

SCIENCE SUB-COMMITTEE REVIEW APPLICATION FORM GUIDELINES

TO APPLICANTS:

(NOTE: Randomized Controlled Trial Applications must be accompanied by a Completed Consort Check List - available at: <http://www.consort-statement.org>)

For those applicants seeking funds to **conduct a randomized controlled trial** please ensure that your **grant application includes** a trial registration number, such as ISRCTN (see attached (last pages of application) editorial: Moher D, Bernstein A. Registering CIHR-funded Randomized Controlled Trials: A Global Public Good. Canadian Medical Association Journal 2004;171:750-751).

Your proposal will be reviewed by the Science Committee of the Research Institute and will be rated as follows:

<u>Scientific Rating</u>		<u>Relevance Rating</u>	
4.5 - 4.9	Outstanding	Not Recommended	- Not Relevant
4.0 - 4.4	Excellent	0	- Low Relevance
3.5 - 3.9	Good	.1	- Moderate Relevance
3.0 - 3.4	Needs Revision	.2	- High Relevance
2.6 - 2.9	Needs Major Revision		
2.5 - lower	Serious Flaws		

You will be advised by letter of the Science Committee's decision and will also be given the unedited comments of the in-depth review. Decisions are reached through discussion and individual reviewers may not always agree in their assessments.

The following areas are addressed by the in-depth reviewers and the committee.

1. **IN ORDER TO BE REVIEWED** your proposal should be no longer than 10 pages, single-spaced, excluding references and appendices. Print type should be no smaller than 12 point, with 1 inch margins. A lay abstract of not more than 300 words should be included, telling what it is you are going to do; and how you are going to do it. The abstract should explain in terms understandable by the general public, what its relevance to health care is.

Appendices should be limited to letters of collaboration, support, questionnaires, photographs and figures (excluding copyrighted questionnaires).

If your proposal is not consistent with reviewers' guidelines, it may be returned to you. The Chairperson of the Science Sub-Committee and the Director of the Research Institute will review any particular applications which may be returned.

Grant applications already formatted for submission to external agencies may be submitted as is for further consultation with the Chairperson of the Science Sub-Committee.

2. Your proposal should clearly state the objectives.
3. Your proposal should include a critical appraisal and presentation of the relevant background literature.
4. Your proposal should include a description of the research methodology or research design such that its adequacy for the stated objectives can be judged. This should include methods of subject selection and recruitment, inclusion-exclusion criteria, methods of data collection, justification of sample size, measures, data analysis, and evaluation of the results. Any intervention, experimental or therapeutic, should be described in sufficient detail that others could replicate it. All procedures that you will use for intervention or data collection should be described clearly with justification.

SCIENCE SUB-COMMITTEE REVIEW APPLICATION FORM GUIDELINES

5. Budget and justification. Is there a cost benefit or cost effectiveness component to your research? If so, describe how this will be carried out. Indicate source of funding and what is covered by these funds. If further support is required from another CHEO investigator who is not a co-applicant or co-investigator, e.g., creatinine measurements - CHEO Biochemistry - provide a statement from the Director of Biochemistry indicating his/her agreement to perform these measurements.

6. Ethical considerations. **Note:** Applications to the Research Institute for R.I. funding, shall be reviewed by the Ethics Committee upon receipt of the Science Sub-Committee's review and comments.

7. Relevance to children's health.

- X How is this related to the priorities of the service departments or the Children's Hospital of Eastern Ontario?
- X What is being added to the knowledge base?
- X In practical terms, what impact will the study findings have on children's health care?
- X Demonstrate the relevance of program evaluation by:
 - o How the results would contribute to new knowledge, and
 - o How it would be generalizable or transferable to other health care settings.

When scientific merit is equal between competing grants, and there are limited funds, the Finance Committee may recommend funding based on ratings of relevance.

8. Please provide the names, addresses, and phone numbers of two peers, see item 11 on Application Form, who could carry out a review of the proposal.

9. It has been the experience of the Science Sub-Committee that those applications that have already been peer-reviewed, either within the originator's department or outside the department tend to be more successful.

10. Principal investigators require signatures from:

- i) **For Medical Staff:** the Department Head
- ii) **For Nursing, Allied and Other Health Staff:** to be determined within each individual PSU whether the required signature be from the Medical and/or Operations Directors **and** the Professional Practice Leaders.

