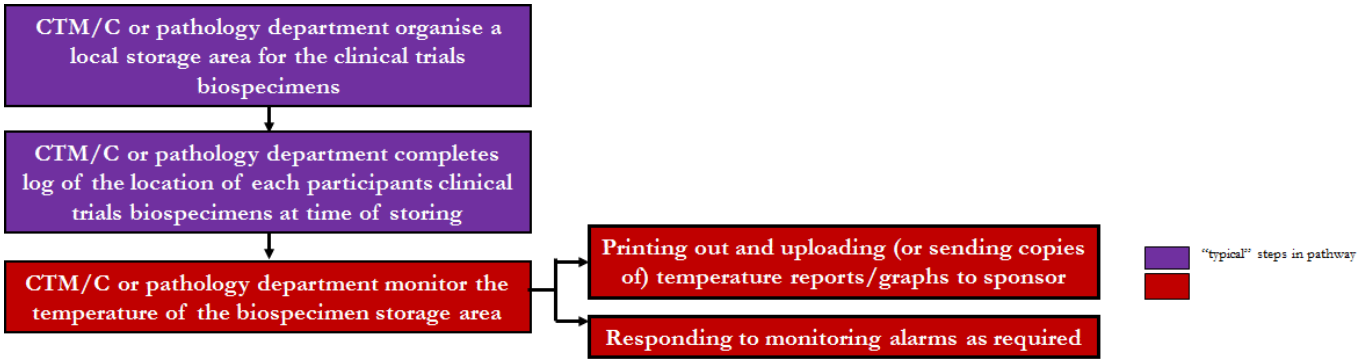
LEARNINGS FROM SITE VISITS

In the majority of cases we found that biospecimens are not stored at local hospitals for prolonged periods of time. Generally they are regularly sent to the sponsor throughout the life of a trial, or at the end of the trial. Where specimens were found to be stored on site, they were generally small amounts and did not consume significant space.

DERIVED PROCESS MAP FOR "BIOSPECIMEN STORAGE"

Figure B.10 presents the typical process involved in biospecimen storage in the **purple** boxes. Optional steps are shown in the **red** boxes.

Figure B.10: Process map for activities included under "biospecimen storage"



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 bottom up costing could not be attempted.

TABLE OF STANDARD COSTS FOR "BIOSPECIMEN STORAGE"

Table B.24 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. 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.24: 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

Item 2.6.1 – Investigator time

Reference number	2.6.1
Item	Investigator time
Sub-list	Site implementation
Category	Clinical resources
Definition	The unit labour cost (fully absorbed hourly rate, i.e. inclusive of overheads) for any activities (clinical or non-clinical) that need to be carried out by an investigator, that are specific to the trial, and that are not covered by an item listed elsewhere on the standard List.
Standard cost	**$226.11** per hour for Principal Investigator **$199.11** per hour for sub/co-investigator

LEARNINGS FROM SITE VISITS

The investigators involved in clinical trials usually include a Principal Investigator (PI) and sub or co-investigators. The PI is almost always a senior medical clinician who is responsible for the clinical trial at a nominated clinical trial site. The sub or co-investigator(s) are also generally medical clinicians, usually less experienced than the PI, who are also involved in recruiting participants, collecting the required trial data etc. in the clinical trial, but will not have the same authority over the clinical trial. All investigators at a given clinical trial site are included on the ethics application.

DERIVED PROCESS MAP FOR "INVESTIGATOR TIME"

Not applicable.

CONSIDERATIONS FOR DERIVING THE COST OF "INVESTIGATOR TIME"

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.25.

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.25. 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.25 shows that the estimated cost per hour ranges from $166.39 to $228.79.

Table B.25: 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	$3,793.80	$99.84	$24.96	$41.60	$166.39
Specialist Year 2	$4,047.70	$106.52	$26.63	$44.38	$177.53
Specialist Year 3	$4,205.00	$110.66	$27.66	$46.11	$184.43
Specialist Year 4	$4,369.70	$114.99	$28.75	$47.91	$191.65
Specialist Year 5	$4,539.70	$119.47	$29.87	$49.78	$199.11
Specialist Year 6	$4,716.70	$124.12	$31.03	$51.72	$206.87
Specialist Year 7	$4,809.50	$126.57	$31.64	$52.74	$210.94
Specialist Year 8	$5,094.00	$134.05	$33.51	$55.86	$223.42
Specialist Year 9	$5,216.50	$137.28	$34.32	$57.20	$228.79

TABLE OF STANDARD COSTS FOR "INVESTIGATOR TIME"

To distinguish between the level of experience between PI and Sub/Co-investigators, a differential standard cost has been calculated. Table B.26 presents the basis for calculating the standard cost for both the PI and Sub or Co –PIs. For a PI, the choice of an hourly rate between AMA levels 8 and 9 (average) was considered reasonable. For Sub/Co-investigators, the choice of an hourly rate at AMA level 5 was considered reasonable. On this basis the standard cost for PI time is set at **$226.11** per hour and for Sub/Co-investigators is set at **$199.11**.

Table B.26: Determination of standard cost for investigator time

Item	Basis	Resource unit (hourly rates)					Unit cost	Standard cost
		Min	25th percentile	Median	75th percentile	Max		
Principal 'investigator time'	Fully absorbed hourly rate	$223.42	N/A	N/A	N/A	$228.79	$226.11	$226.11
Sub or co-'investigator time"	Fully absorbed hourly rate	$166.39	N/A	N/A	N/A	$228.79	$199.11	$199.11

Item 2.6.2 – Research nurse time

Reference number	2.6.2
Item	Research nurse time
Sub-list	Site implementation
Category	Clinical resources
Definition	The unit labour cost (fully absorbed hourly rate, i.e. inclusive of overheads) for any activities (clinical or non-clinical) that need to be carried out by a research nurse, are specific to the trial, and are not covered by an item listed elsewhere on the standard List.
Standard cost	**$74.79** per hour for research nurse

LEARNINGS FROM SITE VISITS

Clinical trials often involve a research nurse or CTN who may or may not also be the Clinical Trials Coordinator (CTC). The role of the CTN varies and can include protocol review, drafting the ethics application, recruitment and coordination of clinical trial participants, collecting and/or processing biospecimens, administering or assisting with treatments within the bounds of their practice code and the evaluation of protocols. We found that the majority of CTNs recruited at each of the sites were senior RNs at the equivalent of a CNS on the salary Awards. Although there were variations across some sites with some filling these positions with RNs (usually Grade 3 or 4) whereas other sites fill the positions with more senior nurses equivalent to a CNC.

DERIVED PROCESS MAP FOR "RESEARCH NURSE TIME"

Not applicable.

CONSIDERATIONS FOR DERIVING THE COST OF "RESEARCH NURSE TIME"

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. As the nursing staff working in the clinical trials area ranged from CNC to RNs, the CNS level was considered a mid-point in terms of level of experience and salary range. Award rates from NSW and Queensland (only publicly available data for most recent year being 2014) were blended to determine the rate used to derive the standard cost. It is noted that there is a national nurses' award that was introduced on 1 January 2010. However the rates have not been updated in the public domain post 2000 so the NSW and Queensland source was chosen to be more representative with current salaries.

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.27. 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.

For the blended rate we have at each point in the pay scale, calculated the hourly rate (based on 38 hours per week) which worked out to be in the range of around $43.37 to $46.38 per hour. Applying the ratios needed to convert to fully absorbed costs, Table B.27 shows that the estimated cost per hour ranges from around $72.28 to $77.30.

Table B.27: Determination of standard cost for research nurse time

CNS	Annual Salary	Weekly Salary	Hourly Rate	Salary Oncost	Institutional Overhead	Fully Absorbed Hourly Rate
Year 1	$85,934.04	$1,648.05	$43.37	$10.84	$18.07	$72.28
Year 2	$91,901.79	$1,762.50	$46.38	$11.60	$19.33	$77.30
Average fully absorbed hourly rate						**$74.79**

TABLE OF STANDARD COSTS FOR "RESEARCH NURSE TIME"

As the nursing staff working in the clinical trials area ranged from CNC to RNs, the CNS level was considered a mid-point in terms of level of experience and salary range. There are two levels of CNS, the choice of an hourly rate between year 1 and year 2 is considered reasonable. On this basis the standard cost is set at **$74.79** per hour, as shown in Table B.28.

Table B.28: Determination of standard cost for research nurse time

Item	Basis	Resource unit (hourly rates)					Unit cost	Standard cost
		Min	25th percentile	Median	75th percentile	Max		
Research nurse time	Fully absorbed hourly rate	$72.28	N/A	N/A	N/A	$77.30	$74.79	$74.79

Item 2.6.3 – Clinical research coordinator

Reference number	2.6.3
Item	Clinical research coordinator (non-research nurse) time
Sub-list	Site implementation
Category	Clinical resources
Definition	The unit labour cost (fully absorbed hourly rate, i.e. inclusive of overheads) for any activities (clinical or non-clinical) that need to be carried out by a clinical research coordinator, are specific to the trial, and are not covered by an item listed elsewhere on the standard List.
Standard cost	**$82.74** per hour for clinical research coordinator (equivalent to CTC) **$93.16** per hour for clinical trials manager (CTM) **$90.78** per hour for CTM/CTC

LEARNINGS FROM SITE VISITS

We found that the role of the clinical research coordinator (more commonly known as a Clinical Trials Coordinator, CTC) varied between those qualified as RNs or those with scientific qualifications (e.g. science graduates) and/or allied health qualifications (e.g. pharmacist). On balance about one third were senior RNs, one third were scientists and one third were pharmacists. As the reasonable costs of an RN was calculated for item 2.6.2, this item focuses on the reasonable cost for a non-research nurse as the clinical research coordinator. It is also worth noting that in addition to the CTC, there is often a position within a hospital department (if the department is involved in many trials at any one time (e.g. oncology)) or across the hospital, known as the Clinical Trials Manager (CTM). The role of the CTM is to coordinate CTCs and is often heavily involved in the site authorisation process (more so than the CTC where the role of CTM exists). The CTM is usually a senior nurse, whose prior position was either a NUM or more commonly a CNC.

