Australian Government

National Health and Medical Research Council

Streamlining the site assessment and authorisation of Clinical Trials

Final Report

June 2017

Contents

Foreword from the CEO of the NHMRC

A healthy Australia depends upon sound, evidence-based healthcare, where both new and routine interventions are assessed for their effectiveness and safety. Clinical trials play a critical role in establishing this necessary evidence for policy makers, practitioners and industry, and can give patients confidence that the efficacy of their treatment has been determined in a rigorous and scientifically robust manner. In addition to the health benefits, clinical trials also bring important career and investment opportunities for Australia.

In a competitive world, it is essential that Australia be seen as an attractive place to conduct clinical trials, with consistent and transparent processes across all jurisdictions. Building on Australia's reputation for high quality and ethical research, NHMRC, the Department of Industry, Innovation and Science, the Department of Health and the States and Territories have been working on a suite of initiatives to improve the clinical trials environment in Australia[1]. Central to this work has been the development of a transparent, timely and efficient clinical trial start-up process.

Through extensive stakeholder consultation, and with the input and guidance of a Research Governance Working Group, NHMRC has developed the Good Practice Process for Site Assessment and Authorisation Phases of Clinical Trial Research Governance (the Good Practice Process).The Good Practice Process spans the clinical trial start-up process from the time a clinical trial sponsor approaches a clinical trial site through to the recruitment of the first participant. It outlines a set of principles and critical success factors for the start-up process, details a set of planning and preparation activities that can better equip a site to commence clinical trials in a timely manner, and proposes a streamlined workflow.

NHMRC piloted the Good Practice Process in 16 clinical trial sites around Australia and provided funding for sites to employ a Clinical Trial Liaison Officer (CTLO) to help implement the process. A majority of sites piloting the process saw significant improvements in timeframes and communication, directly as a result of the engagement of a CTLO. Having a dedicated person to fulfil this role allowed sites to provide a central point of information for clinical trial sponsors and researchers, gather data on start-up performance metrics and ensure the Good Practice Process was effective.

The results have been extremely encouraging, though it is clear that there are certain areas where more streamlining is required. Therefore, whether you represent a clinical trial site or a clinical trial sponsor, or you are a clinical researcher, I encourage you to review the Good Practice Process and the report on the Pilot Program, and consider how you can contribute to improving the clinical trial start-up process in Australia.

I would like to thank everyone involved in the development and piloting of the Good Practice Process. It is a clear demonstration of how working together can lead to the development of evidence-based policy and practice which will ultimately benefit the health of our community.

Professor Anne Kelso AO

Chief Executive Officer

National Health and Medical Research Council

[1] Information on these initiatives is available at https://nhmrc.gov.au/research-policy/clinical-trial-reform.

Executive summary

With input from a research governance working group, in late 2014 NHMRC developed a Good Practice Process for the Site Assessment and Authorisation Phases of Clinical Trial Research Governance (GPP) as a mechanism to reduce clinical trial start-up times within hospitals and other clinical trial sites.[2]

Central to the GPP is the role of the Clinical Trial Liaison Officer (CTLO), who works across clinical trial sponsors, researchers and the research office to facilitate communication, coordinate activities and shepherd applications through an often complex workflow.

Between 2015 and March 2017, the GPP was piloted in two phases. The first pilot phase, conducted at 16 sites across Australia, including public hospitals, private hospitals and universities, sought to determine whether implementation of the GPP with respect to clinical trials sponsored by commercial entities (including pharmaceutical and medical device companies and contract research organisations) could result in streamlined clinical trial approval processes and a reduction in clinical trial commencement times. A report setting out the findings of Phase I was published in October 2016.

This report sets of the results of Phase II of the pilot and provides an analysis of the results from both Phases. In Phase II, 9 of the original 16 sites were funded to continue to collect data and to focus on those areas identified in Phase I. The nine sites were chosen on the basis of whether they had the resources to continue the pilot and whether they could meet the requirements of the second Phase which was to: (i) collect further data across the spectrum of trials; and (ii) focus on a smaller number of areas for improvement.

During the pilots, the resultant time to completion of phases of the site assessment and authorisation process was measured through collection of 10 metrics. Reductions in timeframes for completion were observed in 7 out of the 10 metrics collected following GPP implementation. These metrics included the time for assessment of ethics review and site specific assessment. Only one timeframe, confirmation of the site selection visit by the sponsor following completion of a feasibility assessment, increased significantly. Importantly, this activity is not considered to be in the control of the trial site.

On average, adoption of the process in Phase I and Phase II led to a decrease in trial commencement time by approximately 100 days, an 18.4% decrease. This result indicates that adoption of the GPP, including appointment of a CTLO, can have a significant impact on clinical trial start-up times.

Notwithstanding the excellent results, there remains an opportunity to reduce timeframes further, especially in those stages of the process that are controlled outside the clinical trial site. Notably, the results demonstrate that there is a clear need for sponsors to optimise their processes; and in some of the governance and authorisation phases measured, this will involve working closely with clinical trial sites to ensure efficient communication between the two entities.

[2] Historical information on the Good Practice Process is archived at: http://webarchive.nla.gov.au/gov/20180615152111/https://www.nhmrc.gov.au/research/clinical-trials/development-good-practice-process-site-assessment-and-authorisation-clinica

Introduction

In the 2013/14 Budget, NHMRC was tasked with, 'improving…the timeliness of the approval processes for clinical trials'. To this end NHMRC commenced a project to develop and test a streamlined site assessment and authorisation process for clinical trials. The purpose of this project was to determine whether implementation of this process had a positive impact on the timeliness of clinical trial commencement, measured as the timeframe from the initial approach from the sponsor to the site through to the site authorisation from the CEO or delegate.[3]

Working with key stakeholders and experts in the area, and guided by the NHMRC's Research Governance Working Group, NHMRC developed the *Good Practice Process for Site Assessment and Authorisation Phases of Clinical Trial Research Governance* (the GPP).

The GPP comprised three key components:

- A set of principles and critical success factors for timely site assessment and authorisation.
- A set of planning and preparation activities that can make a site more responsive to commencing clinical trials.
- A streamlined workflow for site assessment and authorisation.

A key component of the GPP was the decision taken to support institutions to appoint a Clinical Trial Liaison Officer (CTLO) as a conduit to facilitate the clinical trial commencement process. Evidence from the UK indicated that having a CTLO dedicated to facilitating communication between the sponsor and site, coordinating activities and shepherding applications through the site assessment and authorisation process greatly improved the timeliness of clinical trial commencement. In order to confirm whether such a role would realise the same impact in Australia, NHMRC provided $50,000 of funding to 16 sites to employ a CTLO to carry out the above activities.

To determine whether implementation of the GPP led to efficiencies in the clinical trial start-up process, the GPP was piloted in two phases at a number of sites around Australia. In Phase I, 16 clinical trial sites around Australia, comprising public hospitals (in both urban and rural/regional Australia), private hospitals and universities were employed. The GPP was implemented over a nine month period and Phase I data was collected over this time. In Phase II, 9 of the original sites were chosen on the basis of their Phase I results, and on whether there was sufficient support from them to continue the pilot. In this Phase, further data was collected so that the entire timescale of a trial from idea to first patient recruitment could be mapped, and also so that a dissection of those areas that proved time-limiting, as judged from the Phase I data, could occur.

The sites were selected on the basis of their interest in conducting these pilot studies, their clinical trial activity and the nature of their site, i.e. whether the site was a public hospital, a private hospital or a university. Noting that the majority of pharmaceutical industry-sponsored clinical trial research is conducted in public hospitals, these hospitals represented the majority of pilot sites. A list of the pilot sites used in Phase I and in Phase II is at **Appendix A**.

Prospective data on the stages of the clinical trial commencement process was collected over this period and compared with data collected prior to GPP implementation. The data from trial sites was then aggregated and analysed to determine any differences in start-up times pre- and post-GPP implementation.

The metrics collected during this period were agreed between NHMRC and the pilot sites. These are shown in Table 1 and also represented diagrammatically. Although the initial aim of the project was to determine the effect of the process on site assessment and authorisation, it was agreed that metrics that related to the time taken to recruit the first patient into the trial would also be collected.

A timeline for the progress of the development and implementation of the GPP is shown in Table 2.

[3] Background to this project is archived at: http://webarchive.nla.gov.au/gov/20180615152111/https://www.nhmrc.gov.au/research/clinical-trials/development-good-practice-process-site-assessment-and-authorisation-clinica

Table 1: Metrics collected during the Pilot studies

Metric	Process Phase	Time period measured
1a-1d	Feasibility Assessment	Date the Confidential Disclosure Agreement is sent to the Principal Investigator to the date the sponsor notifies the site of site selection.
2	Document Preparation	Date the sponsor notifies the site of site selection to the date valid site assessment/ethics review documentation is submitted to the institution.
3	Ethics Review	Date a valid ethics review application is provided to the institution to the date an ethics approval notification is provided to the (Co-ordinating) Principal Investigator.
4	Site Assessment	Date a valid site assessment application is provided to the institution to the date the site assessment is finalised.
5	Site Authorisation	Date a valid site assessment has been finalised to the date the site authorisation is granted by the CEO or their delegate.
6	First Patient Recruitment	Date site authorisation is granted to the date the first participant is recruited into the clinical trial.

