CT:IQ
Clinical Trials:
Thinking Smarter

FLEXIBLE TRIAL DESIGN CHECKLIST:

How clinical trials can be designed to be more flexible in Australia

CONTENTS

Published by CT:IQ

Purpose

This checklist is for clinical trial sponsors, researchers, decision-makers and reviewers. It describes how using flexible options in clinical trials can comply with Australian and international regulations and standards. It is intended as a high-level guide. Sponsors will need to discuss the details of their trial design with the relevant regulators, following their usual processes.

Definitions

The term 'flexible trial delivery' (FTD) describes methods that can be used to design trials that can respond to the needs of participants and address any barriers to their participation. In this document we use this broad term to encompass a range of trial delivery methods including, but not limited to, 'decentralised clinical trials' and 'teletrials'. There are many ways that we can offer flexibility to participants, and new technologies, such as wearable patches and home testing kits, are continuing to create more options.

For more information about flexible trial delivery, see our companion tool: Introduction to Flexible Trial Delivery.

In this document, the term 'remote' refers to activities that are undertaken outside of the physical trial site rather than at a geographical location. As such, 'remote' activities can take place in all parts of Australia.

The term 'third-party providers' refers to parties who may be contracted to provide services as part of the trial conduct where these services are part of their usual training and scope of practice. When there is a difference in requirements, we have specified if they are involved in healthcare related activities ('local healthcare providers') or delivering trial services such as shipping investigative products or technology requirements ('service providers').

All other providers who are performing activities that require trial specific training and delegation are considered part of the clinical trial staff. This includes staff at the main or other trial locations (e.g. 'satellite sites').

Scope

This document highlights guidance specific to flexible ways of working in clinical trials from both Australian and international sources. It does not cover all available guidance documents that discuss how to design a clinical trial. Reference sources were:

- National Statement on Ethical Conduct in Human Research (NHMRC, 2025)
- Recommendations Paper on Decentralised Elements in Clinical Trials (EMA, 2022)
- Draft ICH E6(R3) Annex 2 (ICH, 2025)
- Conducting Clinical Trials with Decentralised Elements (FDA, 2022)
- Guideline on computerised systems and electronic data in clinical trials (EMA, 2023)
- Digital Health Technologies for Remote Data Acquisition in Clinical Investigations (FDA, 2023)
- National Standard Operating Procedures for Clinical Trials (including teletrials) (Clinical Trials Project Reference Group, 2020)
- Safety monitoring and reporting in clinical trials involving therapeutic goods (NHMRC, 2016)

Although several of the international guidance documents to which we refer focus on trials using therapeutic goods, the checklist has been designed to apply to all trial intervention types.

This checklist is part of a broader CT:IQ project on Tools for Flexible Trial Delivery which includes additional resources.

The checklist is meant to supplement other relevant resources, such as:

- local laws and regulations,
- guidance from your reviewing ethics or research governance bodies,
- guidance relevant to your participant group or intervention.

This checklist covers what you should think about when deciding which types of flexibility are possible for your trial, either during the design phase or as needed during delivery. It has been designed to cover the essentials, rather than every possible situation. As with all trial design, advice on trial design should be sought from people with relevant lived experience.