DERIVED PROCESS MAP FOR CLINICAL RESEARCH COORDINATOR TIME"

Not applicable.

CONSIDERATIONS FOR DERIVING THE COST OF "CLINICAL RESEARCH COORDINATOR TIME"

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 investigated to support the calculation including:

- Victorian Public Health Sector, (medical scientists, pharmacists and psychologists) Enterprise Agreement 2012-2016;
- Health Professional and Medical Salaries (State) Award; and
- Health Employees' Pharmacists (State) Award.

For both hospital scientists and pharmacists Awards there were multiple salary points within the award. Based on observations the assumption has been made to use hospital scientist's salary rates within the Grade 3 and Grade 4 range, as detailed in Table B.29 below. For pharmacists the range between Grades 3 to 5 were considered in determining the standard cost (see Table B.30).

There was no award for a scientific based research coordinator role that could be identified. The site visits confirmed that CTC 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) as no award for a CTC exists. Table B.29 for medical scientists and Table B.30 for pharmacists shows the variation in salary range between Victoria and NSW for weekly salary and the median for each salary point.

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 and

Table B.30. 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.

Table B.29: Medical Scientist salary range in NSW and Victoria for Grade 3 and 4

Award Grade	NSW Weekly Salary	Vic Weekly Salary	Median Weekly Salary	Hourly Rate	Salary On-costs	Institutional Overheads	Fully absorbed Hourly Rate
Grade 3 - 1st year	$1,761.64	$1,659.70	$1,710.67	$45.02	$11.25	$18.76	$75.03
Grade 3 - 2nd year	$1,817.60	$1,716.80	$1,767.20	$46.51	$11.63	$19.38	$77.51
Grade 3 - 3rd year	$1,853.81	$1,761.80	$1,807.81	$47.57	$11.89	$19.82	$79.29
Grade 3 - 4th year	N/A	$1,880.50	$1,880.50	$49.49	$12.37	$20.62	$82.48
Grade 4 - 1st year	$1,944.04	$1,945.20	$1,944.62	$51.17	$12.79	$21.32	$85.29
Grade 4 - 2nd year	$2,003.00	$1,945.20	$1,974.10	$51.95	$12.99	$21.65	$86.58
Grade 4 - 3rd year	$2,042.70	$2,046.60	$2,044.65	$53.81	$13.45	$22.42	$89.68
Grade 4 - 4th year	N/A	$2,046.60	$2,046.60	$53.86	$13.46	$22.44	$89.76
Grade 4 - 5th year	N/A	$2,250.90	$2,250.90	$59.23	$14.81	$24.68	$98.72
Fully absorbed (average) hourly rate							**$84.93**

Table B.30: Pharmacist salary range in NSW and Victoria for Grade 3, 4 and 5

Award Grade	NSW Weekly Salary	Vic Weekly Salary	Median Weekly Salary	Hourly Rate	Salary On-costs	Institutional Overheads	Fully absorbed Hourly Rate
Grade 3 - 1st year	$1,999.60	$1,659.70	$1,829.65	$48.15	$12.04	$20.06	$80.25
Grade 3 - 2nd year	$2,055.10	$1,716.80	$1,885.95	$49.63	$12.41	$20.68	$82.72
Grade 3 - 3rd year	N/A	$1,761.80	$1,761.80	$46.36	$11.59	$19.32	$77.27
Grade 3 - 4th year	N/A	$1,880.50	$1,880.50	$49.49	$12.37	$20.62	$82.48
Grade 4 - 1st year	$2,055.10	$1,945.20	$2,000.15	$52.64	$13.16	$21.93	$87.73
Grade 4 - 2nd year	$2,124.90	$1,945.20	$2,035.05	$53.55	$13.39	$22.31	$89.26
Grade 4 - 3rd year	N/A	$2,046.60	$2,046.60	$53.86	$13.46	$22.44	$89.76
Grade 4 - 4th year	N/A	$2,046.60	$2,046.60	$53.86	$13.46	$22.44	$89.76
Grade 4 - 5th year	N/A	$2,250.90	$2,250.90	$59.23	$14.81	$24.68	$98.72
Grade 5 - 1st year	$2,189.60	N/A	$2,189.60	$57.62	$14.41	$24.01	$96.04
Grade 5 - 2nd year	$2,244.60	N/A	$2,244.60	$59.07	$14.77	$24.61	$98.45
Fully absorbed (average) hourly rate							**$88.40**

In order to calculate a standard cost for a CTM, the top of the CNC range (i.e. Grade 3) was considered to be reasonable (Table B.31) with the average of year 1 and 2 calculated. Unfortunately only NSW data was publicly available.

Table B.31: CNC Grade 3 salary range in NSW

Award Grade	NSW Weekly Salary	Hourly rate	Salary On-costs	Institutional Overheads	Fully absorbed Hourly rate
CNC Grade 3 Year 1	$2,104.60	$55.38	$13.85	$23.08	$92.31
CNC Grade 3 Year 2	$2,143.70	$56.41	$14.10	$23.51	$94.02
Fully absorbed (average) hourly rate					**$93.16**

TABLE OF STANDARD COSTS FOR "CLINICAL RESEARCH COORDINATOR"

Site visits found that the role of CTM/C was filled equally with either RNs, medical scientists and/or pharmacists. Based on this observation a weighted hourly rate of the three salaries groups that have been calculated above in 2.6.2, and 2.6.3 is the basis that has been used to derive the standard hourly rate for a CTM/C, as shown below in Table B.32.

Table B.32: Determination of standard cost for Clinical Trials Manager/Coordinator

Item	Position filled by	Basis	Resource unit (hourly rates)					Unit cost	Standard cost
			Min	25th percentile	Median	75th percentile	Max		
CTC	Clinical research coordinator	Fully absorbed hourly rate	$72.28	N/A	N/A	N/A	$77.30	$74.79	$74.79
	Medical scientist	Fully absorbed hourly rate	$75.03	N/A	N/A	N/A	$98.72	$84.93	$84.93
	Pharmacist	Fully absorbed hourly rate	$80.25	N/A	N/A	N/A	$98.45	$88.40	$88.40
Fully absorbed (average) hourly rate									**$82.74**
CTM	CNC	Fully absorbed hourly rate	$92.31	N/A	N/A	N/A	$94.02	$93.16	$93.16
CTM/CTC	Average of CTM and CTC	Fully absorbed hourly rate	$88.40	N/A	N/A	N/A	$93.16	$90.78	$90.78

Item 2.6.4 – Interpreter services

Reference number	2.6.4
Item	Interpreter services
Sub-list	Site implementation
Category	Clinical resources
Definition	The unit labour cost (fully absorbed hourly rate, i.e. inclusive of overheads) for any activities that need to be carried out by an interpreter that are specific to the trial.
Standard cost	**$53.91** per hour

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 had interpreters (for at least the most common languages) available on site. Those sites that used contracted interpreter services were not able to provide advice on the typical fees paid. Where interpreters were used, sites reported it was often difficult to source them and the CTM/C spent considerable time in ensuring that all parties including the participant, their family and the interpreter was available.

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, 2014.

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.33. 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 B.33 shows that the cost per hour ranges from $51 to $56.

Table B.33: 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	$59,552.00	$1,145.23	$30.54	$7.63	$12.72	$50.90
Second year	$61,091.00	$1,174.83	$31.33	$7.83	$13.05	$52.21
Third year	$63,070.00	$1,212.88	$32.34	$8.09	$13.48	$53.91
Fourth year	$64,671.00	$1,243.67	$33.16	$8.29	$13.82	$55.27

Source: http://www.health.nsw.gov.au/careers/conditions/Awards/hsu_he_interpreters.pdf

TABLE OF STANDARD COSTS FOR "INTERPRETER SERVICES"

The choice of an hourly rate for a Grade 3 Interpreter at third year level is considered reasonable. Table B.34 presents the basis for the standard cost which is set at $53.91 per hour.

Table B.34: 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	$53.91	$53.91

Item 2.6.5 – Ward bed days

Reference number	2.6.5
Item	Ward bed days
Sub-list	Site implementation
Category	Clinical resources
Definition	The unit cost (fully absorbed daily rate, i.e. inclusive of overheads) for a patient admitted to a ward to receive clinical services (including monitoring) that are specific to the trial (i.e. the services do not represent standard care).
Standard cost	**$1,130** per day

LEARNINGS FROM SITE VISITS

Patients who attend as part of a clinical trial generally do so on an outpatient basis, where they receive treatment and assessment by relevant medical professionals. For some trials however, it is required to admit a patient to hospital, due to the nature of the treatment being provided. Examples of such clinical trials included Phase 1 trials, or patients that are admitted for a device trial or a surgical procedure based trial. Where sites were involved in such trials they reported that the cost of admission was not usually factored into the budgets they negotiated. A number of sites reported to not consider taking on clinical trials where an admission was required as it was difficult to access hospital beds.

