Australian Clinical Trials Alliance

Discussion Paper: integrated consent – a tiered approach to consent for comparative effectiveness trials

June 2020

ACTA gratefully acknowledges operational funding from the Australian Government's Medical Research Future Fund

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ACKNOWLEDGEMENTS

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Concepts adapted from a consultation to develop a consent template for pragmatic trials conducted by the National Health Service (NHS) Health Research Authority.[1]

ACTA workshop participants.

USE OF THIS DOCUMENT

ACTA requests that the following acknowledgement is included in any documents that are developed using knowledge gained from this document.

> [name of organisation, trial or individual] acknowledges the contribution of ACTA to the development of applying a integrated consent approach in clinical trials (reference: Australian Clinical Trials Alliance (ACTA) Discussion Paper: integrated consent – a tiered approach to consent for comparative effectiveness trials). To assist in identifying the usefulness and impact of its work, ACTA is collating 'use-cases'. If this document has influenced your consent documents or process, please notify ACTA at info@australianclinicaltrialsalliance.org.au, title: example of applying ACTA integrated consent approach.

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PURPOSE

This document outlines a risk-proportionate approach to seeking consent for comparative effectiveness trials. It describes a tiered approach to the presentation of trial information, so that Participant Information Sheets/Consent Forms (PICFs) are shorter, and potential participants have more choice over the amount of information they read before signing the consent form.

This document is part of a broader work program to provide guidance on a range of consent models for trials across all risk levels (see **Appendix 1**). It is referenced in Appendix 1 as 'Integrated consent with a concise PICF'.

KEY POINTS

- The Australian Government supports clinical research as a core business of the health system, embedded within routine care.
- While medical science advances have improved patient care and health outcomes, evidence of the comparative effectiveness of interventions in common use remains inadequate.
- Embedding comparative effectiveness trials (CETs) into routine care will accelerate the generation of this evidence.
- Traditional methods for the design and conduct of randomised controlled trials are ill suited to CETs. As a result, many socially valuable CETs are not even attempted. Transformational approaches are required.
- Consent should be commensurate to the risks and complexities of a trial. Long, legalistic consent documents are likely to reduce comprehension, increase anxiety, and may inadvertently subvert the consent process.
- Patients could be asked to participate in trials in a more satisfactory and straightforward manner that is aligned with clinical care and already supported by the Australian ethical and regulatory framework.

BACKGROUND

The Australian Clinical Trials Alliance (ACTA) supports clinical trial networks to conduct efficient and timely research. To support the embedding of comparative effectiveness research into the health system ACTA is addressing the barriers that prevent this research from being conducted. The goal is for patients (in both primary and secondary care) to be recruited 'at point of care', to enable many more studies, particularly comparative effectiveness trials (CETs), to be completed quickly and cost effectively.

This document focuses on CETs, although the principles apply to other research. CETs compare the benefits and harms of interventions commonly used in routine care. Unlike premarket trials that evaluate efficacy in well-defined and controlled settings, their primary goal is to generate 'real-world' evidence of effectiveness. CETs therefore adopt pragmatic designs, so they can be embedded into clinical care. Therefore, CETs place little or no extra risks or burdens on participants compared to standard care.

Consent is central to the ethical conduct of research, but in recent years the traditional informed consent process for clinical trials has become long and complex. PICFs are widely criticised for being written in a way that obscures important detail[2], for reducing understanding and recall, and for focusing on the need for institutions to mitigate risk.[3,4]

There is growing consensus that traditional informed consent may poorly suit CETs[5,6,7], and patients often reject these trials due to an exaggerated and disproportionate perception of risk[8]. Moreover, the emphasis on the PICF ignores the context in which the consent process takes place, which also involves a discussion with health professionals. Systematic reviews illustrate the importance of the discussion in improving participant understanding.[9,10]

Recent advances, such as the widespread use of electronic health records and the development of novel trial designs, motivate and enable the integration of research and clinical care. This has helped to increase the number of CETs conducted as an integral part of service delivery. However, to further enable widespread embedding of CETs into routine care, many experts call for more pragmatic interpretations of ethical and regulatory frameworks or, where appropriate, revisions of these frameworks.[11–13] But in Australia, the National Statement already enables and encourages a flexible approach to consent that could be better utilised.[14,15]

This document describes an **integrated consent** model that enables valid consent to be obtained using a proportionate, risk-based approach. It was developed with ACTA's Embedding Clinical Trials in Routine Care Reference Group and incorporates feedback from a multi-stakeholder workshop in March 2020 that used concepts from a consultation in the UK which culminated in a tailored process and PICF template for pragmatic trials.[1]

WHAT IS MEANT BY INTEGRATED CONSENT?