Table 2: Development process and timeline

Date	Activity
May 2013	Announcement of Budget measure providing funds for NHMRC to improve the timeliness of the approval processes for clinical trials.
September 2013	National Forum on Clinical Trial Research Governance
December 2013	Streamlined Research Governance meeting
May 2014	National consultation on the draft GPP
October 2014	Outcomes of the national consultation published
November 2014	Review and finalisation of the GPP by NHMRC's Research Governance Working Group
June 2015	Draft GPP published and Phase I of the Pilot Program commenced
Early November 2015	Interim reports provided from Phase I Pilot Program sites
Late November 2015	Meeting of Pilot Program sites and clinical trial sponsors/Clinical Research Organisations.
March 2016	Final reports received from Phase I Pilot Program sites
June 2016	Phase II of the Pilot Program commenced
October 2016	Phase I report published
December 2016	Phase II of the Pilot program completed
June 2017	Draft Phase II report prepared

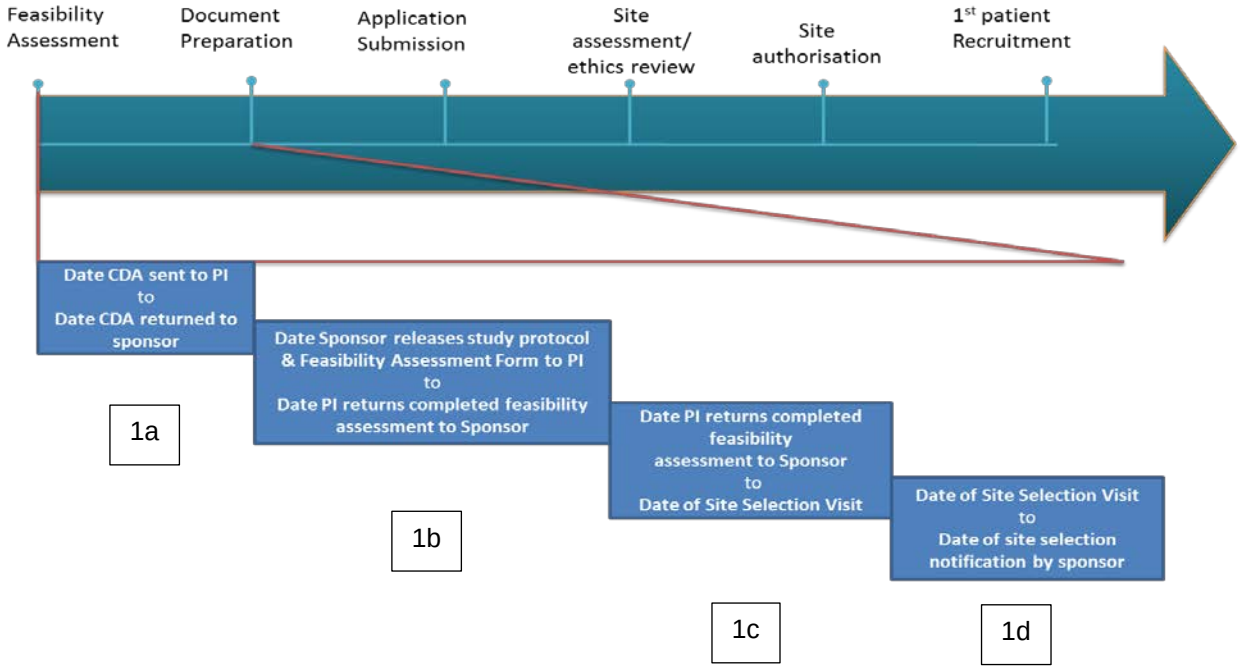
Metrics Collected during Pilot studies

The following metrics were used to determine the impact of the GPP. They span the site assessment and authorisation process from the first measurable indication of a viable approach by a sponsor (the signing of a Confidential Disclosure Agreement) through to the recruitment of the first clinical trial participant. These allowed the entire process to be broken down into its constituent parts, and the precise impact of the GPP to be determined.

These metrics can be used by clinical trial sites to examine their current processes, understand where delays are being introduced and set benchmarks for the site assessment and authorisation process. They align with the workflow outlined in the GPP.

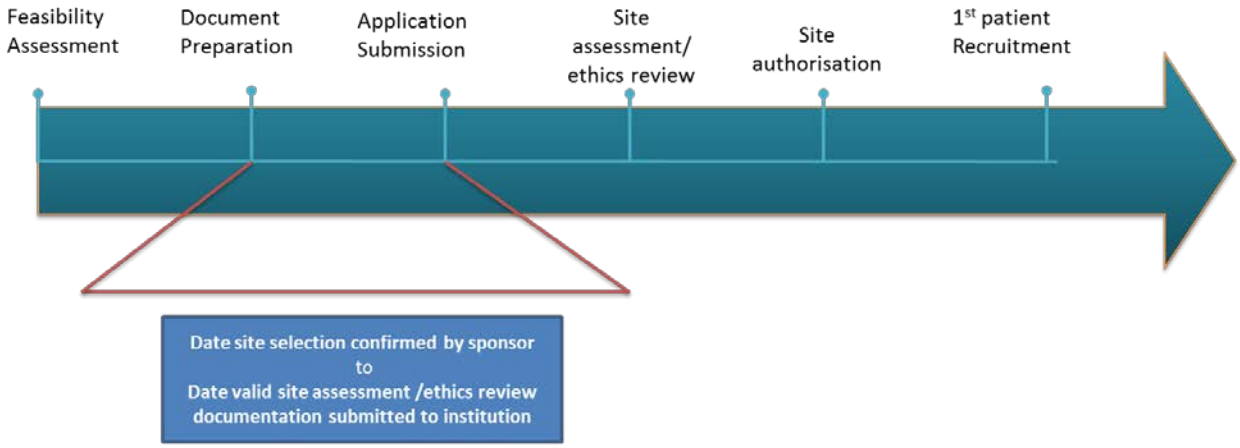
Metric 1a-1d – Feasibility assessment

This metric, broken down into four sub-metrics (1a-1d), measures the time taken for the Feasibility Assessment phase. Overall, it measures the number of days from when the Confidential Disclosure Agreement is sent to the Principal Investigator (PI) until the sponsor notifies the site of its intention to use the site in the trial (site selection).



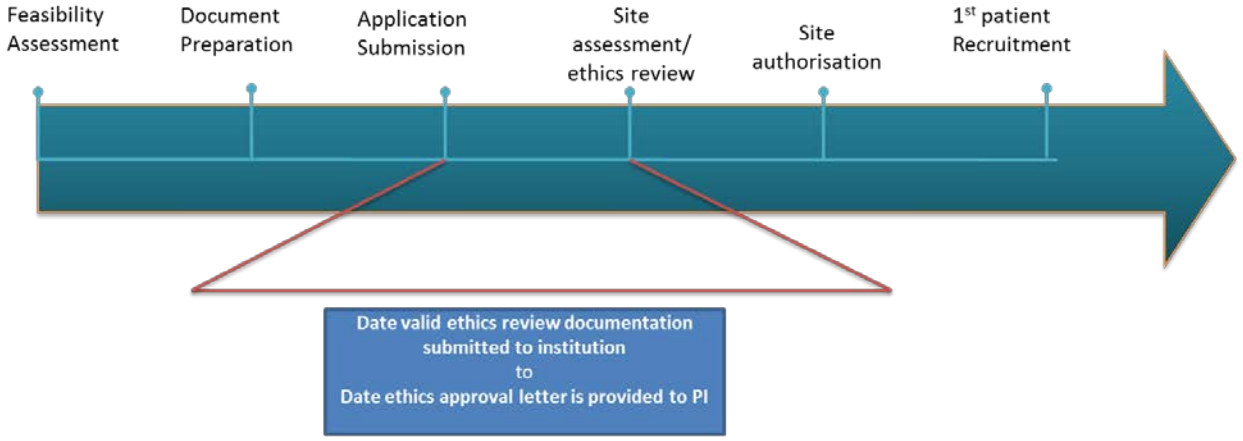
Metric 2 – Document preparation

This metric measures the number of days from when the sponsor notifies the site of site selection until valid site assessment/ethics review documentation is submitted to the institution. In this context a 'valid' application relates to one that has all the required components, but has not yet been reviewed or accepted.