DERIVED PROCESS MAP FOR "WARD BED DAYS"

Not applicable.

CONSIDERATIONS FOR DERIVING THE COST OF "WARD BED DAYS"

Where a patient is admitted to hospital as part of a clinical trial, it is important to recognise the cost of treating the patient while an admitted patient. A cost for ward bed days has been identified based on the NHCDC data. The NHCDC data from 2012-13 was used, where the cost components or cost 'bucket' breakdown was available. Each component was reviewed and assessed as to whether it should be included or not in calculating the standard cost. Cost components including allied health (as captured under item 2.3.8) imaging (as captured under item 2.3.3), pathology (as captured under item 2.3.2), theatre costs (as captured under item 2.6.6) etc., have not been included in the calculation of the standard cost, as these costs have been identified separately in other items and/or are typically outside the cost of a ward bed-day. The components included in the derived standard cost for a ward bed-day have been chosen as so to ensure that costs have not been double counted with costs in other items/activities. The 2012-13 costs have been indexed as per the National Efficient Price Determination for 2013-14 indexation rate. The costs calculated have been based on are the national costs, inclusive of all states/territories.

TABLE OF STANDARD COSTS FOR "WARD BED DAYS"

Table B.35 presents the basis for calculating the standard cost per ward bed-day as $1,130 per day.

Table B.35: Determination of standard cost for ward bed days

Cost Component	Direct Costs	Overhead Costs	Total Costs	ALOS	Cost per Day	Cost per Day indexed 4.7%*
Total Cost	$1,832	$1,176	$3,007	2.79	$1,080	**$1,130**

Source: National Hospital Cost Data Collection Cost Weights for AR-DRG version 6.0x, Round 17 (2012-13) *Index as per National Efficient Price Determination 2013-14;http://www.ihpa.gov.au/internet/ihpa/publishing.nsf/content/CA25794400122452CA257B15007D6F12/$File/2013-14%20NEP%20Determination.pdf

Item 2.6.6 – Clinic/theatre time

Reference number	2.6.6
Item	Clinic/theatre time
Sub-list	Site implementation
Category	Clinical resources
Definition	The unit cost (fully absorbed hourly rate, i.e. inclusive of overheads) for a patient spending time in clinic and/or theatre to receive clinical services (including investigations) that are specific to the trial (i.e. the services do not represent standard care)
Standard cost	**$980** per theatre/clinic hour (excluding medical costs)

LEARNINGS FROM SITE VISITS

The theatre time in the case of surgical and/or device clinical trials was discussed at the site visits. Where clinical trials involved a surgical or procedural element, there was little data, if any, captured. Through consultations it was found that in some cases a procedure will take longer to perform if part of a clinical trial, either due to it being a new technique, or due to additional images and data being recorded as part of the study or use of a laparoscopic approach replacing a more invasive procedure. Interestingly it was noted that conversely in some cases the trial procedure was shorter in time that the traditional method and in these instances it was thought that it was equally important to recognise the 'saving' generated through a reduction in theatre time, as it was where additional cost is incurred by an organisation due to increased procedure/theatre time.

DERIVED PROCESS MAP FOR "CLINIC/THEATRE TIME"

Not applicable.

CONSIDERATIONS FOR DERIVING THE COST OF "CLINIC/THEATRE TIME"

In order to source data to calculate an hourly rate for clinic/theatre time, State/Territory Health department as well as sites involved in the study were asked to supply theatre costs per min or hour excluding medical costs (as these cost elements have been identified elsewhere (e.g. items 2.3.6 and 2.6.1). Data were provided on hospitals in Queensland, South Australia and New South Wales.

TABLE OF STANDARD COSTS FOR "CLINIC/THEATRE TIME"

Table B.36 presents the resource units, in hours, which were calculated from the provided data. Due to the variability in the types of theatre (in terms of scale and complexity of services provided), the median was considered the best basis for setting the standard cost of $980 per theatre hour.

Table B.36: Determination of standard cost for clinic/theatre time

Cost component description	Resource unit (hours)					Unit cost	Standard cost (median)
	Min	25th percentile	Median	75th percentile	Max		
Total theatre costs excluding medical costs per hour	$229	$704	$980	$1,605	$2,805	N/A	$980

Item 2.6.7 – Outpatient time

Reference number	2.6.7
Item	Outpatient time
Sub-list	Site implementation
Category	Clinical resources
Definition	The unit cost (fully absorbed daily rate, i.e. inclusive of overheads) for a patient receiving clinical services in an outpatient department.
Standard cost	Delete from list

LEARNINGS FROM SITE VISITS

Through both consultations with sites and through the public consultation process, this item appeared to duplicate other items in the list (e.g. mainly items 2.3.6, 2.3.7 and 2.3.8) as these are the reasons that most clinical trials patients would be attending an outpatient clinic (i.e. to see a specialist, nurse or allied health professional). For these reasons we agree suggesting that this item be deleted from the list.

DERIVED PROCESS MAP FOR "OUTPATIENT TIME"

Not applicable.

CONSIDERATIONS FOR DERIVING THE COST OF "OUTPATIENT TIME"

Not applicable.

TABLE OF STANDARD COSTS FOR "OUTPATIENT TIME"

Suggest to delete the item from the revised NHMRC list.

Item 2.7.1 – Lead site coordination

Reference number	2.7.1
Item	Lead site coordination
Sub-list	Site implementation
Category	Trial operation
Definition	The activities conducted only at the lead site associated with the ongoing coordination and management of all the nominated sites participating in the clinical trial (i.e. excludes those activities conducted at the lead site that are specific to that site's participation in the clinical trial but includes activities associated with coordinating information flow to and from the Lead HREC, sponsor and other site).
Standard cost	**$2,436.81** per clinical trial per annum where there are four or less clinical trials sites involved **$5,100.08** per clinical trial per annum where there were more than four sites involved in the clinical trial.

LEARNINGS FROM SITE VISITS

Observations that were obtained on the additional for sites that have undertaken the role of lead site coordination largely involved the flow of information. It was not so much of the doing that most saw should be covered by this item as the doing is covered by other items (e.g. item 2.9.1 - amendment preparation, item 2.7.2 - reporting for serious adverse events (SAEs), annual reports etc.). However most sites reported that coordinating the flow of information to and from other sites was what needed to be covered by this item. Most stakeholders found it difficult to quantify how much time this took and the number of hours required was very trial dependent. However the estimates provided were on a per year basis (not per trial) averaged out over times where lead site coordination is very involved (e.g. at the start and end of the trial and when protocol amendments are provided etc.). Most reported it was the role of the CTM/C to take on this role but there was a need for the PI to also be involved in some aspects.

DERIVED PROCESS MAP FOR "LEAD SITE COORDINATION"

Not applicable.

CONSIDERATIONS FOR DERIVING THE COST OF "LEAD SITE COORDINATION"

The most typical process identified involved the CTM/C with some oversight provided by the PI, as such in order to derive a standard cost for the lead site coordination, professional time was chosen as the most suitable resource unit.

TABLE OF STANDARD COSTS FOR "LEAD SITE COORDINATION"

Table B.37 presents the basis for calculating the standard costs for lead site coordination activity per year. The median shows that a CTM/C spends a week per year per clinical trial and the PI one day per year per clinical trial on lead site coordination activities. However as the number of sites impacts on the workload for the lead site a differential standard cost based on number of sites was factored into setting the standard cost for lead site coordination activities.

Table B.37: Typical personnel, resources and unit cost involved in lead site coordination

Activities	Personnel involved	Resource unit (hours)					Unit cost	Standard cost (25th percentile/ median)
		Min	25th percentile	Median	75th percentile	Max		
Lead site coordination (≤ 4 sites)	Clinical Trials Manager/Coordinator*	7.50	16.88	37.50	54.38	75.00	$90.78	$1,532.37
	Principal Investigator*	2.00	4.00	7.50	8.00	15.00	$226.11	$904.44
Total								**$2,436.81**
Lead site coordination (> 4 sites)	Clinical Trials Manager/Coordinator∞	7.50	16.88	37.50	54.38	75.00	$90.78	$3,404.25
	Principal Investigator∞	2.00	4.00	7.50	8.00	15.00	$226.11	$1,695.83
Total								**$5,100.08**

Note: The calculated hourly rate (fully absorbed) for a PI is presented in item 2.6.1 and for the CTM/C in item 2.6.3. * Standard cost calculated based on 25th percentile ∞ Standard cost calculated based on median. Totals may not be exactly additive due to rounding errors.

Table B.37 presents the resource units, in hours, required for each activity by specific personnel. Due to the variability in the resources required for the lead site coordination, the 25th percentile was considered the best basis for setting the standard cost of **$2,436.81** per year per clinical trial where there are four or less clinical trials sites involved and the median was considered the best basis for setting the standard cost of **$5,100.08** per year per clinical trial where there were more than four sites involved in the clinical trial.

