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Prepared for the National Health and Medical Research Council

Refinement of the standard list of items associated with conducting Clinical Trials in Australia

Final Report – Incorporating Revised List

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Executive Summary

HealthConsult was engaged by the National Health and Medical Research Council (NHMRC) in May, 2014, to undertake a:

> ***"consultation process to support the development of a revised list of standard items for clinical trials' (and to develop the revised list)"***

HealthConsult used a four stage methodology that embraced a wide ranging consultative process to gather the views of a representative set of the diverse range of stakeholders involved in the conduct of clinical trials in Australia. These stakeholders came from the commercial sector (pharma, device, biotech), potential trial host sites (public hospitals, private hospitals, stand-alone Phase 1 trial facilities), Contract Research Organisations (CROs), Collaborative Research Groups (CRGs) Clinical Trial Alliances/Networks, Third Party Trial Centres, and Institutions (Universities, Research Institutes). The revised List, as presented in Chapter 3, was then derived by undertaking a thematic analysis of the information produced by the consultative process and reviewing the written submissions received.

A key point made by stakeholders was that a set of principles should be developed that are published along with the List and the associated table of standard costs. It is considered that 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 suggested set of principles, developed primarily from the feedback provided by stakeholders during this project is:

- The principal purpose of the List and the associated table of standard costs (once derived and published by the Independent Hospital Pricing Authority (IHPA)) is to provide an authoritative reference point for the negotiation of a trial budget between a trial funder/sponsor and a health service that wishes to host and/or conduct a trial.
- The List has been developed principally with reference to hospitals (public or private) as the host health service. It is acknowledged that many of the items on the List may also be applicable to other health services that host and/or conduct trials (e.g. community based health services, general practices, and purpose-built Phase 1 Trial Centres).
- The List is only intended to cover activities associated with clinical trials that are undertaken at, or by, a health service that hosts and/or conducts a clinical trial. There are many other stakeholders (trial funders, trial sponsors, Contract Research Organisations (CROs), Clinical Trial Cooperative Groups or Networks, and 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 includes some items where significant contributions to undertaking the activities are made by other than the trial hosts site (e.g. preparation of the HREC application often involves substantial work by the trial funder/sponsor). Such items are included on the revised List, as there is still work required by the trial host sites. The amount of work required by the trial host site does vary depending on the contributions made by other involved stakeholders (e.g. trial funder/sponsor, CROs). This variation should be dealt with in setting the price for these items by negotiation between the trial funder/sponsor and the health service that wishes to host and/or conduct a trial (with reference to the IHPA standard cost).
- 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 will have an associated standard cost (once derived and published by IHPA), which represents an independent determination of the typical cost of the activity/service covered by each item. The development of a budget, including the setting of a price for each item, for a specific clinical trial remains a subject for negotiation between the trial funder/sponsor and the health service that wishes to host and/or conduct a trial.

- The List is only intended to cover activities/services that are common to the conduct of clinical trials in health services (not all activities/services may apply to all trials). Activities/services 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 that wishes to host and/or conduct a trial.
- The revised List has been developed following consultation with, and input from, a wide range of stakeholders including potential trial funders/sponsors from the commercial, collaborative research/trial group, and academic sectors. In this process, it was acknowledged that, although the principal point of reference for development of the initial List was commercially funded/sponsored trials, the items now included on the revised List typically apply to all trials (see principle below).
- Many health services currently choose to support investigator initiated/academic clinical trials to a greater extent than industry sponsored trials by meeting a larger part of their costs through charging lower fees. The List is not intended to provide incentives or disincentives to this practice, merely to define the usual activities/services associated with hosting and/or conducting a trial and their typical cost (once published by IHPA). Therefore, 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.
- 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 health services would have provided to any patient for his/her condition if he/she had not been enrolled in the clinical trial are used in the negotiations around setting trial budgets.

As experience grows in the use of the revised List, there may be scope to make it applicable to an even wider range of clinical trials and trial participants. However, prior to any increase in the intended scope, it is considered important that the table of standard costs derived for the revised List becomes an accepted reference point for the negotiation of a trial budget between a trial funder/sponsor and a health service that wishes to host and/or conduct a trial.

It is understood that the next step in the development process will be to refer the revised List to IHPA for the determination of an associated table of standard costs. Unlike the 2013 study that generated the initial table of standard costs, it is suggested that IHPA be given the flexibility to make modifications to the items on the revised List, if it is considered necessary to arrive at a more representative and homogenous cost. It is expected that there will be little need for such refinement, but some additional flexibility afforded to IHPA in this regard may improve the next version of the table of standard costs. Naturally any change to the items suggested by IHPA should be approved by the NHMRC (as the custodian of the List) before it is implemented for costing purposes.

Finally, it is suggested that the development of a costing template, which makes it simple to use the standard List of items 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, 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.

1

Introduction

HealthConsult was engaged by the National Health and Medical Research Council (NHMRC) in May, 2014, to undertake a:

> ***"consultation process to support the development of a revised List of standard items for clinical trials' (and to develop the revised list)"***

This Chapter presents the project background and objectives; and summarises the methodology used by HealthConsult to conduct the assignment, including the number of stakeholders consulted and the types of organisations that they represented.

1.1 BACKGROUND – INITIAL DEVELOPMENT AND COSTING OF THE LIST

The NHMRC developed a standard List of 63 items associated with the conduct of clinical trials in Australia in early 2012 (the 'List'). On 28th November 2012, the then Minister for Health, directed the Independent Hospital Pricing Authority (IHPA) to determine the national efficient price (NEP) for each item on the List. In March 2013, IHPA engaged HealthConsult to develop, in consultation with a broad range of stakeholders, a table of standard costs for the List. The report of this work the "HealthConsult Report"), titled *Development of a Table of Standard Costs for Conducting Clinical Trials in Australia* was produced in June 2013. Subsequently, a *National Efficient Price Determination Standard List of Clinical Trials Items* (the "IHPA Determination") was released by IHPA in November, 2013.