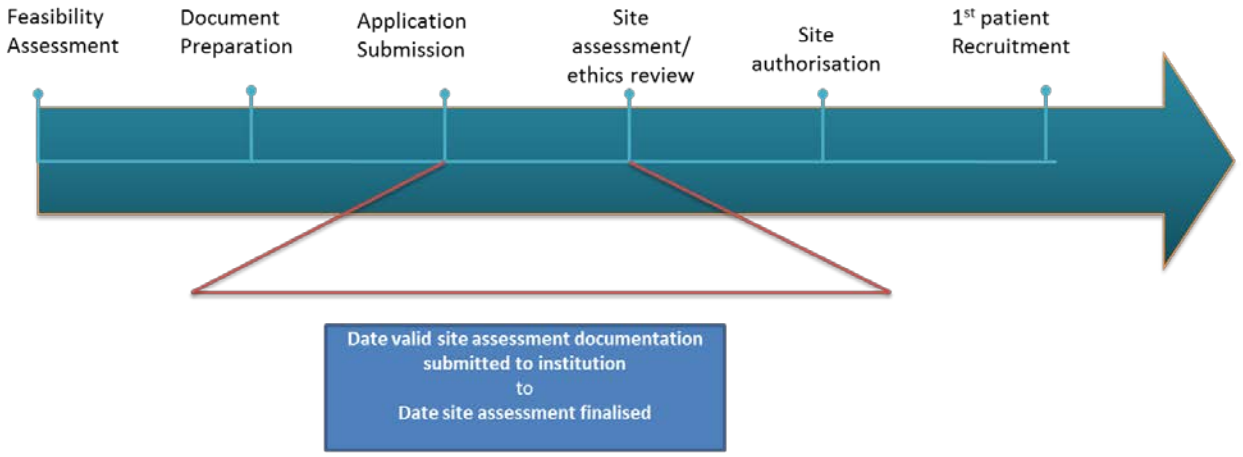
Metric 3 – Ethics review

This metric measures the number of days from when a valid ethics review application is provided to the institution until an ethics approval notification is provided to the Principal Investigator. In this context a 'valid' application relates to one that has all the required components, but has not yet been reviewed or accepted. It is considered best practice, when practical, to complete the ethics review and research governance review in parallel, hence metric 3 and metric 4 span the same timeframe.



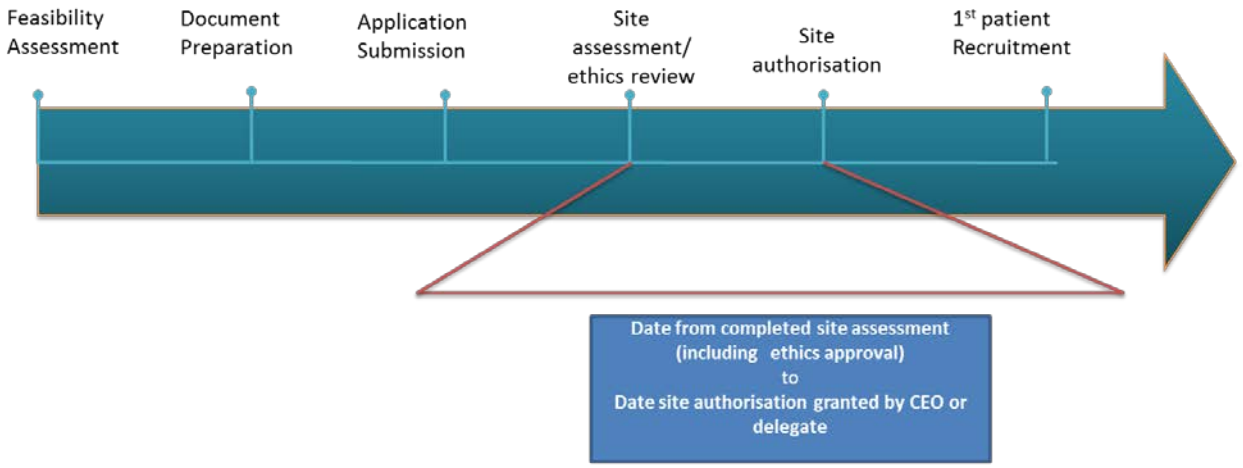
Metric 4 – Site assessment

This metric measures the time taken for the site assessment phase. It measures the number of days from when a 'valid' site assessment application is provided to the institution until the site assessment is finalised. In this context a 'valid' application relates to one that has all the required components, but has not yet been reviewed or accepted. It is considered best practice, when practical, to complete the ethics review and research governance review in parallel, hence metric 3 and metric 4 span the same timeframe.



Metric 5 – Site authorisation

This metric measures the time taken for site authorisation. It measures the number of days from when a valid site assessment (which may include the granting of ethics approval, depending on multi-site ethics approval arrangements) has been finalised (that is, one that has been reviewed, found to be acceptable and a recommendation is made to the CEO or their delegate that they approve the application) until the site authorisation is granted by the CEO or their delegate.



Metrics 6 and 7 – Date of site authorisation to date of first patient recruitment

This period uses two metrics to measure the time taken for the first participant to be recruited into the clinical trial. Metric 6 measures the number of days from when site authorisation is granted to the time that site activation by the commercial sponsor occurs. This period was not overtly measured during Phase I, but the conduct of Phase II has enabled collection of this information. Metric 7 measures the period from site activation until the first participant is recruited into the clinical trial.

These time periods are not traditionally considered to be a part of the site assessment and authorisation process, but are essential metrics to ensure that the clinical trials are progressing as planned. The time taken to first patient recruitment is also a key metric for clinical trial sponsors, as the timeliness of the site assessment and authorisation process is somewhat immaterial if it then takes much longer than expected to recruit the participants.

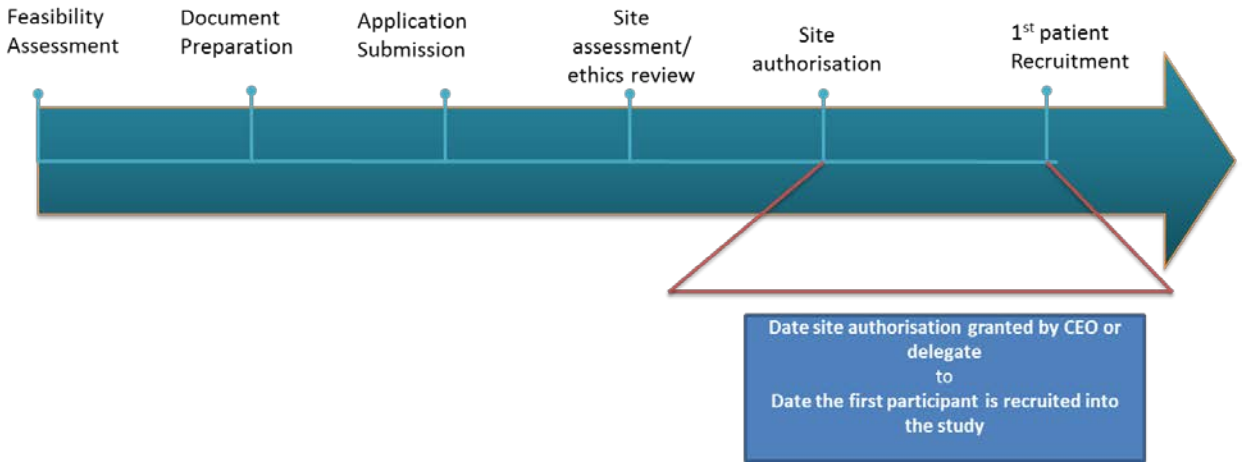


Table 3: Aggregated Phase I and Phase II data		Pre GPP				Post GPP						
Metric Number		**Metric Description**		**N**	**Mean**	**SD**		**N**	**Mean**	**SD**		**Mean change**		**Reduced variation?**
1a		Date CDA sent to PI TO Date CDA returned to Sponsor		149	20.6	94.2		187	13.6	37.8		**33.9% decrease**		**YES**
1b		Date Sponsor releases study protocol and feasibility assessment form to Principal Investigator (PI) TO Date PI returns completed feasibility assessment to Sponsor		128	14.6	41.4		165	14.5	27.1		**0.9% decrease**		**YES**
1c		Date PI returns completed feasibility assessment to Sponsor TO Date of Site Selection Visit		132	58.2	79.8		149	72.8	110.7		**25.1% increase**		**NO**
1d		Date of Site Selection Visit TO Date of Site Selection Notification by sponsor		156	36.6	59.8		196	27.6	47.8		**24.4% decrease**		**YES**
2		Date site selection confirmed by sponsor TO date valid site assessment/ ethics review documentation submitted to institution (whichever is later)		95	199.6	141.9		127	155.5	86.5		**22.1% decrease**		**YES**
3		Date valid ethics review documentation submitted to institution TO Date ethics approval letter is provided to PI		233	59.9	54.6		306	56.4	53.7		**5.9% decrease**		**YES**
4		Date valid site assessment documentation submitted to institution TO Date site assessment finalised		273	21.9	41.5		457	10.7	25.9		**51.2% decrease**		**YES**
5		Date from completed site assessment (including ethics approval) TO Date site authorisation granted by the CEO or delegate		269	4.4	27.2		370	1.8	7.3		**58.4% decrease**		**YES**
6		Date from site authorisation granted by the CEO or delegate TO Date of site activation by Sponsor		214	44.9	53.1		210	36.7	39.9		**18.3% decrease**		**YES**
7		Date of site activation by Sponsor TO Date the first participant is recruited into the study		169	65.5	78.8		91	40.7	66.9		**37.9% decrease**		**YES**