Item 2.7.2 – Administration, monitoring and reporting

Reference number	2.7.2
Item	Administration, monitoring and reporting
Sub-list	Site implementation
Category	Trial operation
Definition	The activities associated with ongoing operation of the trial at the trial site that occur post initiation of the trial. Includes liaison with investigators and/or sponsor (including the monitors), preparing materials for, and involvement in, monitoring visits, CRF completion, data collection and entry, endpoint recording, accrual reporting, safety and adverse event reporting, review of SAE reports, managing clinical trial documentation, retrieving medical and/or clinical records, invoicing, and annual reporting including annual ethics report and final report.
Standard cost	**$1,073.32** per clinical trial per annum for administration activities; **$45.39** per eCRF or CRF per participant per visit**;** **$234.03** per monitor visit (including remote monitoring visits); **$77.23** per review of line listing/SAE reports; and **$745.65** per clinical trial per annum for reporting activities – other annual reporting; **$251.69** per SAE and/or incident report prepared.

LEARNINGS FROM SITE VISITS

Through the consultation process with clinical trial departments it was found that there were discrete activities within item 2.7.2 which could differ in volume per clinical trial (e.g. the number of monitoring visits, the number of SAE etc.) and others that were known in volume (e.g. annual ethics report, annual governance report etc.).

Monitoring visits were found to be relevantly consistent in nature with the attendance of the sponsor to the site to complete a review of trial documentation and follow-up questions with the relevant staff members. General comments that were noted was the increasing occurrence of remote monitoring replacing some monitoring visits. Comments were also received in relation to change in sponsor or CRO staff or inexperienced staff performing monitoring visits significantly increased the time sites were required to participate in monitoring visits.

The amount of time per patient that was spent by the CTM/C to complete CRF reporting varied significantly. Some of the variations in time were attributable to the type and nature of the clinical trial. However an additional theme that emerged at almost every site was the impact of the platform on which the eCRF software operated on which could dramatically increase (or decrease) the amount of time it took to record the data required (e.g. 10 minutes to two hours to enter a similar amount of data). A frequent suggestion from the sites to sponsors was for them to standardise the applications used to one or two platforms, being the most efficient and easiest to use interface.

The reporting of adverse and serious adverse events (SAEs) reporting was also noted. The majority of these events could be reported in a reasonable period of time, however, if the event occurred in another hospital or the outcome was catastrophic then this significantly increased the amount of time that was required to complete the necessary reporting requirements.

Sites also reported the increasing (and additional) time required by PIs to review line listings (e.g. an email sent to the PI, which required them to log in so they could be identified as having reviewed the, for example, SAE) that were now being circulated by sponsors.

DERIVED PROCESS MAP FOR "ADMINISTRATION, MONITORING AND REPORTING"

Figure B.12 presents the typical activities included under administration, monitoring and reporting activities in the **purple** boxes.

Figure B.12: Process map for activities included under "administration, monitoring and reporting"

Administration activities include administration tasks that occur post the establishment phase, including
- managing clinical trial documentation;
- retrieving medical and/or clinical records;
- invoicing;
- organising and maintaining virtual private network (VPN) access;
- liaison with investigators and/or sponsor.

Monitoring activities include:
- review of line listings (i.e. SAE reports etc) which are sent directly to the PI;
- CRF or eCRF completion;
- preparing materials for, and involvement in, the monitoring visit (including remote visits); etc.

Reporting activities include:
- accrual reporting;
- safety and adverse/incident event reporting;
- annual governance reporting;
- annual ethics report; etc.

CONSIDERATIONS FOR DERIVING THE COST OF "ADMINISTRATIVE, MONITORING AND REPORTING"

The most typical process identified involved time of the CTM/C, oversight provided by the PI, and supporting department personnel time, as such in order to derive a standard cost for the administration, monitoring and reporting activities, professional time was chosen as the most suitable resource unit.

TABLE OF STANDARD COSTS FOR "ADMINISTRATION, MONITORING AND REPORTING"

Table B.38 presents the basis for calculating the standard costs for six discrete activities which come under administration, monitoring and reporting. Due to variability in the resources required for the six discrete activities either the 25th percentile or median has been suggested as the basis for calculating the standard cost. Whether the 25th percentile or median has been suggested is based on the occurrence at which the discrete activities occurs. For example, when suggesting the standard cost for a given discrete activity is set annually then the median has been suggested. Where it has been calculated per activity or per participant the 25th percentile has been suggested. However where the clinical trial site is a lead site it is suggested that the min is the basis for 'administration activities' and 'reporting activities – other annual reporting' as there is some overlap in the activities and resources presented in Table B.38.

Table B.38: Typical personnel, resources and unit cost involved in administration/monitoring and reporting

Activities	Personnel involved	Resource unit (hours)					Unit cost	Standard cost (25th percentile or median)
		Min	25th percentile	Median	75th percentile	Max		
Administration activities*	Principal Investigator	0.50	0.50	0.75	2.25	6.00	$226.11	$169.58
	Clinical Trials Manager/Coordinator	1.00	2.88	9.00	15.75	39.00	$90.78	$817.02
	Other Support Departments	0.25	1.00	1.00	4.00	15.20	$86.72	$86.72
Total								**$1,073.32**
Monitoring activities - eCRF or CRF reporting∞	Clinical Trials Manager/Coordinator	0.17	0.50	1.50	3.00	75.00	$90.78	$45.39
Total								**$45.39**
Monitoring activities - preparing and involvement in monitoring visit∞	Principal Investigator	0.08	0.25	0.38	0.92	1.50	$226.11	$56.53
	Clinical Trials Manager/Coordinator	0.50	1.00	3.00	6.50	11.50	$90.78	$90.78
	Other Support Departments	0.25	0.50	1.00	1.00	1.00	$86.72	$86.72
Total								**$234.03**
Monitoring	Principal Investigator	0.05	0.14	0.25	0.25	1.00	$226.11	$31.84

Activities	Personnel involved	Resource unit (hours)					Unit cost	Standard cost (25th percentile or median)
		Min	25th percentile	Median	75th percentile	Max		
activities - review of line listing/SAE reports∞	Clinical Trials Manager/Coordinator	0.08	0.50	1.00	2.50	12.00	$90.78	$45.39
Total								**$77.23**
Reporting activities – other annual reporting*	Principal Investigator	0.50	0.50	1.50	2.00	2.00	$226.11	$339.17
	Clinical Trials Manager/Coordinator	0.50	2.00	4.00	4.25	8.00	$90.78	$363.12
	Other Support Departments	0.08	0.25	0.50	0.50	1.00	$86.72	$43.36
Total								**$745.65**
Reporting activities – – preparing SAE and/or incident reports∞	Principal Investigator	0.25	0.42	0.66	2.50	7.50	$226.11	$93.84
	Clinical Trials Manager/Coordinator	1.00	1.50	4.00	10.38	45.00	$90.78	$136.17
	Other Support Departments	0.17	0.25	0.50	0.75	8.00	$86.72	$21.68
Total								**$251.69**

Note: The calculated hourly rate (fully absorbed) for a PI is presented in item 2.6.1 and for the CTM/C in item 2.6.3. The hourly rate (fully absorbed) for personnel from supporting departments is based on a blended hourly rate of a hospital scientist (i.e. Grade 3/4 hospital scientist) and pharmacist (i.e. Grade 3/5 pharmacist). * Standard cost has been based on the median. ∞ Standard cost has been based on the 25th percentile. Totals may not be exactly additive due to rounding errors.

Table B.38 presents the resource units, in hours, required for each activity by specific personnel. Due to the variability in the resources required for the six discrete activities within administration, monitoring and reporting activities, either the 25th percentile or median was considered the best basis for setting the standard cost of: **$1,073.32** per clinical trial per annum for administration activities; **$45.39** per eCRF or CRF per participant per visit**;** **$234.03** per monitor visit (including remote monitoring visits); **$77.23** per review of line listing/SAE reports; **$745.65** per clinical trial per annum for reporting activities – other annual reporting; and **$251.69** per SAE and/or incident report prepared.

Item 2.8.1 – Participant time

Reference number	2.8.1
Item	Participant time
Sub-list	Site implementation
Category	Participant related
Definition	The unit cost for the time involved in participating in the clinical trial. This item is only intended to be used for Phase 1 healthy volunteer trials, where payment for participant time is the norm. Any provision for participant payment would be described in the Clinical Trial Agreement and in the Patient Information and Consent Form and will have been considered by the Lead HREC.
Standard cost	**$49.19** per hour

LEARNINGS FROM SITE VISITS

Except for healthy participants usually involved in Phase 1 clinical trials, we found that participant time was not reimbursed. For those trials where reimbursement for time was provided it was on the basis of per outpatient appointment rather than per hour of participant time.

However as the item relates to a unit of cost for the participant time involved in a given clinical trial, we searched the grey literature for a source.

DERIVED PROCESS MAP FOR "PARTICIPANT TIME"

Not applicable.

CONSIDERATIONS FOR DERIVING THE COST OF "PARTICIPANT TIME"

In order to calculate a standard cost for participant's time, a grey literature search was conducted to identify consumer hourly rates available in the public domain for similar activities. Table B.39 presents the sourced rates which are considered to provide a representative range to assist in calculating a standard cost for participants' time within a clinical trial.

