

Ethical Principles for the Conduct of TROG Clinical Trials

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Summary: The aim of this policy statement is to ensure the protection of the rights, safety and wellbeing of trial participants.

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Applies to: TROG full, affiliate and lifetime members; TROG staff

Approved by: TROG Chief Executive Officer

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Revision Chronology:

Vs 1: 31 Jan 1997	New policy
Vs 2: 15 Oct 2008	Document rewritten to be TROG-specific.
Vs 3: 09 Mar 2011	Addition of regulations. Consistency check with protocol template. Update of references.
Vs 4: 06 Dec 2013	Addition of regulations. Consistency check with other TROG Policy Statements. Update of references.
Vs 5: 28 Mar 2017	Addition of regulations. Update to sections 2.2, 2.3, 3.2, 3.3, 3.4, 3.6 and of the references.

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1.0 GENERAL PRINCIPLES

All research conducted under the auspices of TROG (whether or not TROG is the lead trials group) is performed in compliance with the principles detailed in the:

- Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects (last amended by the World Medical Association, 2008)¹
- Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice E6(R2)²
- Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) annotated with TGA comments (Australia, July 2000)³
- Australian Code for the Responsible Conduct of Research (2007)⁴
- Guideline on the Regulation of Therapeutic Products in New Zealand. Part 11: Clinical Trials - Regulatory Approval and Good Clinical Practice Requirements (January 2015)⁵
- National Statement on Ethical Conduct in Human Research, (Australia, 2007)⁶
- Ethical Guidelines for Intervention Studies: Revised edition (NZ 2012)⁷
- Values and Ethics - Guidelines for Ethical Conduct in Aboriginal and Torres Strait Islander Health Research (Australia 2003)⁸
- Statement on Consumer and Community Participation in Health and Medical Research (Endorsed 7th December 2001)⁹
- Ethical Guidelines for Intervention Studies, Revised edition (New Zealand, 2012)¹⁰
- Standard Operating Procedures for Health and Disability Ethics Committees, New Zealand Ministry of Health, 2012 (<http://ethics.health.govt.nz/operating-procedures>)¹¹
- Guidelines for the Use of Human Tissue for Future Unspecified Research Purposes. New Zealand Ministry of Health: 2007 (<http://www.health.govt.nz/publication/guidelines-use-human-tissue-future-unspecified-research-purposes-0>)¹²
- Current TROG Policy Statements (<http://www.trog.com.au/Policy-statements>)

TROG investigators are also required to comply with all other Australian and New Zealand national requirements that are applicable to research involving human participants including all privacy legislations.

It is not the intention of this policy to repeat information from the above documents but to provide TROG investigators a summary of the main areas covered in relation to the ethical conduct of clinical trials and to therefore assist them to easily locate additional relevant information.

Specific templates and procedures, such as the TROG protocol template, have been implemented by TROG in order to ensure compliance to the above documents.

2.0 GUIDELINES REQUIRING FURTHER EXPLANATION

2.1 Note for Guidance on Good Clinical Practice annotated with TGA comments (Australia)

The Note for Guidance on Good Clinical Practice (GCP) is an internationally accepted standard for the designing, conducting, recording and reporting of clinical trials.

The Therapeutic Goods Administration (TGA) has adopted CPMP/ICH/135/95 in principle but has recognised that some elements are, by necessity, overridden by the National Statement (see section 2.2) and therefore not adopted and that others require explanation in terms of 'local regulatory requirements'.

Section of the international GCP guidelines not adopted by the TGA:

Section 3: Institutional Review Board/ Independent Ethics Committee

Sections of the international GCP guidelines explained further by the TGA:

Section 4.8: Informed Consent of Trial Subjects

Section 5.5.11: Retention of Records by Sponsors of Clinical Trials

Section 5.17: Adverse Drug Reaction Reporting

2.2 National Statement on Ethical Conduct in Human Research (Australia)

The National Statement is designed to clarify the responsibilities of institutions and researchers for the ethical design, conduct and dissemination of results of human research; and review bodies in the ethical review of research.

The values set out in Section 1: Values and principles of ethical conduct – respect for human beings, research merit and integrity, justice and beneficence – help to shape the relationship between the researcher and research participants as one of trust, mutual responsibility and ethical equality. For this reason, the term research 'participant' is used rather than 'subject' and is applied throughout all TROG documentation.

Other sections of particular relevance to TROG researchers include:

Chapter 2.2: General Requirements for Consent;

Chapter 3.3: Interventions and Therapies, including Clinical and Non-clinical Trials, and Innovations (which also provides definitions of Phase I-IV clinical trials);

Chapter 5.2: Responsibilities of Researchers, and;

Chapter 5.5: Monitoring Approved Research.

Researchers, Institutions and Human Research Ethics Committees (HRECs) are advised to use the NHMRC web site to ensure that they are accessing the current version of the National Statement, and to check regularly for updates. It is the responsibility all users of the National Statement, including HRECs, Research Offices and researchers to ensure the current version is being used in establishing research proposals and undertaking any ethical review that occurs on or after the date of release of any update.

2.2.1 NSW Supplement to the National Statement of Ethical Conduct in Human Research

To assist all those concerned with the lawful and ethical conduct of research in the NSW public health system, NSW Health has developed the NSW Supplement to the National Statement of Ethical

Conduct in Human Research (NSW Supplement)¹³. The NSW Supplement summarises relevant New South Wales law and policy.