Integrated consent is where patients provide consent at their point of care, often as part of the routine clinical discussion.

Integrated consent:

- includes a concise, focused PICF (paper or electronic) normally less than five pages
- can link to additional information for participants who want it
- permits some information to be disclosed to participants verbally (if written consent to receive the intervention(s) is not required outside the trial setting)
- provides sufficient information to decide whether to participate
- includes consumer input wherever possible.

WHAT IS MEANT BY 'SUFFICIENT INFORMATION TO DECIDE WHETHER TO PARTICIPATE'?

For consent to be legally valid, it must be voluntary (freely given without pressure or duress), given by a person with the necessary mental capacity who has been adequately informed. For participation to be adequately informed, the National Statement requires disclosure of *sufficient information* to enable an adequate understanding of the **purpose, methods, demands, risks and potential benefits** of the research (2.2.2). Knowledge of **reasonable alternatives** is also considered necessary for decision-making when other treatments or interventions are available.

For CETs, there is a dual purpose for treatment, 1) clinical care, and 2) obtaining generalisable knowledge to improve the care of future patients[16]. As well as understanding that they are being offered treatment for their disease condition, prospective participants must also understand:

- **That treatment is being offered in a research context, and that participation is voluntary**
- **The aims of the research – the use of data to obtain generalisable knowledge to benefit others**
- **The extent to which the research may alter their care.**

The information in **bold** is considered the *key information* that a prospective participant (or their authorised representative) should be given to decide whether to participate.* Clinicians supplement consent for standard care with information on the material differences between the study and standard care.[16]

Note: The Australian Commission on Safety and Quality in Health Care (ACSQH) publish guidance on preparing and writing documents for consumers.[17,18] These guidance documents should be used to support the development of concise, readable PICFs that end-users can comprehend.

WHY SEPARATE THE KEY INFORMATION FROM OTHER INFORMATION?

The National Statement requires that trial information, '*be presented in ways suitable to each participant*' (2.2.3). Some studies show that patients are often happy to make decisions on much less information than is currently provided in a traditional PICF.[19] Others suggest some patients would have liked more information than was provided.[20] Exercising choice is challenging when all trial information is contained within a single document, particularly as potential participants are expected to sign to confirm that they have read and understood all information. Even if PICFs are sectioned into 'general and trial-specific' or 'key and supplementary', patients are still overwhelmed when presented with a PICF that runs to many pages. Instead, participant should be able to choose the amount of information they read before signing the consent form.

For some CETs, this approach could include:

1) A concise PICF supplemented by the verbal discussion during the clinical consultation when treatment is offered, which together provide sufficient information to make an informed decision about participation (Tier 1).
2) Separate, user-friendly methods to access additional study information, for example, from a trial website or leaflet (Tier 2).

The primary information should clearly explain how additional information is accessed.

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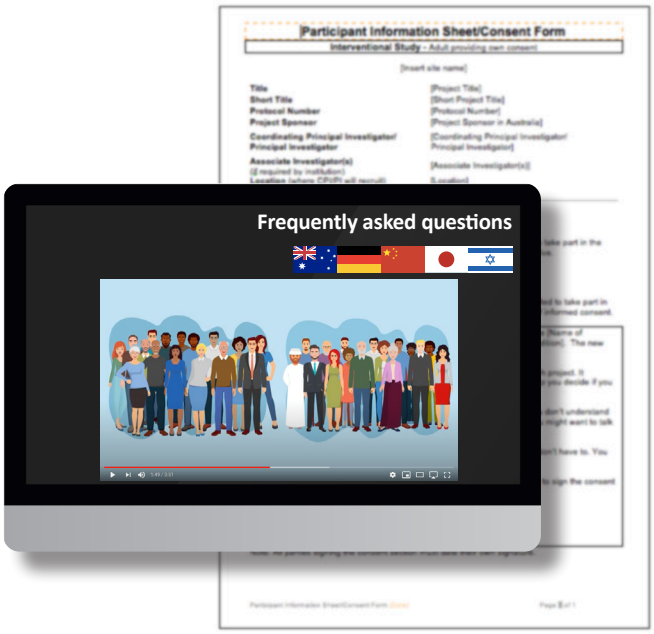
* As a general principle, the more a comparative effectiveness trial deviates from established practice, the greater the amount of information required in the PICF.

AN ILLUSTRATION OF INTEGRATED CONSENT

Tier 1: Key information



Tier 2: Extra information

Integrated consent differs from traditional consent in two ways: 1) the use of a tiered approach, and 2) the use of mixed methods for information provision.