Table B.39: Rates to determine an average hourly rate for participant costs

Source	per hour
Health Consumers Qld – (Oct 2014)	$46.75
Medicines Australia – (June 2014)1.601-2.6 litre (1,601-2,600cc)	$100.00
Association of Participating Service Users – APSU (Vic consumer representative body – July 2013)	$25.00
NMHCCF – consumer and carer participation policy: framework for mental health sector (June 2010 – ACT Health)	$25.00
Average hourly rate	**$49.19**

Source: http://hcq.org.au/wp-content/uploads/2012/11/HCQ-Consumer-Remuneration-Rates-Oct-2014.pdf; https://medicinesaustralia.com.au/about-us/corporate-policy/policy-and-remuneration/; http://sharc.org.au/wp-content/uploads/2014/08/1.3-Remuneration.pdf; http://www.mhccact.org.au/cms/media/user_uploads/caucus/consumer_carer_participation_policy_options.pdf

TABLE OF STANDARD COSTS FOR "PARTICIPANT TIME"

Table B.40 presents the basis for calculating the standard costs for participant time per hour.

Table B.40: Determination of standard cost for participant costs

Item	Resource unit (hourly rates)					Unit cost	Standard cost (average)
	Min	25th percentile	Median	75th percentile	Max		
Cost per hour	$25	N/A	N/A	N/A	$100	$49.19	$49.19

The average was considered reasonable as being a clinical trial participant is more involved than being part of a committee.

Item 2.8.2 – Participant Costs

Reference number	2.8.2
Item	Participant costs
Sub-list	Site implementation
Category	Participant related
Definition	The costs that may be necessarily incurred by a trial participant due to participating in the trial. May include transport to and from the trial location, car parking, meal allowances (where extended time attendance is required), and overnight accommodation costs where participants need to travel significant distances to and from the trial locations and/or need to stay in close proximity to the trial site for an extended period. Any provision for reimbursement of participant costs would be described in the Clinical Trial Agreement and in the Patient Information and Consent Form and will have been considered by the Lead HREC.
Standard cost	**$183** per night for accommodation **$25.35** per breakfast meal **$28.55** per lunch meal **$48.65** per dinner meal Car travel per km by car type Car parking – at cost incurred

LEARNINGS FROM SITE VISITS

The majority of sites visited provided *reasonable* reimbursements to clinical trial participants within the bounds of the funding provided by the sponsor. Reimbursements were largely related to car parking, meals, car travel (per km) and for accommodation, where possible if funds were available. In some instances, especially in relation to travel, some sites were encouraging these costs to be directly reimbursed by the sponsor on the presentation of receipts or the provision of a capped amount per participant again provided directly by the sponsor. Most sites reported as they were not set up to do invoicing it was a very time consuming process that most try to pass back to the sponsor.

DERIVED PROCESS MAP FOR "PARTICIPANT COSTS"

Not applicable.

CONSIDERATIONS FOR DERIVING THE COST OF "PARTICIPANT COSTS"

The basis for calculating the standard cost for participant costs was based on:

- **Car Travel:** the Australian Taxation Office (ATO) states that realisable costs in relation to car travel is based on per kilometre by the type of car (refer to Table B.40).
- **Overnight Accommodation**: the ATO states that being realisable costs in relation to overnight accommodation, for annual salary less than $112,610, a nightly rate for each capital city (i.e. from $132 for Hobart to $233 for Perth). The average of the rate for overnight accommodation in the capital cities has been used to calculate the standard cost of $183 per night (see Table B.41).
- **Breakfast**: the ATO states that realisable costs in relation to a breakfast meal, for annual salary less than $112,610, by capital city (although it was noted the rate was generic and did not vary depending on location). The calculated standard cost for a breakfast meal is $25.35 (see Table B.41).
- **Lunch**: the ATO states the realisable costs in relation to a lunch meal, for annual salary less than $112,610 is by capital city (although it was noted the rate was generic and did not vary depending on location). The calculated standard cost for a lunch meal is $28.55 (see Table B.41).
- **Dinner**: the ATO states the realisable costs in relation to a dinner meal, for annual salary less than $112,610, is by capital city (although it was noted the rate was generic and did not vary depending on location). The calculated standard cost for a dinner meal is $48.65 (see Table B.41).

- **Car Parking**: Car parking varies greatly dependent on location and the length of the clinical trial specific visit. As such it is suggested that car parking is reimbursed (by receipt) at the cost that has been incurred.

TABLE OF STANDARD COSTS FOR "PARTICIPANT COSTS"

Table B.41 and Table B.42 presents the basis for calculating the standard costs for participant costs per occurrence.

Table B.41: ATO suggested allowance for car travel by km and type of car

Ordinary	Rotary	Rate per km
1.6 litre (1,600cc) or less	0.8 Litre (800cc) or less	$0.65
1.601-2.6 litre (1,601-2,600cc)	0.801-1.3 litre (801-1, 300cc)	$0.76
2,601 litre (2,601cc) and over	1.301 litre (1,301cc) and over	$0.77

Table B.42: ATO suggested allowance for accommodation and meals

Item	Resource unit (hourly rates)					Unit cost	Standard cost
	Min	25th percentile	Median	75th percentile	Max		
Overnight Accommodation	$132	N/A	N/A	N/A	$233	$183	$183
Breakfast	$23.35	N/A	N/A	N/A	$23.35	$23.35	$23.35
Lunch	$28.55	N/A	N/A	N/A	$28.55	$28.55	$28.55
Dinner	$48.65	N/A	N/A	N/A	$48.65	$48.65	$48.65

Source: http://law.ato.gov.au/atolaw/view.htm?docid=TXD/TD201419/NAT/ATO/00001&PiT=99991231235958

Item 2.9.1 – Amendment preparation and submission

Reference number	2.9.1
Item	Amendment preparation and submission
Sub-list	Site implementation
Category	Amendment processing
Definition	The activities associated with 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. Also includes responding to HREC and/or RGO queries and/or requests for additional information and forwarding copies of relevant authorisations (once obtained) and associated documentation to the trial funder/sponsor.
Standard cost	**$128.47** per minor amendment **$238.09** per major amendment **$113.06** per participant if re-consenting is required as a result of the amendment.

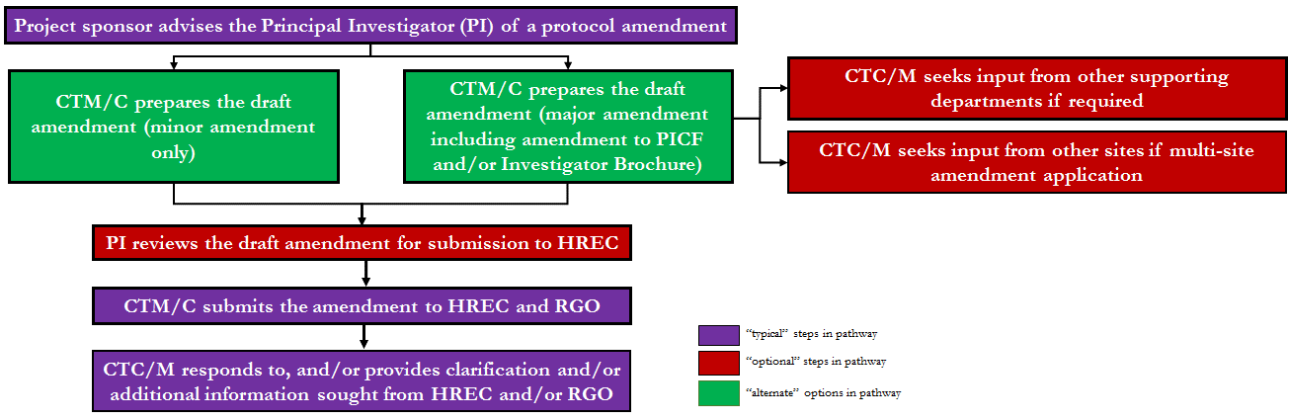
LEARNINGS FROM SITE VISITS

The time required to complete the preparation of an amendment varied depending on the nature and type of amendments. Amendments of a purely administrative nature (e.g. additions or deletion of staff involved in the clinical at a site) were minor in nature and not so time consuming. Where there were major amendments including impact on changes to the PICF, these were considered significant and would require in some cases large investment of time. Again as referred in activities above, the standard and quantity of documentation provided, especially in sponsor trials influenced the time required by usually the CTM/C to spend on preparing these documents. It was also found that whether the RGO was involved varied by site.

DERIVED PROCESS MAP FOR "AMENDMENT PREPARATION AND SUBMISSION"

Figure B.13 presents the typical process involved in amendment preparation and submission process in the **purple** boxes. Optional steps are shown in the **red** boxes and alternative pathway in **green** boxes. Note: the role of the HREC office and/or RGO office is included under item 2.9.2 'amendment review".

Figure B.13: Process map for activities included under "amendment preparation and submission"



CONSIDERATIONS FOR DERIVING THE COST OF "AMENDMENT PREPARATION AND SUBMISSION"

The personnel involved in amendment preparation and submission varied depending on who the sponsor organisation was for the clinical trial. For investigator-initiated and/or collaborative clinical trials, the principal author was the proposed PI and/or their Fellow. For industry sponsored clinical trials, the principal author was the CTM/C. As such in order to derive a standard cost for amendment preparation and submission process, professional time was chosen as the most suitable resource unit.

TABLE OF STANDARD COSTS FOR "AMENDMENT PREPARATION AND SUBMISSION"

Table B.43 presents the basis for calculating the standard costs for amendment preparation and submission activity per amendment that is processed. A different standard cost has been calculated based on minor (based on 25th percentile) and major amendments (based on median). In addition, a standard cost for re-consenting has been calculated. It is important to note that the max for the PI was driven by investigator-initiated and/or collaborative clinical trials where the preparation of amendments is undertaken by the PI (or their Fellow) and little or no involvement of the CTM/C.