While the IHPA Determination was considered a useful guidance on some of the costs of clinical trials, a number of issues have been identified by stakeholders since its release late last year. Specifically, it was considered that the items on the List should be applicable to both commercially sponsored and academic trials, as well as to pharmaceutical and medical device trials. Concerns were raised as to whether the List should focus on only those activities conducted at the trial host sites rather than all activities associated with clinical trials. As a result, the NHMRC was asked by the Department of Health to conduct work to refine the standard list of clinical trial items.

As part of the review project, HealthConsult engaged with a wide range of key stakeholders who conduct, or are otherwise involved in the conduct or governance of, clinical trials in Australia. The consultations allowed a determination of the significance of the cited and other concerns relating to the List, so they could be taken into account in developing the revised List.

1.2 PROJECT REQUIREMENTS

The project requirements, as set out in the Request for Offer (RFO) document stated that the project team was required to:

(1) Consider the 2013 HealthConsult Report and 2013 IHPA Determination and industry feedback related to these documents.

(2) Identify critical distinctions between items on the List (or not on the List) as follows:
   a. items related to pharmaceutical trials only;
   b. items related to medical device trials only;

c. items related to both pharmaceutical and medical device trials;
d. items related to the conduct of commercially-sponsored clinical trials only;
e. items related to the conduct of academic or 'investigator-initiated' clinical trials only;
f. items related to the conduct of both commercially-sponsored clinical trials and the conduct of academic or 'investigator-initiated' clinical trials;
g. items for which the associated costs are incurred by trial host sites only;
h. items for which the associated costs are incurred by the trial sponsor or the sponsor's agent only;
i. items for which the associated costs are incurred by trial host sites and by the trial sponsor or the sponsor's agent; and
j. items that are costs of clinical trials but for which a standard fee is not generally applied or which is otherwise difficult to determine.

(3) Identify key stakeholders who could provide valuable input into a revised standard items List.

(4) Consult with these stakeholders.

(5) In consultation with NHMRC, develop a revised standard items List.

The RFO also set out two other requirements as follows:

- analysing the implications of the determination that an item is a standard component of clinical trials versus its status as a component of standard care delivered by the healthcare institution to patients who are both receiving treatment or care and also participating in a clinical trial.
- making recommendations regarding how these implications relate to the inclusion of an item on the standard items list for costing purposes.

1.3 PROJECT METHDOLOGY

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

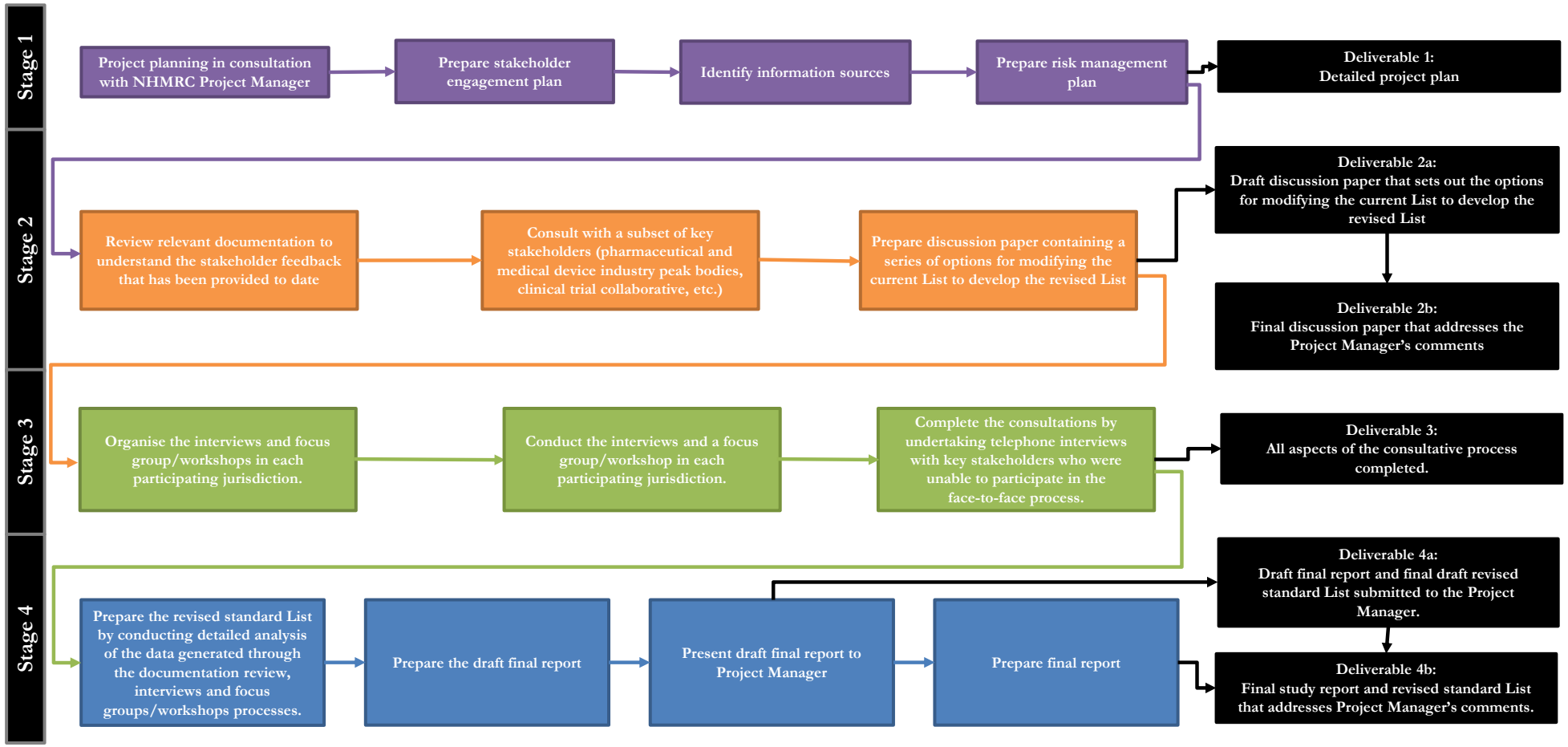
(1) **Stage 1:** Project planning which included the development of the stakeholder engagement and risk management plans.

