Prepared for the Independent Hospital Pricing Authority

Development of a Table of Standard Costs for Conducting Clinical Trials in Australia

Public Consultation Paper

IHPA is calling for submissions on this Consultation Paper by the closing date of Tuesday, 28th April, 2015

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24th March 2015

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Introduction

The Independent Hospital Pricing Authority (IHPA) has appointed HealthConsult to undertake a project to *"provide a table of standard costs for conducting Clinical Trials in Australia"*. This Chapter briefly sets out the context for the project and the purpose of this Consultation Paper.

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, 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. 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 the IHPAs *Determination of the Standard Table of Costs for Conducting Clinical Trials in Australia* (published in November, 2013).

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 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 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 (specifically, clinical trial costs that are not deemed ~~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 the 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 COAG Health Council meeting scheduled for 7th August, 2015). This Consultation

paper describes the work that ~~it~~ is proposed will be undertaken to create the information base that will allow IHPA to comply with the Direction.

1.2 CONSULTATION ON THE DEVELOPMENT OF THE TABLE

This **Consultation Paper has been produced to underpin a process of stakeholder consultation around development of the Table through inviting public submissions**. In particular:

- Throughout the paper there are questions posed and approaches proposed that relate to how the Table of standard costs will be developed. Stakeholders are invited to provide specific feedback on the questions and/or to indicate the suitability or otherwise of the proposed approaches, where possible, with reasons and suggestions for alternative approaches;
- **IHPA is calling for submissions on this Consultation Paper.** Submissions must be emailed as MS Word or RTF attachment to **submissions.ihpa@ihpa.gov.au** by **5.00pm EST on Tuesday 28th April 2015**. All submissions will be published on the IHPA website unless respondents specifically identify any sections that they believe should be kept confidential due to commercial or other reasons.
- HealthConsult is also undertaking a series of targeted consultations in April and May 2015 via interviews and focus groups to seek input from a range of invited stakeholders.

Potential respondents to this invitation for submissions should note that the approaches proposed in this Consultation Paper have not been endorsed by the Pricing Authority. They are presented as a mechanism for gauging stakeholder views, as well as to provide a basis for identifying the methodological refinements that may be required to produce a fit-for-purpose Table of standard costs. HealthConsult will have regard to the contents of submissions made, as well as the results of the investigations undertaken with invited stakeholders, in developing a table of standard costs for each item on the NHMRC revised List for consideration by the Pricing Authority.

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 a summary of the structure of the List. The full set of items in the revised List with proposed definitions is then 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 the Independent Hospital Pricing Authority (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~~ may apply to ~~all~~ other 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.

Comment [LC1]: Suggest you try to make the point in a new sentence. I understand that you are trying to make the point that pricing practices vary among sponsors. I believe that the point of this exercise is to try to address the pricing practice differences between hospitals. Most sponsors pay all Australian sites the same for the same trial; the problem is that when one hospital is a lot higher than the other that higher price tends to be applied to all sites, thus making Australia in general more expensive.

- 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 of 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 OVERVIEW OF THE LIST OF STANDARD ITEMS

The revised List 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 Closeout). The previous items have been retained, where appropriate, and reorganised into the new structure. The revised List has a reference numbering system structured as a.b.c, where 'a' is the sub-list number, 'b' is the category number, and 'c' is the item number within each category. Table 2.1 summarises the features of the List, including the number of sub-lists; and the number of categories and items within each sub-list.

Table 2.1: Brief descriptive analysis of the NHMRC's standard 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 the 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 Closeout	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**	

3

Costing the list of standard items for clinical trials

This Chapter presents the proposed approach to deriving a standard cost for each item on the revised list.

