

## Guidelines for the progression of trials through TROGs trial timeline – from new proposal to completion

Document Number: TPS E3

Version: 7

Effective date: 31 January 2017

Number of pages: 9

**Summary:** The aim of this policy statement is to describe the progression of a trial through TROGs trial timeline and to provide specific guidelines for each phase (i.e. new proposal, development, activation, open, closed and completed).

**Author:** TROG Central Operations Office

**Applies to:** TROG Membership and TROG staff

**Approved by:** TROG Chief Executive Officer and Research Manager

**Review date:** July 2018

<b>Revision Chronology:</b>	Vs 1: 13 Sep 1999	New Policy
	Vs 1: amended 23 May 2000	Inclusion of protocol amendment guidelines
	Vs 2: 05 Sep 2008	Update of existing sections and addition of sections pertaining to the conduct of trials
	Vs 3: 21 Sep 2012	Update of existing sections according to current TROG processes.
	Vs 4: 14 Mar 2013	Clarification of timing of allocation of a TROG number
	Vs 5: 16 Dec 2013	Clarification of submission requirements for out of session Category B new proposals. Renaming title of policy to reflect contents.
	Vs 6: 03 Aug 2015	Documentation of new process for new proposals
	Vs 7: 31 Jan 2017	Added new category of trial, further defined TROG involvement, addition of a TROG Development Number

---

## Contents

1.	<b>TROG TRIAL TIMELINE</b> .....	4
2.	<b>NEW PROPOSALS</b> .....	4
2.1	Types of new proposals .....	4
2.1.1	Level of TROG involvement – Category B and Category C .....	4
2.2	New proposal submission process.....	6
2.2.1	The Role of the TROG Subspecialty groups .....	7
2.2.2	The Role of the TROG ASM.....	7
3.	<b>APPROVED FOR DEVELOPMENT</b> .....	8
4.	<b>OPEN</b> .....	8
5.	<b>CLOSED TO ACCRUAL</b> .....	9
6.	<b>CLOSED TO FOLLOW-UP</b> .....	9
7.	<b>COMPLETED TRIALS</b> .....	9
7.1	Back-up and Archiving of Trial Data.....	9
8.	<b>REPORTING</b> .....	10
9.	<b>SUBSTUDIES</b> .....	10

---

## TROG TRIAL TIMELINE

### NEW PROPOSAL

**DEFINITION:** A new trial concept, protocol synopsis or full protocol submitted to TROG for consideration of further development.

**Start:** New proposal application form received by TROG

**End:** New proposal approved for development

### APPROVED FOR DEVELOPMENT

**DEFINITION:** This phase commences when a new proposal is approved for development by the TROG Scientific Committee (TSC).

**Start:** New proposal approved for development

**End:** Trial development milestones met, ethics approval obtained & first trial site is activated

### OPEN

**DEFINITION:** A trial is considered open when all TROG trial development milestones have been met, ethics approval has been obtained and the first site is activated .

**Start:** When the first trial site is activated

**End:** Accrual of last participant

### CLOSED TO ACCRUAL

**DEFINITION:** A trial is considered closed to accrual after the last participant has been recruited. Patients will be in follow up.

**Start:** Accrual of last participant

**End:** The final visit of the last participant in follow-up

### CLOSED TO FOLLOW-UP

**DEFINITION:** A trial is considered to be closed to follow-up when all participants have completed the required follow-up period and all participant data has been collected.

During the closed to follow-up phase the database will be cleaned, final analyses will occur, manuscripts will be submitted for publication and close out of trial sites will commence. These activities will be monitored by the TROG Central Operations Office and the TSC will be notified when all are complete.

**Start:** The final visit of the last patient in follow-up

**End:** Official notification from the TSC indicating that trial is completed

### COMPLETED

**DEFINITION:** A trial is considered to be completed when all analyses have been performed and published, the trial database has been locked, trial sites have been closed and records archived.

---

## 1. TROG TRIAL TIMELINE

The timeline of a TROG clinical trial is categorised into the following six stages:

1. New proposal
2. Approved for development
3. Open to accrual
4. Closed to accrual
5. Closed to follow-up
6. Completed

TROG requires specific requirements and/or milestones to be sufficiently met before the trial can commence from one stage to the next. These requirements are described in detail below.

## 2. NEW PROPOSALS

TROG aims to foster and promote the design and execution of high quality clinical trials involving Radiation Therapy (RT) and which require multi-centre participation. If your proposal fits these aims, it is suitable for submission as a new proposal. If in doubt, contact the TROG Central Operations Office (TCOO).

The Investigator who prepares and presents a new trial proposal to TROG will be referred to as the 'Trial Proponent' until the trial has been approved by TROG for further development, the Trial Proponent will then be referred to as the Trial Chairperson.

