QUEENSLAND HEALTH TELETRIALS PILOT ANALYSIS REPORT

Prepared by

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Queensland Health (QH)

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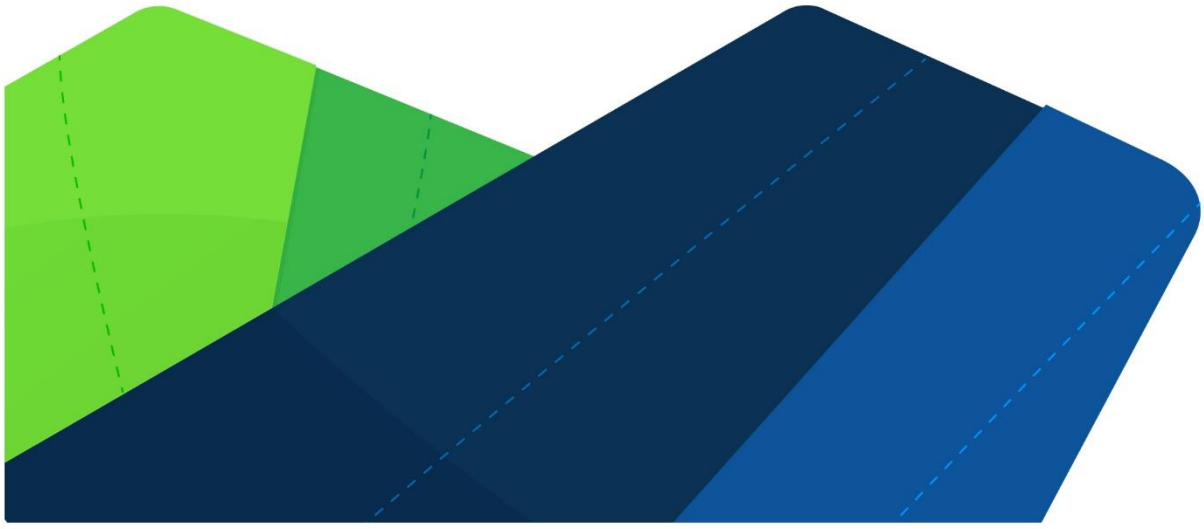

Queensland Government

Queensland Health Teletrials Pilot Analysis Report

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Summary

A Queensland Health pilot project of the use of telemedicine in clinical trials, under a quality assured framework, has shown that:

- **The data produced is acceptable for commercially sponsored research destined for marketing applications to regulators.**
- **The teletrials model enables rural and remote patients to access clinical trials closer to home.**
- **Teletrials is an efficient way of increasing clinical trials capability and training of regional sites in Good Clinical Practice (GCP).**
- **There is broad national support for the implementation of a uniform teletrials model.**

Background

Clinical trials are prospective research studies on human participants that are designed to answer specific questions about biomedical or behavioural interventions, including new treatments such as novel vaccines, drugs, dietary choices, dietary supplements, and medical devices.

Owners (or Sponsors) of therapeutic products are required to conduct clinical trials to generate safety and efficacy data before they can sell those products in any markets.

Governments of those markets have strict regulations about how clinical trials are conducted and how trial data is quality assured. This has led to Sponsors having very high monitoring standards and controls over clinical trial sites. Ensuring the scientific validity of clinical trial data requires resource intensive administrative processes and compliance with global standards such as the International Council for Harmonisation of Good Clinical Practice (ICH-GCP). The compliance costs and resources limit the number of sites a Sponsor can activate for a single trial, and this has meant many regional patients have been only able to access clinical trials in metropolitan centres.

Queensland Health has strategically invested in State-wide telemedicine infrastructure to facilitate the best treatments, at the right time and place for regional and remote patients. The challenge of exploring and developing the use of telemedicine to facilitate the opening of regional clinical trials sites, in an acceptable and cost effective way for commercially sponsored clinical trials, was undertaken by Queensland Health at the request of clinical researchers.

The Queensland Clinical Trials Coordination Unit (QCTCU) of the Department of Health ran a pilot project to develop the framework, quality assurance requirements and processes for health system-wide teletrials implementation. This work was supported by the Commonwealth Department of Health under the Project Agreement *Encouraging More Clinical Trials to Australia*. Under the Project

Agreement, in 2017, Queensland Health was awarded $1.2 million over four years to establish QCTCU and among other projects, to develop and implement a teletrials model. This work will also inform a National approach to teletrials, so ultimately any patient, anywhere will have access to relevant clinical trials, in the same way as their metropolitan counterparts, without the need to venture far from home.