3.1 PRINCIPLES TO BE USED IN COSTING THE NHMRC REVISED LIST OF STANDARD ITEMS FOR CLINICAL TRIALS

The standard costs will be derived using the following principles:

- **Activity based costing for each item on the list will be used as the preferred method**. Where possible, items will be costed on an activity basis from first principles. A protocol based approach will be used that develops process maps (where necessary), defines the resource units associated with each step in the process map, and determines standard unit costs for each resource. These three pieces of information will be used to derive an overall standard cost for each item on the NHMRC List where activity based costing from first principles is used.
- **Unit costs will be externally derived.** Where items on the NHMRC list are costed from first principles, the unit costs for the resource units used to determine standard costs will come from secondary sources (e.g. the National Hospital Costs Data Collection (Round 17) held by the IHPA or other published costs schedules; various Awards, classifications and pay rates under which hospital staff are employed; various charges levied by ethics committees, clinical trial auspice/coordinating bodies (only where these charges become a cost to the health service that hosts a clinical trial); and so on);
- **Standard costs will be based on representative practice**. The timeframe available to the study are such that constructing a prospective data collection that attempts to measure actual costs for each item across a statistically significant number of trials and trial sites is not possible. The study will thus determine standard costs by investigating the actual processes used across a number of trial sites, but the standard costs will not be based on the mean of a series of measurements. Rather, standard costs will be based on a synthesis of the process maps derived from the field work that identifies the most representative practices through review by an Expert Reference Group (i.e. standard costs may be determined at mean, median, 25th percentile, etc.).
- **Where activity based costing principles cannot be used, standard costs/price schedules will be used without amendment.** For some items on the List (e.g. clinical services such as medical/nursing consultations or diagnostic tests), there is insufficient time available to the study to validate pre-existing cost/price schedules (i.e. activity based costing from first principles will not be possible). In these circumstances, generally accepted standard cost/price schedules (e.g. MBS fees for diagnostic tests) will be used. Consideration will be given, based on evidence, to any adjustments that may need to be applied if the services are provided in the context of a clinical trial. Where there are multiple cost/price schedules available for an item, all cost/price schedules will be examined and the most commonly accepted cost or price will be used to determine the standard cost.

Comment [LC2]: Not sure if this refers to the principles table above (NHMRC principles)?

Comment [LC3]: It would be useful to know who is on Group, who the members represent, or where to find this information, or at least categories and total number.

Comment [LC4]: It would be useful if this were defined – eg 50th percentile. Or is the group waiting to see what the range of costs is? In some instances there will be relative uniformity of costs, in others there will be wide variation.

- **Actual practices will be investigated in a number of clinical trial sites through fieldwork**. As, for items costed from first principles, ~~the standard costs will not be calculated as the mean of a~~ series of measurements, purposeful random selection of field work sites is not required. ~~However,~~ the sampling strategy will ensure that the hospitals selected for field work are reasonably representative of the settings in which clinical trials are conducted in Australia (i.e. provide 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); location of hospital (metropolitan, regional); and sector of hospital (public, private).

- **Standard costs will be determined on a fully absorbed basis.** The determined costs will 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 will be transparent**. For each item on the NHMRC 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 are used to derive the standard cost of an item, they will be referenced (subject only to any limitations imposed by commercial confidentiality).

- **Standard costs will be measured, not prices.** The study will produce a Table of standard costs, there will be no mark-up on measured costs for pricing purposes (i.e. as with the NEP for public hospitals set by the IHPA, the NEP for items associated with clinical trials, that IHPA is required to produce by Ministerial Direction, will equal the measured standard cost). Users of the Table of standard costs will be free to refer to it as they wish for the processes of negotiating budgets for the establishment of clinical trials.

Comment [LC5]: As above

Comment [LC6]: Please re-phrase for meaning.

Comment [LC7]: Consider including a sentence to ensure the overhead costs are not charged on top of standard costs:
'Should sites charge an overhead in a clinical trial, the standard costs in the table would not be applicable as a guide to costs'.

Comment [LC8]: Please define/explain the NEP

Consultation questions
Are the principles for developing the Table of standard costs reasonable?
Are there any principles that should be modified or deleted? Should additional principles be adopted?
Please suggest wording changes and/or additional principles where necessary.

3.2 COSTING THE SITE AUTHORISATION SUB-LIST

Table 3.1 provides details of the proposed costing method for the ~~seven~~ main items on the site authorisation sub-list.

Comment [LC9]: Perhaps make it clear that this is not and does not attempt to be an exhaustive list.

