

# Policy Statement



Trans Tasman Radiation Oncology Group

ABN: 45 132 672 292

Calvary Mater Newcastle, Locked Bag 7, HRMC, NSW 2310, Australia

Telephone: +61 (0)2 401 43911 Fax: +61 (0)2 401 43902

[trog@trog.com.au](mailto:trog@trog.com.au)

[www.trog.com.au](http://www.trog.com.au)

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## Quality Assurance in TROG Clinical Trials

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**Summary:** The purpose of this policy is to outline procedures adopted by TROG to ensure world-class excellence in the design and management of Quality Assurance in TROG clinical trials.

**Author:** TROG Central Operations Office

**Applies to:** TROG Trials

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<b>Revision Chronology:</b>	Vs 1: 21 Sep 1999	New Policy
	Vs 2: 24 Sep 2008	Update of existing sections
	Vs 3: 26 Mar 2015	Revision of policy

## CONTENTS

1. INTRODUCTION .....	3
2. GOVERNANCE .....	3
3. RISK ASSESSMENT .....	4
3.1 Levels of Quality Assurance .....	4
4. CREDENTIALLING .....	4
4.1 Facility Questionnaire .....	4
4.2 Trial-Specific Benchmarking Exercise .....	4
4.3 Dosimetric Quality Assurance .....	5
5. INDIVIDUAL CASE REVIEW .....	5
6. ACKNOWLEDGEMENTS .....	6
APPENDIX 1 .....	7

## **1. INTRODUCTION**

Quality assurance (QA) provides the framework to allow verification of data accuracy and protocol compliance via the review of source documentation. The QA processes ensure that any safety issues for patients on a trial are identified as soon as possible, and highlight issues which may require amendment to the protocol to facilitate smooth running of a trial.

## **2. GOVERNANCE**

The TROG Technology and Quality Manager is a member of the TROG Scientific Committee and also reports to the TROG Board. The TROG Scientific Committee is informed of trial QA progress and any arising trial or operational issues.

Based at the TROG Central Operations Office (TCOO), the QA team consists of multi-professional staff covering all areas of clinical trial and scientific work. The team provides support and assistance with the development and management of a trial's QA program. Each TROG trial has a trial-specific QA program, depending on the questions posed and technologies used, which is designed and agreed upon in conjunction with the Trial Management Committee (TMC).

The TCCO QA team conducts the following:

- development of trial-specific QA programs including risk assessment, tolerance criteria and review audits
- management of trial QA programs including requests for source data, checking radiotherapy treatment plan data integrity in review software, liaising with reviewers and reporting results
- training of reviewers and site users in Central Quality Management System (CQMS) and review software programs, including MIM (MIM Software, Cleveland, Ohio, USA) and SWAN (Research Physics Unit, Sir Charles Gairdner Hospital, Perth, Australia)
- liaising with equipment manufacturers to facilitate QA processes and data export for site users
- development and maintenance of standardised naming for contouring
- implementing processes within the policy frameworks for the credentialling of centres
- conducting site dosimetric audit visits

In order to address the implementation of new technologies into TROG trials, the New Technologies and Techniques Committee (NTTC) works proactively to identify priorities and develop standardised procedures for inclusion in the research portfolio. The NTTC conducts the following in collaboration with the TCOO:

- establish a database of existing relevant activities and outcomes
- identify priorities for emerging technologies
- develop a framework for the implementation of new technologies
- source information regarding international 'best practice' for radiation oncology clinical trials QA procedures
- initiate small sub-groups for new technologies to identify the requirements and procedures for implementation in TROG clinical trials
- review all guidelines on an annual basis

- provide a quarterly report to the Scientific Committee

The TROG QA team is a member of the Global Quality Assurance of Radiation Therapy Harmonisation Group which aims to harmonise and improve the QA of radiation therapy implemented worldwide as it pertains to multi-institutional cooperative clinical trials for the treatment of cancer. Collaborative links have also been formally recognised between TROG and the Danish Head and Neck Cancer Group (DAHANCA) and UK Radiotherapy Trials Quality Assurance (UK RTTQA) in acknowledgement of common purpose in the development of clinical trial radiotherapy quality assurance procedures and practices. The opportunity to share knowledge, processes and information with these groups will facilitate the conduct of TROG clinical trials.

### 3. RISK ASSESSMENT

#### 3.1 Levels of Quality Assurance

Trials are assessed on their level of risk based on the following three categories with increasing levels of QA intervention:

- A. Level I: No RT question, or RT dose not critical
- B. Level II: RT is standard in both arms
- C. Level III: RT is the research question, specifically the technology/technique being tested

QA Activity	Facility Questionnaire	Dosimetric Audit	Benchmarking	Case Review (Real-Time and/or Post-treatment)
Level I	-	-	-	✓
Level II	✓	-	✓	✓
Level III	✓	✓	✓	✓

With the increasing clinical use of advanced treatment techniques, including IMRT and VMAT, TROG QA has issued detailed information on the QA requirements for Inversely Planned Treatments: *Guidelines for the use of inversely planned treatment techniques in Clinical Trials: IMRT, VMAT, TomoTherapy, Version 2.0, March 2014* available on the TROG website ([www.trog.com.au](http://www.trog.com.au))

### 4. CREDENTIALLING

#### 4.1 Facility Questionnaire

The facility questionnaire is web-based and consists of a generic module, covering equipment and facilities, and the information is held centrally.

