

Policy Statement



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Protocol Amendments for TROG Trials

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Summary: The aim of this policy statement is to describe the review and approval process for TROG trial amendments

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Applies to: TROG Trial Management Committee members, Central Trial Coordinators, TROG Scientific Committee members, TROG staff

Approved by: TROG Chief Executive Officer and Research Manager

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	Vs 2: 11 Apr 2017	Update category of amendments and TSC approval process

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1 AMENDMENT DEFINITION

A Protocol Amendment is defined by the TGA ICH Good Clinical Practice guidelines as ‘a written description of a change(s) to, or formal clarification of, a protocol’¹. For the purpose of this document, changes to other trial documentation that are an extension of the protocol, such as the Group Specific Appendix (GSA), Participant Information and Consent Form (PICF) and RT Planning Delivery and QA Guidelines, are considered to be protocol amendments.

Amendments may occur at any time during the trial lifetime and may be a result of the following:

- Immediate issues that have a significant impact on the safety of the patient (commonly related to the intervention being studied).
- Feedback from sites in relation to Radiation Therapy (RT) planning techniques, timing of patient assessments and the practicalities of patient eligibility criteria.
- A change to the type of data being collected i.e. to ensure that all required data relating to the outcomes and endpoints are collected and available for analysis. Protocol amendments for closed trials may occur to ensure that all data collected is analysed and published.
- Publication of new information that results in an ethical requirement for the protocol and PIC to be amended (such as changes to a specific standard of care).

Protocol amendments can be classified as substantial and non-substantial. This Policy Statement explains the differences between the categories and describes the correct processes to follow to obtain TSC approval for a protocol amendment.

1.1 Substantial Amendments

Substantial amendments refers to an amendment to the protocol or any other supporting documentation, that is likely to affect to a significant degree^{4,5};

- the safety or physical or mental integrity of the subjects of the study;
- the scientific value of the study;
- the conduct or management of the study;
- or the quality or safety of any investigational medicinal product used in the trial.

These may include changes to⁵;

- the design or methodology of the study, or to background information affecting its scientific value;
- the procedures undertaken by participants;
- the study documentation such as participant information sheets, consent forms, questionnaires;
- the sponsor(s) or sponsor’s legal representative;
- the Trial Management Committee or appointment of a new Trial Chair
- the insurance or indemnity arrangements for the study
- the risk/benefit assessment for the study or any change relating to the safety or physical or mental integrity of participants
- the definition of the end of the study

1.2 Non-substantial Amendments

Non-substantial amendments are amendments that do not affect the safety of trial participants or the scientific validity, scope, or ethical rigour of the trial. These amendments may include⁵;

- minor changes to the protocol or other study documentation, e.g. correcting errors, updating contact points, minor clarifications
- changes in funding arrangements
- changes in the documentation used by the research team for recording study data
- changes in the logistical arrangements for storing or transporting samples
- extension of the study beyond the period specified in the application form

2 AMENDMENT REVIEW AND APPROVAL PROCESS

2.1 Initiation of Protocol Amendment

To initiate a protocol amendment, the Trial Chairperson, in consultation with the TMC, shall;

1. Amend the protocol and/or accompanying documents (e.g. PICF, GSA) as required, ensuring that all changes are tracked.
2. If applicable, prepare a statement outlining if the proposed amendments introduce any new risks to participants (e.g. changes to confidentiality provisions, physical or psychological risks, increased time commitments etc.)
3. Document that the protocol amendment has been reviewed and agreed upon by all members of the TMC (this can be in the form of minutes from a TMC meeting)
4. If applicable, generate a document summarising the changes (please see appendix 1 for the template summary of changes document)
5. Determine if changes are required to the Case Report Forms or database
6. Submit the above documents for review and approval by the trial sponsor

2.2 Amendment review and approval of TROG studies

Review and approval of an amendment will be dependant of the category of the trial (e.g. Category A, Category B etc.), the category of the amendment and/or the level of TROG's involvement in the trial.

