ANZICS CTG Policy on Conflict of Interest Issues in Clinical Research

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Scope

This document will refer throughout to the commercial industry. The considerations expressed can equally be taken to apply to manufacturers of therapeutic, monitoring or diagnostic devices. It will also refer throughout to the researcher, as its primary aim is to provide a policy for the Australian and New Zealand Intensive Care Society (ANZICS) Clinical Trials Group (CTG), which exists solely to i improve outcomes of intensive care patients and their families by fostering an exceptional, collaborative research community The researcher is understood to be involved in a trial that has been endorsed or supported by the ANZICS CTG. The focus of this document will be on issues pertaining to conflicts of interest in the arena of intensive care research. It is not intended to be a discussion of all facets of research ethics.

The document has been based largely on the ANZCA document “Guidelines for the relationship between fellows and the healthcare industry”, the RACP document “Ethical guidelines in the relationship between physicians and the pharmaceutical industry” and on the references cited at the end of the document.

General Principles

1. The primary concern of the researcher must remain the patient, for whom – directly or indirectly – the researcher and the intensive care unit (ICU) provide clinical care.

2. There should be formal and open acknowledgment by the researcher receiving financial or material support from the commercial industry in order to conduct research.

3. Researchers should not allow their names or the name of the ANZICS CTG to be associated with any form of direct advertising, unless the commercial nature of their involvement is

clearly
stated and there has been prior approval by the ANZICS CTG. An association, in the form of ANZICS CTG endorsement or support of a trial, between the ANZICS CTG and any commercial product, does not imply endorsement of the product. A disclaimer to this effect should be included in industry advertising material.

4. In any commercial arrangement between a researcher and the commercial industry, if the ANZICS CTG is directly or indirectly involved, the final agreement must be subject to the approval of the ANZICS CTG Committee. If negotiations are conducted in a personal capacity, no mention of an ANZICS CTG affiliation can be made.

5. A "conflict of interest" between the interests of academic research and the interests of the pharmaceutical industry is a difficult concept to encapsulate but has potentially powerful negative connotations. It has been suggested that the notion of a "conflict of interest" might usefully be replaced with that of a "duality of interest" which recognises that, in a given situation, a researcher might have more than one interest. Such dualities should be openly reported as suggested above, and judgements about their significance, and whether any "conflict" exists, should be made by independent observers. The independent observer will generally be the ANZICS CTG Committee, unless the Committee members themselves decide that impartiality cannot be guaranteed, in which case the matter will be referred to the ANZICS Board.

6. Each ANZICS CTG endorsed or supported study must have a register of financial interests for investigators. Researchers unwilling to disclose financial interests for the purposes of the register cannot be involved in study design, patient recruitment or study analysis. The register will be maintained by the ANZICS CTG Committee and will be confidential. The format of the register follows this document as Appendix 1. This form may be signed by the chief investigator on behalf of the management team where they are certain that no conflict of interest exists. If there is a conflict of interest to declare then the individual concerned must fill out an individual conflict of interest form.

Specific Issues

Conduct of sponsored clinical trials

This discussion will pertain only to commercial industry-sponsored trials. For conduct of non-sponsored trials researchers should consult standard references including the references cited below.

1. Study Design

- The study must have a credible scientific basis, rather than evaluating or promoting a product.
- The study must conform to the academic standards of non-sponsored studies – predefined methods, appropriate statistics, ethical approval and a written budget. Patient consent and confidentiality must be assured and the potential risks to patients need to be considered.

2. Researcher-Sponsor relationship

- The researcher must not derive direct personal or financial benefit from the conduct of a sponsored trial, other than adequate compensation for personal expenses arising from the trial. The amount of compensation must relate to income or time lost and should be administered under a formal contractual arrangement open to scrutiny. Remuneration should be paid into a fund subject to institutional guidelines, and be used solely to execute the study. Researchers must inform the ANZICS CTG Committee if such an arrangement is in place for an ANZICS CTG-endorsed study.
- If remuneration to a researcher is based on a *per capita* basis for patient recruitment, the ANZICS CTG Committee must approve all such arrangements. As above, such remuneration should be paid into an institutional fund.
- An institutional fund is a fund that is administered and controlled by the hospital or institution in which the research is being performed, or in the case of university employees, a university administered fund. As such it must be subject to the financial regulations of that institution, even if the funds are used for the purposes of intensive care research alone. A fund which is controlled by the researcher is not necessarily subject to such external control and is more open to perceptions of financial impropriety.