Specific techniques and technologies are covered by short questionnaires, e.g. IMRT/VMAT/TomoTherapy. Information is transferrable across TROG trials using that technique.

#### 4.2 Trial-Specific Benchmarking Exercise

The benchmarking exercise aims to ensure the centre's ability to comply with the trial protocol and the QA review process. The benchmarking exercise may include a contouring and/or planning exercise with external

review by independent reviewers (appointed by the TMC) using TROG plan review software including MIM [i] or SWAN [ii].

If there is more than one investigator per trial site, consideration may be given to modifying the benchmarking requirement in that the sampling procedure is applied to each investigator rather than each trial site.

#### **4.3 Dosimetric Quality Assurance**

- All centres will be asked to provide evidence, by report, of an external level 1 audit by a recognised body, such as Australian Clinical Dosimetry Service (ACDS), within the last 2 years. Reports from other recognised bodies, eg RPC, may be submitted to the TROG QA office for consideration.
- Clinical trial data robustness relies on the equivalence of delivered dose in each participating centre. Traditionally this has been validated by a level 3 dosimetric audit site visit by a trial representative, using the same phantom and equipment at each centre. It has been the responsibility of each trial to cover the QA procedures as required. In some instances, it has been possible for other trials to accept credentialling reports. TROG QA regards the validity of the level 3 audit report as up to 5 years, and will discuss any issues with individual centres.
- Due to limited resources, it is not always possible to make the credentialling site visits. TROG is working on alternative approaches, which would enable efficient timescales for the credentialling process.
- International centres wishing to take part in TROG trials are invited to submit evidence of dosimetry audits, from recognised bodies, to TROG QA for consideration.
- All centres using TomoTherapy shall have an external dosimetry audit to assess the delivered dose and ensure consistency of delivered dose for comparison with linear accelerator treatment deliveries.
- VMAT, i.e. dynamic gantry modulated delivery with inverse planning, is regarded as a new technique and each centre wishing to use VMAT in TROG trials must provide evidence of an external dosimetry audit. There are differences in planning and delivery techniques between the manufacturers, e.g. in gantry and dose modulation prioritising. The external audit is therefore only valid for the specified equipment, however exceptions may be granted.
- Other new treatment delivery techniques, including Cyberknife, will require the centre to have an external dosimetry audit – contact TROG QA for advice.
- Each trial will set the tolerance criteria for acceptance, for both point dose accuracy and planar dose accuracy [iii, iv].

#### **5. INDIVIDUAL CASE REVIEW**

Individual case reviews (ICR) will be timed according to the level of risk for the treatment technique and may include pre-treatment and/or post-treatment radiotherapy reviews. Pre-treatment reviews allow for any protocol variations to be corrected prior to the patient commencing treatment. Tolerance limits for key protocol criteria are developed for review in consultation with the TMC.

QA ICR sampling rate should consider factors such as whether the trial involves a new technique, participation of a new or international trial site and the sample size of the patients to be recruited to the trial.

The following sample rates may be implemented:

- All cases reviewed
- A 2-phase review process will be implemented:
  - Phase 1 - at least the first 5 patients from each trial site. If the initial review results are acceptable the trial site proceeds to Phase 2.
  - Phase 2 - at least 1-in-5 of the subsequent patients registered on the trial are reviewed.

TROG QA develops trial-specific QA checklists used to request copies of source documentation for each case requiring review.

Audit programs for the ICR of key trial criteria including eligibility, chemotherapy, surgery, quality of life and device compliance will be developed in consultation with the TMC.

## **6. ACKNOWLEDGEMENTS**

TROG appreciates the support of the members of the TROG New Technologies and Techniques Committee; the TROG Scientific Committee and the Membership.

## APPENDIX 1

### QA OVERVIEW CHECKLIST

This checklist provides an overview of QA requirements and is intended to support investigators.

Area	Comments
TROG protocol template	The protocol template covers all areas to be addressed, and is available from TROG COO
Multi-Disciplinary trial QA team	Each team member should have good clinical experience. The team may be drawn from different centres and cover all professional disciplines.
QA program [ to assess compliance with trial protocol]	Contact TROG QA office for advice and information on requirements and documentation specific to the trial, including facility questionnaire and benchmarking case.  Discuss QA requirements including dose-volume constraints and definitions of minor/major violations.
Centre credentialling requirements	Contact TROG QA office to discuss the category of credentialling required, and any previous audits which may be relevant for this trial
Notification to centres	Inform centres of specific requirements, e.g. external dosimetry audit for new technique, via protocol and RTQA Guidelines

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<sup>i</sup> Comprehensive Solutions for Radiation Oncology. 2013 26 Nov 2013]; Available from: <http://www.mimsoftware.com/>.

<sup>ii</sup> Ebert, M., et al., Detailed review and analysis of complex radiotherapy clinical trial planning data: Evaluation and initial experience with the SWAN software system. Radioth Oncol 2008. 86: p. 200-210.

<sup>iii</sup> Low, D., et al., A technique for the quantitative evaluation of dose distributions. Med Phys 1998. 25: p. 656-661.

<sup>iv</sup> Hussein, M., et al., A comparison of the gamma index analysis in various commercial IMRT/VMAT QA systems. Radiotherapy and Oncology, 2013.