### 2.1 Types of new proposals

Four types of New Proposals are accepted by TROG:

- **Category A** : An investigator-initiated trial that is submitted by a full TROG member to be considered for sponsorship by TROG.
- **Category B**: A trial that has been initiated by a recognised national or international Collaborative Trials Group and where TROG would act in the role of the Australian/New Zealand (ANZ) sponsor. Trial in this category may have an existing protocol (or protocol in development). The intention of a new proposal submission in this category would be that the trial is carried out under the joint auspices of TROG and the group concerned.
- **Category C**: As per category B, but TROG will not act in the role of ANZ sponsor of the trial, the trial is for endorsement by TROG only.
- **Category D**: An investigator-initiated project or registry that involves data capture, data mining or secondary analysis.

#### 2.1.1 Level of TROG involvement – Category B and Category C

A group or institution seeking collaboration with TROG may indicate the level of TROG involvement as follows:

1. TROG Sponsorship
2. TROG Quality Assurance (QA) procedures
3. TROG Trial Coordinating Centre
4. TROG Endorsement
5. A combination of the above

---

### **2.1.1.1 TROG Sponsorship**

In this scenario the lead group may be an international trials group seeking additional trial participants from Australia and New Zealand. Collaboration with TROG would allow access to TROG trial sites across Australia and New Zealand and lead to increased accrual.

TROG will act as the sponsor for TROG sites and the study will be included to TROG's clinical trial insurance policy. Trial procedures specific to TROG must be documented within the body of the protocol if possible. If this is not possible TROG recommends that these procedures are documented in a Group Specific Addendum (GSA). A GSA will include TROG trial specific ethical and regulatory information as well as specific data management procedures for TROG trial sites. A template GSA is available to the TROG membership via the TROG website.

The TROG logo should be included on the protocol (where possible) and a TROG member included on the TMC. The protocol (final draft or finalised version) and, if applicable, the GSA is to be submitted to the TROG Scientific Committee (TSC) prior to the allocation of a TROG number.

TROG will include the study's details on the TROG clintrial refer app and the website, and promote the study within the TROG membership.

Participants recruited to the study from TROG sites will be counted towards TROGs reportable accrual totals.

### **2.1.1.2 TROG QA procedures**

The lead group may seek to collaborate with TROG on an intellectual level or as a contract organisation only.

If TROG is involved in an intellectual level, TROG would be required to have input into the development of the protocol (or input into existing information within the protocol) particularly with regards to QA procedures. The TROG logo will be included on the protocol and a TROG member included on the Trial Management Committee (TMC). The protocol (final draft or finalised version) is to be submitted to the TROG Scientific Committee (TSC) prior to the allocation of a TROG number. Trial procedures specific to TROG must be documented within the body of the protocol or in the RTQA guidelines if possible. If this is not possible TROG recommends that these procedures are documented in a Group Specific Addendum (GSA).

In some instances, a lead group may request TROGs QA services on a contractual basis only. In this scenario TROG would be contracted to perform QA services only and would not have any influence on the design of the protocol or QA procedures. TROG QA may put forward recommendations for consideration by the group but cannot enforce these recommendations. For contracted services, a TROG number will not be allocated, the TROG logo would not appear on the protocol nor will TROG be included in any publications apart from in the acknowledgements.

### **2.1.1.3 TROG Trial Coordinating Centre Services**

If the Lead Group is seeking to collaborate with TROG for accrual purposes, TROG can provide a quote for Trial Coordinating Centre services. TROG and the Lead Group will need to determine the level of this service and the quote will be tailored accordingly.

In some instances, a lead group may request TROG coordination services on a contractual basis only. In this scenario TROG would be contracted to perform coordination services only and would not have any influence on the design of the protocol. For contracted services, a TROG number will not be

---

allocated, the TROG logo would not appear on the protocol nor will TROG be included in any publications apart from in the acknowledgements.

#### **2.1.1.4 TROG Endorsement**

The lead group may seek endorsement by TROG. The TROG Scientific Committee will review the protocol and may put forward recommendations for consideration by the group but cannot enforce these recommendations. The committee will allocate a TROG number to the trial once they are satisfied of its scientific merit.

The TROG logo should be included on the protocol (where possible) and a TROG member included on the TMC. TROG will include the study's details on the TROG clintrial refer app and the website, and promote the study within the TROG membership.

Participants recruited to the study from TROG sites will NOT be counted towards TROGs reportable accrual totals.

## **2.2 New proposal submission process**

The time to submit a new proposal depends on its category;

- **Category A** proposals are to be submitted in response to the call for new proposals that is sent out in second half of each year.
- **Category B and C** proposals may be submitted to TROG at any time thought out the year.
- **Category D** proposals may be submitted to TROG at any time thought out the year. Depending on the complexity of the project, the proposal may require presentation at the annual scientific meeting prior to being accepted for development.

