



CT:IQ
Clinical Trials:
Thinking Smarter



Flexible Trial Delivery Case Studies



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PURPOSE

CT:IQ has worked with its members and the Flexible Trial Delivery project team to develop this suite of Australian case studies. They are intended as illustrations for how clinical trials can be adapted to be more accessible for participants. The case studies demonstrate flexibility that has been introduced at the protocol and site implementation levels, as well as for an individual participant.

FTD Case Study 1:

IMPACCT strategies for palliative and chronic care research

Case study provided by: University of Technology Sydney

For more information contact: Professor Meera Agar, itcc@uts.edu.au

CONTEXT OF THE TRIAL AND FLEXIBLE METHODS USED

Description of trial aim	<p>Trials of end-of-life symptom management therapies and strategies. Medications used are usually already on the market, but are being tested for a different population, route or indication.</p>
Trial size and location(s)	<p>The groups trials are usually short (days to weeks long) due to the participants stage of life.</p> <p>There is a focus on inclusion/exclusion criteria being as short/simple as possible. The participants are those who have the disease or symptom and who would be most likely receive the treatment in a real-world setting.</p> <p>The trials are usually multi-site due to low population numbers and limited recruitment potential at any single site. The sites are mostly metropolitan due to palliative service locations. There have been a small number of trials which include larger regional services, and none yet in remote locations due to logistics and very low recruitment populations. One trial in development will include a remote location.</p> <p>Sample sizes vary according to the primary outcome calculations, ranging from very low in pilot or feasibility studies, to 200+ for phase 3 studies.</p> <p>Trials often ask for carer input as well (burden of care, impact of symptoms), and most trials also collect health economic data to support assessment of the impact of the symptom and/or treatment.</p>
Sponsor	<p>The sponsor is usually the University of Technology Sydney, for Collaborative Group approved trials. Trials often focused on questions arising from clinical practice of the group's members. Work is conducted with competitive/local funding.</p>
Why were flexible trial elements used?	<p>The participant population is in a delicate stage of life where any research activity needs to fit in with the time available and their physical, emotional and cognitive capacity, and the existing burden on the families. This means there is a focus on meeting participants where they are (with visits offered at their home), or times with existing clinical visits, and a focus honouring their time and contribution.</p>

What flexible elements were used?	<p>Main flexibility around the timing and location of visits.</p> <ul style="list-style-type: none"> • If there are multiple assessments at a visit, they are scheduled to allow for fatigue and illness. Assessments are prioritised: <ul style="list-style-type: none"> ◦ safety related assessments done first ◦ assessments related to the primary outcome (usually symptom management) done second ◦ assessments related to secondary outcomes done if time permits. • Assessments done mostly by self-report rather than testing or physical assessment. If possible, reviews done by telephone to limit number of people visiting the home. • All visits have windows (usually +/-1 or 2 days) to enable participants to attend to other appointments, family matters and their quality of life. • Timing of symptom collection adjusted to reflect the expected changes in the symptom of interest, with a focus on collecting the minimum information required to enable an assessment of changes. <p>The group also uses the idea of “pre-consent” where participants discuss trials with staff before the symptoms appear while they still have capacity. Because the population is generally not tech savvy, these conversations usually happen in person.</p> <p>To date, trials with electronic data collection have not gone well. The participants are too unwell to focus on learning the new technology, or are unable to attend to the technology themselves. When given a choice, participants have chosen a paper completed instrument over electronic.</p>
How was flexibility added?	<p>These approaches are fundamental to the research that the group does and are used at all sites. Protocols build in the flexibility around visits, data collection method and always take into account the burden of each visit.</p>