2.3 Ethical Guidelines for Intervention Studies (New Zealand)

The Guidelines accord with key international guidance, including the World Medical Association Declaration of Helsinki: Ethical principles for medical research involving human subjects (WMA 2008), the International Ethical Guidelines for Biomedical Research Involving Human Subjects (CIOMS 2002) and the ICH Harmonised Tripartite Guideline: Guideline for good clinical practice (ICH 1996). Sections that contain information that is particular to implementing research in New Zealand include:

Section 4: Justice

Section 6.22: Features of Informed Consent

Section 8: Compensation for Injury

These guidelines set out the established ethical standards that all researchers must meet when undertaking health and disability research, whether or not that research requires health and disability ethics committee review. These guidelines are also of use to ethics committees, research sponsors and for training and educating researchers.⁷

The New Zealand Ministry of Health's Standard Operating Procedures (2012)^{Error! Reference source not found.}¹ support Ethics review by clearly defining the role of Ethics Committees and the review process, and providing rules and guidance for implementing the Guidelines.

2.3.1 Cultural Considerations (New Zealand)

All research in New Zealand must undergo review from a Māori cultural perspective before locality approval will be granted as part of the Ethics review process. Areas of review include assessing how the proposed research will impact health-related inequalities in New Zealand, ensuring that the proposed informed consent process is culturally appropriate, and identification of any ethical issues of significance to Māori. There are specific cultural considerations for any research involving tissue, in particular for tissue that needs to be overseas from New Zealand. For any research involving tissue for future unspecified research, consult the Guidelines for the Use of Human Tissue for Future Unspecified Research Purposes (Wellington: Ministry of Health 2007)¹².

3. TROG SPECIFIC PROCEDURES

The following procedures have been implemented as measures to ensure compliance by TROG and its members with the regulatory and ethical guidelines specified in Section 1.

3.1 Protocols

TROG has developed a protocol template to comply with regulatory and ethical guidelines specified in Section 1 along with the SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) statement.^{14, 15}

The TROG protocol template is provided to all TROG Trial Chairpersons of a Category A trials when a trial is approved for further development by the TROG Scientific Committee.

3.2 Group Specific Appendix

For Category B trials (i.e trials developed by another research group, where TROG is acting in the role of ANZ sponsor), a Group Specific Appendix (GSA) will be required to comply with regulatory and ethical guidelines specified in Section 1.

The TROG GSA template is provided to all TROG Trial Chairpersons of a Category B trial when the trial is approved for further development by the TROG Scientific Committee.

3.3 Participant Information Sheet and Consent Form

The template/master Participant Information Sheet and Consent Form (PICF) should be a separate document to the protocol (i.e. not included in the appendix) so that when changes occur the entire protocol does not need to be submitted for HREC approval.

The format of the PIC and instructions for the content will depend on the ethics committee undertaking the review and the region in which they are located. See following websites for examples:

- <http://www.health.vic.gov.au/clinicaltrials/application-instructions.htm> (for everything)
- http://www0.health.nsw.gov.au/policies/gl/2007/GL2007_016.html (PIC)
- <http://hrep.nhmrc.gov.au/toolbox/standardised-forms> (PIC)

TROG specific information to be inserted into the trial PIC can be found in the TROG protocol template.

3.4 Protocol Approval by the TROG Scientific Committee

All final protocols, GSAs, Radiotherapy Planning Delivery and QA Guidelines and PICFs, and any amendments to these documents, must be approved by the TROG Scientific Committee prior to being submitted to an ethics committee.

Prior to ethics submission, the TROG Representative and Trial Chairperson must sign the protocol/GSA signature page. A copy of this page must be forwarded to the TROG Central Operations Office.

3.5 Agreements

In order to ensure the ethical conduct of clinical trials, TROG implements Clinical Trial Research Agreements (CTRAs) which detail responsibilities and obligations of TROG and other parties i.e. Trial

Site, Trial Coordinating Centre, Collaborating Groups. Each trial must finalise all CTRAs required for trial infrastructure (including any industry sponsorship agreements) prior to the trial commencing accrual. Contracts for each Trial Site will be finalised as part of each site's activation requirements. Refer to the TROG Policy Statement: Trial Development Resources for further information.

3.6 Ongoing Monitoring of Compliance

TROG ensures ongoing compliance to the regulatory and ethical guidelines specified in Section 1 through the following methods:

- standard trial site activation requirements across all participating sites
- requesting and monitoring bi-annual trial specific progress reports
- regular TROG Scientific Meetings to discuss the ongoing conduct of all trials
- Annual Scientific Meetings where all trial chairperson are requested to present current information to the TROG membership

Further information on methods used to monitor the conduct of TROG trials can be found in TROG Policy Statement TPS E3 Trial Development and Conduct Guidelines.

4. LEGISLATION AND GUIDELINES - PRIVACY AND CONFIDENTIALITY

Maintaining high standards of conduct with respect for the privacy of individuals and the confidentiality of information is essential for all personnel involved with the conduct of clinical research.

Collection, use, disclosure and storage of data associated with TROG clinical trials must be compliant with the Privacy Act 1998 (Aust) and associated Guidelines to the National Privacy Principles¹⁶, relevant Australian State and Territory legislation and the Privacy Act 1993 (NZ)¹⁷.

In addition to the above regulations and guidelines, principle 2.11 of TGA ICH GCP guidelines states that the confidentiality of records that could identify subjects should be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirements.

The NHMRC National Statement also outlines privacy and confidentiality issues; and covers additional areas such as the use of human tissue samples (chapter 3.4) and human genetic research (chapter 3.5)⁵. The New Zealand Ethical Guidelines for Intervention Studies, Revised edition (2012) outlines privacy requirements in Section 7.¹⁰

5. REFERENCES

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