(2) **Stage 2:** First round stakeholder consultations with a subset of key stakeholders leading to the production of a discussion paper presenting a series of options/opportunities for revising the List. This paper was then used as the basis of a broader consultative process, so that stakeholder input could be received on the merit of the options before any revisions to the List were undertaken.

(3) **Stage 3:** Roll-out of the broad stakeholder consultation process, which included one or two-day visits to the States/Territories for the conduct of one on one interviews and focus groups. The consultations on revising the List were integrated with those undertaken by HealthConsult as part of the project to gather feedback on the NHMRC's discussion paper on good practice for research governance associated with clinical trials. This strategy enabled a much wider range of stakeholders than would otherwise have been possible to have input into the development of the revised List.

(4) **Stage 4:** Analysis of the stakeholder feedback to develop a draft revised List. Finalisation of the revised List and the associated report (this document) after receiving feedback from the NHMRC's Project Manager.

Figure 1.1: Overview of the four stage methodology used



1.4 CONSULTATION PARTICIPANTS

The consultation process was conducted in the period from 10th July to 22nd August, 2014. As already indicated, the process was run in parallel with the consultations for obtaining feedback on the NHMRC's discussion paper on a '*Good practice process for research governance'* associated with clinical trials. This process worked very well as many stakeholders had an interest in, and contributed to, both consultations.

As shown in Table 1.1, there were 26 face to face interviews held with a total of 51 attendees and seven focus Group Sessions held with a total of 101 attendees across five States and one Territory, as part of the consultation process. These stakeholders represented the commercial sector (pharma, device, biotech), potential trial host sites (public hospitals, private hospitals, stand-alone Phase 1 trial facilities), Contract Research Organisations (CROs), Collaborative Research Groups (CRGs) Clinical Trial Alliances/Networks, Third Party Trial Centres, and Institutions (Universities, Research Institutes). In most of these interviews and focus groups, stakeholders provided feedback on both the streamlined research governance and the revision to the standard List discussion papers.

Table 1.1: Number of stakeholders involved in consultation process by jurisdiction

State/Territory	Email Invitations	Focus Group Registrations	Focus Group Attendances	Face-to-face interviews (participants)
New South Wales	155	36	15 &15	11 (21)
Victoria	116	21	9 &21	5(12)
Queensland	81	26	20	2 (5)
Western Australia	42	14	13	2(4)
South Australia	74	12	8	1 (2)
Tasmania	9	0	NA	0
Australian Capital Territory	7	0	NA	4 (7)
Northern Territory	5	0	NA	0
Other (National bodies)*	24	0	0	0
Grand Total	**513**	**116**	**101**	**26 (51)**

*where appropriate representatives from National bodies attended State Focus Groups Sessions or were interviewed face-to-face

As a result of the discussions, HealthConsult received four follow-up written submissions relating to the revision of the List (two from Pharmaceutical companies, one from a private hospital group, and one from a CRG). Additionally, a number of stakeholders took the opportunity to remind HealthConsult that they had made submissions as part of the 2013 IHPA process of developing the table of standard costs for the List. Stakeholders advised that the suggestions they has made for revising the List as part of this public consultation process still represented their views (revising items on the List was not part of the scope of the IHPA study, only the development of a standard costs).

Thus, the consultative process gathered the views of a diverse range of stakeholders involved in the conduct of clinical trials in Australia. HealthConsult reviewed all the written material received (including the submissions made to the 2013 IHPA consultation process) and undertook a thematic analysis of the information produced by the 2014 consultative process in order to develop the revised List of standard items that is presented in Chapter 3.

2

Key principles underpinning revision of the List

This Chapter sets out the key principles that have been used in preparing the revised List. The principles are derived from a thematic analysis of the information provided by stakeholders, in response to the discussion paper, through the interview and focus group processes, and written submissions.

2.1 SCOPE OF THE ACTIVITIES ON THE LIST

Most of the activities on the current List are typically undertaken at or by clinical trial sites (e.g. protocol review, study set-up) but some are not (e.g. preparation of research protocol, trial centre set-up and development). Stakeholders were asked whether the List should be restricted to activities that are typically conducted at clinical trial sites, or whether it should reflect all the activities involved in a clinical trial (including those typically carried out by trial funders/sponsors, Contract Research Organisations (CROs), Clinical Trial Cooperative Groups/Networks and/or Third Party Trial Centres).

Stakeholders pointed out that there was not a not a 'one size fits all' approach. There are clinical trials, particularly investigator initiated trials, where some activities that are commonly undertaken by CROs and/or Third Party Trial Centres need to be performed at trial sites. But, a common and recurring theme in the consultations was that this first redevelopment of the List should focus on 'getting the List right' for the most commonly occurring scenario, as less common scenarios could be dealt with by exception when applying the List. The clear majority view was that the List should focus only on activities that are typically conducted at or by trial host sites.

Conclusion: The revised List is intended to cover activities that are typically conducted at or by trial host sites.