IMPACT OF FLEXIBLE TRIAL ELEMENTS ON THE CONDUCT OF THE TRIAL

Data collection	<p>The focus on how visits are scheduled ensures that safety data is always collected, and triages other data collected.</p> <p>The participant population is carefully considered to avoid duplicate assessments.</p> <p>The reasons for incomplete data are systematically collected to capture participant fatigue or inability to respond.</p>
Recruitment/retention	<p>These ways of working are critical to researching this highly vulnerable population, and greatly increase their recruitment and retention into clinical research. Without these methods, it would be difficult to test new clinical practices in this population.</p> <p>Recruitment strategies are always pre-planned and customised for each site in order to maximise the potential recruitment and are reviewed frequently. Despite this, recruitment is low, with high dropout rates between referral to the study, screening and baseline.</p> <p>Systematic data is collected regarding referral patterns and reasons why screening does not progress in order to monitor the recruitment strategies and consider any protocol issues.</p> <p>Retention rates are good, indicating that the protocol design suits the intended population.</p>

Review process	<p>Most sites are embedded in the palliative care services, where the PI is already providing care to the participant.</p> <p>To date there have been no issues with respect to HREC or RGO review, over and above the issues that relate to all trials. HREC and RGO have allowed flexibility in design to maximise recruitment and retention, including telephone data collection. Reasonable questions regarding burden have been considered as part of the review process.</p>
Contracts	<p>The trials from this collaborative group use the standard Medicines Australia Clinical Trial Research Agreement for collaborative Trials without difficulty. Service agreements are put in place for 3rd parties such as external pharmacy providers for Direct to Patient IMP management. UTS owns a licence for REDCap for data entry, which is developed and managed centrally.</p>
Finances	<p>Use of a central external pharmacy significantly reduces the cost of multiple clinical trial pharmacies, there is one single fee structure in place. The IMP is couriered to site/patient/PI as required, the cost of which is covered by the funding, and remains less than multiple pharmacies, a full costing will be underway shortly.</p>

OVERALL THOUGHTS

Key strengths

Early consumer input maximises the potential to design trials where the participant population is considered and trial design is pared back to reflect the population (instead of the perfect patient), and the capacity of the participant population to complete the required assessments. Flexibility in visit schedules, data collection and even inclusion/exclusion criteria enable recruitment to trials in an otherwise very challenging space.

Differently next time

The trials are constantly evolving as regulations, technology and expectations change. Electronic technology capture is very challenging and is approached with caution.

Advice to others

Trials can have flexibility built in with careful consideration. Inclusion of consumers is critical, also consider inclusion of those who collect the data or assess the participants to ensure that the future participant burden, capacity and abilities are considered up front.

Patients want to contribute, even at the very end of life, the trials need to respect this and enable participation in order to expand the evidence base for clinical care.

FTD Case Study 2:

IMP access at sites without clinical trial pharmacists

Case study provided by: NT Health

For more information contact: Emilie Meier or Teana Brewster-O'Brien

CONTEXT OF THE TRIAL AND FLEXIBLE METHODS USED

Description of trial aim	To measure how well a new hormone therapy works compared to standard hormone therapy (tamoxifen, anastrozole, letrozole, or exemestane) in people 18+ with early breast cancer that is ER+ and HER2-.
Trial size and location(s)	Recruitment target: 6000 globally, across 31 countries. Locally, four per year over recruitment period. Initially recruiting at tertiary hospital in MM2 (regional centre) location, with intention to extend recruitment to a Teletrial site at a secondary hospital in MM6 (remote community) location. Recruitment closed before the MM6 site recruited any participants.
Sponsor	Large international industry Sponsor.
Why were flexible trial elements used?	This way of working was established to facilitate clinical trial medication access for patients in the MM6 location, as the Investigational Medicinal Product (IMP) required 24-hour temperature monitoring (storage 15-25C) until received by the patient. It was not possible for the Sponsor to supply directly to the site, due to lack of local staff and suitable storage facilities.
What flexible elements were used?	Established an agreement with the Sponsor that the IMP would be dispensed at the MM2 site, then shipped to the MM6 location via courier. A MM2 site pharmacist would then undertake IMP activities utilising a mobile pharmacist model. Alternatively, a delegated Clinical Trial Co-ordinator (CTC) at the site could undertake activities, pending availability and capacity.
How was flexibility added?	Flexibility was initiated at the site with the support of the sponsor and would apply to all participants at the site.