A. Design for success

	A. 1. Engage Early
☐	Collaborate with consumer partners to develop the design of the proposed FTD elements, ensure that they are suitable and identify training and support needs for participants, especially for any data entry or investigational product management tasks participants will be conducting (1,2).
☐	Engage with sites (including the relevant ethics and institutional review bodies), healthcare professionals, and investigators to align operational approaches and identify training and support needs for staff to deliver FTD elements(1).
	A.2. Design with participants at the centre
☐	Place the rights and safety of participants over all other interests in deciding whether to use FTD elements in a trial (1).
☐	Weigh any transfer of burden to trial participants and/or investigators caused by using FTD elements against the potential benefits to participants, investigators, and scientific knowledge (1).
☐	Confirm that clinical trial insurance or other arrangements are in place to cover any harm to participants or staff or damage resulting from remote trial procedures (3).
	A.3. Design for trial validity
☐	Consider the suitability of conducting the informed consent procedure remotely, including any necessary in-person procedures required for screening (4,5).
☐	Consider the suitability of conducting some or all trial activities remotely including site capacity, participant preferences, and any clinical need for in-person interaction. Note that some trial activities may be easier for sites to conduct remotely than others, and some trial activities may have more benefits to participants if conducted remotely (3,6).
☐	Consider the suitability of making the investigational product available remotely (e.g. to participants or third-party providers). This includes assessing the risk profile of the investigational product, relevant labelling or prescribing requirements, training needed for administration, and shipping and storage requirements (7,8).
☐	Consider if FTD elements are likely to have a significant impact on the trial's scientific validity, data integrity, risk-benefit ratio, or ability to protect trial participants. If so, document these impacts in a risk-benefit assessment with the mitigation actions that will be put in place (1).
☐	Specify in the protocol, the Data Management Plan and/or the trial monitoring strategy how the potential for data variability caused by FTD elements will be minimised (9,10).
	A.4. Establish monitoring and data management systems
☐	Ensure the safety monitoring plan takes the flexible nature of the trial into account. This may require additional detail on how adverse events and treatment errors are to be collected and addressed if local healthcare providers are involved, and how data will be transferred in a timely manner (11).
☐	If using remote patient monitoring devices (including wearables and sensors), articulate what data profile would constitute an adverse event, how often this data will be reviewed, and the care responses in place (11).
☐	Incorporate any specific risks associated with the FTD elements into a proportionate trial monitoring strategy (12,13,14).
☐	Consider how you will mitigate any safety issues that arise during the trial associated with the FTD elements. This may include having options for site-based trial delivery methods.
☐	Ensure that all data collection systems and mechanisms for remote access to trial data have met relevant legal and regulatory requirements (14,15,16).
☐	Establish a Data Management Plan, which clearly describes the flow, storage and handling of all sources of data in the trial (16,17).
☐	Consider responsibilities for the regular calibration and maintenance of any devices for data collection, investigative product storage, or sample processing (e.g. scales, centrifuge) which are used outside of research sites (18).

B. Support participants during the trial

	B.1. Participant flexibility
☐	Set up systems to seek, record and update participant preferences for how they will undertake trial activities.
☐	Ensure there are systems for tracking and updating how to best contact participants during the trial. This is especially important for participants who may only be seen virtually (19).
	B.2. Remote consent
☐	Ensure secure means for potential participants to communicate directly with an investigator or their delegate when providing consent (20).
☐	Establish a process for recording and verifying that potential participants have received information, any discussions between an investigator or their delegate and the potential participant, and the giving of consent (20).
☐	Consider alternative channels for providing information about the trial, depending on participant preferences (e.g. paper, electronic or audio methods) (20).
	B.3. Remote trial activities
☐	Develop guidance for site staff about any individual participant circumstances that would not be amenable to remote trial procedures and outline possible alternatives (5).
☐	Ensure the necessary education and support is provided to participants for all trial activities, including administration of the investigational product and using any devices or apps. This may be delivered in-person and/or using video training resources.
☐	Provide suitable training and help desk resources to participants and third-party providers who are inputting data into the trial database (e.g. if they are entering data directly into an app or device) (19).
☐	Establish systems and guidance for site staff and third-party providers on protecting the privacy of in-home and telehealth visits, including for participants who share their home with others (6).
☐	Ensure there are systems in place for the Primary Investigator to oversee any remote supply of investigational product(s) to participants and/or third-party providers (e.g. GP clinics, pharmacies etc), including the return and destruction of any unused investigational product and/or product recall (7,21).
☐	Establish procedures for participants or the staff supporting them to return study devices and equipment at the end of the study, and for the repair and replacement of lost or broken study devices or equipment.
	B.4. Remote safety reporting and management
☐	Ensure that participants have clear advice on how to seek medical assistance and/or contact trial staff for unscheduled visits by telehealth or an in-person visit when needed (11).
☐	Ensure the protocol specifies how and by whom adverse events will be identified and assessed, and any care provided when it is impractical to travel between the participant location and the central site in a timely manner (6).
☐	If using remote patient monitoring devices (including wearables and sensors), informed participants how often the data will be reviewed for safety events (11).