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

Item number	Item	Costing method	Costing basis	Develop 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 trial site	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
1.1.2	Protocol review	Primary costing, protocol based	per trial site	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
1.1.3	Feasibility determination	Primary costing, protocol based	per trial site	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
1.2.1	Preparation of the HREC application	Primary costing, protocol based	per trial site	Yes	• Identify resource units (minutes of labour) required to complete for each activity in process map. Should not be included in costing if the sponsor prepares the documentation	• Use 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 trial site	Yes	• Identify resource units (minutes of labour) required to complete for each activity in process map. Should not be included in costing if the sponsor prepares the documentation	• Use 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 trial site	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
1.3.2	Site processing and review	Primary costing, protocol based	per trial site	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

Comment [LC10]: This is usually a very quick activity and not paid-for by commercial sponsors. There is concern that its inclusion in the document may encourage sites to try to seek payment for it, which may deter sponsors from doing initial feasibility in Australia.

Comment [LC11]: Again not usually paid work.

Comment [LC12]: Would eb worth artcliculaitng that this is an on-site pre-study (and pre-contract) activity, which is not usually paid for.

Comment [LC13]: This is a significant area for confusion. The PI is expected to review (but often does not) and then forward the application to ethics. We have reports that sponsors will often also do the PI's cover letter.

Comment [LC14]: It would be ideal to seek input from an IEC on how they determine the charges. IEC members are usually not paid.

Comment [LC15]: Other countries do not usually have this, which leaves Australia out of step internationally and less attractive as a result - particularly if the sponsor does the preparation anyway.

Review of Table 3.1 demonstrates that it is intended to attempt primary costing using a protocol based approach for deriving the standard costs of all seven items on the site authorisation sub-list.

Consultation questions
Is the proposed method for deriving the standard costs for each item on the NHMRC sub-list for site authorisation reasonable?
Are there any items for which the costing approach should be modified?
Please suggest alternative costing approaches where appropriate.

3.3 COSTING THE SITE IMPLEMENTATION SUB-LIST

Table 3.2 provides details of the proposed costing method for the ~~31~~ main items on the site implementation sub-list.

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

Item number	Item	Costing method	Costing basis	Develop process map?	Method for determining resource units	Method for assigning unit costs to resource units
2.1.1	Start-up meetings	Primary costing, protocol based	per trial site	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
2.1.2	Departmental set up	Primary costing, protocol based	per trial site	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
2.1.3	Trial specific equipment set-up and maintenance	Primary costing, protocol based, with reference to external cost/fee schedules	per trial site	yes	• Identify resource units (minutes of labour and equipment costs (e.g. hire or purchase costs) (from charge schedules) needed acquire and maintain trial-specific equipment	• Use external source (e.g. relevant Award) to determine hourly rate (including provision for overhead) for each category of labour used and external source (e.g. schedule of charges) to determine typical unit cost for equipment hire/purchase and maintenance

Comment [LC16]: This is not an item usually charged for in other countries.

Comment [LC17]: Again, this is not usually charged for in other countries. If sites commence billing for Site Initiation Visits, we suggest a nominal standard cost. Australia often charges a 'start-up' fee (which would cover all of these activities). It is a source of contention for Australian sponsors trying to convince international offices to include Australia in the study.

Comment [LC18]: Suggest removing this line item as it is highly variable.

Item number	Item	Costing method	Costing basis	Develop process map?	Method for determining resource units	Method for assigning unit costs to resource units
2.2.1	Pre-screening activity	Primary costing, protocol based	per service (patient screened)	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
2.2.2	Recruitment activity	Primary costing, protocol based	per service (patient recruited)	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
2.3.1	Initial patient Sscreening and health assessment (includes informed consent)	Primary costing, protocol based with reference to external cost/fee schedules	per service	yes (only for the trial specific data collection and reporting activities)	• Identify resource units (minutes of labour) required to complete for each activity in process map • Identify applicable items on the MBS that correspond to the clinical services provided	• Use an adjusted MBS fee for the services as a surrogate for unit cost, where the service is deemed to not be part of standard of care • Use an adjusted MBS fee as a surrogate for unit cost, where the service is deemed to be part of standard of care to reflect the extra resource required to comply with the requirements of the trial protocol
2.3.2	Laboratory tests and procedures (where applicable, trial-specific, non-standard care)	Primary costing, protocol based with reference to external cost/fee schedules	per service	yes (only for the trial specific data collection and reporting activities)	• Identify resource units (minutes of labour) required to complete for each activity in process map • Identify applicable items on the MBS that correspond to the clinical services provided	• Use an adjusted MBS fee for the services as a surrogate for unit cost, where the service is deemed to not be part of standard of care • Use an adjusted MBS fee as a surrogate for unit cost, where the service is deemed to be part of standard of care to reflect the extra resource required to comply with the requirements of the trial protocol