IMPACT OF FLEXIBLE TRIAL ELEMENTS ON THE CONDUCT OF THE TRIAL

Data collection	Once established, this way of working will increase access to clinical research in MM6 locations, increasing the diversity of the participant pool,
Recruitment/retention	This flexibility allowed for the recruitment of participants at the MM6 site to remain a possibility.
Review processes	The MM6 site was a satellite site to the MM2 site. This relationship and allocation of activities/responsibilities was outlined in the Teletrial Supervision Plan, and reviewed by the RGO.
Contracts	An account was established with the courier to provide temperature-controlled and -monitored freight of the IMP.
Finances	The cost of shipping was to be charged to the Australian Teletrial Program's account and reimbursed by the Sponsor (~\$1000 per consignment, quarterly). Although there is no CT pharmacist at the satellite site, a CT pharmacist at the primary site was still required to dispense the IMP, and as the cost of freight is reimbursed by the Sponsor, it is cost-neutral to the site.

OVERALL THOUGHTS

Key strengths of this approach were improved flexibility and capacity increasing, as supply does not hinge on the availability of a delegated pharmacist at the MM6 location. Because we knew that the MM6 location was desirable to the sponsor from the Site Initiation Visit (SIV) at the MM2 location we were able to work on this from that early stage. The sponsor acknowledge we are an emerging site with limited clinical trial experience at the time of the SIV. This type of approach would need to be done on a case-by-case basis and in negotiation with the Sponsor. It hinges on the MM2 site dispensing the IMP prior to sending. It would not have been an option for the MM6 CTC to receive it and supply to the patient.

FTD Case Study 3: International participant travel

Case study supplied by: Alexion Pharmaceuticals, Inc

For more information contact: Leila Lotfi, Head of Country Operations

CONTEXT OF THE TRIAL AND FLEXIBLE METHODS USED

Description of trial aim	Testing an Investigational Medical Product (IMP) for a rare disease clinical trial, with a randomised double-blind design. Participants were adults with the stated rare disease.
Trial size and location(s)	Multicentre global clinical trial. This scenario impacted just one Australian participant.
Sponsor	Large multinational pharmaceutical company sponsor, with local affiliate as country sponsor.
Why were flexible trial elements used?	Flexible elements were used because one participant needed to maintain dosing while traveling in Canada. Since the trial requires biweekly dosing, the participant would otherwise have been unable to travel for an extended period during enrolment. This flexibility prevented protocol deviations and ensured the participant did not miss doses or experience long dosing gaps, protecting both protocol compliance and safety. Supporting this flexibility has also positively impacted the participant's well-being and trial retention.
What flexible elements were used?	The IMP and ancillary supplies were shipped internationally directly to the participant's accommodation via a speciality courier, ensuring cold-chain requirements with temperature loggers. This process involved ethics and governance review, patient-specific consent for data disclosure, and sponsor-led insurance and legal review to ensure coverage was maintained throughout.
How was flexibility added?	<p>Contracts for supply and shipping were amended; TGA approval for export was obtained; data privacy consent for international data sharing was developed and signed; ethics/governance review was sought regarding the plan; insurance coverage was clarified, with PI documentation arranged as required; and bespoke courier logistics and storage solutions were sourced.</p> <p>These adaptations were operationally managed rather than included in the original protocol.</p>

