Thoracic Oncology Group Australasia

STUDY ENDORSEMENT POLICY

CONTENTS

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ABBREVIATIONS AND DEFINITIONS

TOGA-led study	A TOGA-endorsed study subject to oversight by TOGA Operations Executive and able to benefit from TOGA insurance policy
CARF	Committee for Audit, Risk and Finance
CCTG	Cancer Cooperative Trials Group
endorsement	The action of supporting a clinical trial or research proposal as a TOGA study
HRQoL	Health-related Quality of Life
ICMJE	International Committee of Medical Journal Editors
NHMRC CTC	National Health and Medical Research Council Clinical Trial Centre
RP	TOGA Research Panel for concept/proposal peer-review
SC	Scientific Committee
substudy	Contained within the protocol of a particular clinical trial
Secondary use of data	A proposal to use existing clinical trial data for a novel hypothesis and analysis
WG	TOGA working group for concept/proposal peer-review

INTRODUCTION

TOGA strives to achieve and maintain a reputation for designing, conducting and publishing high-quality clinical trials and research that contribute to evidence-based health care in thoracic malignancies. The advantages to an individual member in developing a clinical trial through the TOGA and seeking TOGA endorsement include potential access to a national network of sites, potential provision of the TOGA track record in successful and high-quality clinical trial design and completion to enhance funding applications and manuscript submissions and access to peer- and consumer-review processes that critique clinical trial design, assess feasibility, equipoise and scientific merit of the proposal and determine support for the trial by the wider membership.

For members involved in the recruitment of participants and conduct of the study, the peer- and consumer-review process that underpins the award of a TOGA-endorsed clinical trial or research proposal gives confidence in the quality of the clinical trial design and conduct, and the potential benefit to advancement in clinical care.

To ensure only high-quality and feasible clinical trials and research studies are conducted by TOGA and to maximise the benefit of peer-review it is necessary to outline a policy and process for TOGA endorsement of a study concept, or application for secondary use of data or research proposal. This process typically comprises peer-review of the study proposal, assessments that the study is feasible and support for the study by the wider membership.

PURPOSE

This policy outlines the minimal criteria, the application process and the requirements for a TOGA-endorsed clinical trial, research proposal or secondary use of data.

SCOPE

- Clinical trial concepts
- Substudy concepts
- Proposals for secondary use of clinical trial data
- Grant applications
- Other proposals where Scientific Committee (SC) Chair or Scientific Chair, TOGA Board of Directors have requested consideration for TOGA endorsement/ peer-review.

GUIDING PRINCIPLES

- Transparent and equitable procedures
- Prioritisation of high-quality research that enhances care of patients with thoracic malignancies
- Consumer involvement in research design
- Maintenance of the TOGA reputation as a leading organisation in thoracic cancer research

RESPONSIBILITIES

Working group or Research Panel

- Scientific critique and feasibility assessment of the proposed research to provide a recommendation to SC

SC

- Review working group (WG) or Research Panel (RP) recommendation
- Conduct peer-review if necessary
- Approve application (TOGA-endorsed project or clinical trial)

CP

- Review concepts and proposals for relevance and appeal to patients

Supportive Care Panel

- Review concepts and proposals for additional incorporation of supportive care studies

Translational Research Panel

- Review concepts and proposals for additional incorporation of translational research studies

Executive Officer

- Assign TOGA study number for endorsed concepts and research proposals
- Facilitate reviews including consumer review and review by National Technical Services for health-related Quality of Life (HRQoL) and health economics as required by Cancer Australia infrastructure funding

SC

- Recommendation to the TOGA Board of Directors re. prioritisation of TOGA resources (if required)
- Decision whether a concept or research proposal will be TOGA-led.
- Agreement that a concept will not benefit from further reviews from National Technical Services as required by Cancer Australia infrastructure funding.
- Endorse use of position statements
- Approve use of TOGA logo or name where peer-review is not conducted by the TOGA SC or WG or RP

Study chair

The Study Chair may choose to use the services of a Trial Centre or other delegate for some or all of these tasks.