Project Overview

The project aim was to implement a standardised teletrials model with satellite regional sites across Queensland (the Project) to improve rural and remote patient access to trials.

Although it is not uncommon for doctors and other clinicians (investigators) to see patients for ad-hoc clinical trial visits at satellite clinics or to conduct interim "telephone" visits, there is no health system-wide standard agreed to conduct an entire clinical trial using video conferencing (i.e.telemedicine) where one Principal Investigator is responsible for patients at satellite sites.

To enable this approach, a quality assurance framework is required so that industry and regulators can be assured of the safety of participants and the quality of data produced at sites where patients are seen by telemedicine. The safety and efficacy of telemedicine for non-clinical trial hospital services has been well established[1] and telemedicine has been successfully implemented in Queensland Health[2]. The ability to translate this innovation into a clinical trial context is a reasonable assumption.

QCTCU led the development of the teletrials quality assurance framework that was tested in a commercially sponsored clinical trial for a breast cancer drug, in the Queensland public hospital system (the Pilot). The pilot informed the final version of the policy and processes that are proposed to be mandated as Standard Operating Procedures (SOPs) in Queensland Health via a Research Ethics & Governance (REG) Health Service Directive. The proposed mandatory standard gives industry the assurance that teletrials conducted in Queensland Health will ensure patient safety, and produce data that will be acceptable to regulatory agencies. In addition to bringing clinical trials

[1] Jhaveri, Divita, Larkins, Sarah, and Sabesan, Sabe (2015) *Telestroke, teleoncology and teledialysis: a systematic review to analyse the outcomes of active therapies delivered with telemedicine support. Journal of Telemedicine and Telecare, 21 (4). pp. 181-188*

[2] Sabesan, Sabe, Senko, Clare, Schmidt, Andrew, Joshi, Abhishek, Pandey, Ritwik, Ryan, Corrine A., Lyle, Megan, Rainey, Natalie, Varma, Suresh, Otty, Zulfiquer, Ansari, Zia, Vaughan, Kerrie, Vangaveti, Venkat, Black, Jason, and Brown, Amy (2018) Enhancing chemotherapy capabilities in rural hospitals: implementation of a telechemotherapy model (QReCS) in North Queensland, Australia. Journal of Oncology Practice, 14 (7). e429-e437

closer to home for patients, recruitment potential increases and workforce capability at regional sites is increased.

The Pilot began in November 2017 with two clusters, the Northern cluster (Townsville, Cairns, Mackay & Mt Isa) and the Gold Coast/Hervey Bay cluster. Three sites with various levels of trial capabilities, who would normally miss out on participating in clinical trials, were involved. Eight satellite staff were upskilled with ICH GCP training and clinical trial experience and 11 regional patients who would otherwise not have been able to participate in clinical trials were enrolled.

Project Timeline

- **2015 -** Professor Sabe Sabeson (Director of Medical Oncology, Townsville Cancer Centre, Townsville Hospital and Health Services, Townsville/ Co-Chair, Australasian Teletrial Consortium Clinical Oncology Society of Australia, Sydney and Chair, QH State-wide Teletrial Working Group) initiates discussion with the Health and Medical Research Team, now the Health Innovation, Investment Research Office (HIIRO) in the Department of Health to champion the Teletrial Initiative.
- **2016 -** Prof Sabeson secures support from members of the Clinical Oncology Society of Australia (COSA), clinical trial sponsors, clinicians, health administrators, and regulatory bodies to develop a national teletrials framework and implementation plan.
- **November 2016** - The Australasian Tele-trial Model is released.
- **August 2017** - HIIRO begins work on operationalising the teletrial model by writing the Australian ICH GCP (Including Teletrials) Standard Operating Procedures (SOPs).
- **November 2017** - The Queensland Health led teletrials pilot is agreed with Eli Lilly and the Monarch E protocol is chosen as the pilot trial.
- **December 2017** - The first iteration of the Australian ICH GCP (Including Teletrials) SOPs (Teletrials SOPs) is publicly released (Version 2) and the teletrial pilot starts.
- **June 2018** - The revised Teletrial SOPs (Version 3) are released incorporating extensive stakeholder input from industry, the sites involved in the pilot, State Departments of Health and the QH Clinical Research Coordinator network.
- **October 2018** - The first rural and remote teletrials patient is recruited.
- **April 2019** - Final Australian ICH GCP (Including Teletrials) SOPs (Version 4) are released incorporating further feedback from the pilot trial sites, the sponsor (Eli Lilly), the Contract Research Organisation (CRO) monitoring the trial (IQVia) and comments from Round 1 consultation on QH's REG Health Service Directive.