2.2 STRUCTURE OF THE LIST

The current List has a three part sub-structure covering "Clinical – Tests and Procedures'; 'Clinical – Trial Support Services' and 'Non Clinical Services'. Many stakeholders noted that this structure may have led to some duplication of activities on the List, particularly between those listed as 'Clinical – Trial Support Services' and those listed as 'Non Clinical Services'. Stakeholders were asked whether it would be better to base the structure of the revised List on the typical life-cycle (or different stages) of a clinical trial. The possible revised structure discussed was:

- Site Authorisation;
- Site Implementation; and
- Site Close-out.

Stakeholders overwhelmingly favoured this life-cycle approach. Many of them indicated that this was the typical structure that was used when negotiating trial budgets (it was found that there was little used being made of the current List in the trial budget negotiation process, notwithstanding the fact that there was a commitment to do so in future). Only one stakeholder expressed support for retention of the current structure of the List.

Conclusion: The revised List is structured according to the clinical trial life-cycle.

2.3 INCLUSION OF ITEMS THAT ARE DEFINED AS FEES ON THE LIST

The current List has a mixture of items that describe activities and items that describe fees. Stakeholders were asked whether it is reasonable/possible/desirable to remove all the fee items from the List and define all items on the basis of activities undertaken. Stakeholders noted and supported the fact that this proposition was an attempt to, at least partially, address the perceived duplication between the 'umbrella' fee items (e.g. Departmental Establishment/Set-up Fees) and the specific activity items (e.g. investigator meetings, staff training).

Overall, stakeholders favoured a streamlined approach. The majority thought that all items should be described as activities, so that the fee items would be redefined on the basis of the activities that the fee was intended to cover. There was a minority view, which considered that it was possible to refer to all items on the List as fees, so long as there was a clear definition of the activities that the fee was intended to fund. Ultimately, these two views are not inconsistent, so in the interests of having a list of activities that can be subsequently costed, the items previously defined as fees have been redefined as activities.

Conclusion: The revised List describes all items as activities, leaving the question of fees to be determined between the trial funder/sponsor and trial site with reference to the cost of the activity as published by IHPA.

2.4 REDUCE EMPHASIS ON PHARMACY DEPARTMENT ACTIVTIES

Many stakeholders had previously observed that the current List has a strong focus on activities associated with pharmaceutical trials, and hence an emphasis on items that deal with activities undertaken by the pharmacy department. Accordingly, stakeholders were asked whether new items should be added to the List so that it is more inclusive of the clinical trial related activities of supporting departments other than pharmacy (e.g. pathology, imaging).

Most stakeholders did not consider this problem significant, citing the fact that the majority of clinical trials have a pharmaceutical as the intervention. They did, however, note that the pharmacy department related items were presented in considerable detail, but the equivalent level of detail was not present for other supporting departments. In contrast, some other stakeholders considered this situation appropriate; as, particularly for tests and procedures undertaken by supporting departments, there is the opportunity to recover costs through charges for clinical services under the current sub-List 1.

Overall, there was strong support for the concept of more 'bundling' of the items relating to pharmacy department activities (i.e. reducing the number of pharmacy department related items, whilst still reflecting the scope of work required) and also including more specific references to activities undertaken by other supporting departments. The revised List attempts to attain this desired balance, noting that departments providing services (e.g. imaging examinations, pathology tests) have the opportunity to cover the clinical trial related costs of these services through the clinical services items on the List.

Conclusion: The revised List includes changes that 'bundle' pharmacy department activities and make more explicit the activities carried out by supporting departments other than pharmacy.

2.5 EXTRA CLINICAL SERVICES ITEMS ON THE LIST

Within the current 'clinical – tests and procedures' services sub-List, there is no item that reflects the provision of accommodation (overnight or day only) by a hospital, or for use of the day procedure suite

(if the clinical service requires admission as a day patient). The professional services provided during such admissions (medical, nursing or allied health time) are explicitly covered by items under the 'clinical – tests and procedures' sub-List, but the support services (e.g. the provision of a ward bed to which the patient is admitted) are not part of an existing item.

Stakeholders noted that some clinical trials require hospitals to admit (overnight or day) patients for close monitoring and/or tests and procedures that are specific to the trial protocol, and not regarded as standard of care. It was also noted that items 3.3.6 to 3.3.8 in the current List deal with this issue, but they have been interpreted as items that relate to the 'participant related' cost (which may be a co-payment), rather than to reflect the ward accommodation provided by the hospital. Accordingly, stakeholders supported the inclusion of items on the revised List that explicitly provide for trial-specific overnight admission and outpatient/day admission to receive clinical services that are not considered to be standard of care.

Conclusion: The revised List includes an item to explicitly cover ward bed-days (including same-day suite) as a clinical resource.

2.6 ACTIVITIES SPECIFC TO TRIAL INTERVENTION TYPE

It has previously been noted that that the List was constructed mainly with reference to activities involved in the conduct of pharmaceutical clinical trials. Stakeholders were asked to consider whether there was a need to add items to the List, and/or modify the List in other ways, to reflect the variety of interventions that are trialled in a clinical setting. Consistent with the advice provided on the scope of the items on the List, stakeholders felt that the List should not be made too long or complicated by adding items that detail activities that only occur rarely in practice (and typically relate to non-pharmaceutical interventions). Besides the specific pharmacy related items (that normally only apply to pharmaceutical trials), stakeholders considered that the other items on the List will apply to most trials regardless of intervention type (e.g. device trials, other medical trials (e.g. radiation oncology trials and surgical trials), service model trials and non-medical trials (e.g. psychotherapeutic or educational trials).

Conclusion: The revised List does not include any additional activities that apply only to trials with a non-pharmaceutical intervention.