Table B.43: Typical personnel, resources and unit cost involved in amendment preparation and submission

Activities	Personnel involved	Resource unit (hours)					Unit cost	Standard cost (25th percentile and median)
		Min	25th percentile	Median	75th percentile	Max		
Amendment preparation and submission	Principal Investigator	0.08	0.19	0.25	0.88	3.00	$226.11	$37.69 / $56.53
	Clinical Trials Manager/Coordinator	0.08	1.00	2.00	4.00	30.00	$90.78	$90.78 / $181.56
Total (minor amendment) ∞								**$128.47**
Total (major amendment) *								**$238.09**
Re-consent participant	Principal Investigator	0.08	0.25	0.50	0.75	2.00	$226.11	$113.06
Total								**$113.06**

Note: The calculated hourly rate (fully absorbed) for a PI is presented in item 2.6.1 and for the CTM/C in item 2.6.3. * Standard cost has been based on the median. ∞ Standard cost has been based on the 25th percentile. Totals may not be exactly additive due to rounding errors.

Table B.43 presents the resource units, in hours, required for each activity by specific personnel. Due to the variability in the resources required for amendment preparation and submission activity, s standard cost for minor amendments has been suggested at **$128.47** per amendment and **$238.09** per major amendment. In additional standard cost of **$113.06** has been suggested (based on the median) per patient if re-consenting is required as a result of the amendment.

Item 2.9.2 – Amendment review

Reference number	2.9.2
Item	Amendment review
Sub-list	Site implementation
Category	Amendment processing
Definition	The activities associated with the review of the amendment documentation by the HREC and/or RGO, including the preparation of any requests for additional information and subsequent consideration of the material provided.
Standard cost	**$35.30** per minor amendment/SAE review by HREC office; **$238.81 per** major amendment/SAE review by HREC office (including it being tabled at HREC meeting), **$35.30** per minor amendment/SAE review by RGO.

LEARNINGS FROM SITE VISITS

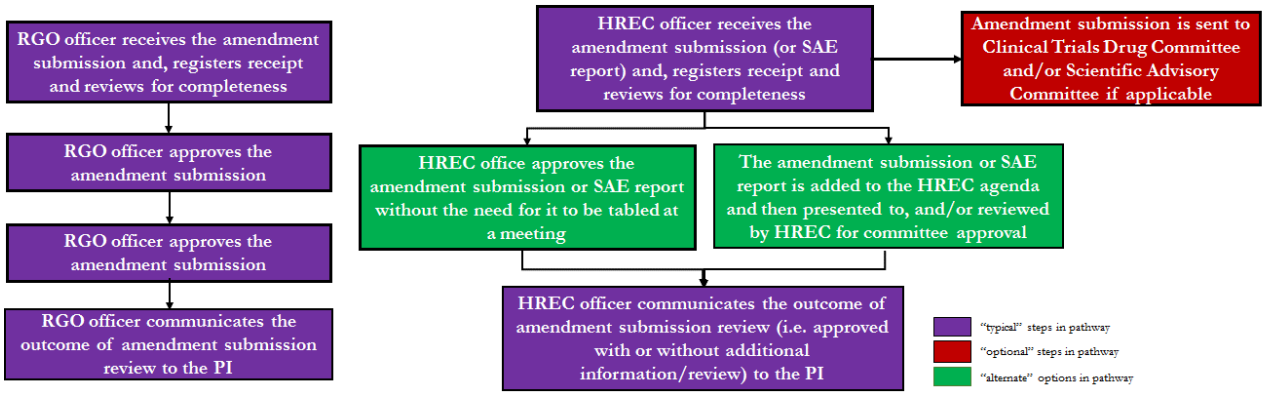
Through the case study visits it was identified that the review of amendments is largely completed by the staff within the HREC office, and sometimes by the RGO, and then authorised (or signed-off) by an appropriate delegated officer within the HREC or RGO. In the majority of cases amendments are collated and incorporated into the meeting agenda paper or tabled and noted at HREC meetings. If the issue under consideration for amendment is deemed in need of conversation at the meeting this will occur. Once the amendment is approved, then relevant communication is sent to the appropriate person by the HREC office and/or RGO.

In addition, the review of SAEs is required by HREC and/or RGO. The process is similar to the process for review and process of amendments to clinical trial protocols. The SAE's are received by the HREC office and, reviewed, collated and incorporated into the meeting agenda paper or tabled and noted at HREC meetings as required. The RGO does not present or table the SAE or amendments at a meeting but ensures the amendment is reviewed and filed with the clinical trial folder.

DERIVED PROCESS MAP FOR "AMENDMENT REVIEW"

Figure B.14 presents the typical process involved in amendment review in the **purple** boxes. Optional steps are shown in the **red** boxes and alternative steps are shown in the **green** boxes.

Figure B.14: Process map for activities included under "amendment review"



CONSIDERATIONS FOR DERIVING THE COST OF "AMENDMENT REVIEW"

The personnel involved in amendment review were ethics and/or research governance officers. While some amendments are tabled/presented at HREC meetings, majority of the time the amendments were minor and reviewed by the HREC officer only by the ethics office staff. As such in order to derive a standard cost for the amendment review process, professional time was chosen as the most suitable resource unit.

TABLE OF STANDARD COSTS FOR "AMENDMENT REVIEW"

Table B.44 presents the basis for calculating the standard costs for amendment review, based on per amendment reviewed/received. A different standard cost has been calculated based on whether the amendment/SAE is minor or major. In addition a separate cost for processing of the amendment or SAE by the RGO office has also been calculated

Table B.44: Typical personnel, resources and unit cost involved in standard cost for amendment review

Item	Personnel involved	Resource unit (hourly rates)					Unit cost	Standard cost (median)
		Min	25th percentile	Median	75th percentile	Max		
Minor Amendment/SAE	HREC officer	0.08	0.25	0.50	1.00	1.50	$70.59	$35.30
Total Minor Amendment/SAE								**$35.30**
Major Amendment/SAE	HREC officer	0.25	1.00	1.00	2.00	2.00	$70.59	$70.59
Presentation and discussion Amendment/SAE review at HREC meeting	Legal	0.08	0.08	0.16	0.25	0.50	$199.11	$31.86
	Medical clinician (x2)	0.08	0.08	0.16	0.25	0.50	$199.11	$63.72
	Scientific/Allied Health (x 2)	0.08	0.08	0.16	0.25	0.50	$85.40	$27.33
	Ethics officer	0.08	0.08	0.16	0.25	0.50	$70.59	$11.29
	Lay person	0.08	0.08	0.16	0.25	0.50	$70.59	$11.29
	Chairperson	0.08	0.08	0.16	0.25	0.50	$142.08	$22.73
Total Major Amendment/SAE								**$238.81**
Amendment/SAE review	RGO officer	0.17	0.31	0.50	0.81	2.00	$70.59	$35.30
Total Amendment/SAE review by RGO								**$35.30**

Note: The calculated hourly rate (fully absorbed) for a medical clinician is presented in item 2.6.1 (co-investigator). The hourly rate (fully absorbed) for reviewers and chair person is based on the median of the co-investigator (see item 2.6.1) and scientist. The calculated hourly rate (fully absorbed) for a scientific/allied health is based on the average hourly rate of a hospital scientist (i.e. Grade 3/4 hospital scientist). The hourly rate (fully absorbed) for personnel from the research and governance office is based on an average salary of $82,587 plus superannuation sourced from averaging four current advertisement for research ethics office and/or governance office in NSW and Qld. It is also assumed that the lay person would be at least equivalent in salary terms to the ethics officer. Totals may not be exactly additive due to rounding errors.

Table B.44 presents the resource units, in hours, required for each activity by specific personnel. Due to the variability in the resources required for the amendment review process, the median was considered the best basis for setting the standard cost of **$35.30** for a minor amendment/SAE review by HREC office, **$238.81** for a major amendment/SAE review by HREC office (including it being tabled at HREC meeting), **$35.30** for a minor amendment/SAE review by RGO.