3. Data Management

- Before the study begins, the degree of access to data by researcher and sponsor should be agreed. Ideally, both parties should have open access to all data.
- There should be a data monitoring and safety committee including representation from the sponsor and from the researcher.

- Statistical analysis should be performed by an independent professional, with subjective endpoints evaluated by an independent, blinded and unbiased committee.

4. Publication of results

- Before the study begins, the intentions regarding publication of results should be clearly stated and agreed upon. Ideally, this would be publication of results, including negative results in a peer-reviewed journal.
- There should be a publication committee to make decisions regarding publication. It is not acceptable for publication to be subject to sponsor approval.
- The responsibility for writing should rest with the researcher. “Ghost writing” by industry scientists is not acceptable.

Industry-sponsored attendance at meetings and travel

The ideal manner for the commercial industry to provide sponsorship is through an independently organised scientific meeting, for which the costs of bringing in invited speakers are defrayed by the sponsorship provided by the industry. The cost of attending such meetings is borne by the individual, for its value to their education. In accepting sponsorship outside these guidelines the researcher must bear in mind certain recommendations:

1. Attendance at a scientific meeting at which the researcher is making a contribution

Sponsorship of an individual researcher to attend meetings of scientific societies for either a scientific contribution or as an organiser is acceptable. The organising committee, not the sponsor, should make actual payment to the individual. Such sponsorship should be acknowledged, and should be of a magnitude judged reasonable by the committee. Individuals offered sponsorship independent of the organising committee should encourage the sponsor to approach the committee. If ANZICS CTG research is to be part of the presentation, then the ANZICSCTG Chair should be notified of the sponsorship.

Meetings organised by the commercial industry will call into question the independence of the invited speaker. For these meetings, the ANZICS CTG Committee must approve the presentation of ANZICS CTG research before it can be presented. Such meetings should not purport to be under the auspices of the ANZICS CTG.

2. Attendance at a scientific meeting at which the researcher is not making a contribution

If the researcher is not making a formal contribution to an industry-sponsored meeting, then the researcher should follow the guidelines approved by their employer. The ANZICS CTG can not be affiliated in any way with such meetings, and the researcher must not be seen to be a representative of the ANZICS CTG, unless the ANZICS CTG Committee has given prior approval.

3. Attendance at other meetings

The commercial industry also provides support for other meetings, such as product launches, hospital grand rounds, local meetings of specialists or departments. As above, the ANZICS CTG cannot be affiliated in any way with such meetings, and the researcher must not be seen to be a representative of the ANZICS CTG, unless the ANZICS CTG Committee has given prior approval.

<u>Industry support for ANZICS CTG meetings</u>

4. Support for venues, speakers and other costs

It is acceptable to approach the commercial industry to provide support for ANZICS CTG meetings. Certain principles should always apply

- Support must never be contingent on alterations in the program, speakers or other aspects of the scientific format of the meeting. The ANZICS CTG Committee alone should arrange the scientific program.
- Support for the costs of a visiting speaker are acceptable as long as such support is acknowledged. If the industry chooses a speaker, then care must be taken to ensure that the presentation is not primarily to promote an individual product. If the chosen issue is known to be a contentious one then there should be a balance of speakers canvassing alternate views.
- It is acceptable for the industry to provide other support in the form of venues, refreshments and so forth. As above, all support must be acknowledged.
- It is acceptable for the industry to exhibit its products at ANZICS CTG meetings.

Other remuneration provided to researchers

Gifts and entertainment

Benefits of whatever kind received from a commercial company must leave an individual's independence of judgement unimpaired. In general, the guidelines of an individual's employer should be followed, and the ANZICS CTG cannot be associated in any way with provision of such goods or services. It is recognised that judgement on these matters may sometimes be difficult. If there is to be any perception that the ANZICS CTG is involved then the matter should be brought to the attention of the ANZICS CTG Chair who may decide whether it should be referred to the ANZICS CTG Committee.

Remuneration for other services

An individual researcher is entitled to remuneration for any consultative or other service he provides to the pharmaceutical industry. There is, however, a substantial risk of potential conflict of interest with ANZICS CTG research, and therefore, such arrangements need to be transparent and open. If the remuneration is not an ongoing service, for example, a one-off fee for a consultation, then notification to the ANZICS CTG Chair should be sufficient disclosure. However, if the researcher is in any way employed or regularly remunerated by the industry, then that arrangement needs to be approved by the ANZICS CTG Committee. The overriding principle must be that full disclosure is the preferred course of action if there is any doubt.