2.7 ACTIVITIES SPECIFIC TO TRIAL SPONSOR TYPE

As the initial List was developed as a result of a recommendation of the report of the Clinical Trials Action Group that investigated the reasons for Australia becoming a less-preferred destination for international pharma trials), the current items were developed with reference to the activities undertaken in pharma sponsored trials. Stakeholders were asked to consider whether items should be added to the List and/or the List should be modified in some other way to better reflect the activities associated with clinical trials where the funder/sponsor is not a pharmaceutical company (i.e. other commercial sponsor, cooperative research group, clinical trial network, or academic institution).

This issue generated considerable discussion in the consultative process, but overwhelmingly the view was that the activities done at, or by, trial host sites associated with clinical trials with non-pharma sponsors are substantially the same as the activities associated with pharma sponsored trials. The difference is in the charging practices of trial sites where many hospitals currently choose to support investigator initiated/academic clinical trials to a greater extent than industry sponsored trials by providing funding through accepting lower fees for items on the List. Stakeholders concluded that the List should not reflect the sponsor type, but instead any issues around non-commercial sponsors should be dealt with when using the revised List and its associated table of standard costs to derive trial budgets.

Conclusion: The revised List does not include any additional activities that apply only to trials with non-pharmaceutical funders/sponsors.

2.8 ACTIVITIES SPECIFIC TO TRIAL SETTING

The sites hosting clinical trials range from hospitals (public or private) through to primary and community services, through to purpose built facilities (particularly for Phase 1 pharmaceutical trials). The List largely focusses on clinical trials conducted in the hospital setting. Stakeholders were asked to consider whether items should be added to the List, and/or the List should be modified in some other way to better reflect trials conducted in non-hospital settings (e.g. in general practices).

Overall, consistent with advice provided on other opportunities to refine the List raised in the discussion paper, stakeholders considered that the purpose (i.e. to have the List and its associated table of standard costs accepted as the authoritative reference point for negotiating clinical trial budgets) would be best serviced by retaining the focus on trials conducted in hospitals (as that is where most trials occur). Two specific issues generated the most discussion. First, the fact that some community based trials require clinicians to travel to see the trial participants. Second, the fact that trials conducted in dedicated Phase 1 facilities require persons (may or may not be patients) to be admitted and closely monitored for an extended period. Ultimately, the majority view was that these circumstances would be best dealt with by exceptions to the List in the context of negotiating budgets for the trials in which they occur.

Conclusion: The revised List does not include any additional activities that apply only to trials in non-hospital settings. Addition of such activities may represent an opportunity for subsequent refinement of the List.

2.9 ACTIVITIES SPECIFIC TO TRIAL PHASE

Pharmaceutical trials are normally categorised into phases from Phase 1 (where researchers test an experimental drug or treatment in a small group of people for the first time to evaluate safety pharmacokinetics, toxicity and tolerability) through to Phase 4 (which are post-marketing approval studies that delineate additional information, including the treatment risks, benefits, and optimal use of a pharmaceutical). As the current List was developed largely with reference to Phase 3 pharmaceutical trials (where the new treatment is compared to the current standard treatment), stakeholders were asked to consider whether items should be added to the List, and/or the List should be modified in some other way to better reflect the activities associated with non-Phase 3 trials.

Again, stakeholders observed that pharmaceutical most trials conducted in Australia were Phase 3, although a few stakeholders noted that this situation is gradually changing with more Phase 1 trials being undertaken. Stakeholders also noted that the List applied equally to Phase 2 trials. There was discussion that there are some key difference for Phase 1 trials, especially first in human trials conducted in dedicated Phase 1 trial facilities. It was noted that by introducing a bed-day item the List became more relevant in this context, as participants in these trials are normally admitted for close pharmacokinetic monitoring. The overall conclusion was that any specifics associated with non-Phase 3 trials could be dealt with by exception and there was no need to add items to the List.

Conclusion: The revised List does not include any additional activities that apply only to non-Phase 3 pharmaceutical trials. Addition of such activities may represent an opportunity for subsequent refinement of the List.

2.10 DEFINING STANDARD OF CARE

It is important to note that, in the context of negotiating a trial budget, the List is intended to be applied only to those clinical services that are over and above standard of care, i.e. the List is not intended to 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. Stakeholders were asked to consider/suggest what type of guidance could be provided on how to differentiate between clinical services that represent standard of care and those that are clinical trial-specific so as to assist users to apply the List as intended.

This issue generated very considerable discussion, as stakeholders recognised the importance and complexity of the problem. It was noted that a clinical service that is standard of care in one trial may not be standard of 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 of 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 discussion about whether standard of care should be defined as part of the trial protocol, and 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 of care in the country where the clinical trial was designed (typically not Australia) may not be standard of care in Australia. So while, ideally, standard of care would be defined in the trial protocol and act as the reference point for discussion, in practice this was not always possible.

Another confounding issue raised by stakeholders was that standard of 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 of 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 of care in the trial context.

Most stakeholders considered that the solution to the problem was to have a clear statement of principles that are published along with the List. One of these principles would be that, in the context of negotiating a trial budget, the costs for clinical services on the List are only intended to be applied for services that are over and above standard of care.

Conclusion: The revised List does not include guidance on determining standard of care but it does include an accompanying statement of principles that make it clear that, in the context of negotiating a trial budget, the costs of clinical services on the List are only intended to be applied to services over and above standard of care.