Key Findings

This project would not have been possible without a large coalition of willing stakeholders and the strategic investment by the Commonwealth Department of Health. An analysis of feedback from stakeholders was undertaken in March 2019 to evaluate the Pilot and inform the final version of the SOPs and QH REG Health Service Directive.

The key project findings are:

1. Commercial Sponsors, including the sponsor for the pilot:
    - support national implementation of a unified teletrials model
    - support the Australian ICH GCP (Including Teletrials) SOPs developed by Queensland Health
    - support the Primary and Satellite site sub-contract with the Medicines Australia/ Medical Technology Association Australia Clinical Trials Research Agreement templates as the header agreement in the annexure. National acceptance and usage of the teletrials sub-contract with header agreement is desirable
    - will provide indemnity to all satellite sites as well as the primary site and this will facilitate public/private and interjurisdictional clusters
    - data quality was assured and no protocol deviations or breaches to the protocol were identified
2. A clinical champion is required to drive policy implementation within health systems.
3. Regular primary and satellite site cluster meetings are needed to consolidate the collaboration between clinical trial, institution management and research governance staff.
4. Significant cross jurisdictional consultation initially utilising the National Mutual Acceptance (NMA) working group infrastructure for national implementation of teletrials is necessary.
5. A Teletrials definition acceptable to all jurisdictions is to be agreed by the NMA with work now to be progressed by an NMA working group.
6. The Teletrial Cluster model is an efficient way of upskilling regional sites compared to establishing them as standalone trial sites.
6. Both primary site and satellite staff found it rewarding to work with multiple sites in collaboration; to see patients gain access to clinical trials closer to home; and to see Research Governance Officers (RGOs) learning from each other and collaborating due to

the Health Service Directive.

7. Patient feedback has been positive and without teletrials, they would not have participated in the clinical trial to access the potentially lifesaving drug. Regional patients are not usually able to relocate or travel vast distances to metropolitan cities.

Table 1 - SOP recommendations of the Teletrials Pilot

Teletrial Model Issue	Teletrial Model Intent	Pilot Actual	Teletrial Pilot SOP recommendation
Satellite Site (SS) Selection	Primary Site (PS) Responsibility	Sponsor visited all SSs for the pilot to confirm acceptance	PS to evaluate and select appropriate SS only at time of potential eligible participant identified at SS, and not at the initiation of the trial unless warranted.
Satellite Site Initiation and training / Investigator Meeting	Primary Site Responsibility	Sponsor visited all SSs to initiate and train SS staff	Sponsor to initiate and train / hold Investigator meeting at PS. PS to initiate and train SS only at time of potential eligible participant identified at SS, and not at the initiation of the trial unless warranted. Refer to Australian ICH GCP (Including Teletrials) SOP 30 & 60 https://www.health.qld.gov.au/hiiro/html/regu/for_researcher/gcp,research-ethics-and-governance-standard-operating-procedures-sop
Satellite Site Monitoring	Sponsor to perform Source Document Verification (SDV) and monitoring for all SSs remotely at PS	Sponsor visited all SSs to perform (SDV) and monitoring	SS to ensure all relevant trial related documentation to be at PS Trial Master File (TM) as stipulated in the Supervision Plan and documented in the monitoring plan. Refer to Australian ICH GCP (Including Teletrials) SOP 30. https://www.health.qld.gov.au/hiiro/html/regu/for_researcher/gcp,research-ethics-and-governance-standard-operating-procedures-sop
Shipment of Investigational Medicinal Product (IMP)	Primary Site Responsibility to dispatch IMP to SS as and when needed.	Sponsor shipped trial IMP to all SSs as all SSs were listed on the Clinical Trials Notification (CTN) and to ensure appropriate cold chain processes were observed.	Sponsor to ship all trial IMP to PS. PS Pharmacy to have validated cold chain processes in place to send IMP to SS only at time of potential eligible participant identified at SS. Refer to Australian ICH GCP (Including Teletrials) SOP 110 https://www.health.qld.gov.au/hiiro/html/regu/for_researcher/gcp,research-ethics-and-governance-standard-operating-procedures-sop
Site identification on the CTN	PS only to be listed on the CTN.	Sponsor created a separate CTN for each SS as IMP was shipped to each SS	Sponsor to list only the PS on the CTN and the Primary Site should keep IMP and ship to the satellite site as required.