Comment [LC19]: This would benefit form being be capped. It is also highly variable. This is usually included in the per-patient cost (eg assume you will screen 4 patients to enrol 1)

Comment [LC20]: Suggest removing this line item, as it comes under screening and patient enrolment or 2.3.1. (unless it is referring to clinical trial promotion or advertising initiatives, in which case suggest clarification of the terminology of this item to avoid double-charging.)

Comment [LC21]: Suggest this be capped.

Comment [LC22]: Most commercially sponsored trials have central labs so this is not applicable. It could be worthwhile including instruction that there is a general expectation that there will be no lab fees where a central lab is used for the study.

Item number	Item	Costing method	Costing basis	Develop process map?	Method for determining resource units	Method for assigning unit costs to resource units
2.3.3	Imaging examinations and procedures (where applicable, trial-specific, non-standard care)	Primary costing, protocol based with reference to external cost/fee schedules	per service	yes (only for the trial specific data collection and reporting activities)	• Identify resource units (minutes of labour) required to complete for each activity in process map • Identify applicable items on the MBS that correspond to the clinical services provided	• Use an adjusted MBS fee for the services as a surrogate for unit cost, where the service is deemed to not be part of standard of care • Use an adjusted MBS fee as a surrogate for unit cost, where the service is deemed to be part of standard of care to reflect the extra resource required to comply with the requirements of the trial protocol
2.3.4	Radiation therapy planning and treatment (where applicable, trial-specific, non-standard care)	Primary costing, protocol based with reference to external cost/fee schedules	per service	yes (only for the trial specific data collection and reporting activities)	• Identify resource units (minutes of labour) required to complete for each activity in process map • Identify applicable items on the MBS that correspond to the clinical services provided	• Use an adjusted MBS fee for the services as a surrogate for unit cost, where the service is deemed to not be part of standard of care • Use an adjusted MBS fee as a surrogate for unit cost, where the service is deemed to be part of standard of care to reflect the extra resource required to comply with the requirements of the trial protocol
2.3.5	Other clinical tests or procedures (where applicable, trial-specific, non-standard care)	Primary costing, protocol based with reference to external cost/fee schedules	per service	yes (only for the trial specific data collection and reporting activities)	• Identify resource units (minutes of labour) required to complete for each activity in process map • Identify applicable items on the MBS that correspond to the clinical services provided	• Use an adjusted MBS fee for the services as a surrogate for unit cost, where the service is deemed to not be part of standard of care • Use an adjusted MBS fee as a surrogate for unit cost, where the service is deemed to be part of standard of care to reflect the extra resource required to comply with the requirements of the trial protocol

Item number	Item	Costing method	Costing basis	Develop process map?	Method for determining resource units	Method for assigning unit costs to resource units
2.3.6	Specialist medical consultations (where applicable, trial-specific, non-standard care)	Primary costing, protocol based with reference to external cost/fee schedules	per service	yes (only for the trial specific data collection and reporting activities)	• Identify resource units (minutes of labour) required to complete for each activity in process map • Identify applicable items on the MBS that correspond to the clinical services provided	• Use an adjusted MBS fee for the services as a surrogate for unit cost, where the service is deemed to not be part of standard of care • Use an adjusted MBS fee as a surrogate for unit cost, where the service is deemed to be part of standard of care to reflect the extra resource required to comply with the requirements of the trial protocol
2.3.7	Nursing services (where applicable, trial-specific, non-standard care)	Primary costing, protocol based with reference to external cost/fee schedules	per service	yes (only for the trial specific data collection and reporting activities)	• Identify resource units (minutes of labour) required to complete for each activity in process map • Identify applicable items on the MBS that correspond to the clinical services provided	• Use an adjusted MBS fee for the services as a surrogate for unit cost, where the service is deemed to not be part of standard of care • Use an adjusted MBS fee as a surrogate for unit cost, where the service is deemed to be part of standard of care to reflect the extra resource required to comply with the requirements of the trial protocol
2.3.8	Allied health services (where applicable, trial-specific, non-standard care)	Primary costing, protocol based with reference to external cost/fee schedules	per service	yes (only for the trial specific data collection and reporting activities)	• Identify resource units (minutes of labour) required to complete for each activity in process map • Identify applicable items on the MBS that correspond to the clinical services provided	• Use an adjusted MBS fee for the services as a surrogate for unit cost, where the service is deemed to not be part of standard of care • Use an adjusted MBS fee as a surrogate for unit cost, where the service is deemed to be part of standard of care to reflect the extra resource required to comply with the requirements of the trial protocol
2.4.1	Staff training (drug specific) where training is in addition to a Site Initiation Visit or Investigator Meeting	Primary costing, protocol based	per trial site	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