3

Revised list of standard items for clinical trials

This Chapter presents the revised List of standard items associated with the conduct of clinical trials. To put the revised List into context, it starts with a series of principles that are intended to guide the use of the revised List, and a summary of the structure of the revised List. The full set of items in the revised List with proposed definitions is then presented. Note that **the current exercise was only about reviewing/refining the activities on the standard List, not revising the associated costs, so no costs are presented.**

3.1 PRINCIPLES TO GUIDE THE USE OF THE STANDARD LIST

There are a number of principles that should be noted by users of the standard List of items. 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 table of standard costs (once derived and published by the Independent Hospital Pricing Authority (IHPA)) is to provide an authoritative reference point for the negotiation of a trial budget between a trial funder/sponsor and a health service that wishes to host and/or conduct a trial.
- The List has been developed principally with reference to hospitals (public or private) as the host health service. It is acknowledged that many of the items on the List may also be applicable to other health services that host and/or conduct trials (e.g. community based health services, general practices, and purpose-built Phase 1 Trial Centres).
- The List is only intended to cover activities associated with clinical trials that are undertaken at, or by, a health service that hosts and/or conducts a clinical trial. There are many other stakeholders (trial funders, trial sponsors, Contract Research Organisations (CROs), Clinical Trial Cooperative Groups or Networks, and 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 includes some items where significant contributions to undertaking the activities are made by other than the trial hosts site (e.g. preparation of the HREC application often involves substantial work by the trial funder/sponsor). Such items are included on the revised List, as there is still work required by the trial host sites. The amount of work required by the trial host site does vary depending on the contributions made by other involved stakeholders (e.g. trial funder/sponsor, CROs). This variation should be dealt with in setting the price for these items by negotiation between the trial funder/sponsor and the health service that wishes to host and/or conduct a trial (with reference to the IHPA standard cost).

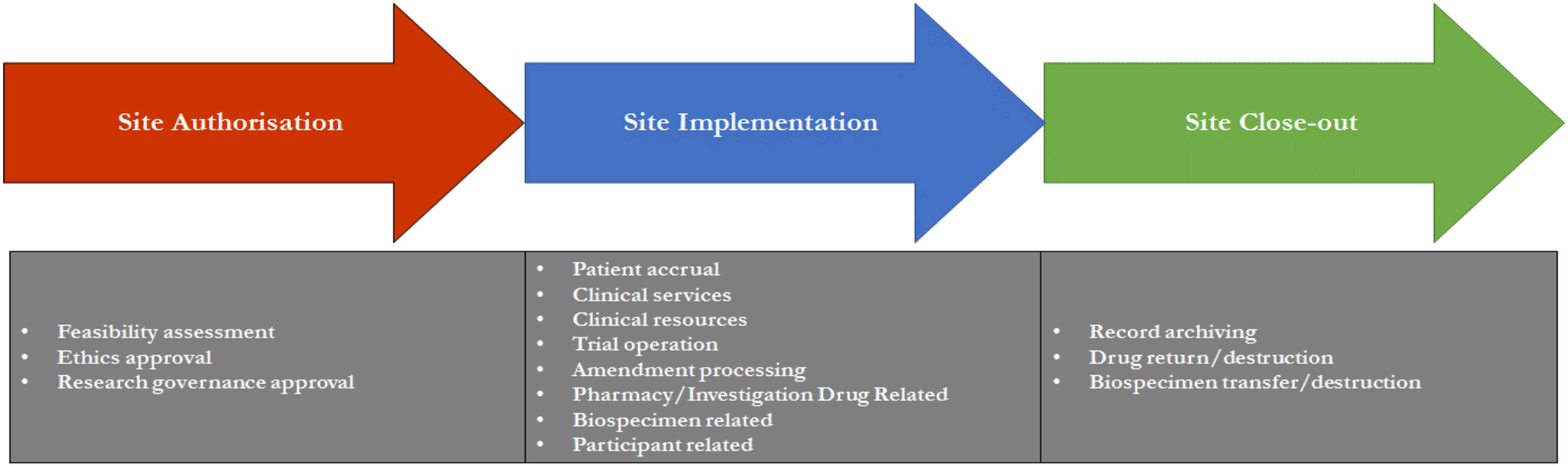
- The List is defined in terms of activities/services, not in terms of prevailing or usual practice fees that are associated with clinical trials. Each activity will have an associated standard cost (once derived and published by IHPA), which represents an independent determination of the typical cost of the activity/service covered by each item. The development of a budget, including the setting of a price for each item, for a specific clinical trial remains a subject for negotiation between the trial funder/sponsor and the health service that wishes to host and/or conduct a trial.
- The List is only intended to cover activities/services that are common to the conduct of clinical trials in health services (not all activities/services may apply to all trials). Activities/services 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 that wishes to host and/or conduct a trial.
- The revised List has been developed following consultation with, and input from, a wide range of stakeholders including potential trial funders/sponsors from the commercial, collaborative research/trial group, and academic sectors. In this process, it was acknowledged that, although the principal point of reference for development of the initial List was commercially funded/sponsored trials, the items now included on the revised List typically apply to all trials (see principle below).
- Many health services currently choose to support investigator initiated/academic clinical trials to a greater extent than industry sponsored trials by meeting a larger part of their costs through charging lower fees. The List is not intended to provide incentives or disincentives to this practice, merely to define the usual activities/services associated with hosting and/or conducting a trial and their typical cost (once published by IHPA). Therefore, 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.
- 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 health services would have provided to any patient for his/her condition if he/she had not been enrolled in the clinical trial are used in the negotiations around setting trial budgets.

As experience grows in the use of the revised List, there may be scope to make it applicable to an even wider range of clinical trials and trial participants. However, prior to any increase in the intended scope, it is considered important that the table of standard costs derived for the revised List becomes an accepted reference point for the negotiation of a trial budget between a trial funder/sponsor and a health service that wishes to host and/or conduct a trial.

3.2 OVERVIEW OF THE LIST OF STANDARD ITEMS

As shown in Figure 3.1, 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. This structure replaces that used in the initial List which was also in three parts, i.e. Clinical – Tests and Procedures, Clinical Trial Support Services, and Non-Clinical Services (the previous items have been retained, where appropriate, and reorganised into the new structure).