- Prepare and submit clinical trial concept form for review,
- Facilitate reviews or provide reasons why additional reviews will not benefit the concept or proposal
- Secure funding
- Prepare grant application/clinical trial protocol
- Oversee study
- Prepare manuscript
- Ensure publication of results

TOGA Committee for Audit, Risk and Finance (CARF)

- Execution of funding contracts

Contract negotiation including TOGA study payments

Clinical Trial Sponsor

- Contract negotiation including TOGA study payments, where applicable

POLICY

Overview

Fundamental to the process of trial endorsement is review by peers and experts to assess the merit of the research question and the feasibility of clinical trial/study design and conduct. A study question can also benefit from the experience of peer-review to develop and refine the concept or proposal.

In TOGA, peer-review and development are conducted by the WG or RP with a recommendation to SC to endorse the proposal. Supplementary reviews by the Consumer Advisory Panel, the supportive care panel, the translational research panel and the Cancer Australia- appointed national technical services for health economics and Quality of Life, and the likelihood of adequate funding, may contribute to the SC decision. If the SC final decision is to endorse the TOGA trial or research study, the clinical trial protocol or research proposal should bear the TOGA logo and endorsement.

Figure ***1*** provides an overview of this process.

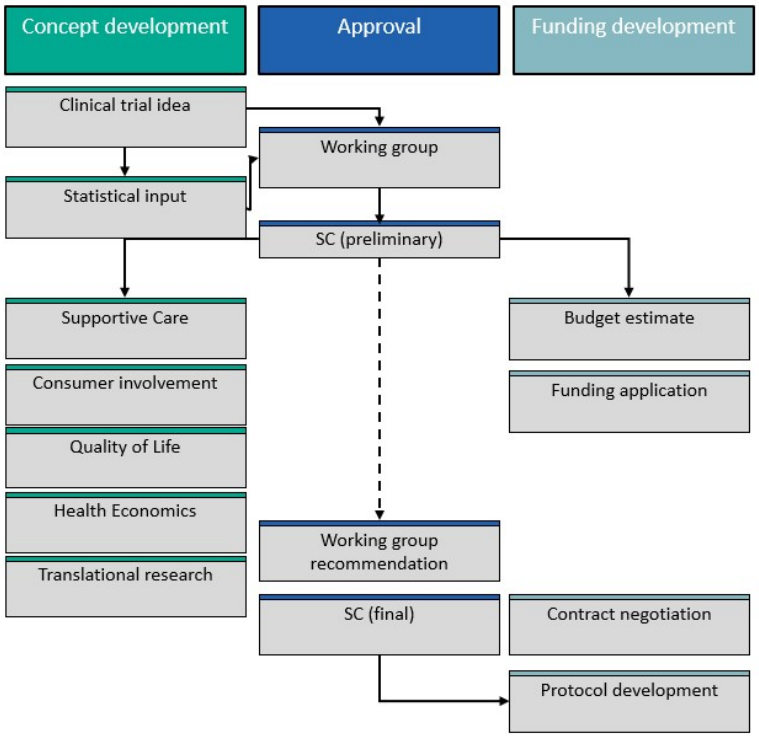

Figure 1 Approval process for TOGA endorsement of a research proposal or clinical trial concept

Benefits of TOGA endorsement

TOGA endorsement offers the following benefits:

- Use of TOGA logo or TOGA acknowledgment on all applications, presentations and publications
- Membership mailouts to recruit sites
- Listing of trial on the TOGA website
- Updates presented at SC meetings (time permitting)

In TOGA a trial can be endorsed, or both endorsed and led by the group, with the latter offering oversight by the TOGA Operations Executive Committee and the option of accessing clinical trial insurance through the CCTG Umbrella Insurance Scheme. TOGA studies may also benefit from

assistance provided by the National Health and Medical Research Council Clinical Trial Centre (NHMRC CTC) to develop a protocol and/or funding application.

Applications to endorse clinical trial proposals may apply for either option, with the final decision being made by TOGA SC, with guidance by the TOGA Board of Directors representatives, if required.

Applications to endorse research proposals that are not clinical trials will not be considered TOGA-led studies. If a proposal is a joint research initiative with another Australasian Cancer Cooperative Trials Group (CCTG), only one CCTG can lead the study. The leading group is usually the group that includes the members most likely to recruit the patients.