Table 4- Allocation of Responsibility for Activities

Metric Number	Activity Description	Change in time	Reduced variation?	Main responsibility
1a	Date CDA sent to PI TO Date CDA returned to Sponsor	**33.9% decrease**	**YES**	**Site**
1b	Date Sponsor releases study protocol and feasibility assessment form to PI TO Date PI returns completed feasibility assessment to Sponsor	**0.9% decrease**	**YES**	**Site**
1c	Date PI returns completed feasibility assessment to Sponsor TO Date of Site Selection Visit	**25.1% increase**	**NO**	**Sponsor**
1d	Date of Site Selection Visit TO Date of Site Selection Notification by sponsor	**24.4% decrease**	**YES**	**Sponsor**
2	Date site selection confirmed by sponsor TO date valid site assessment/ ethics review documentation submitted to institution (whichever is later)	**22.1% decrease**	**YES**	**Sponsor and site**
3	Date valid ethics review documentation submitted to institution TO Date ethics approval letter is provided to PI	**5.9% decrease**	**YES**	**Site**
4	Date valid site assessment documentation submitted to institution TO Date site assessment finalised	**51.2% decrease**	**YES**	**Site**
5	Date from completed site assessment (including ethics approval) TO Date site authorisation granted by the CEO or delegate	**58.4% decrease**	**YES**	**Site**
6	Date from site authorisation granted by the CEO or delegate TO Date of site activation by Sponsor	**18.3% decrease**	**YES**	**Sponsor**
7	Date of site activation by Sponsor TO Date the first participant is recruited into the study	**37.9% decrease**	**YES**	**Site**

Results and Discussion

Implementation of the Good Practice Process

The purpose of the pilot program was to determine the degree of efficiency that could be realised by implementation of a best practice approach to site assessment and authorisation of clinical trials. The pilot was split into two phases. Phase I involved the use of 16 sites representing public, private and university entities. This Phase, funded by money from the *Expediting clinical trials in Australia* initiative, enabled collection of data across some activities required before commencement of trials, but was limited by the length of time taken to commence the trial (an average of 526 days). Following the conclusion of Phase I and the collection and analysis of data, it became clear that further data collection was required to ensure that any conclusions made about the commencement of trials in Australia would be robust.

Phase II involved nine sites, which were a subset of those used in Phase I. The nine sites were chosen on the basis of whether they had the resources to continue the pilot and whether they could meet the requirements of the second Phase which was to: (i) collect further data across the spectrum of trials, and (ii) focus on a smaller number of areas for improvement. The only difference between Phase I and Phase II in terms of data collection was a separation of metric 6 (time from site authorisation to first patient recruitment) into two separate metrics: (i) time from site authorisation to site activation; and (ii) time from site activation to first patient recruitment. This separation is important as it facilitates a better attribution of responsibilities within commencement activities (see Table 4 for details).

Table 3 provides the aggregated results from Phase I and Phase II. For eight of the nine time points measured, there was a decrease in the time taken to complete the process following implementation of the GPP of greater than 20% in each case. Overall, this resulted in an average decrease of around 100 days in the clinical trial commencement process.

Overall, the time taken for clinical trial commencement decreased from an aggregated mean time of 526 days to 430 days. This is exciting progress, but reinforces the need to keep working to reduce timeframes where possible.

Summary of results

Significance

Table 3 shows that following the completion of Phase II, time points were able to be collected from a large number of trials across the range of commencement activities. With one exception, that being the time from site activation to first patient recruitment, more data was able to be collected during the pilots than was made available beforehand.

Table 3 also shows that only 2 of the time points have a significantly high standard deviation, reducing the significance of their contribution. In metric 1c, the time from the date PI returns completed feasibility assessment to Sponsor to the date of the site selection visit, the time post-GPP has increased even from the result in Phase I. The reasons for this are discussed below. However, it is notable that, at least from the perspective of improving processes within clinical trial sites, this metric is one that is controlled by sponsors and, as such, cannot be influenced to any great degree by sites. The robustness of all other results has increased in all other cases, indicating an increased efficiency in these activities.

Key Reductions in time

While all other time points have decreased, a number have decreased more significantly. The marked decrease in times of time points 1d, 2, 4 5, 6 and 7 is encouraging and reflects process improvement. For example, in metric 4, the mean time taken to complete the site assessment review has decreased by approximately 50% to 10.7 days. While anecdotally, some institutions can complete this phase in around 1-2 days, it nevertheless negates common arguments made around the inefficiency of site assessment. Taken together with metric 3, time taken for ethics review, the combined time period for this part of the process is around 69 days.

Increases in time- Feasibility assessment

Feasibility assessment is a stage of the research governance process that is often overlooked as a mechanism to ensure that there are appropriate resources for a trial and also as a means to prevent wastage of resources on trials that will not be able to be completed. One part of the feasibility assessment which was measured during the pilot studies was the timeframe measured from when the PI returns the completed feasibility assessment to the Sponsor to the date Site Selection Visit (metric 1c). This metric increased over the period of the GPP from a mean of 58-78 days. Even given the variability in the timeframes associated with the activity, a process which occupies this length of time is clearly one that should be considered for optimisation. The most likely explanation for the failure of the GPP to reduce this timeframe is that, as the date of the site selection visit is wholly a decision of the sponsor, this activity is not impacted by process improvement at a site level. As such, any change in timeframe is independent of the site. If this assumption is correct, this observation demonstrates that increases in timeframe, and timeframe variability can result from activities that are outside the control of the site. Thus, there is an opportunity to work with sponsors and Contract Research Organisations to determine ways in which the timeframe for this metric to reduce this significant time delay.

Impact on critical metrics

Ethics and site-specific assessment review

The metrics collected during the GPP include a number which have been the focus of much work in Australia. Two in particular are notable. These are the time taken for ethics review (metric 3) and the time for finalisation of the site-specific assessment (metric 4). The availability of data for these metrics reflects both their position in the clinical trial commencement process and their importance in providing an indication of the 'research governance' timeframe.

The time taken to complete both processes has been shown to decrease following GPP implementation. The timeframe related to ethics review is significant because it is within the proposed 60 day limit set in the report of the Clinical Trials Action Group ('the CTAG Report') in 2011[4]. Significant attention has been placed on this timeframe as one that is a barrier to timely clinical trial commencement. However, the results demonstrate that this phase seems to be completed effectively through use of the GPP.

While the combined timeframe of 69 days for metrics 3 and 4 exceeds the 60 day benchmark envisaged in the CTAG report of the Clinical Trial Action Group[5] it is important to note that this pilot project did not specify the use of parallel review, where both ethics and site assessment information is considered simultaneously, as compared to sequential review, where the ethics review process is completed before the site assessment process begins.. Secondly, it is important to understand that these results are conservative and that they are simply an aggregated mean. This means that in many cases, the time taken for this process would be significantly less than the 69 days quoted. For example, the range of times for ethics review range from 7 days to 328 days with a median of 56 days. Parallel review would likely result in reduced timeframes and, as such, should be considered in all cases as far as possible.

At this time, while it may be possible to optimise some processes further, in many cases, the times will already have been optimised. For example, one site reported an average time for site authorisation of less than two days, and another, 7 days for ethics review. As times for ethics review are to some extent fixed, in most cases, the minimum time for review would be the time required for consideration by a scientific review committee, in addition to the two week time required for submission and the time for review and provision of approval letter. Anecdotally, approval in most cases is not provided on first review, thereby requiring some reconsideration. An obvious means to reduce timeframes, therefore, lies in the quality of information that is provided to an ethics committee in the first instance. It is tempting to speculate on whether the recent launch of the Human Research Ethics Application (HREA), by the NHMRC, will lead to decreased review times, based on the provision of comprehensive information in the first place negating the need for multiple (and time-consuming) revision and re-review.

---

[4] *Clinically competitive: boosting the business of clinical trials in Australia*. (2011) Report of the Clinical Trial Action Group http://www.industry.gov.au/industry/IndustrySectors/PharmaceuticalsandHealthTechnologies/ClinicalTrialsActionGroup/Pages/Library%20Card/Clinical_Trials_Action_Group_Report.aspx.

[5] Ibid.

Site authorisation, Site Activation and First participant Recruitment

Even though the time taken for ethics review and site-specific assessment has decreased, this must be considered in the context of the remainder of the process. As highlighted in Tables 3 and 4, the subsequent stages offer some room for improvement and optimisation. Pleasingly, the time taken for site authorisation has decreased to a mean of 1.8 days, reflecting an ability to either upwardly manage effectively, or implementation of a process that incorporates appropriate delegation for sign off this activity.