Future Directions

The project's final product *The Australian ICH GCP (Including Teletrials) SOPs* and associated sub-contract template have been developed to incorporate the recommendations from the *Clinical Oncology Society of Australia's (COSA) Australasian Tele-trial Model – A National Guide to Implementation*.

These SOPs and subcontract template have been made freely available to all jurisdictions, and a working group has formed within the National Mutual Acceptance Scheme to further progress national policy agreement. Queensland Health will be the jurisdictional custodian of the Australian ICH GCP (Including Teletrials) SOPs.

A State-wide training strategy concerning the implementation of the Teletrials Model, Australian ICH GCP (Including Teletrials) SOPs and Australian Teletrials sub-contract will be developed and implemented across Queensland.

Conclusion

The vision of providing state of the art infrastructure and a standard operating environment for clinical trial related services to clients not only in the densely populated areas but also to clients in the rural and remote areas of Queensland has been achieved in a way that is acceptable to commercial clinical trial Sponsors. The outcomes of the pilot project are expected to facilitate further teletrials across Australia over the next few years and this can be supported by the implementation of a unified teletrials model.

Acknowledgements

The QCTCU gratefully acknowledges the Commonwealth Department of Health and thanks the research community for their input and involvement in this project, particularly the COSA Teletrials Consortium, Medicines Australia and its member organisations, Cooperative Clinical Trial Groups, COSA Queensland Health (QH) advisory group, QH State-wide Teletrial Working Group, QH State-wide Cancer Clinical Network and pilots at the Northern Cluster and the Gold Coast/Hervey Bay Cluster in Queensland and Orange/Dubbo Cluster in New South Wales, QH Clinical Research Coordinator Network and other State Health jurisdictions, QH Research Governance Officers (RGOs), Contract Research Organisations (CROs) and pharmaceutical company representatives.

Appendices

Bush cancer patients travel hundreds of kilometres for life-saving treatment. *ABC Landline* Jennifer Douglas First posted 21 May 2018, 7:03am, Updated 26 Sep 2018, 4:17pm [Accessed 20 July 2019]
https://www.abc.net.au/news/2018-05-21/cancer-patients-travel-hundreds-of-kilometres-for-treatment/9758072

New trial saves lives *Townsville Bulletin* 21 November 2018 pg.13
https://www.townsvillebulletin.com.au/

Saving lives webcam consultations for rural and regional areas *Daily Mercury, Mackay QLD* Zizi Averill November 22 2018 pg. 1,3. https://www.dailymercury.com.au/

Townsville Hospital and Health Service Media- News Release 20 November 2018
Telehealth brings drug trials to the regions
https://www.health.qld.gov.au/townsville/about/media-news-releases-2018/telehealth

Townsville Hospital rolls out country first *Townsville Bulletin* Tess Ikonomou 21 November 2018 p.g.10 https://www.townsvillebulletin.com.au/

Trial to close the gap in rural areas *Weekly Times, Rural Weekly* 23 November 2018 pg. 8
https://www.weeklytimesnow.com.au/news/rural-weekly

Treating remote cancer patients with telehealth *Health Report ABC* interview with Professor Sabe Sabesan Monday 10 December 2018 5:45PM [Accessed 20 July 2019]
https://www.abc.net.au/radionational/programs/healthreport/treating-remote-cancer-patients-with-telehealth/10599286

Letter of appreciation from COSA re: Qld implementation of Teletrials

Clinical Oncology Society of Australia

10 October 2018

Karen Thompson
Senior Director
Health Innovation, Investment and Research Office
Queensland Department of Health
Karen.Thompson3@health.qld.gov.au

Dear Ms. Thompson,

We would like to express our gratitude for the work done by HIIRO to implement the Australasian Tele-Trial Model in Queensland. We would especially like to thank Melissa Hagan and her team for their excellent contribution to this achievement. Queensland is leading Australia in this ground-breaking initiative which will ensure equity of access to clinical trials for patients in regional and rural Australia.

Under the leadership of Professor Sabe Sabesan we look forward to continuing our collaboration with HIIRO in the future.

Yours sincerely

Marie Malica
Chief Executive Officer

Cancer Council
(Affiliated with Cancer Council Australia)

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