Review of the trial question

Poor-quality research proposals or study design can lead to research waste (1), due to inadequate recruitment and premature termination of a study, or publication of poor-quality research. Determining the merit of the trial question includes assessing:

- Is the question of appropriate scientific merit?
- Does the research question demonstrate sufficient equipoise?
- Does the study answer a question relevant to clinical practice and/or consumer priorities?
    - Where the study is investigating an existing variation in practice, information on current practice may be required to adequately identify the variation in practice.
- Is the study appropriately powered to definitively answer the clinical question?
- Is the choice of comparator arm appropriate?
- Has a consumer advocate been involved in the design of the proposal?
- Do consumer advocates agree that the research study is appealing and of benefit to patients?

Feasibility review

The peer-review process should assess the feasibility of the study, examining the following areas:

- appropriateness of eligibility criteria to facilitate recruitment and applicability of results beyond the study population,
- sufficient alignment with common clinical practice and availability of protocol-mandated non-investigational treatments, laboratory testing or supportive care. Surveys of existing practices by members may identify areas of the trial design that are misaligned with standard of care.

Consideration should also be given to likelihood of funding and provision of study drug, if required.

Requirements for a proposal seeking endorsement

Proposals are to be designed and submitted by a current TOGA member(s). There is no requirement for the submitting member to serve on a TOGA committee, advisory group or WG&RP.

Proposals can be submitted either as a concept (see APPENDIX 1), research proposal or a brief paragraph, and will require presentation at a WG&RP and/or SC meeting. The presentation at the meeting should be approximately 10 mins allowing adequate time for review and discussion after the presentation. Requests for presentation/review should be made to info@thoraciconcology.org.au

The presentation should cover:

- Background and rationale including evidence of a search that there are no current local trials that will compete for recruitment, or trials that examine the same question overseas
- Aim/hypothesis
- Trial treatment and any points where it does not align with local standard of care treatment
- Trial population
- Study design (consider a schema)
- Statistics including endpoint/objectives and, if possible, power calculation

- Potential significance of trial results, and implementation beyond the trial setting
- Feasibility and key questions for consideration

Endorsement process

TOGA convenes standing WG or RP of consumers and health professionals reflecting the multidisciplinary membership to assist with review and development of clinical trial concepts and research proposals. The WG&RP are:

i. Early NSCLC
ii. Advanced NSCLC
iii. Mesothelioma, SCLC and other thymic cancers
iv. Supportive and palliative care
v. Translational Research

Members of the WG&RP review proposals submitted as a clinical trial concept or research proposal and provide a recommendation to the SC regarding TOGA endorsement. The SC then considers the WG or RP recommendation and review and may conduct its own review of a concept or proposal. In some cases, the SC may conduct a review without the assistance of the WG&RP.

If the SC agrees to endorse the TOGA study, and a concept or proposal has been received by the TOGA Executive Officer, a TOGA study number is assigned by the TOGA Executive Officer. This number is the year the concept or proposal was approved by SC, followed by a hyphen and a 3-digit sequential number for all concepts or proposals approved in the calendar year. E.g TOGA 19-003. The researcher submitting the clinical trial concept or research proposal will be informed of successful endorsement and the TOGA number via letter, as outlined in APPENDIX 2.

Unsuccessful outcomes or further considerations for study design will be communicated via the SC chair or delegate.

Conditions of endorsement

If a TOGA- endorsed study has not already progressed for review by the Cancer Australia- appointed National Technical Services for HRQoL and health economics, these reviews will be facilitated by the Executive Officer, unless the Study Chair, SC chair and Scientific Chair, Board of Directors, or delegate, agree that the study will not benefit from these reviews.

TOGA-endorsed clinical trials should abide by the 'Integrated Addendum To ICH E6(R1): Guideline For Good Clinical Practice ICH E6(R2) annotated with TGA comments' (2), 'The Australian Code for the Responsible Conduct of Research, 2018' (3),'The National Statement on Ethical Conduct in Human Research (2007) updated 2018' (4), 'The Australian Clinical Trial Handbook version 2.2 October 2018' (5) and subsequent amendments to any of these documents and other applicable regulations where required e.g Medsafe 'Guideline on the Regulation of Therapeutic Products in New Zealand' (6). To the best of their ability, researchers of successfully TOGA-endorsed trials should identify the trial by the TOGA study number and use the TOGA logo on study-related documentation, presentations etc.