The time to site activation (metric 6) is an activity where they may be some room for improvement. Like site selection, this activity is considered to be the sole responsibility of the sponsor and represents a period where the finalisation of a number of steps may have to occur. These have been listed[6] as:

- Negotiating a financial contract
- Providing clinical supplies
- Obtaining other documents from site (CVs, financial disclosure, etc)
- Set-up or installation of specialist equipment, such as dedicated drug storage facilities

While site activation can incorporate a number of steps considered earlier in the GPP, those listed above remain the key rate limiting steps. In particular, contract and budget development[7]. Though these aspects have been considered earlier in the process, providing supplies and other resources in an efficient manner may remain a barrier to site activation. The average time taken for site activation is 36.7 days, a decrease of 8.2 days or 18%.

The final metric collected represented the time from site activation to first patient recruitment. Much information has been collected in this area, including the production of a report by the Department of Health on the barriers to Recruitment and Accruals in Clinical Trials[8]. While it is recognised that there are barriers that must be overcome through the use of novel recruitment strategies, that is outside the scope of this report. However, what is noticeable is that following implementation of the GPP, the time taken for this activity decreased. Once again, it is possible that some part of this activity can be done in parallel with site activation, thereby decreasing time to clinical trial commencement further

Many of the sub-processes within these phases can be accomplished in parallel and where possible this should be the aim, rather than having sequential phases. The data collection was not able to elucidate instances where these stages overlapped, so that the overall average timeframe post-GPP implementation (430 days) may be slightly less.

Impact of the Clinical Trial Liaison Officer

The impact of the Clinical Trial Liaison Officer (CTLO) was a key contributor to the positive effect of GPP implementation. This is not unexpected as similar, though perhaps more dramatic, results were obtained in the UK when this role was introduced. The reason for the success of this approach lies in the role and ability of the CTLO to form a conduit between researchers, sponsors and hospital/ site administrators. By performing these functions, CTLOs can speed up the review and approval processes. Although timeframes observed during the GPP have been shown to decrease significantly, timeframes in the UK were found to decrease by a greater amount, indicating that other processes may be able to be streamlined, and additionally that the UK may be able to influence process standardisation and workflow efficiencies to a greater extent than Australia.

Sites that introduced the CTLO position observed that the impact of the CTLO included the following aspects:

- The CTLO was able to remove a significant burden from investigators by being the first point of contact for sponsors, and resulted in faster response times.

[6] Gen Li *Site Activation: The key to more efficient trials (2008) PharmExec.com* http://www.pharmexec.com/site-activation-key-more-efficient-clinical-trials.
[7] Diego A. Martinez et al., *Activating clinical trials: a process improvement approach*. (2016) Trials. 2016; 17: 106. Published online 2016 Feb 24. doi: 10.1186/s13063-016-1227-2.
[8] *Scoping and analysis of recruitment and retention in Australian clinical trials* Final report from the Department of Health.(2016) < http://www.health.gov.au/internet/main/publishing.nsf/Content/Clinical-Trials>.

- The CTLO has the potential to increase the alignment of research activity with the organisation's strategic objectives.
- The CTLO was able to determine the gaps that cause delays in trial commencement by analysing metrics and making recommendations to streamline the relevant processes.
- The CTLO was effective in increasing awareness within the organisation around factors that can be targeted to support clinical trials.
- The CTLO could facilitate open communication with sponsors and CROs on site capability and performance.

If implemented widely, the effect of the CTLO could positively effect change within the organisation with respect to the importance of clinical research and the efficiency with which it may be conducted. However, only by resourcing this position effectively at major clinical trial sites can efforts at reaching the necessary level of efficiency to be globally competitive be realised.

The following key areas of focus are considered to be those which can be part of the role of the CTLO:

Reviewing and streamlining a site's clinical trial start-up processes.

- Working with site staff to assess infrastructure and staff availability required for the conduct of clinical trials with each department.
- Implementing the GPP and monitoring progress, including performance measurements.
- Developing resources related to the GPP and clinical trial start-up process, including Standard Operating Procedures and Key Performance Indicators.

Providing a central point of contact and information, and improving communication between sponsors, researchers and site administrative staff.

- Working to establish a central repository for the documentation required by external sponsors.
- Working to communicate site research capabilities and areas of clinical interest to clinical trial sponsors.
- Establish contacts and relationships with all key stakeholders, including clinical trial sponsors, contract research organisations, researchers and administrators.

'Shepherding' applications through the site assessment and authorisation process.

- Working with the Principal Investigator and Site Staff to ensure they can demonstrate that they can recruit sufficient numbers of participants.
- Working with clinical trial sponsors to ensure all relevant documentation is available to conduct the capacity planning exercise with local service departments.
- Working with the Principal Investigator and site staff to assess the proposed budget and clinical trial agreement.
- Tracking the progress of individual applications through the site assessment and authorisation process and intervening as necessary to minimise delays.

Conclusions

NHMRC has completed a two-phased pilot of its GPP. This enabled consolidation of a sizeable dataset across all activities involved in the commencement of a commercially sponsored clinical trial in Australia. By implementing the GPP, clinical trial commencement time, based on an aggregated mean of data from each of the sub-processes analysed, was reduced by 96 days 100 from 526 days to 430 days.

At first blush, the mean time taken for clinical trial commencement would seem to be excessive, especially when a comparison of the 70 day benchmark set by the UK NIHR with respect to the period from submission of a valid application to first patient recruitment is considered[9]. The results from this study indicate that the mean time for this period in Australia was 146.3 days, having been reduced from 196.6 days, a reduction of 27%. Though impressive, two other factors should be considered when interpreting all of the data: (i) no information was collected on whether these activities were collected in parallel or sequentially; and (ii) the data is a conservative estimate as it is an aggregation of all time-points from trials, including those that were significant outliers. Thus it is likely that time taken for the commencement of the majority of trials would be significantly less than the 430 days. This is important because anecdotally, some CROs can consistently facilitate trial commencement within 180 days, a benchmark that would be globally competitive.

It is clear from the data that implementing the GPP, including employing a Clinical Trial Liaison Officer, can significantly reduce the time taken for clinical trial commencement. Of the ten metrics being measured in the pilot program, seven showed a significant reduction in the number of days taken for that stage of the clinical trial start-up time following the implementation of the GPP. Of these seven metrics, six also showed a reduced variability following the implementation of the GPP.

Combining all the average times in the above table, implementing the GPP can save around 100 days (Pre = 526 days, Post = 430 days) a 19 % decrease in timeframe. This figure differs from that observed from analysis of the Phase I data (410.5 days). This result is solely down to the variability of one metric (metric 1c- Time from the date that the PI returns the completed feasibility assessment to Sponsor to the Date of Site Selection Visit. While it is disappointing that this timeframe has increased, thereby reducing some of the gains made elsewhere, it must be remembered that this activity is one that is considered to be solely the responsibility of the sponsor. In addition, as there was an increase in variability of the results from this metric, it indicates vastly different processes and efficiencies occur in a company specific manner.

Not only can the GPP reduce the timeframe of the clinical trial start-up process, it can increase predictability. A reduced variability was seen in nine of the ten metrics. Reduced variability in timeframes will provide more predictability around how long a certain stage of the clinical trial start-up process will take. Some of the areas for future focus remain those highlighted in the previous version of this report. As such they are reiterated again as follows:

- For some sites, the process represents a significant cultural change, and research offices are experiencing difficulty in engaging researchers and departments;
- Communications with sponsors can still be sporadic, or not include the research office at all;
- Budget negotiations, contract agreement and insurance matters still appear to present a significant barrier to the streamlining of clinical trials site assessment and authorisation;
- The need to collect additional metrics has, for some sites, highlighted inflexibility in IT systems, often necessitating manual data collection and curation, which takes a significant amount of time and effort.

As noted above, following the GPP, the overall average start-up time was 430 days. This still provides a number of opportunities for improvement. From the data presented, the average time taken from the confirmation of site selection by the sponsor to the submission of valid site assessment/ethics review documentation (whichever is later) to the institution (Metric 2), even after implementing the GPP, was considerable, at 155.5 days. This stage would appear to be an ideal candidate for further exploration to understand where and why delays are occurring. In

[9] *The* **NIHR Performance in Initiating** *and Delivering Clinical Research (70 day benchmark) and the NIHR Clinical Research Network High Level Objectives: a description of purpose, definition and differences.*<https://www.nihr.ac.uk/02.../NIHR-Metrics-Comparison-CCF-December-2013.pdf>

addition, looking to streamline the site activation stage and continue to decrease patient recruitment times will be of significant benefit. Given that the greatest variability in the entire process appears to occur within activities that are largely the responsibility of sponsors, it is perhaps time to move away from the mantra that governance takes too long and instead focus on working with sponsors who are able, through having regional autonomy, to improve the way in which they conduct their side of the site assessment and authorisation process.