Item number	Item	Costing method	Costing basis	Develop process map?	Method for determining resource units	Method for assigning unit costs to resource units
2.4.2	Stock management (marginal costs)	Primary costing, protocol based	per trial site 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
2.4.3	Drug preparation and dispensing (marginal costs)	Primary costing, protocol based	per trial site 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
2.5.1	Biospecimen collection and processing (central labs)	Primary costing, protocol based	per service (specimen collection and processing)	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
2.5.2	Biospecimen storage	Primary costing, protocol based	per trial site 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
2.6.1	Investigator time	Reference to external labour cost schedules	rate per minute	no	• Minutes of investigator time	• Use 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 minute	no	• Minutes of research nurse time	• Use external source (e.g. relevant Award) to determine hourly rate (including provision for overhead) for each category of labour used
2.6.3	Clinical research coordinator (non-research nurse) time	Reference to external labour cost schedules	rate per minute	no	• Minutes of clinical research coordinator time	• Use external source (e.g. relevant Award) to determine hourly rate (including provision for overhead) for each category of labour used
2.6.4	Interpreter services	Reference to external labour cost schedules	per service (interpreter service used)	no	• Minutes of interpreter time	• Use 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 (non-standard-care)	Reference to external cost/fee schedules	per bed-day	no	• Number of bed days	• Use external source (e.g. NHCDC) to determine bed-day cost (including provision for overhead) for each category of bed-day used

Comment [LC23]: There is a concern that sites will collect government funding for the bed as well as sponsor funding. Perhaps the government could absorb the cost for this?

Item number	Item	Costing method	Costing basis	Develop process map?	Method for determining resource units	Method for assigning unit costs to resource units
2.6.6	Clinic/theatre time (non-standard-care)	Reference to external cost/fee schedules	per minute	no	• Minutes of theatre time	• Use external source (e.g. NHCDC) to determine standard per minute theatre cost (including provision for overhead)
2.6.7	Outpatient time (non-standard-care)	Reference to external cost/fee schedules	per minute	no	• Minutes of outpatient clinic time	• Use external source (e.g. NHCDC) to determine standard per minute outpatient clinic cost (including provision for overhead)
2.7.1	Lead site coordination	Primary costing, protocol based	per trial	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	Administration, monitoring and reporting	Primary costing, protocol based	per trial site per quarter	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
2.8.1	Participant time	Reference to external cost/fee schedules	per hour/day	no	• Number of hours/day	• Use external source (e.g. relevant reimbursement schedule) to determine standard hourly rate (including provision for overhead)
2.8.2	Participant costs	Reference to external cost/fee schedules	per bed-day	no	• Number of km travelled • Number of nights' accommodation • Number of meals	• Use external source (e.g. relevant reimbursement schedule to determine standard cost (including provision for overhead) for each category of participant costs
2.9.1	Ethics ~~A~~amendment preparation and submission where not performed by the study sponsor	Primary costing, protocol based	per service (per amendment)	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
2.9.2	Amendment review – Ethics Committee Fees	Primary costing, protocol based	per service (per amendment review)	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
New item (standard)	Unscheduled patient visits for Serious Adverse Event or other unscheduled event	Primary costing, protocol based	per service (per amendment review)	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

Comment [LC24]: We suggest removing this line item; or be clear if the sponsor or the government is funding the item - to guard against sites collecting from both.