TOGA also undertakes, to the best of their ability, a commitment to publish all endorsed clinical trials and research proposals in the highest possible quality journals. A lay summary of research outcomes should also be prepared and made available to participants.

The completion of any major milestones need to be provided to the TOGA Executive Officer via info@thoraciconcology.org.au. As a guide the following milestones and documents should be provided:

- Study activation
- Closure of recruitment
- Conference presentations
- Journal publications

- Media articles (including social media)

Clinical trials and research proposals endorsed by TOGA should endeavour to include a payment ranging from 5-10% of any payment milestones to TOGA where the clinical trial budget can accommodate such payments. This should be discussed with the TOGA Scientific Chair, Board of Directors or delegate, and clinical trial Sponsor prior to the signing of any clinical trial funding agreements for TOGA-led studies.

Authorship and acknowledgement of TOGA

TOGA does not provide TOGA guidelines for authorship, but suggests that the '*Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals'* (7), developed by the International Committee of Medical Journal Editors (ICMJE) guide authorship decisions. These recommendations aim to ensure that all listed authors have meaningful and substantive contribution to the work and take public responsibility for their contribution to the work.

Another potential beneficial reference when deciding criteria for authorship and indexing of author names in PubMed is Fontantanarosa et al (8).

In multi-network studies, it is suggested that sites and investigators affiliated with the TOGA be clearly identified. This will ensure TOGA is citable on all PubMed searches. Options for doing this include:

- 'The X Study Investigators "for" Thoracic Oncology Group of Australasia'
- 'Listed investigators, "and" the X Study Investigators "for" Thoracic Oncology Group of Australasia'
- 'Listed individuals, the X Study Investigators, the X Institution "for" Thoracic Oncology Group of Australasia'

Retraction of endorsement

TOGA reserves the right to retract endorsement of a trial, but in doing so will consider if it will affect continuation of the clinical trial.

International clinical trials

TOGA also welcomes proposals for participation in international clinical trials. If the protocol has already been written, the protocol synopsis (rather than the clinical trial concept form) should be submitted for WG&RP/SC review using the same process as outlined in the approval column above. In addition, an international collaboration requires an assurance that the study will be conducted to the same or higher standards than those required in Australia, and a delegation of responsibilities between the international sponsor and the local sponsor..

Internationally-led clinical trials do not require review by Cancer Australia- appointed National Technical Services unless there is an opportunity to include further studies in the protocol. However, internationally-led clinical trials may require an appendix to detail compliance and feasibility in the local context.

Every endeavour should be made to secure acknowledgement of TOGA in internationally-led clinical trials, including but not limited to, the registration of a trial on a WHO-approved registry and acknowledgement of participation on any publication, presentations or other collateral produced by the international group.

Request for clinical trial data for substudies or novel study questions

Proposals for substudies or entirely novel study questions may require access to data from another TOGA clinical trial. These proposals need to undergo peer-review and endorsement as outlined above and in

Figure 2, but also require the permission of the TOGA Study chair and trial sponsor from the original study that collected the data.

The effort in collecting the original study data should be recognised as a significant contribution to the substudy or novel study questions when considering authorship for the substudy or new study question.