2.2.1 Category A trials:

All amendments must be submitted to the TROG Central Operations Office (TCOO) for review prior to being submitted to the TSC for approval, via the TSC secretary.

Throughout the review process, the TSC secretary shall be the liaison between the TSC and the Trial Chairperson/s and shall be responsible for coordinating the review process in a timely manner.

2.2.1.1 *Substantial Amendments*

When a substantial amendment is received, the TSC secretary will forward the amendment and associated documents to the TSC chair for review. The TSC chair will then review the amendment and, at their discretion and depending on the nature of the change, will;

1. Approve the amendment as a representative of the TSC
2. Request the full TSC to review and comment on the amendment (via written correspondence), prior to approval
3. Request that the amendment be tabled at the next TSC meeting for further discussion (via telco or face-to face), prior to approval
4. Request feedback from the applicable TROG subspecialty group prior to approval
5. Request feedback from the TROG membership at the next Annual Scientific Meeting prior to approval

2.2.1.2 Non-substantial Amendments

When a non-substantial amendment is received, the TSC secretary will forward the amendment to the TROG CEO and Research Manager for approval as a representative of the TSC. The TSC chair will be notified by the TSC secretary of the non-substantial amendment.

Please note: Prior to the amended protocol being submitted to ethics for approval, the TROG Representative and Trial Chairperson must sign the applicable signature page. A copy of this page is to be forwarded to the TROG Central Operations Office.

2.2.2 Category B trials:

Amendments to Category B trials must be submitted to the TROG Central Operations Office (TCOO) and the TSC will be notified of the amendment by the TSC secretary.

If the Group Specific Appendix (GSA) or the TROG specific PICF is required to be amended in response to the protocol amendment, then the TSC will be required to approve these changes as per sections 2.2.1.1 or 2.2.1.2.

Please note: Prior to the amended GSA being submitted to ethics for approval, the TROG Representative and Trial Chairperson must sign the applicable GSA signature page. A copy of this page is to be forwarded to the TROG Central Operations Office.

2.2.3 Category C trials:

TROG is to be notified of any changes to the protocol or trial documentation. The TSC secretary will notify the TSC of the amendment.

2.2.4 TROG QA involvement:

If the TROG QA team is responsible for the radiotherapy quality assurance, then any amendments involving changes to the radiotherapy treatment must be submitted to the TROG QA team.

Depending on the nature of the change, these may also be required to be reviewed by the TSC and/or the NTTC prior to distribution to applicable Human Research Ethics Committees (HRECs), institution Regulatory Governance Officers (RGOs)^{2,3} and/or participating trial sites.

3 PROTOCOL AMENDMENT REGULATORY APPROVALS

Once provided with the TSC approval documentation for the amended protocol, the Trial Chairperson (which may be via the central trial coordinator) will be responsible for ensuring that the amended protocol and summary of changes document are submitted to the main approving ethics committee for review.

Once approved by the main HREC, the Trial Chairperson will distribute the amended documents to all principal investigators (PI). The PI and delegated staff are required to obtain approval from their local ethics and/or governance prior to implementing the amended documents in their participating centres^{2,3}. The PIs are to notify the Central Trial Coordinator when the approvals have been granted.

4 REFERENCES

1. Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) annotated with TGA comments, Therapeutic Goods Administration, Australia, July 2000. Available at: <http://www.tga.gov.au/industry/clinical-trials-note-ich13595.htm>
2. National Statement on Ethical Conduct in Human Research (2007) incorporating all updates as at May 2015. Available at: <http://www.nhmrc.gov.au/guidelines-publications/e72>
3. Australian Code for the Responsible Conduct of Research. Available at: <http://www.nhmrc.gov.au/guidelines-publications/r39>
4. SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials). (2013). Protocol amendments. Available at: <http://www.spirit-statement.org/protocol-amendments/>
5. Health Research Authority. NSH. Definitions of substantial and non-substantial amendments and Substantial and non-substantial amendments. Available at: <http://www.hra.nhs.uk/research-community/during-your-research-project/amendments/definitions-of-substantial-and-non-substantial-amendments/>