1) **A tiered approach**

   The National Statement permits the use of a tiered approach stating: '*staged or tiered information should be considered in order to address variations in the needs or characteristics of potential participants*' (3.1.26 (b)). Therefore, participants should be able to sign a consent form without having to read the additional information in second tier, knowing that more comprehensive information can be accessed at any time.

2) **Mixed methods to provide information**

   The National Statement requires researchers to consider whether consent information, '*is best communicated through speech, writing, some other way, or a combination of these*' (5.2.17 (a)). It allows consent to be, '*expressed orally, in writing or by some other means … depending on the nature, complexity and level of risk of the research*' (2.2.5). Therefore, for CETs with risks comparable to standard care, information may be expressed orally and need not always be duplicated in the PICF. Instead, the PICF could refer to the conversation and encourage participants to ask questions.[1]

   Note: The National Statement does not require a trial to be formally classified as low risk for consent information to be provided orally. However, 2.2.5 of the National Statement should be considered.

ARE THERE ANY PRE-CONDITIONS FOR THE USE OF INTEGRATED CONSENT?

- Trial risks and burdens are comparable to the risks and burdens posed by standard care.
- In addition to usual ethical requirements for clinical trials, the specific ethical requirements for CETs should be met.[21] For example:
  - > There must be a properly informed uncertainty about the comparative merits of the treatments or interventions being tested.
  - > There should be sufficient evidence the choice of comparators is appropriate (the HREC should be satisfied that allocation to one or other treatment arm is no less reasonable than the allocation in actual practice).

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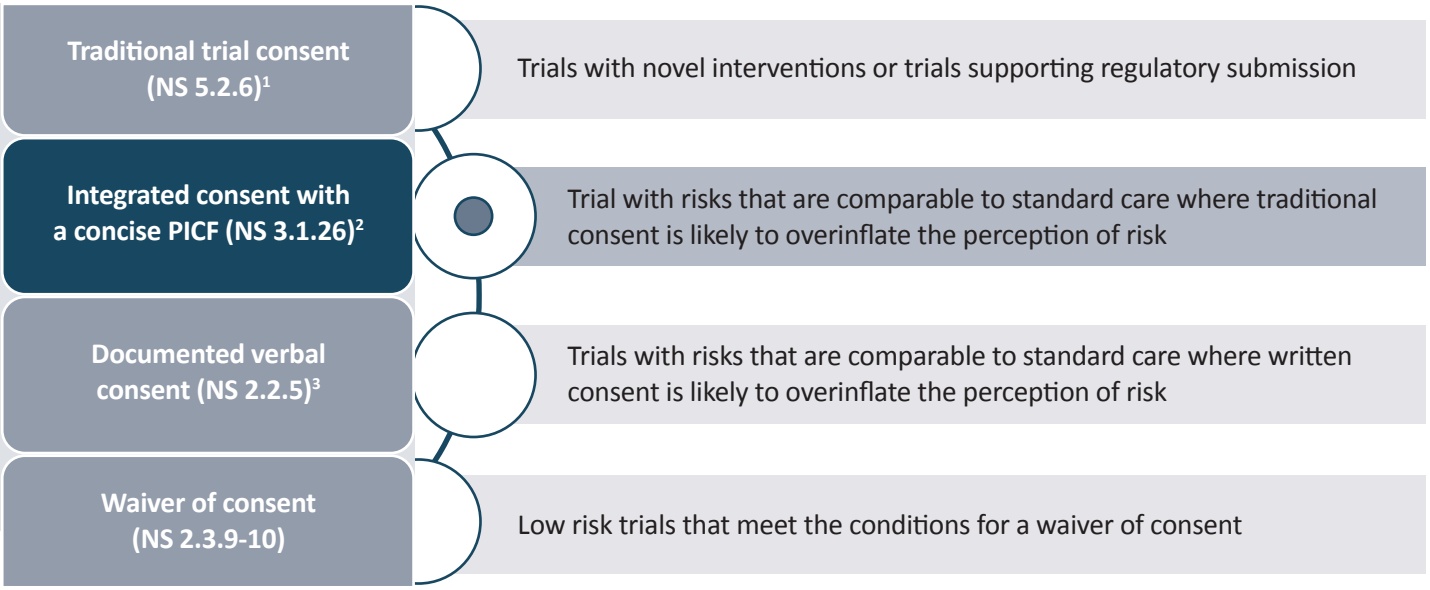
APPENDIX 1: ILLUSTRATION OF INTEGRATED CONSENT IN THE CONTEXT OF OTHER OPTIONS



1. Where current models and forms are used.
2. Standard care means care that is widely recognised as established practice.
3. Verbal consent is obtained in a way that allows participants' decisions to be clearly established and documented.

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