Appendix A – GPP pilot program sites (Phase I)

The Canberra Hospital (ACT)

Royal North Shore Hospital (NSW)

Melbourne Health (VIC)

Monash Health (VIC)

Barwon Health (VIC)

Peninsula Health (VIC)

Royal Children's Hospital Melbourne (VIC)

St Vincent's Hospital Melbourne (VIC)

Princess Margaret Hospital (WA)

Metro South Hospital and Health Service (QLD)

Sunshine Coast Hospital and Health Service (QLD)

Queensland University of Technology (QLD)

Central Adelaide Local Health Network (SA)

Northern Adelaide Local Health Network (SA)

Women's and Children's Health Network (SA)

The University of Tasmania/Royal Hobart Hospital/Launceston General Hospital (TAS)

GPP pilot program sites (Phase II)

Royal North Shore Hospital (NSW)

Melbourne Health (VIC)

Monash Health (VIC)

Royal Children's Hospital Melbourne (VIC)

St Vincent's Hospital Melbourne (VIC)

Princess Margaret Hospital (WA)

Metro South Hospital and Health Service (QLD)

Central Adelaide Local Health Network (SA)

The University of Tasmania/Royal Hobart Hospital/Launceston General Hospital (TAS)

Attachments

Attachment 1 – Good Practice Process for Site Assessment and Authorisation Phases of Clinical Trial Research Governance

Good Practice Process for Site Assessment and Authorisation Phases of Clinical Trial Research Governance

v2.3

September 2016

Version control

Version	Date	Author
1.0	1 June 2015	NHMRC
1.1	6 July 2015	NHMRC
2.0	25 July 2016	NHMRC
2.1	10 August 2016	NHMRC
2.2	31 August 2016	NHMRC
2.3	28 September 2016	NHMRC

Introduction

Clinical trials are an important element of health and medical research and are required for the evaluation of the safety and effectiveness of interventions or treatments. To ensure the safety of research participants, the integrity of each research project, the effective use of research funds and the responsible conduct of research, all clinical trials are subject to a process of institutional assessment prior to their commencement. The framework, systems and processes leading to the authorisation and commencement of a clinical trial at a research site are commonly referred to as 'research governance'.

A wide range of stakeholders, including the pharmaceutical industry and clinical trial practitioners have raised concerns about the length of time taken to commence clinical trials in Australia, and particularly about the time taken to complete research governance in Australia. Reducing delays in the commencement of clinical trials will help to increase Australia's attractiveness as a destination for global sponsors to conduct clinical trials.

In order to alleviate this situation, the Australian Government, through the National Health and Medical Research Council (NHMRC) is taking steps to streamline the research governance process in order to reduce delays in clinical trial commencement. The expertise of key stakeholders from public and private hospitals, jurisdictions, industry, academia and medical research institutes, and organisations involved in conducting clinical trials in Australia has been utilised to develop a Good Practice Process to enable efficient and effective site assessment and authorisation of clinical trials. It is believed that if this Process is adopted, it will lead to a decrease in the time taken for clinical trials commencement.

In developing the Good Practice Process, two key improvements that would reduce the time taken to commence clinical trials have been proposed by the development group:

1. An increased commitment to planning, preparation and ongoing support for clinical trials within those institutions where clinical trials are conducted; and

2. A change to the order in which the activities within the assessment and authorisation process are conducted, whereby key assessment activities occur much earlier.

- The proposed order in which activities can be completed in the Good Practice Process represents a paradigm shift from the way in which the site assessment and authorisation process has traditionally been conducted. The majority of site assessment activities can be completed not just at the same time as, but prior to, ethical review being undertaken, rather than be delayed until all documentation is submitted. In this way, ethics and governance review can be carried out in parallel rather than sequentially.

The Good Practice Process comprises three parts:

- Principles and Critical Success Factors: A set of high-level principles and critical success factors that set out the ideal features of a research governance process.
- Planning and Preparation activities: A group of activities that apply to all clinical trials rather than be specific for a given clinical trial, and support the site's ability to attract, accept and promptly commence clinical trials.
- Site Assessment and Authorisation activities: Activities that set out a process that will streamline the review and approval of a clinical trial.

To ensure the Good Practice Process is both implementable and realises improvements in clinical trial start-up times, NHMRC has piloted the Good Practice Process in 16 clinical trial sites across 7 states and territories.

As part of the pilot program, NHMRC also provided each site with seed funding to employ a Clinical Trial Liaison Officer. The role of the Clinical Trial Liaison Officer includes reviewing and streamlining the site's clinical trial start-up processes, providing a central point of contact between sponsors, researchers and site administrative staff and 'shepherding' applications through the site assessment and authorisation process.

The pilot program has demonstrated that implementing the Good Practice Process, including employing a Clinical Trial Liaison Officer, can significantly improve clinical trial start-up times. A report detailing the improvements realised under the Good Practice Process is available on the NHMRC website.

Definitions

Site - an institution (or group of institutions) that resource, conduct and manage clinical trials that come under one final research governance authorisation sign off.

Sponsor – an individual, organisation or group taking on responsibility for securing the arrangements to initiate, manage and finance a study.

Research Governance - a process used by an organisation for the oversight, assessment, authorisation and monitoring of research conducted at one or more of its sites or under its auspices[10].

Site Assessment - a process that assesses research against institutional requirements.

Site Authorisation - a determination by an organisation that a research project to be conducted at one or more of its sites or under its auspices satisfies organisational requirements and may commence at the site/s over which it exercises its authority. Site authorisation is the outcome of the site assessment process.

Ethical review - a process to explore the ethical issues presented by, and implications of, a research project.

Ethical approval - a determination by an ethics review body that a research project satisfies ethical standards and requirements, including, but not limited to, the NHMRC/ARC/AVCC National Statement on Ethical Conduct in Human Research.

Feasibility Assessment- a process to determine whether a clinical trial site has the capacity and capability, including resources, expertise and participant pool to carry out a specific clinical trial.

[10] A research governance framework includes good research culture and practice, organisational strategy, role definition and accountabilities, risk, resource and financial assessment and management, compliance with legal, regulatory and contractual requirements, competencies and training of personnel, site assessment, scientific review, ethical review and approval, site authorisation, monitoring of research, and management of conflicts of interest, complaints and allegations of research misconduct.

Principles and Critical Success Factors

Overview

A number of principles and critical success factors underpin the Good Practice Process. These are relevant to any existing research governance process, and are intended to address key areas to improve the research governance approval process.

Principles

Timeliness

Principle: Minimise timeframes.

Sites should seek to minimise the timeframes for activities undertaken during the research governance process. By recording the time taken for key components of the research governance process to take place, sites can use empirical measurements to identify where delays occur, and the impact of subsequent measures to reduce them. Forward planning of all activities can help to reduce the timeframes for the research governance process.

Transparency and communication

Principle: There should be open, transparent and effective communication between all stakeholders involved in the clinical trial and associated governance activities.

- Open and effective communication both between sites and sponsors and within a site, is a key feature of an effective and efficient site assessment process. This can be implemented by activities such as:
- providing sponsors with a dedicated contact person at the site (the Clinical Trial Liaison Officer);
- providing sponsors with regular updates on the progress of the site assessment and authorisation for their clinical trial;
- developing an internal communication plan;
- sponsors providing as much information and documentation prior to the site assessment process;
- developing and using Standard Operating Procedures;
- reaching early agreement about costs that may be incurred in the trial and the costs that will be paid for by the sponsor, including what constitutes standard care; and
- transparency in the calculation of costs associated with conducting clinical trials at the site.

Critical Success Factors

1. Clearly documented roles and responsibilities.

Clearly documented roles and responsibilities will:

- help avoid the duplication and/or omission of activities within the research governance process;
- identify people who can provide guidance on different aspects of the governance process; and
- identify when delegated responsibilities are required to avoid delays in the governance process.

2. Early assessment of the feasibility of the clinical trial with applicable service areas.

Delays in the site authorisation process can occur when the feasibility is not confirmed with appropriate service areas (pharmacy, radiology, pathology etc.) early on, even during the concept development stage. These service areas often have competing priorities, and clinical trials may require specialist services that are outside the normal activities of the service area. As negotiating these services can take some time, commencing a feasibility assessment as early as possible allows other aspects of feasibility to be determined in parallel.

3. Conduct of site assessment, where possible before, or in parallel with, ethics review.

Under the Good Practice Process (Figure 1) ethics review and the site assessment are essentially independent processes up until the final site assessment activity. As such, the preparation of site assessment documentation should take place before, or in parallel with, the preparation of ethics review documentation. Similarly, site assessment should take place before, or in parallel with, the ethics review.

4. Completion of as many site assessment activities as possible in parallel.

A number of site assessment activities are independent of one another. As such, these activities can be carried out in parallel. By having a clearly mapped process these independent activities can be identified. Carrying out as many activities in parallel should reduce the time taken for site assessment and authorisation.

5. Minimisation of unnecessary re-review of documentation.

By clearly outlining and promulgating the roles and responsibilities associated with the research governance process, unnecessary re-reviewing of documentation can be avoided. An example of where there may be an opportunity to obviate the need for a re-review of documentation is where patient information and consent forms are considered by the research governance office prior to review by an ethics committee to ensure that they reflect how the trial was going to be conducted.

6. Implement and review clinical trial planning and preparation activities.

The planning and preparation activities are ongoing activities that, rather than being specific to any given clinical trial, are aimed at ensuring the site is ‘ready, willing and able’ to carry out clinical trials. These include ensuring appropriate resourcing for clinical trials is in place and that appropriate processes and procedures to ensure that clinical trials can take place effectively and efficiently are in place. Appropriate review of relevant processes will ensure they are in place and fit for purpose.