IMPACT OF FLEXIBLE TRIAL ELEMENTS ON THE CONDUCT OF THE TRIAL

Data collection	No anticipated loss of data; the patient continued dosing at the scheduled interval, and follow-up visits to protocol schedule were maintained before and after the trip.
Recruitment/retention	Retention was maintained: the participant remained enrolled and compliant with the protocol, avoiding a protocol deviation or withdrawal.
Review processes	Additional review by ethics, site governance, and legal/privacy officers was required for the international element and data privacy. The trial "site" remained the Australian centre where participant was enrolled, with oversight preserved remotely.
Contracts	This process required contract amendments with the courier, the use of a Canadian consignee, and patient-specific documentation for import/export and insurance. All aspects were organised and overseen by the Sponsor from Australia.
Finances	This approach incurred costs from international shipping, cold-chain solutions, insurance & legal review. These costs were absorbed by inhouse Sponsor team.
Environmental impact	Increased environmental impact due to international air freight and cold-chain packaging. This was unavoidable as due to the trial randomisation & blinding, it was not possible to source or dispense IP from a trial location in Canada.

OVERALL THOUGHTS

The flexibility of this approach supported protocol adherence, patient safety, and trial integrity, but required extensive coordination, customised documentation, and increased costs for the Sponsor. Initially, the requirements were unclear and there was no precedence, so considerable effort went into identifying what measures were required and could be completed and gathering input from multiple stakeholders. Although this process was resource-intensive for the sponsor, it was not seen as a barrier due to the sponsor's commitment to patient centricity - particularly in rare disease clinical trials, where every effort is made to meet individual patient needs.

In the future, starting with a detailed plan and early stakeholder engagement would help streamline the process and anticipate requirements. For others using this approach, it is recommended to ensure thorough preparation, clear communication among all parties, and a strong focus on patient-centred solutions to continue to drive the best outcome.

FTD Case Study 4:

Virtual and direct-to-participant IBS supplement trial

Case study provided by: Central Pharmacy Logistics

For more information contact: Rima Darwiche or Emily Bandiera

CONTEXT OF THE TRIAL AND FLEXIBLE METHODS USED

Description of trial aim	Trial tested the safety and efficacy of a complementary investigational medicine.
Trial size and location(s)	This Phase 2 trial aimed for a participant population size of 60-100 individuals, with 62 participants fully assessed in that stage. This number, combined with Phase 1 participants, is expected to result in approximately 100 participants for the final analysis. There were 5 sites in total, with a mixture of private and public hospital sites. Participants were primarily on the Australian East Coast and South Australia.
Sponsor	The sponsor was a small Australian biotech/collaborative research group.
Why were flexible trial elements used?	As the participant group are in the younger 18-65 year old age bracket, a virtual approach was thought to be more compatible with their lifestyle and time constraints.
What flexible elements were used?	<p>Virtual and direct-to-patient elements were used to recruit participants and retain them in the trial.</p> <p>The trial used e-consent, and participants were screened by phone and by completing an at-home stool sample collection to determine eligibility. Test kits were mailed by participants to the diagnostic lab, who contacted the clinic with the results. The study coordinator then contacted Central Pharmacy Logistics (CPL, a supply chain company with a focus on direct-to-patient model) with the randomisation details and CPL shipped the appropriate kit (including the investigational medical product, IMP) to participants</p> <p>When participants received the IMP, they were instructed to read a temperature card and to contact the study coordinator if the temperature storage conditions were unacceptable.</p>
How was flexibility added?	These approaches were built into the protocol and used for all participants.

IMPACT OF FLEXIBLE TRIAL ELEMENTS ON THE CONDUCT OF THE TRIAL

Impact on data collection	We were able to collect more data quickly as this study had a fast rate of recruitment.
Impact on recruitment/retention	Retention rate was high at over 90% when industry standard for a traditional clinical trial is 50% retention.
Impact on review processes	The Research Governance Office and HREC were supportive of the virtual trial design, perhaps because it was a supplement rather than a potent chemical.
Impact on contracts	The central pharmacy used their regular shipping contracts with a courier who has SOPs on direct-to-patient delivery, with the sites and principal investigators maintaining overall responsibility. Delegation logs were prepared at sites for IMP to be shipped to participants. ePROs and other e-technologies were used to ensure informed consent, randomisation appropriately and participant privacy at all times.
Impact on finances	For this trial it is difficult to know what the financial cost of direct-to-patient IMP management would have been as it was done this way from the beginning, however it is expected to have positively impacted the budget as there was less drop out and retention was high, hence more data in a shorter time.