New proposal synopsis forms and instructions are available on the TROG website

<http://www.trog.com.au/New-proposals>.

On submission, the proposal will be referred to selected experts for an independent scientific assessment as well as the appropriate TROG Subspecialty Group (see section 2.2.1). The scientific assessments will then be discussed by the TSC or its sub group, the New Proposal Committee (NPC).

Feedback will be sought from the TROG membership through the circulation of the new proposal summary along with an invitation for sites to complete an Expression of Interest (EOI) survey. This circulation will allow discussion within institutions and comments which will be fed back to the new proponent. The results of the returned EOIs will allow for the TSC or NPC to confirm interest from the TROG membership.

The TSC will base their decision for approving a proposal on the following;

- Potential for the proposal to alter clinical management practices for the better, improved treatment outcome which may either relate to improvement of the results of treatment or to the reduction of treatment morbidity or improved cost-effectiveness of treatment.  
This will involve an assessment of the degree of benefit to individual patients that may be demonstrable as a result of the successful completion of the trial, together with an estimate of the total number of patients likely to benefit nationally and internationally.  
The assessment will also include the relevance of the proposal in question to international initiatives (i.e. will the result still be relevant to ongoing international progress when it is finally obtained). The feedback questionnaire can be utilised to provide a more detailed appraisal than the Yes/No vote

- 
- Likelihood of successful completion in proposed time frame (this includes availability of trial coordination support and results of EOI surveys).
  - New Trial Chairperson (i.e. all other considerations being equal, a proposal with a potential new Trial Chairperson should be given priority).
  - New area/field of research for TROG
  - Recommendations of the TROG Subspecialty Group

If the new proposal is not approved, the proponent will be encouraged to modifying the new proposal according to the feedback provided and/or re-submit the proposal at a later date. Past experience has indicated that support for trials with similar endpoints changes from year to year and investigators are encouraged to re-submit should they wish to do so. There may be more compelling data (either pilot or from elsewhere) to support a trial proposal previously rejected. Institutions may have proceeded with a trial regardless of TROG support and if successful accrual has occurred this provides a good reason for a trial to be reconsidered. However, patients accrued prior to TROG approval will not be able to be included in the analysis of the TROG trial.

### **2.2.1 The Role of the TROG Subspecialty groups**

TROG has moved towards a subspecialty approach to assist in ensuring proposed clinical trials are relevant, supported, competitive and likely to be completed in a timely fashion.

If there is a TROG subspecialty group applicable to the new proposal, all Trial Proponents are encouraged to present the new proposal at a group meeting for discussion and feedback prior to submitting to TROG.

Once a new proposal has been submitted to TROG, it will be forwarded to the Subspecialty Group Chair/s and/or Executive Committee for review. It is recommended that the proposal is discussed in a general meeting, or at the ASM breakout session, for further membership feedback.

The group chair/s is to provide formal feedback to the New Proposal Committee on the proposal, along with a recommendation for the proposal to proceed to further development or not. If the proposal is presented during the TROG ASM, these recommendations will also be presented to the meeting delegates in the Subspecialty Group feedback session.

### **2.2.2 The Role of the TROG ASM**

One of the major roles of the ASM is to hear and assess new proposals and determine whether there is general support based on scientific merit for a trial proposal to proceed to further development.

The Trial Proponent will be required to make a presentation of the proposal on the first day of the ASM, either in the Subspecialty Group break out session (if available for the tumour group) or in the main meeting. The allocated time for this presentation will allow time for questions from the floor. If all questions are not resolved during the allocated time, the session Chairman will direct the Trial Proponent to discuss unresolved issues further with specific members attending.

Further time is allotted at the ASM on the second day for each Category A and applicable Category D proposals to be presented to all the meeting delegates. A discussant will also be required to critique the proposal after this second presentation. The discussant will be appointed by either the TSC, NPC or the TROG Subspecialty Group Chair/s.

Full members are required to vote on each Category A and applicable Category D proposal at the Annual Scientific Meeting to proceed to further development.

---

### 3. APPROVED FOR DEVELOPMENT

The trial phase of “Approved for Development” commences when a new proposal receives approval from the TROG New Proposal Committee for development for proceed. On approval a TROG Development (TD) Number will be allocated e.g. TD 17.01.

To complete the development phase a new trial must fulfil the requirements of the following trial development milestones to the satisfaction of the TSC:

1. Protocol finalised and TROG number allocated
2. Statistical Requirements
3. Trial Budget and Funding
4. Trial Management Committee
5. Trial Coordinating Centre
6. Quality Assurance
7. Case Report Forms (CRFs) and Database
8. Indemnity
9. HREC approval
10. Contractual and Regulatory Documentation

Please refer to TROGs Trial Development Resources (available on the TROG website) for detailed information on the requirements of each of the above milestones.