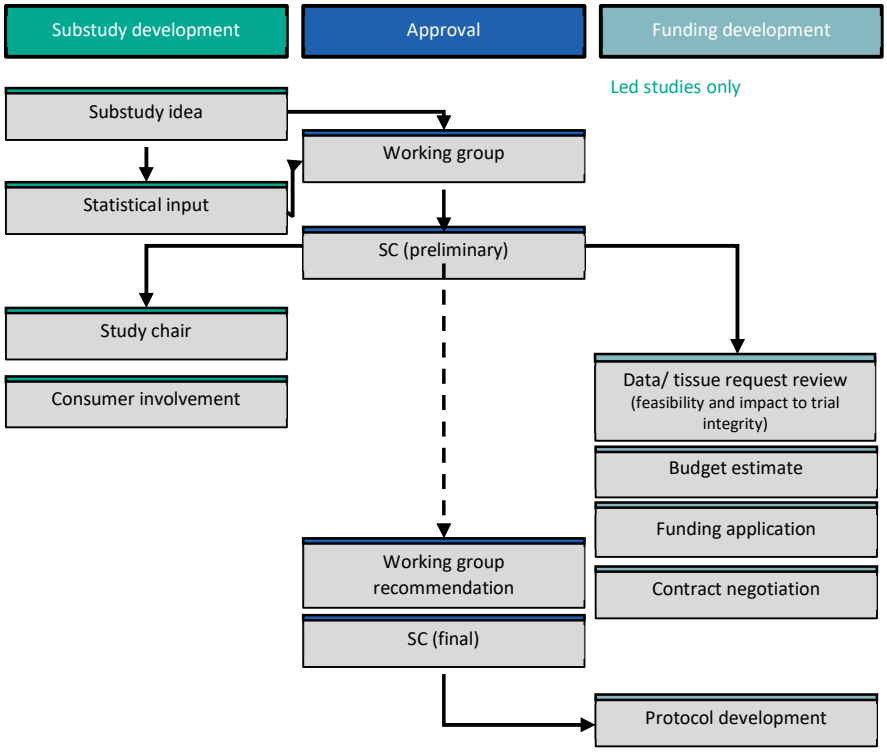

Figure 2 Approval and endorsement of a substudy or novel question using existing study data

Endorsement of position statements

TOGA may be requested to endorse particular position statements. Where these have already undergone peer-review by experts in the field, the decision whether to endorse the statement, and brand with the TOGA logo or name, will be made by the TOGA Board of Directors.

REFERENCES

1. Altman DG (1994) The scandal of poor medical research. *BMJ* 308:283
2. Integrated Addendum To ICH E6(R1): Guideline For Good Clinical Practice ICH E6(R2) annotated with TGA comments https://www.tga.gov.au/publication/note-guidance-good-clinical-practice Accessed 11 May 2020.
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4. The National Statement on Ethical Conduct in Human Research (2007), updated 2018. https://www.nhmrc.gov.au/about-us/publications/national-statement-ethical-conduct-human-research-2007-updated-2018 Accessed 11 May 2020.
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7. International Committee of Medical Journal Editors. Recommendations for the conduct, reporting editing, and publication of scholarly work in medical journals. http://www.icmje.org Updated December 2019. Accessed 10 May 2020.
8. Fontantanarosa P, Bauchner H, Flanagin A (2017) Authorship and team science. *JAMA*. 318: 2433-2437.

APPENDIX 1 TOGA CLINICAL TRIAL CONCEPT FORM

Contact Name		Date	
Link to bio showing research interests		Email	
Study Title			
Lay summary			
Background and rationale			
Aim			
Primary Objectives			
Secondary Objectives			
Tertiary/correlative Objectives			
Hypotheses			
Study design			
Population and setting			
Interventions			
Outcomes and measures			
Study procedures			
Statistical considerations			
Feasibility	.		
Significance			
Funding			

Risks	

Please submit your concept outline to info@thoraciconcology.org.au

APPENDIX 2 SAMPLE LETTER CONFIRMING TRIAL ENDORSEMENT

<Date>

By email:

<email address>

Dear *<member proposing the concept or proposal>*,

Re: TOGA endorsement of research proposal

This is to confirm that the following research proposal has been reviewed and approved by the Scientific Advisory Committee (SC) of the Thoracic Oncology Group of Australasia (TOGA):

Protocol number: *<TOGA XX/XXX>*

Study title:

Date of approval:

Please notify the TOGA Executive Officer on info@thoraciconcology.org.au of the completion of major milestones of your research project including, but not limited to:

- Study activation
- Close to recruitment
- Conference presentations
- Publication
- Preparation and distribution of a lay summary to research participants

Please note that endorsement of the proposal by TOGA does not equate to TOGA being sponsor of the study.

Yours sincerely,

TOGA SC Chair