Researchers' personal finances and conflicts of interest

It is impossible to lay down precise guidelines in this area, but a useful general principle might be that an impartial observer would not consider that financial interests in the company involved had significantly influenced a researcher's judgement about the place of a commercial agent. Such interests might include:

- Share holdings or options
- Board membership
- Paid employment
- Fellowships or other grants

It is not expected that researchers divest themselves of personal assets, or otherwise modify their financial dealings in order to participate in ANZICS CTG trials. It is expected, however, that individual researchers remain aware of the potential for duality of interest issues to arise, and of the potential adverse effect on the ANZICS CTG of any perception of impropriety. It must be the responsibility of the individual to recognise a potential duality, and the appropriate response should be disclosure to the ANZICS CTG Chair, who should decide whether it is a matter for the ANZICS CTG Committee to discuss. The question of spouses or dependent children having financial interests in commercial companies may also arise. Again, it is difficult to formulate precise guidelines, but the general principles mentioned above should apply, and the researcher should err on the side of caution and disclosure, if in doubt.

Potential solutions to duality of interest issues will vary according to the circumstances. If a researcher has a substantial and direct financial interest in a study outcome, (for example a

major stockholding or regular paid employment directly related to ANZICS CTG research) then, in most cases, he should not be involved in study design or direction, patient recruitment or consent, or data analysis. Alternatively, if the researcher is willing, the assets may be divested until the study is published. In the case of less substantial interests (for example, small stockholding, or occasional consulting fees, unrelated to ANZICS CTG research) the disclosure may be sufficient.

Assets such as stocks or options held by immediate family members may be viewed as creating a duality of interest in the same way as if the researcher held them. The guiding principle must be how the public would view such arrangements, and divesting assets by transferring them to family members might not be perceived as resolving a potential duality. This area is obviously difficult, and each case will need to be treated on its merits.

In the rare event of a researcher holding a patent (with or without commercial sponsorship) for a product, then full disclosure to the ANZICS CTG Committee is absolutely essential if the research is to be ANZICS CTG endorsed or supported. Individuals holding patents are not necessarily excluded from participating in research, but the guiding principle again should be how the public would view such arrangements.

In all cases of potential duality of interest, any publications should make mention of interests held or retained by the researcher during the study period.

Other recommendations

The specific recommendations in the document above will cover most situations. In any situation not covered by this document, a researcher concerned about a potential duality of interest should contact the ANZICS CTG Chair and the ANZICS CTG Chair can decide whether to refer the matter to the ANZICS CTG Committee.

The ANZICS CTG Committee or a subcommittee of the Committee should review these guidelines at an interval determined by the Committee.

References

Royal Australian College of Physicians. Ethical guidelines in the relationship between physicians and the pharmaceutical industry. RACP, Sydney, 2000
http://RACP.edu.au/members/fyi/resources/pharm
Australian and New Zealand College of Anaesthetists. Guidelines for the relationship between fellows and the healthcare industry. ANZCA, Melbourne, 2000.
http://anzca.edu.au/publications/profdocs/profstandards
National Heart, Lung, and Blood Institute. Guidelines for Avoiding Conflicts of Interest in Multicenter Clinical Trials.
http://www.nhlbi.nih.gov/funding/policies/coi-res.htm
Van McCrary S, Anderson CB, Jakovljevic J, Khan T, McCullough LB, Wray NP, Brody BA. A national survey of policies on disclosure of conflicts of interest in biomedical research. N Engl J Med 2000 Nov 30;343(22):1621-6.

Appendix 1: Register of Interests for Clinical Trials

Name _____

1. Do you have a personal or financial interest in the outcome of this study ?

   ☐YES ☐NO

2. Where the study involves investigation of a company's products, please answer the following questions:

   2.1. Do you directly own shares or options in that company ? YES☐ NO☐

   2.2. If you answered yes to Q2.1, please indicate if the current value of those shares or options is: less than $1000 ☐

   $1000 - $50000 ☐

   over $50000 ☐

   2.3. Have you received any payment from the company for services rendered? If so, please give details below

   _____

   _____

   _____

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   2.4. Have you received any hospitality or gifts from the company? If so, please give details below

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3. Please indicate if any immediate member of your family has any personal or financial interest in the outcome of the study

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4. Please declare below any other duality or conflict of interest that you may have in relation to this study

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