7. Use active management strategies for key steps in the clinical trial start-up process.

Applying active management strategies, such as employing dedicated personnel to manage the site assessment and authorisation process can reduce the time taken for site assessment and authorisation.

The role of the Clinical Trial Liaison Officer (CTLO)

The role of the Clinical Trial Liaison Officer is central to the Good Practice Process. By focusing on three key activities, the CTLO can greatly improve the clinical trial start-up timeframe. These activities are detailed below, and should be considered when developing a job description for a CTLO position.

Reviewing and streamlining a site's clinical trial start-up processes.

- Working with site staff to assess infrastructure and staff availability required for the conduct of clinical trials with each department.
- Implementing the Good Practice Process and monitoring progress, including performance measurements.
- Developing resources related to the Good Practice Process and clinical trial start-up process, including Standard Operating Procedures and Key Performance Indicators.

Providing a central point of contact and information, and improving communication between sponsors, researchers and site administrative staff.

- Working to establish a central repository for the documentation required by external sponsors.
- Working to communicate site research capabilities and interests to clinical trial sponsors.
- Establish contacts and relationships with all key stakeholders, including clinical trial sponsors, contract research organisations, researchers and administrators.

'Shepherding' applications through the site assessment and authorisation process.

- Working with the Principal Investigator and Site Staff to ensure they can demonstrate that they can recruit sufficient numbers of participants.
- Working with clinical trial sponsors to ensure all relevant documentation is available to conduct the capacity planning exercise with local service departments.
- Working with the Principal Investigator and site staff to assess the proposed budget and clinical trial agreement.
- Tracking the progress of individual applications through the site assessment and authorisation process and intervening as necessary to minimise delays.

Planning and Preparation

Overview

The planning and preparation activities are not specific to a particular clinical trial. Rather, they are ongoing activities that ensure the institution is best placed to attract, accept and promptly commence clinical trials. For example, ensuring relevant staff have current Good Clinical Practice certification reduces delays in clinical trial start-up times resulting from researchers having to renew their certification before commencing the trial.

The planning and preparation activities have been listed according to the person or entity responsible. Depending on the structure of a specific organisation, there may be some overlap in the responsibilities. Institutions should use the responsibilities as a guide and implement the activities as appropriate for them.

Activities and responsibilities

Sponsor/Contract Research Organisation

- Use standard research agreements/contracts (such as those available from Medicines Australia, http://medicinesaustralia.com.au/issues-information/clinical-trials/clinical-trials-research-agreements/).
- Review trial protocols, patient information and consent forms and other appropriate documentation to ensure it is compatible with the Australian context before providing to investigators.
- Maintain adequate training and an experienced clinical trials team.

Principal investigator and other researchers as applicable

- Complete and maintain current and acceptable Good Clinical Practice training.
- Maintain a current CV in an institutional database.
- Maintain professional registrations.
- Maintain professional indemnity insurance.

Human Research Ethics Committee/Ethics office

- Document and promote processes to efficiently manage clinical trial ethics applications.
- Use certified ethical review processes for multi-centre clinical trials and single site trials as appropriate.
- Utilise the current national ethics application form.
- Adopt standardised ethical review forms, templates and processes.
- Publish HREC meeting dates and deadlines.
- Encourage the use of standard patient information and consent form templates.

Institution/Research office

- Establish and communicate clinical research priorities and objectives.
- Promote capacity to conduct clinical trials.
- Have clearly documented roles and responsibilities.
- Put in place ongoing clinical trial planning and preparation activities and review as appropriate.
- Maintain certification for ethics review processes related to multi-centre clinical trials and single site trials as appropriate.

- Make template documents, standard operating procedures, policies and other guidance available on an institutional website and ensure any changes are widely disseminated.
- Accept single ethics review without further ethics review (unless an additional specialist HREC review is required).
- Comply with national standards and processes for research governance frameworks including, as far as possible, the Good Practice Process.
- Ensure all staff involved in clinical trials have the appropriate training.
- Use active management strategies to ensure that the various steps in the clinical trial start-up process occur within mandated timeframes.
- Use nationally agreed site assessment document templates when available.
- Use standard research agreements/contracts (such as those available from Medicines Australia, http://medicinesaustralia.com.au/issues-information/clinical-trials/clinical-trials-research-agreements/) in accordance with applicable State or Territory requirements.
- Develop and report on clinical trials key performance indicators.
- Provide the infrastructure for and promote the electronic submission of documents.
- Utilise (or incorporate into existing documents) national standard operating procedures for site assessment, where available.
- Publish costs for clinical trial-related activities and services (with reference to Independent Hospital Pricing Authority advice where applicable).

Implementation of the planning and preparation activities

In order to implement the above planning and preparation activities, sponsors and sites should:

- Review current clinical trial planning and preparation activities and responsibilities.
- Compare current planning and preparation activities and responsibilities to those detailed in the Good Practice Process.
- Identify which planning and preparation activities can be, and need to be implemented.
- Develop an implementation plan, including timeframes, responsibilities, measures of success and provision for periodic review.
- Implement the appropriate planning and preparation activities.
- Carry out a periodic review of the implementation status and impact of the planning and preparation activities.

Site Assessment and Authorisation for each clinical trial

Overview

For the purposes of the Good Practice Process, the site assessment and authorisation process commences when a sponsor is considering a site for a clinical trial (the beginning of the Feasibility Assessment stage) and ends when site authorisation has been granted (the end of the Site Authorisation stage).

Figure 1 outlines the high level activities, roles and responsibilities for the various components of the site assessment and authorisation process. This should be used as an overview of the clinical trial start-up process and a guide to the general responsibilities of the various stakeholder groups, which may vary between institutions.

Figure 2 expands on the information in Figure 1, and details a proposed workflow and responsibilities for an institution carrying out a site assessment for an individual trial. In this detailed workflow, a number of activities should be carried out in parallel – this will increase the efficiency of the assessment and authorisation process. However, some activities are dependent on the outcome of previous activities, and are depicted as such.

Clinical Trial – Feasibility Assessment to Site Authorisation

	Feasibility Assessment	Document Preparation	Document Submission	Site Assessment and Ethics Review	Site Authorisation
Commercial Sponsor / CRO	• Identify and decide on potential trial sites, Principal Investigators, Coordinating Principal Investigator and lead HREC • Consider patient recruitment requirements and sample size required for protocol • Establish if potential sites are using nationally agreed standards, guidelines, contracts, standard costs etc, and, if not, identify any issues that might have an impact on the suitability of a potential site	• Develop/provide research protocol and draft contract/budget • Recommend standard of care definition(s) in the research protocol • Submit a Non-Disclosure Agreement or Confidentiality Agreement to the PI • Finalise all documents required by PIs and CPIs to fulfil ethics and site assessment requirements		• Receive copy of ethics approval certificate/letter and approved documents from CPI or HREC	• Receive site authorisation/s from PIs • Register trial with clinical trials registry if not previously registered • Notify trial to TGA if required
Principal Investigator/s	In association with institution (as appropriate): • Determine whether participation requirements are acceptable • Determine capacity of proposed project team to participate in a trial within the proposed time frame • Determine whether sufficient participant recruitment can take place at site	• Determine institutional requirements for site assessment and authorisation • Communicate with sponsor re. document requirements • Finalise all documents for site assessment • Review documents with institution as necessary	• Submit site assessment documents to institution	• Receive copy of ethics approval certificate/letter from CPI and provide to institution	• Receive notification of site authorisation from institution and provide to sponsor
CPI/delegate	• Determine capacity and time required to prepare ethics application	• Finalise documents for submission to HREC • Review ethics application documents with HREC administrator (or equivalent) as necessary	• Submit ethics application to HREC	• Receive HREC approval certificate/ letter and approved documents and provide to PIs	
HREC			• Accept ethics application and record in database	• Conduct ethics review (including preceding or concurrent scientific review) • Communicate with CPI if further information or amendments are required during review • Provide approval letter and documents to CPI or CRO/Sponsor	
Institution (RGO, Research Director, CFO etc)	In association with the Principal Investigator/s (as appropriate): • Determine if clinical trial is consistent with institution's mission and research priorities • Assess availability of required institutional resources • Identify any other contribution the institution may make to the clinical trial • Communicate any special requirements that are specific to the institution and/or jurisdiction to the Sponsor	• Approve proposed contract and budget • Engage early with relevant support departments or equivalent • Provide advice on institutional requirements for site assessment and authorisation as required	• Accept documents for site assessment and record in database	• Assess site assessment documents • Monitor or coordinate delegate review/s and approval/s • Receive HREC approval certificate/ letter and approved documents from the PI • Liaise with PIs as required regarding any further required documentation • Complete assessment	• Authorise clinical trial (CEO or delegate) • Notify PI of site authorisation

Figure 1. The high level activities, roles and responsibilities for the various components of the site assessment and authorisation process