Comment [LC25]: Not usually paid for in Australia, As it is highly variable, we suggest removing from this exercise.

Comment [LC26]: As this is highly variable, we suggest mentioning this and noting it is subject to ethics approval.

Comment [LC27]: This is always done by the sponsor.

Item number	Item	Costing method	Costing basis	Develop process map?	Method for determining resource units	Method for assigning unit costs to resource units
	Telephone assessment of patient	Primary costing, protocol based	per service (per amendment review)	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

Review of Table 3.2 demonstrates that it is intended to attempt primary costing using a protocol based approach either fully or partially for deriving the standard costs of 22 of the 31 items. Standard cost for the other nine items will be derived by reference to published or otherwise available cost/fee schedules.

Consultation questions
Is the proposed method for deriving the standard costs for each item on the NHMRC sub-list for site implementation reasonable?
Are there any items for which the costing approach should be modified?
Please suggest alternative costing approaches where appropriate.

3.4 COSTING THE SITE CLOSEOUT SUB-LIST

Table 3.3 provides details of the proposed costing method for the ~~four~~ main items on the site closeout sub-list.

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

Item number	Item	Costing method	Costing basis	Develop process map?	Method for determining resource units	Method for assigning unit costs to resource units
3.1.1	Site closeout visit (face to face)	Primary costing, protocol based	per trial site	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
3.2.1	Archiving of trial records	Primary costing, protocol based	per trial site	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
3.3.1	Drug return/destruction	Primary costing, protocol based	per trial site	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
3.4.1	Biospecimen return/destruction	Primary costing, protocol based	per trial site	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

Comment [LC28]: This is usually included in the per patient budget, like site monitoring visits, but may be covered under 'reporting and monitoring / admin'. That same item could also apply to this visit. Suggest removing this line item as it is out of step with other countries.

Comment [LC29]: Suggest this is moved to the pharmacy section, to ensure it is not no double-charged.

Comment [LC30]: Suggest this is moved to the pharmacy section, to ensure it is not no double-charged.

Review of Table 3.3 demonstrates that it is intended to attempt primary costing using a protocol based approach for deriving the standard costs of all four items on the site closeout sub-list.

Consultation questions
Is the proposed method for deriving the standard costs for each item on the NHMRC sub-list for site close out reasonable?
Are there any items for which the costing approach should be modified?
Please suggest alternative costing approaches where appropriate.

3.5 POTENTIAL NEED FOR ADJUSTMENTS TO STANDARD COSTS

Review of the existing materials 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 are expected to have different costs experiences to the typical adult population. For example, there are trials targeted at children; and trials that involve significant participation of patients from known higher need groups e.g. people from Indigenous or culturally and linguistically diverse backgrounds. There may be a need to consider adjustments to the standard costs for trials that are likely to involve high proportions of participants from these groups.
- **Location of trial sites**. Some trial sites may be located in remote regional and rural areas, where it is known that there may be ~~higher~~ different cost experiences (e.g. for participant travel, or for the unit cost of clinical labour). There may be a need to consider adjustments to the standard costs for trials where sites are located in remote regional and rural areas.
- **Standard of care services, and services over and above standard of 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 of care). It is acknowledged that general principles that allow standard of care services to be distinguished from non-standard of care services are difficult to define. Ultimately, the determination of standard of 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 proposed 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 of 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 of care, and another, lower cost, for when the test is standard of 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.

Comment [LC31]: Please clarify which table this refers to.

Consultation questions
Is there a need to provide for adjustments to the standard costs based on any for the identified factors?
Are there other factors that should be considered for potential adjustments to the standard costs?
Please suggest methods for adjusting standard cost to account for the factors where considered necessary.

Appendix A: Revised list of items for clinical trials

This Appendix presents the revised List of standard items associated with the conduct of clinical trials in Australia, as developed by the NHMRC. Note that these lists are not exhaustive, and conversely items on the list may not be applicable to all trials.