C. Build and support trial teams

	C.1. Clarify roles and responsibilities
☐	Determine whether any local healthcare providers engaged in delivering FTD elements should be listed as a member of the trial team. Considerations include if the providers need to be trained in the trial protocol, and their involvement differs from activities they are qualified to perform in their clinical practice (6).
☐	For local healthcare providers that do not need to be listed as a member of the trial team, make sure an audit trail exists for trial activities (e.g. list the company they work for in the delegation log and establish a way of recording the tasks each staff member has completed) (6).
☐	Clearly describe the responsibilities of any third-party providers in the protocol or related documents and make sure these are outlined in a service agreement between the third-party provider and the contracting party (either the sponsor or the site) (22).
☐	Detail how the Principal Investigator will maintain oversight of the conduct of the trial, including activities that have been delegated to third-party providers. This could be done through a Supervision Plan (23).
	C.2. Third party providers
☐	Develop clear training and informational materials and provide help desk resources for those undertaking FTD elements (e.g. if local pharmacies are dispensing the investigational product, they will need sufficient information to answer common questions from participants and/or access to a help desk). This should include training and resources for those who are inputting data as part of FTD (e.g. a standardised data directory) (21,19).
☐	Establish clear communication systems between service providers and sponsors to discuss the trial. For trials including investigational products, this includes drug accountability, return and destruction of unused investigational product and/or product recall.
	C.3. Safety monitoring
☐	Review the safety monitoring plan and unblinding protocols with third-party providers for feasibility (24).
☐	Establish procedures for reporting adverse events experienced during visits at all location types and by all staff or third-party providers interacting with participants or their data (3,25).
☐	Consider what information site staff need to collect about adverse events and how this information will be collected and/or verified remotely. This may include providing training to third-party providers (especially local healthcare providers) about the information to be collected, how to collect it, and actions to take if abnormal findings are identified (22).
☐	If using local testing or imaging facilities for safety monitoring, ensure there is a timely data transfer system for review of reports by investigators (25).

References

1. EMA: Recommendation Paper on Decentralised Elements in Clinical Trials, 1. Introduction, Scope and General Considerations
2. Draft ICH G6(R3) Annex 2, para 3.1 Engagement and Communication
3. EMA: Recommendation Paper on Decentralised Elements in Clinical Trials, 5. Trial Related Procedures at Home
4. NHMRC: National Statement on Ethical Conduct in Human Research, 3.1 The elements of research
5. Draft ICH E6(R3) Annex 2, 2.2 Informed Consent Considerations
6. FDA: Conducting Clinical Trials With Decentralized Elements, Part B Remote Clinical Trial Visits and Clinical Trial-Related Activities
7. FDA: Conducting Clinical Trials With Decentralized Elements, Part G Investigational Products in a DCT
8. Draft ICH E6(R3) Annex 2, 3.6 Investigational Product Management (Sponsor)
9. Draft ICH E6(R3) - Annex 2, 3.2 Protocol and Trial Design
10. FDA: Conducting Clinical Trials With Decentralized Elements, Part A. DCT Design and Conduct
11. FDA: Conducting Clinical Trials With Decentralized Elements, Part I Safety Monitoring in DCT
12. EMA: Recommendation Paper on Decentralised Elements in Clinical Trials, 7. Trial Monitoring
13. Draft ICH E6(R3) Annex 2 3.8 Sponsor Oversight
14. EMA: Guideline on computerised systems and electronic data in clinical trials
15. FDA: Digital Health Technologies for Remote Data Acquisition in Clinical Investigations
16. FDA: Conducting Clinical Trials With Decentralized Elements, Part D Roles and Responsibilities
17. EMA Recommendation Paper on Decentralised Elements in Clinical Trials, 6. Data collection and management including defining and handling source data
18. FDA: Digital Health Technologies for Remote Data Acquisition in Clinical Investigations, C. Verification, Validation, and Usability Evaluations of Digital Health Technologies
19. EMA: Recommendation Paper on Decentralised Elements in Clinical Trials, 2. Clinical trial oversight: roles and responsibilities
20. EMA: Recommendation Paper on Decentralised Elements in Clinical Trials, 3. Informed Consent Process
21. EMA: Recommendation Paper on Decentralised Elements in Clinical Trials, 4. Delivery of Investigational Medicinal Products and Administration at Home
22. EMA Recommendation Paper on Decentralised Elements in Clinical Trials, 2. Clinical Trial Oversight: Roles and Responsibilities
23. CTPRG: National Standard Operating Procedures for Clinical Trials, including Teletrials in Australia. SOP 2: Investigator Responsibilities
24. NHMRC: Safety monitoring and reporting in clinical trials involving therapeutic goods. Part 1 IMP Trials C. An Overview of Safety Monitoring and Reporting Responsibilities. Responsibilities of the Sponsor; and Part 2 IMD Trials C. An Overview of Safety Monitoring and Reporting Responsibilities. Responsibilities of the Sponsor
25. Draft ICH E6(R3) Annex 2, 3.6 Investigational Product Management (Investigator)