Appendix C – Site Close-out

Item 3.1.1 – Site close-out visit

Reference number	3.1.1
Item	Site close-out visit
Sub-list	Site close-out
Category	Site close-out visit
Definition	The activities that occur at the end of a trial as part of the attendance by the sponsor (and/or representative) at the clinical trial site for a series of meetings with personnel that were involved in the trial. Includes verifying that the study procedures have been completed, all relevant data have been collected and transferred to the sponsor, preparing and implementing plans to un-blind/unmask and debrief site staff; and, if relevant, arranging for the study intervention to be returned to the responsible party or prepared for destruction, the activities undertaken to confirm that the site's clinical trial obligations have been met and post study obligations are understood. Covers the provision of assurances that the relevant data have been collected and transferred, and ensuring, where relevant, that the study intervention is returned to the sponsor and/or is destroyed in accordance with the sponsor's requirements.
Standard cost	**$821.26** per clinical trial

LEARNINGS FROM SITE VISITS

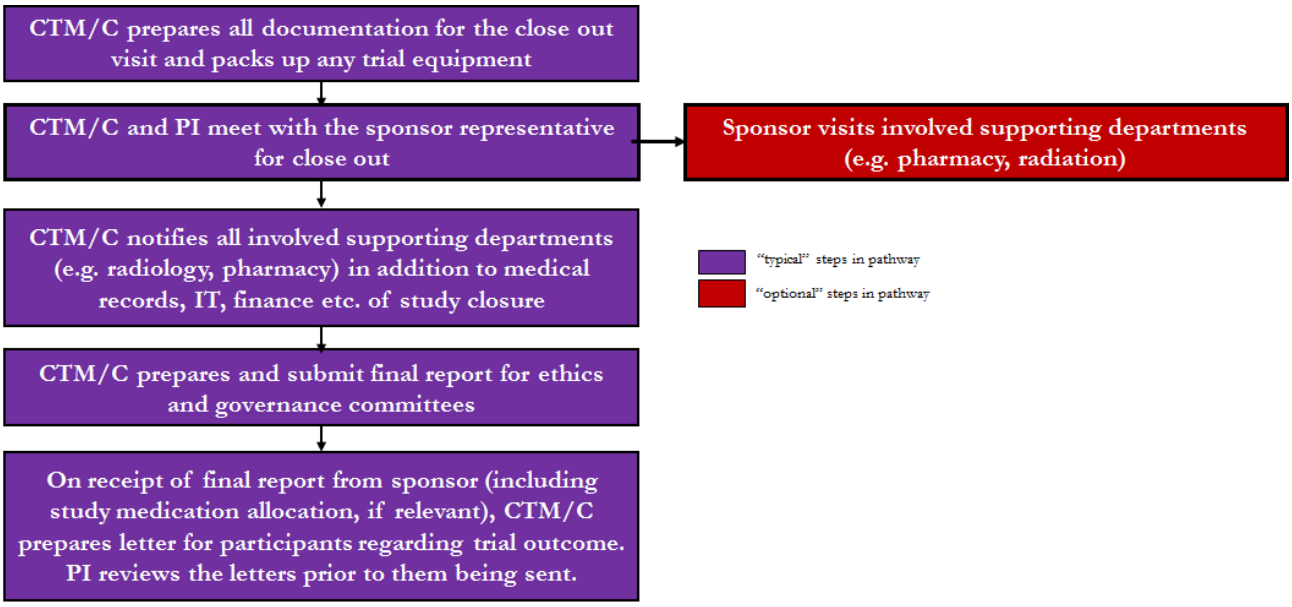
The majority of sites visited indicated that close-out visits were carried out for industry sponsored trials, not so much for collaborative group trials. Preparation (e.g. undertaking a final review of all trial information, addressing any outstanding questions on data issues, packing up and returning any trial equipment) and coordination of the close-out visit was largely undertaken by the CTM/C. The CTM/C sometimes met with supporting departments to advise the close of the clinical trial and to gather any outstanding information. On the day of the visit, the sponsor (or their representative) would spend most of the day with the CTM/C, have a brief meeting with the PI and also meet with supporting departments as required (e.g. usually pharmacy if it was a drug trial). The CTM/C would also prepare and submit the final ethics report.

A number of sites reported that even after the close-out visit, some follow-up with patients occurs. Some studies required the CTM/C to contact patients and complete questionnaires through interview at defined time intervals after a trial had 'closed' (e.g. one year after the trial, two years after the trial). Resources and time involved in completing these activities is generally not recognised or monitored by sites. Some sites also get requests that require them to get files out of archive to answer sponsors questions. Again this is not factored into their budgets.

DERIVED PROCESS MAP FOR "SITE CLOSE-OUT VISIT"

Figure C.1 presents the typical process involved in site close-out visit in the **purple** boxes. Optional steps that were found have been provided in the **red** boxes.

Figure C.1: Process map of activities included under site close-out visit



CONSIDERATIONS FOR DERIVING THE COST FOR "SITE CLOSE-OUT VISIT"

The most typical process identified for the site close-out visit activities included the CTM/C, PI and personnel from involved supporting departments. As such in order to derive a standard cost for the site close-out visit process, professional time was chosen as the most suitable resource unit. It should be noted that the standard cost assumes only one supporting department is visited and consumes only the median time of one personnel in that supporting department.

TABLE OF STANDARD COSTS FOR "SITE CLOSE-OUT VISIT"

Table C.1 presents the standard costs for site close-out visit activity per clinical trial.

Table C.1: Typical personnel, resources and unit cost involved in site close-out visit

Activities	Personnel involved	Resource unit (hours)					Unit cost	Standard cost (median)
		Min	25th percentile	Median	75th percentile	Max		
Close-out visit	Principal Investigator	0.17	0.25	0.33	0.75	4.00	$226.11	$75.37
	Clinical Trials Manager/Coordinator	0.50	2.25	7.50	8.50	25.00	$90.78	$680.85
	Other supporting departments	0.50	0.50	0.75	1.00	2.00	$86.72	$65.04
Total								**$821.26**

Note: The calculated hourly rate (fully absorbed) for a PI is presented in item 2.6.1 and for the CTM/C in item 2.6.3. The hourly rate (fully absorbed) for personnel from supporting departments is based on a blended hourly rate of a hospital scientist (i.e. Grade 3/4 hospital scientist) and pharmacist (i.e. Grade 3/5 pharmacist). Totals may not be exactly additive due to rounding errors.

Table C.1 presents the resource units, in hours, required for each activity by specific personnel. Due to the variability in the resources required for the site close-out visit process, the median was considered the best basis for setting the standard cost of **$821.26** per clinical trial.

Item 3.2.1 – Archiving of trial records

Reference number	3.2.1
Item	Archiving of trial records
Sub-list	Site close-out
Category	Record archiving
Definition	The activities associated with archiving the trial records for the required period. Includes the boxing up of all trial material ready for archiving/storage as well as the secure storage of the material for up to the agreed number of years.
Standard cost	**$272.34** for archiving activities performed by the clinical trial host department; **$86.72** for archiving activities performed by supporting departments per clinical trial; **$1,575.00** storage fee which assumes storing 3.5 boxes for 15 years at $30.00 per box.

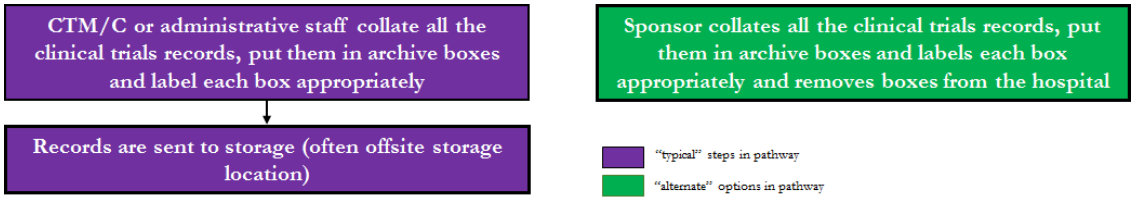
LEARNINGS FROM SITE VISITS

At the conclusion of a clinical trial it is necessary for the clinical trial records be collated, put into archive boxes and each box to be appropriately and clearly labelled. This was found to be completed by either the CTM/C (or sometimes by administrative staff within the clinical trials area) or the sponsor themselves. The boxed clinical trials records were then generally sent to an offsite storage provider or to the sponsor, as there was generally insufficient space for storage on site.

DERIVED PROCESS MAP FOR "ARCHIVING OF TRIAL RECORDS"

Figure C.2 shows the typical process involved in g archiving of trial records in the **purple** boxes. Alternative steps have been provided in **green** boxes.

Figure C.2: Process map of activities included under archiving of trial records



CONSIDERATIONS FOR DERIVING THE COST FOR "ARCHIVING OF TRIAL RECORDS"

The most typical process for archiving of trial records identified involved the CTM/C. Supporting department (e.g. pharmacy, pathology) staff also need to archive their records at the end of the trial. As such in order to derive a standard cost for the archiving of trial records process, professional time was chosen as the most suitable resource unit. However as hospitals incur secure storage fees for 15 years this is also included.

TABLE OF STANDARD COSTS FOR "ARCHIVING OF TRIAL RECORDS"

Table C.2 presents the standard costs for archiving of trial records per clinical trial.

Table C.2: Typical personnel, resources and unit cost involved in archiving of trial records

Activities	Basis	Resource unit (hours)					Unit cost	Standard cost (median)
		Min	25th percentile	Median	75th percentile	Max		
Archiving of trial records	Clinical Trials Manager/Coordinator	1.00	1.25	3.00	4.00	15.00	$90.78	$272.34
	Supporting departments	0.17	1.00	1.00	2.13	15.00	$86.72	$86.72
Box storage	Per box charge for 15 years	8.50	8.50	30.00	41.25	45.00	$30.00	$450.00
	Average number of boxes per trial	2.00	2.00	3.50	8.00	20.00	-	$1,575.00

Note: The calculated hourly rate (fully absorbed) for the CTM/C in item 2.6.3. The hourly rate (fully absorbed) for personnel from supporting departments is based on a blended hourly rate of a hospital scientist (i.e. Grade 3/4 hospital scientist) and pharmacist (i.e. Grade 3/5 pharmacist). Totals may not be exactly additive due to rounding errors.