OVERALL THOUGHTS

The key strength of this approach was the low withdrawal rate. At end of the trial this was about 7-8% or even less when other parameters are applied, with most withdrawal by placebo participants. Current industry standard for withdrawal from a “traditional” trial are 50% on average. This trial design worked well but not suitable for every IMP. The low-risk, oral nature of the IMP and its temperature stability made it appropriate for this trial.

FTD Case Study 5: START Trial prescribing process

Case study provided by: The George Institute
For more information contact: Helen Monaghan

CONTEXT OF THE TRIAL AND FLEXIBLE METHODS USED

Description of trial aim	The SGLT2 inhibitors As first line therapy to prevent Renal decline in Type 2 diabetes (START) trial is a multi-centre, double blinded, 1:1 randomised trial. The aim is to evaluate the comparative effects of the SGLT2 inhibitor dapagliflozin compared to metformin on annual decline in eGFR when used
Trial size and location(s)	500 participants across Australia and Sri Lanka In Australia, sites were GP practices across NSW, QLD and VIC. In Sri Lanka
Sponsor	The Sponsor is The George Institute for Global Health, a multinational not for profit clinical research institute.
Why were flexible trial elements used?	The study design involved the direct shipping of study drug from Syntro (a global investigational medical product (IMP) management company) to participant's homes, so a solution had to be found to get signed prescriptions
What flexible elements were used?	<p>The George Institute is acting as the site (as well as being the Sponsor and trial coordinating centre) for this trial, and had to ensure that scripts for trial medication were signed by qualified physicians prior to being sent to Syntro Pharmacy to trigger despatch to participant's homes.</p> <p>A solution was developed with The George Institute IT team utilising a study specific MS Teams site.</p> <ul style="list-style-type: none"> ■ There are mechanisms in place to allow a team member to select the participant number and the visit type, along with other information relevant to the assessment. ■ A pdf report is generated and a copy of the report is sent to one of the Central Trial Physicians (who have previously provided signed scripts) asking for review of the report and confirmation that the script can proceed. ■ Once confirmation is received, a script template is populated and the script is generated with the physician's signature. ■ A copy is faxed to Syntro with the original version following by post. ■ The trial team monitored temperature forecasts during summer months for departure and arrival cities before confirming shipments could be safely dispatched. The temperature requirements of the IMP were storage under 30C with mean temp of 25C. Transient spikes of up to 40C were permitted as long as they didn't exceed 24h.
How was flexibility added?	This flexibility was planned from the beginning of the trial and is outlined in detailed manual of procedures.

IMPACT OF FLEXIBLE TRIAL ELEMENTS ON THE CONDUCT OF THE TRIAL

Data collection	This exercise didn't really impact the data collection, but rather enabled study drug to be managed centrally and sent directly to participant's homes.
Recruitment/retention	There wasn't an effect on recruitment (which has been incredibly challenging for this trial) but anecdotally it worked well for participants having the medication delivered and they were generally happy with this approach.
Review process	We looked upon this as a legal issue rather than an ethical issue. We didn't deviate from the fact that a registered physician had to physically sign the scripts. We just found a way to enable this to happen via trial physicians located at The George Institute (as the site) and Syntro the central pharmacy. In the PISCF it was explicit that trial drug would be sent from Syntro to a participant's home.
Contracts	There is a contract with Syntro Pharmacy to despatch the trial medication directly to participants.
Finances	This approach meant that more assessments could be done by phone as drug was being sent to participants homes which meant lower cost assessments. Additionally having one pharmacy rather than multiple is a cost saving.
Environmental impact	Not specifically although it did mean that participants didn't have to travel to a local pharmacy to collect trial medication and we didn't have to set up multiple pharmacy agreements and associated paperwork.