A.1 SITE AUTHORISATION

The first sub-list itemises the activities from feasibility assessment through to site authorisation of a clinical trial. Table A.1 shows that there are seven items on this sub-list in three different categories. It also contains the proposed revised definition for each item.

Table A.1: The NHMRC 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.
Ethics Approval	Preparation of the HREC application (where not completed by the sponsor)	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. Only time site staff spends on this activity should be included.

Comment [LC32]: Suggest removing as it is out of step with other countries.

Comment [LC33]: Suggest removing as it is out of step with other countries.

Comment [LC34]: This is never paid for by sponsors in other countries. Will make Australia out of step with other countries. It is a matter for the sites and not for the sponsor.

Major category	Item	Reference number	Definitions
	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~~ Ethics review fee
Site-specific assessment	Preparation of the SSA application by the project team (where not completed by the sponsor)	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 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) 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.

Comment [LC35]: This is already captured.

Comment [LC36]: This involves two separate and discrete fees: 1. prep time (which the sponsor usually conducts), and 2. the governance fee. These activities both make Australia out of step with other countries, which do not charge this.

Comment [LC37]: The sponsor completes the CTN form, as it is part of the ethics package that is sent to sites.

Comment [LC38]: Suggest removing from this section, as it is out of place.

A.2 SITE IMPLEMENTATION

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 A.2 shows that there are 31 items on this sub-list in nine different categories. It also contains the revised definition for each item.

Table A.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, eCRF, 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 – trial-specific costs only) 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.

Comment [LC39]: Suggest removing. This is not paid for, as there is no contract in place at this time.

Comment [LC40]: This is highly variable, and we suggest removing.

Major category	Item	Reference number	Definitions
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 (including patient consent)	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 (no central lab)	2.3.2	• Laboratory clinical services including pathology, histopathology, haematology, chemical, microbiology, immunology, tissue pathology, cytology, genetics, etc.
	Imaging examinations and procedures (no central imaging)	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 (non-standard)	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 (non-standard)	2.3.6	• Clinical consultations services provided by medical specialists, General Practitioners (GPs), dentists and any other registered medical practitioner.
	Nursing services (non-standard)	2.3.7	• Clinical services provided by enrolled, registered and specialist nurses, midwifes and nurse practitioners.
	Allied health services (non-standard)	2.3.8	• Clinical services provided by registered allied health professionals (e.g. pharmacists, physiotherapists, dieticians, occupational therapists).

Comment [LC41]: See earlier comment. Suggest capping, but appropriate cap is too variable to estimate.

Comment [LC42]: This should only apply to advertising, etc. Screening (screen fail or enrolled patients) is included elsewhere.

Comment [LC43]: Recommend differentiating between when there is central labs / imaging and when there is not as the costs are entirely different. If there is a central lab, for instance, you only pay for processing time and sample storage.

Major category	Item	Reference number	Definitions
Pharmacy / Investigation Drug Related	Staff training (drug specific) (where not included in the Site Initiation Visit / Investigator Meeting)	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 (trial-specific; marginal costs)	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 (trial-specific; marginal costs)	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 (trial-specific; marginal costs)	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. Marginal costs only should be included, so if, for example, a freezer is shared between studies, the average portion of the ongoing freezer maintenance cost only should be included
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.

Major category	Item	Reference number	Definitions
	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 of 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 of 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, all on-site sponsor ~~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.
Amendment Processing	Amendment preparation and submission (where prepared by site staff)	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.~~

Comment [LC44]: High probability of sites over-charging. Currently usually only charged by Phase 1 units. Suggest removing or making this Phase 1 specific.

Comment [LC45]: High probability of sites over-charging.

Comment [LC46]: This is usually covered in the general admin. Suggest this item is limited to protocol amendments only.

Comment [LC47]: Should this be EC?

A.3 SITE CLOSEOUT

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 A.3 shows that there are four items on this sub-list in four different categories. It also contains the revised definition for each item.

Table A.3: The NHMRC sub-list of standard items associated with clinical trials for Site Closeout with definitions

Major category	Item	Reference number	Definitions
~~Site closeout visit~~	~~Site closeout 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.

Comment [LC48]: This item ought to be included in on-site visits above.

Comment [LC49]: Perhaps move to pharmacy section.