Table C.2 presents the resource units, in hours, required for each activity by specific personnel. Due to the variability in the resources required for the archiving of trial records process, the median was considered the best basis for setting the standard cost of **$272.34** for the host department and **$86.72** for supporting departments per clinical trial. For the storage fee assuming on average 3.5 boxes per clinical trial for 15 years at the median of $30.00 per box, the standard cost for archiving storage fee is **$1,575.00**

Item 3.3.1 – Drug return/destruction

Reference number	3.3.1
Item	Drug return/destruction
Sub-list	Site close-out
Category	Drug return/destruction
Definition	The activities associated with the return of the trial drugs to the sponsor and/or the destruction of the trial drugs according to the institution's policy, sponsor requirements (if applicable), safe operating practices and the requirements of the trial.
Standard cost	**$72.24** per drug return/destruction process

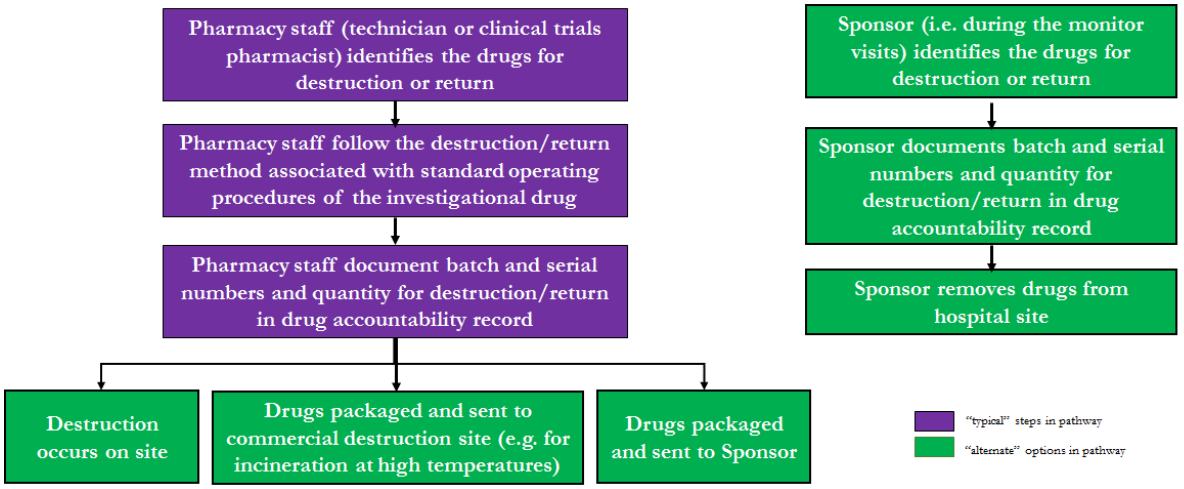
LEARNINGS FROM SITE VISITS

Most sites reported that drug return/destruction occurs throughout the trial not just at close-out. The process involves either the pharmacy technician or clinical trials pharmacist boxing up and returning excess stock to the sponsor or alternatively the site undertakes drug destruction process as per the site process. Under either method all relevant accountability records are updated. Some sites also reported that the monitor does this as part of their visits while the trial is active or as part of the close-out visit.

DERIVED PROCESS MAP FOR "DRUG RETURN/DESTRUCTION"

Figure C.3 shows the typical process involved in completing drug return/destruction in the **purple** boxes. Alternative steps have been provided in **green** boxes.

Figure C.3: Process map of activities included under site selection including drug return/destruction process



CONSIDERATIONS FOR DERIVING THE COST FOR "DRUG RETURN/DESTRUCTION"

The most typical process identified involved both the pharmacy technician and pharmacist, as such in order to derive a standard cost for the drug return/destruction process, professional time was chosen as the most suitable resource unit. As drug return/destruction is performed by pharmacy staff (e.g. technician and/or clinical trials pharmacist), this has been reflected in the rate that has been applied to derive the standard cost.

TABLE OF STANDARD COSTS FOR "DRUG RETURN/DESTRUCTION"

Table C.3 present the standard costs for drug return/destruction process, based on each time the process is undertaken (i.e. per drug return/destruction process). Obviously if the sponsor undertakes the activities then the standard cost calculated is not relevant.

Table C.3: Typical personnel, resources and unit cost involved in drug return/destruction

Activities	Personnel involved	Resource unit (hours)					Unit cost	Standard cost (median)
		Min	25th percentile	Median	75th percentile	Max		
Drug return/ destruction	Pharmacy technician	0.25	0.50	0.88	1.00	4.00	$57.30	$50.14
	Pharmacist	0.08	0.23	0.25	0.25	0.25	$88.40	$22.10
Total								**$72.24**

Note: The calculated hourly rate (fully absorbed) for pharmacist is average hourly rates for Grade 3/5 pharmacist (as defined in 2.6.3). The calculated hourly rate (fully absorbed) for pharmacy technician is average hourly rates for Grade 1 pharmacist. Totals may not be exactly additive due to rounding errors.

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 drug return/destruction process, the median was considered the best basis for setting the standard cost of **$72.24** per drug return/destruction process.

Item 3.4.1 – Biospecimen return/destruction

Reference number	3.4.1
Item	Biospecimen return/destruction
Sub-list	Site close-out
Category	Biospecimen return/destruction
Definition	The activities associated with the transfer of biospecimens obtained throughout the trial to a tissue bank (if provided for by the trial protocol) and/or the destruction of biospecimens according to the institution's policy, sponsor requirements (if applicable), safe operating practices and the requirements of the trial.
Standard cost	**$85.04** per biospecimen return/destruction process. Note the loading associated with item 2.3.2 already incorporates destruction of biospecimens for those biospecimens covered under the MBS. Hence item 3.4.1 is only relevant for biospecimen return and/or destruction not included under the MBS.

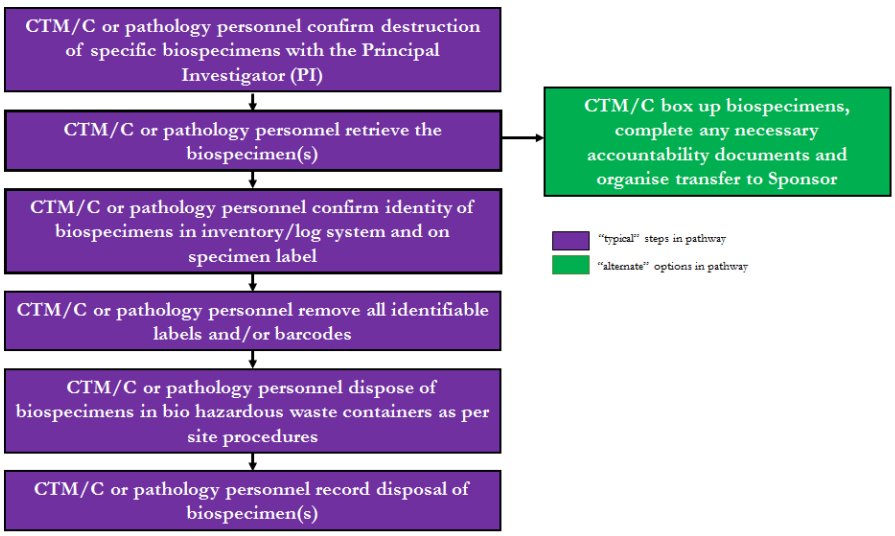
LEARNINGS FROM SITE VISITS

Most clinical trial sites reported that biospecimens are not often stored on the hospital site, unless they are investigator-initiated trials, and therefore there is hardly any biospecimen return/destruction being undertaken by the clinical trials hospital. However, in the rare circumstances that this occurs, it is usually work undertaken by the CTM/C or pathology staff and involves either boxing up the specimens or sending them to the sponsor. Alternatively, sites destroy the biospecimens according to their site rules. Under either method all relevant accountability records need to be updated.

DERIVED PROCESS MAP FOR "BIOSPECIMEN RETURN/DESTRUCTION"

Figure C.4 shows the typical process involved in biospecimen return/destruction in the **purple** boxes. Alternative steps are shown in the **green** boxes.

Figure C.4: Process map of activities included under site selection including biospecimen return/destruction process



CONSIDERATIONS FOR DERIVING THE COST FOR "BIOSPECIMEN RETURN/DESTRUCTION"

The most typical process identified involved pathology personnel destroying and/or returning the biospecimens, as such in order to derive a standard cost for the biospecimen return/destruction process, professional time was chosen as the most suitable resource unit. As biospecimen return/destruction is most typically completed by pathology staff, this has been reflected in the rate

that has been applied to derive the standard cost. It is important to note that although the CTM/C may be involved the most typical process involves pathology personnel.

It is important to note that the MBS loading associated with item 2.3.2 already incorporates destruction of biospecimens for those biospecimens covered under the MBS. Hence item 3.4.1 includes biospecimen return and/or destruction for only those biospecimens not included under the MBS.

TABLE OF STANDARD COSTS FOR "BIOSPECIMEN RETURN/DESTRUCTION"

Table C.4 presents the standard costs for biospecimen return/destruction process per clinical trial.

Table C.4: Typical personnel, resources and unit cost involved in biospecimen return/destruction

Activities	Personnel involved	Resource unit (hours)					Unit cost	Standard cost (median)
		Min	25th percentile	Median	75th percentile	Max		
Biospecimen return/destruction	Pathology staff	0.50	0.63	1.00	1.75	3.00	$85.04	$85.04
Total								**$85.04**

Note: The hourly rate (fully absorbed) for pathology staff is based on a hospital scientist (i.e. Grade 3/4 hospital scientist). Totals may not be exactly additive due to rounding errors.

Table C.4 presents the resource units, in hours, required for each activity by specific personnel. Due to the variability in the resources required for the biospecimen return/destruction process, the median was considered the best basis for setting the standard cost of **$85.04** per clinical trial.