OVERALL THOUGHTS

The strength is that we were able to utilise trial physicians employed by The George Institute. This is an approach that could be replicated by other trial teams recruiting through general practice or in the community where trial medication is being sent directly to participants.

FTD Case Study 6: Regional satellite site

Case study provided by: WA Country Health Service (WACHS)

For more information contact: Nadine Herren, [WA Country Health Service - Clinical trials](#)

CONTEXT OF THE TRIAL AND FLEXIBLE METHODS USED

Description of trial aim	Reduce blood phosphate and associated complications by reducing dietary phosphate intake in patients on dialysis
Trial size and location(s)	23 sites, across Australia Case study relates to a site with a Perth tertiary hospital and a WA regional hospital.
Sponsor	An Australian university
Why were flexible trial elements used?	The trial for dialysis patents was based in the city. Many renal failure patients are living in rural, regional and remote areas and have difficulty travelling to the city to participate in clinical trials.
What flexible elements were used?	The Perth tertiary hospital added the WA regional hospital as a Satellite Site. The Principal Investigator (PI) in Perth provided oversight to the Satellite Site to enable the delivery of clinical trial activities. All trial visits were conducted while patients were undergoing routine dialysis in the regional dialysis unit. This option was available for patients living close to the regional hospital so that they could take part without having to travel 8hrs or more to Perth.
How was flexibility added?	<i>Contractual Arrangements</i> The Medicines Australia Clinical Trial Research Agreement (CTRA) between the Sponsor and the trial site institution was amended to include Satellite Site clauses, and the Teletrial sub-contract was executed by the trial site institution and the satellite site institution. <i>Research Ethics and Governance Review</i> A WA Research Ethics and Governance Working Group was established to design a streamlined co-review process for Teletrials across separate intuitions. The Research Governance Offices of the two institutions worked collaboratively to review the addition of the Satellite Site. Both institutions authorised the Satellite Site. <i>Trial Coordination</i> Trial Coordination, governance, leadership and support was provided by the WACHS Trial Centre who arranged appropriate contracts, ethics and governance submission, Teletrial training, reporting and on-site support for the Satellite Site and Principal Investigator. <i>Principal Investigator Oversight</i> The Principal Investigator travelled to the regional health service for the first week of the trial to conduct training, site initiation visit (SIV), delegation and consent the first patients. Ongoing oversight was provided through PI review of blood results, data on entered into the electronic Case Report Form (eCRF) and via self-monitoring visit reporting by the WACHS Trial Centre. The Satellite Site design was not built into the protocol, rather it was detailed in the Teletrial Supervision Plan.

IMPACT OF FLEXIBLE TRIAL ELEMENTS ON THE CONDUCT OF THE TRIAL

Data collection	Including a Regional, Rural and Remote (RRR) satellite site enabled the inclusion of data from country patients who are overrepresented in this therapeutic area. Strengthening the validity of trial data and applicability to the real-world setting.
Recruitment/retention	Addition of a satellite site facilitated the rapid recruitment of 10 country participants who would have otherwise been unable to participate.
Review processes	The “site” was the site of the Principal Investigator who had responsibility for activities conducted at a separate geographical location. The trial site was named the primary site and the country site was named a satellite site.
Contracts	Teletrial sub-contracts used between the Primary and Satellite sites.
Finances	Utilising that Teletrial model allowed the primary site to receive \$5000 in Teletrial support payments and the satellite site to receive \$700.00 per patient. This was supplemented by the provision of deployed clinical trial coordinators to site funded by the Australian Teletrial Program and in-kind support by hospital staff. Without this support it would have been difficult for the Primary site to set up the Satellite Site and for the Satellite Site to be included.

OVERALL THOUGHTS

The strength of the approach was improved access to a broader group of patients enabling representation from country patients and testing of the intervention in a real-world setting. Adding a satellite site also enabled rapid recruitment of additional patients and upskilling of the regional workforce in clinical trial conduct.

To streamline the approach and improve timelines, detailed stakeholder engagement with all parties involved would be commenced prior to the proposal of a specific trial.