Figure 3.1: Illustration of the structure of the revised standard List of items associated with clinical trials



As with the initial List, the revised List also 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 3.1 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 3.1: 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 Close-out	4	5	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**	**43**	

The revised List has 43 items, which compares to 61 items on the original List. In defining the revised List, working definitions have been proposed for each item. It is suggested that these definitions be adopted for costing purposes by IHPA, with some flexibility provided to IHPA to allow refinement of the working definitions where necessary so that they reflect as closely as possible the activities that have been costed for the standard table of costs.

3.3 SITE AUTHORISATION

The first sub-list itemises the activities from feasibility assessment through to site authorisation of a clinical trial. Table 3.2 shows that there are seven items on this sub-list in three different categories. It contains the proposed working definition for each item.

Table 3.2: The NHMRC sub-list of standard items associated with clinical trials for Site Authorisation with proposed working 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 review of the clinical trial protocol within the potential clinical trial host unit (e.g. oncology, respiratory, etc.) and the relevant supporting departments (e.g. pharmacy, pathology, radiology, radiation therapy, other clinical specialties, clinical trials office/governance office, etc.) for scientific merit and local interest. 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 overall 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 and research priorities; ➢ likelihood of being able to recruit suitable types and numbers of patients; ➢ availability of staff and other resources required to undertake the trial; ➢ the capacity and capability of the site to provide the clinical services required by the trial; ➢ the clinical services that will be considered to 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	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 participant information and consent form (PICF), processing of country specific regulatory documents (e.g. the Clinical Trial Notification *(*CTN*)* Scheme form), safety and/or biosafety reports, insurance and indemnity documents, trial agreements, 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, the subsequent consideration of the material provided and the issuance of final ethics approval.

Major category	Item	Reference number	Definitions
Research Governance Approval	Preparation of the SSA application	1.3.1	• The activities associated with the preparation and submission of the Site Specific Assessment (SSA) application form (or equivalent), 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. 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.
	Research governance review	1.3.2	• The activities associated with the review of the research governance application (Site Specific Assessment (SSA) Form or equivalent) by the Research Governance Office (or Research Office or equivalent), including the preparation of any requests for additional information, the subsequent consideration of the material provided, and the issuance of final site authorisation.

3.4 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 3.3 shows that there are 31 items on this sub-list in nine different categories. It contains the proposed working definition for each item.

Table 3.3: The NHMRC sub-list of standard items associated with clinical trials for Site Implementation with proposed working definitions

Major category	Item	Reference number	Definitions
Trial initiation	Start-up meeting	2.1.1	• The activities that occur at the start of the clinical trial as part of the attendance by the sponsor (and/or representative) at the clinical trial site for a series of meetings with personnel to be involved in the trial. Includes any required handover over 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.
	Investigator meetings	2.1.2	• The activities associated with the organisation and the attendance (off trial site and/or by tele/video conference) of the principal or co-investigators and/or clinical trials manager/coordinator at meetings about the clinical trial.
	Departmental set up	2.1.3	• 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, ensuring the processes for randomisation of patients are in place, preparation/communication of 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	2.1.4	• 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.

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, the informed consent process, organising the screening visit (which includes any required assessments and/or tests), and documenting all the recruitment activity (irrespective of the number of potentially eligible participants that fail the screening assessment).
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.
	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 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, GPs, dentists and any other registered medical practitioner.
	Nursing services	2.3.7	• Clinical consultation services provided by enrolled, registered and specialist nurses, midwifes and nurse practitioners.
	Allied health services	2.3.8	• Clinical consultation services provided by recognised allied health professionals (e.g. pharmacists, physiotherapists, dieticians, occupational therapists, psychologists, etc.).
Clinical resources	Investigator time	2.4.1	• The unit labour cost (*fully absorbed hourly rate, i.e. inclusive of overheads)* that will be used to negotiate a fee (i.e. agree on required number of hours) for any activities (clinical or non-clinical) that need to be carried out by an investigator, are specific to the trial, and are not covered by an item listed elsewhere on the standard List.
	Research nurse time	2.4.2	• The unit labour cost (*fully absorbed hourly rate, i.e. inclusive of overheads)* that will be used to negotiate a fee (i.e. agree on required number of hours) 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	2.4.3	• The unit labour cost (*fully absorbed hourly rate, i.e. inclusive of overheads)* that will be used to negotiate a fee (i.e. agree on required number of hours) 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.

Major category	Item	Reference number	Definitions
	Interpreter services	2.4.4	• The unit labour cost (*fully absorbed hourly rate, i.e. inclusive of overheads)* that will be used to negotiate a fee (i.e. agree on required number of hours) for any activities that need to be carried out by an interpreter that are specific to the trial.
	Ward bed days	2.5.5	• The unit cost (*fully absorbed daily rate, i.e. inclusive of overheads)* that will be used to negotiate a fee (i.e. agree on required number of days) for a patient spending time on 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	2.4.6	• The unit cost (*fully absorbed hourly rate, i.e. inclusive of overheads)* that will be used to negotiate a fee (i.e. agree on required number of hours) for a patient spending time in theatre to receive clinical services (including investigations) that are specific to the trial (i.e. the services do not represent standard of care)
Trial operation	Lead site coordination	2.5.1	• 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).
	Administration, monitoring and reporting	2.5.2	• The activities associated with ongoing operation of the trial at the trial site that occur post the trial initiation Phase. Includes liaison with investigators and/or sponsor (including the monitors), preparing materials for, and involvement in, monitor 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.
Amendment Processing	Amendment preparation and submission	2.6.1	• 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 and authorisation	2.6.2	• 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, the subsequent consideration of the material provided, and the issuance of HREC and/or RGO authorisation.
Pharmacy / Investigation Drug Related	Staff training (drug specific)	2.7.1	• 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.
	Drug stocking	2.7.2	• 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.). The drug stocking activity also covers stock management which includes expiry management (e.g. labelling and re-labelling (due to extension of the expiry date of the drug), recording and storing used/returned drugs; data entry associated with returning any expired or unused drugs, returning unused/used drugs to sponsor, etc.).
	Drug preparation and dispensing	2.7.3	• 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 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)	2.8.1	• 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.