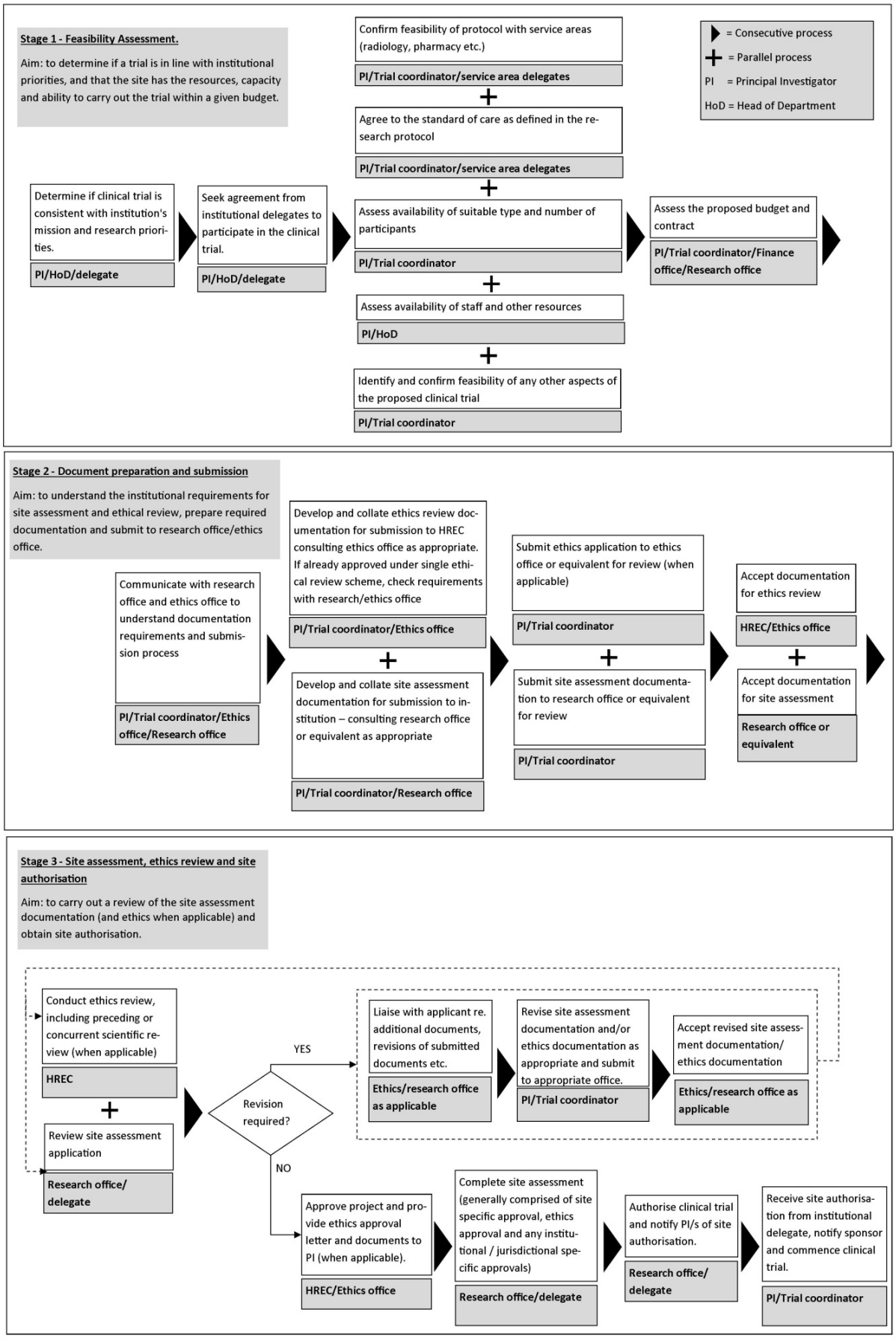

Stage 1 - Feasibility Assessment.
Aim: to determine if a trial is in line with institutional priorities, and that the site has the resources, capacity and ability to carry out the trial within a given budget.
= Consecutive process
= Parallel process
PI = Principal Investigator
HoD = Head of Department
Determine if clinical trial is consistent with institution's mission and research priorities.
PI/HoD/delegate
Seek agreement from institutional delegates to participate in the clinical trial.
PI/HoD/delegate
Confirm feasibility of protocol with service areas (radiology, pharmacy etc.)
PI/Trial coordinator/service area delegates
Agree to the standard of care as defined in the research protocol
PI/Trial coordinator/service area delegates
Assess availability of suitable type and number of participants
PI/Trial coordinator
Assess availability of staff and other resources
PI/HoD
Identify and confirm feasibility of any other aspects of the proposed clinical trial
PI/Trial coordinator
Assess the proposed budget and contract
PI/Trial coordinator/Finance office/Research office
Stage 2 - Document preparation and submission
Aim: to understand the institutional requirements for site assessment and ethical review, prepare required documentation and submit to research office/ethics office.
Communicate with research office and ethics office to understand documentation requirements and submission process
PI/Trial coordinator/Ethics office/Research office
Develop and collate ethics review documentation for submission to HREC consulting ethics office as appropriate. If already approved under single ethical review scheme, check requirements with research/ethics office
PI/Trial coordinator/Ethics office
Develop and collate site assessment documentation for submission to institution – consulting research office or equivalent as appropriate
PI/Trial coordinator/Research office
Submit ethics application to ethics office or equivalent for review (when applicable)
PI/Trial coordinator
Submit site assessment documentation to research office or equivalent for review
PI/Trial coordinator
Accept documentation for ethics review
HREC/Ethics office
Accept documentation for site assessment
Research office or equivalent
Stage 3 - Site assessment, ethics review and site authorisation
Aim: to carry out a review of the site assessment documentation (and ethics when applicable) and obtain site authorisation.
Conduct ethics review, including preceding or concurrent scientific review (when applicable)
HREC
Review site assessment application
Research office/ delegate
Revision required?
YES
NO
Liaise with applicant re. additional documents, revisions of submitted documents etc.
Ethics/research office as applicable
Revise site assessment documentation and/or ethics documentation as appropriate and submit to appropriate office.
PI/Trial coordinator
Accept revised site assessment documentation/ ethics documentation
Ethics/research office as applicable
Approve project and provide ethics approval letter and documents to PI (when applicable).
HREC/Ethics office
Complete site assessment (generally comprised of site specific approval, ethics approval and any institutional / jurisdictional specific approvals)
Research office/delegate
Authorise clinical trial and notify PI/s of site authorisation.
Research office/ delegate
Receive site authorisation from institutional delegate, notify sponsor and commence clinical trial.
PI/Trial coordinator

Figure 2. Proposed workflow and responsibilities for carrying out a site assessment for an individual trial.

Stage 1 - Feasibility Assessment

The aim of this stage is for the site to determine if a proposed trial is consistent with institutional mission, values and priorities, and that the site has the resources, capacity, including the participant population, and ability to carry out the trial on time, to recruitment target and within a given budget.

The Feasibility Assessment stage spans the activities from when a sponsor approaches an institution or individual investigator with a clinical trial proposal until the review of the proposed budget and contract to ensure they are appropriate.

The desired outcome is agreement between all stakeholders that all aspects of a trial are feasible, the trial budget is acceptable to all stakeholders and that a draft contract is agreed upon.

Stage 2 - Document Preparation and Submission

The Document Preparation and Submission stage spans the activities from when the Principal Investigator (or equivalent) determines the site requirements for documentation to the submission of ethics review and site assessment documents to the reviewing offices.

The aim of the Document Preparation and Submission stage is for the Principal investigator/s or other appropriate stakeholders to understand what documentation and supporting evidence is required for institutional site assessment and ethics review, prepare the required documentation and submit that documentation to the institutional research office and ethics office as appropriate.

The desired outcome is the submission, within an appropriate timeframe, of a complete and accurate set of site assessment and ethics review documentation to the appropriate institutional offices.

Stage 3 - Site Assessment, Ethics Review & Site Authorisation

The Site Assessment, Ethics Review and Site Authorisation stage spans the activities from when the appropriate bodies review the site assessment documentation and ethics application to the final granting of site authorisation.

The aim of the Site Assessment, Ethics Review and Site Authorisation stage is for a review of the site assessment documentation and, when applicable, ethics documentation to be carried out, revised when necessary, and for the clinical trial to be granted site authorisation.

Implementation

In order to implement the site assessment and authorisation activities outlined in the Good Practice Process, it is recommended that institutions carry out the following process:

1. Review the current institutional site assessment and authorisation process;
2. Compare the current institutional site assessment and authorisation process to that detailed in the Good Practice Process;
3. Identify which components of the Good Practice Process are not currently in place;
4. Develop an implementation plan, including timeframes, responsibilities, measures of success and provision for periodic review;
5. Develop and/or modify existing Standard Operating Procedures that accompany each stage of the site assessment and authorisation process;
6. Put appropriate performance measurements in place;
7. Implement site assessment and authorisation activities; and
8. Carry out periodic review as appropriate.