Trial Chairpersons have the right to refuse to circulate widely any ‘Draft’ protocol at any stage in development up until a ‘Final’ protocol is approved by the TSC. TROG members are expected to understand that refusal to circulate a draft may be in the best interests of successful initiation of some trials and is not intended to exclude participants. TROG members are encouraged to communicate freely with the Trial Chairperson as this will help in the strategy development, review by other potential investigators and activation stages of trial development.

### 4. OPEN

A trial will be moved to the TROGs open trial portfolio when all TROG trial development milestones have been met, ethics approval has been obtained and the first trial site has been activated.

Formal notification of the open trial status will be sent to the Trial Chairperson by the TSC.

The following TROG Policy Statements on the TROG website are applicable to the open to accrual phase of a trial.

- TPS E2 Ethical Principles
- TPS E4 Adverse Event Definitions Reporting and Scoring
- TPS E6 Quality Assurance Guidelines
- TPS E8 Trial Management Committee Responsibilities
- TPS E9 Data Monitoring Committee Guidelines
- TPS E13 TROG Protocol Amendment Guidelines



---

## **5. CLOSED TO ACCRUAL**

A trial is considered closed to accrual after the last patient has been recruited. During the closed phase, patients will complete follow up and in some instances the interim and/or main analyses may occur and publications may arise.

The following TROG Policy Statements on the TROG website are applicable to the open to accrual phase of a trial.

- TPS E2 Ethical Principles
- TPS E8 Trial Management Committee Responsibilities
- TPS E9 Data Monitoring Committee Guidelines
- TPS E10 Authorship, Publication and Spokesmanship
- TPS E13 TROG Protocol Amendment Guidelines

## **6. CLOSED TO FOLLOW-UP**

During the closed to follow-up phase the database will be cleaned, final analyses will occur, manuscripts will be submitted for publication and close out of trial sites will commence. These activities will be monitored by the TROG Central Operations Office and the TSC will be notified when all are complete.

The following TROG Policy Statement and guidelines available on the TROG website may be applicable to the closed to follow-up phase of a trial.

- TPS E2 Ethical Principles
- TPS E8 Trial Management Committee Responsibilities
- TPS E9 Data Monitoring Committee Guidelines
- TPS E10 Authorship, Publication and Spokesmanship

TROG Trial Site Close-out Guidelines for Category A trials, and applicable Category B and C, the locked database is to be transferred to TROG Central Operations Office prior to the trial moving to the completed stage (please see section 7.1). If an investigator would like access to the data for the purpose of secondary analysis, they are to apply to the trial chair and the TSC as per TPS E12 Secondary Analysis.

Terminated, discontinued or suspended trials will be categorised as closed to follow-up until formal closeout procedures have occurred.

## **7. COMPLETED TRIALS**

A trial is considered to be completed when the final follow-up has occurred, the trial database has been locked, all analyses as detailed in the protocol have been performed and published, trial sites have been closed and records archived.

### **7.1 Back-up and Archiving of Trial Data**

As indicated in TROG's Authorship, Publication and Spokesperson Guideline, once a trial has been ratified as a TROG trial, and TROG is the lead group, the data collected for that trial belong to TROG regardless of where they reside and of the source of the funding for the data management. Accordingly, while the trial

---

coordinating centre will house and retain the data, a copy of the final data set used for the final analysis should be archived within the TROG Central Operations Office.

## **8. REPORTING**

The progression of trials through TROGs trial timeline will be monitored by the TSC via biannual progress reports that are required to be submitted to TCOO. This applies to all categories of trials. The TCOO will provide the Trial Chairperson with the relevant progress report template.

Non-compliance in submitting the reports will be noted by the TSC.

## **9. SUB STUDIES**

A sub study is essentially an add-on study to the main protocol designed to ask a separate research question and includes new data collection from some or all of the trial subjects from the main protocol.

Ideally a sub study should be developed in parallel with the main study to ensure minimal impact on patient assessment schedules and maximise accrual.

In the instance when a sub study is developed after the main study has been opened to accrual, a concept letter for the proposed sub-study must be forwarded to the TCOO for review and approval by the TSC. The sub study concept letter must include:

- A description of the sub study including its hypothesis, aim and objectives
- Any impact on the main protocol (i.e. are visit schedules different to those in the main protocol?)
- Specific efficacy, safety or other assessments
- Statistical power and summary of planned analysis.

A separate Patient Information Sheet and Consent Form (PIC) may also be required for enrolling trial participants into the sub study.

A separate TROG number will not be allocated, alternatively the sub study will fall under the same TROG number as the main study.

As with the main study, publications or presentations arising from the sub study must be approved by the TROG Publications Committee prior to journal submission.