Major category	Item	Reference number	Definitions
	Biospecimen storage	2.8.2	• 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.
Participant related	Participant time	2.9.1	• The unit cost (fully absorbed hourly rate, i.e. inclusive of overheads) that will be used to negotiate a fee (i.e. agree on required number of hours) 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 then 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	2.9.2	• 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.

3.5 SITE CLOSE-OUT

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 3.4 shows that there are five items on this sub-list in four different categories. It contains the proposed working definition for each item.

Table 3.4: The NHMRC sub-list of standard items associated with clinical trials for Site Close-out with proposed working definitions

Major category	Item	Reference number	Definitions
Site close-out visit	Preparation for close-out visit	3.1.1	• The activities associated with preparing for the study close-out visit. 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.
	Study close-out visit	3.1.2	• 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 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 dugs 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.

4

Conclusions and suggestions for further refinement

This Chapter sets out some conclusions and suggestions for further refinement of the List. It starts by addressing the NHMRC's requirement to make a distinction between the applicability of items on the revised List, and then makes some suggestions for further refinement, including through the process of IHPA revising the associated table of standard costs.

4.1 DISTINCTIONS BETWEEN ITEMS ON THE LIST (OR NOT ON THE LIST)

The project requirements required the identification of critical distinctions between items on the List (or not on the List). In responding to this requirement, it is highlighted that the stakeholders consulted overwhelmingly expressed a preference for a shorter List that contains a core set of items that are applicable to the activities conducted at, or by, clinical trial sites for the majority of trials. It was thought that this approach would be better than developing a longer List that attempted to cover all activities associated with clinical trials, even though some of them occur infrequently.

In this context, Table 4.1 sets out the questions posed by the NHMRC, and the answers generated through the process of analysing the stakeholder feedback. There is a little duplication between the contents of Table 4.1 and Section 2.2 in Chapter 2, hopefully this duplication adds clarity, in terms of answering the questions posed.

Table 4.1: Responses to the distinctions between items of the List requested by the NHMRC

Areas where disntiction requested	Distinctions identified
• items related to pharmaceutical trials only	• the only items on the revised List that relate specifically to pharmaceutical trials are those activities undertaken by the pharmacy department (2.7.1 to 2.7.3 and 3.3.1)
• items related to medical device trials only	• there are no items on the revised List that relate only to medical device trials
• items related to both pharmaceutical and medical device trials	• aside from the items identified as being pharmaceutical trial specific, all items on the revised List potentially relate to pharmaceutical and medical device trials
• items related to the conduct of commercially-sponsored clinical trials only	• there are no items on the revised List that are considered to relate only to commercially-sponsored trials
• items related to the conduct of academic or 'investigator-initiated' clinical trials only;	• there are no items on the revised List that are considered to relate only to academic or 'investigator-initiated' trials
• items related to the conduct of both commercially-sponsored clinical trials and academic or 'investigator-initiated' clinical trials;	• all items on the revised List potentially relate to commercially sponsored clinical trials and academic or 'investigator-initiated' trials
• items for which the associated costs are incurred by trial host sites only;	• as per the stakeholder advice, the revised List only includes items where, at least, part of the associated cost is incurred by trial host sites
• items for which the associated costs are incurred by the trial sponsor or the sponsor's agent only;	• as per the stakeholder advice, the revised List excludes the items that were on the initial List where the associated costs was typically incurred by the trial sponsor or the sponsor's agent
• items for which the associated costs are incurred by trial host sites and by the trial sponsor or the sponsor's agent	• all items on the revised List potentially have associated costs incurred by trial host sites and by the trial sponsor or the sponsor's agent

Areas where disntiction requested	Distinctions identified
• items that are costs of clinical trials but for which a standard fee is not generally applied or which is otherwise difficult to determine.	• as per the stakeholder advice, fee charging practices vary, but there is a tendency for trial host sites to contribute more to the costs of investigator initiated trials than commercial trials by charging lower fees (particularly for ethics and governance processes) • in the context of a properly conducted activity based costing study with some prospective data collection there is no item on the revised List for which a cost cannot be determined; for items where the predominate practice is for trial host sites to purchase the service, the standard costs can be determined by reference to the typical charge.

4.2 DEVELOPING THE ASSOCIATED TABLE OF STANDARD COSTS

As highlighted above, in the context of a properly conducted activity based costing study, it is considered that a standard cost can be determined for every item on the List. For a few items, where the predominant practice is for trial host sites to purchase the services from an external provider, the standard costs may best be determined with reference to the typical charge.

Unlike the 2013 costing study, it is suggested that IHPA be given the flexibility to make modifications to the items on the List, if it is considered necessary to arrive at a more representative and homogenous cost. Naturally, any change to the items suggested by IHPA should be approved by the NHMRC (as the custodian of the List) before it is implemented for costing purposes.

4.3 DEVELOPING A SUPPORTING COSTING TEMPLATE

A number of stakeholders highlighted the work done in the United Kingdom (UK) by the National Institute of Health Research (NIHR) as part of an initiative to increase the number of clinical trials undertaken in the UK. One part of this work was the production of a costing template (in Excel) that can be used by clinical trial funders/sponsors and potential trial host sites to work up and negotiate a trial budget. Stakeholders, some of whom had recently worked in the UK health system, advised that the template was a valuable tool in standardising the approach to determining clinical trial budgets.

During the consultation process some stakeholders from pharma companies advised that they have already developed costing templates. A few of these templates were 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 costing 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 suggested that the development of such a template be considered as part of the process of revising the table of standard costs associated with the List.