11. If this is a resubmission of a grant you are required to complete a Previous Review Form ([available on RI website under "Funding & Forms"](#))

Type of Research-Please Check Appropriately

- Clinical Trial
 - Randomized Control Trial (See application form guidelines)
 - Trial Registration Number (if applicable) _____
- Allied Health
- Basic Science
- Program Evaluation
- Qualitative Research
- Other _____

1. **Project Title:** _____

2. **Principal Investigator:**

Name: _____
Title: _____
Address: _____
Tel. No.: _____

3. **Co-Investigators:** _____

4. **Where will research be conducted?** _____

5. **Briefly describe the space, furniture and telephone requirements for the project (e.g., wet lab, animal surgery, office space, etc.)**

SCIENCE SUB-COMMITTEE REVIEW APPLICATION FORM

6. Anticipated Start Date: _____
Completion Date: _____

7. Source of funding applied for (List all sources):

	YES	NO
CHEO Research Institute	_____	_____
CHEO Trust Funds	_____	_____
External Agencies	_____	_____
Drug Companies	_____	_____
Other	_____	_____

8. Name, Title, and Signature of
(All) applicant(s)

Principal Investigator

Signature

Co-Investigator(s)

Signature

Co-Investigator(s)

Signature

Co-Investigator(s)

Signature

Co-Investigator(s)

Signature

SCIENCE SUB-COMMITTEE REVIEW APPLICATION FORM

9. PLEASE NOTE SIGNATURE CHANGES. Your signature indicates your awareness of the project and its resource implications.

I) For Medical Staff

_____	_____	_____	_____
Department Head	Department	Signature	Date

II) For Nursing, Allied and Other Health Staff (as determined within each PSU)

_____	_____	_____	_____
PSU Medical and/or Operations Director	PSU Program	Signature	Date

_____	_____	_____	_____
Professional Practice Leader	Profession	Signature	Date

10. For internal funding (Research Institute funding) use the attached budget form.

11. Please list below, two possible reviewers for your project.

_____	_____
Name of Reviewer #1	_____

	Title, Address, Phone & e-mail

_____	_____
Name of Reviewer #2	_____

	Title, Address, Phone & e-mail

12. **Three copies plus original to:**

Administration Office
Children's Hospital of Eastern Ontario
Research Institute
401 Smyth Road
Ottawa, Ontario K1H 8L1

SCIENCE SUB-COMMITTEE REVIEW APPLICATION FORM

BUDGET

FUNDS REQUESTED FOR _____ month _____ year to _____ month _____ year

PERSONNEL

<u>Name</u>	<u>Position</u>	<u>Estimated % Time Expenditure</u>
_____	_____	
_____	_____	
_____	_____	
_____	_____	
_____	_____	
_____	_____	
_____	_____	
	Personnel Expense	_____
	Employer's Contribution to Fringe Benefits	_____
	<u>TOTAL PERSONNEL EXPENSES</u>	_____

EQUIPMENT

<u>Description</u>	<u>Unit Cost</u>	<u>Estimated Expenditure</u>
_____	_____	
_____	_____	
_____	_____	
_____	_____	
	<u>EQUIPMENT TOTAL</u>	_____

SCIENCE SUB-COMMITTEE REVIEW APPLICATION FORM

SUPPLIES & SERVICES

(Include, where appropriate, telephone installation, rental, and long distance)

SUPPLIES & SERVICES TOTAL

TRAVEL

(1) Travel involved in the collection of data

TRAVEL TOTAL

OTHER EXPENSES

OTHER TOTAL

TOTAL COST OF PROJECT

SCIENCE SUB-COMMITTEE REVIEW APPLICATION FORM CHECK LIST

Have the following aspects been dealt with in the proposal:

YES	NO	
<input type="checkbox"/>	<input type="checkbox"/>	Signature(s) of investigator and all co-investigators
<input type="checkbox"/>	<input type="checkbox"/>	Signature(s) of all relevant department head(s)
<input type="checkbox"/>	<input type="checkbox"/>	Signatures of clinic directors or others (e.g., school boards) who have approved the project with regard to the use of staff, services, or equipment
<input type="checkbox"/>	<input type="checkbox"/>	A lay abstract
<input type="checkbox"/>	<input type="checkbox"/>	Identified known or possible risks to subjects
<input type="checkbox"/>	<input type="checkbox"/>	Precautions taken to deal with known or possible risks to subjects
<input type="checkbox"/>	<input type="checkbox"/>	Informed consent form
<input type="checkbox"/>	<input type="checkbox"/>	Animal Care Committee approval
<input type="checkbox"/>	<input type="checkbox"/>	Pharmacy and Therapeutics Committee approval
<input type="checkbox"/>	<input type="checkbox"/>	Method of informing the family physician
<input type="checkbox"/>	<input type="checkbox"/>	Procedures used in the conduct of the research, including design, methods of data collection, and analysis
<input type="checkbox"/>	<input type="checkbox"/>	Critical appraisal of relevant literature
<input type="checkbox"/>	<input type="checkbox"/>	Statement of relevance to children's health
<input type="checkbox"/>	<input type="checkbox"/>	Ethical considerations
<input type="checkbox"/>	<input type="checkbox"/>	Budget

SCIENCE SUB-COMMITTEE REVIEW APPLICATION FORM

MULTICENTER STUDY/CLINICAL TRIAL

Request to Participate

OBJECTIVES

- 1) A brief statement of the objective(s) of the study.
- 2) Rationale

A discussion of the justification for the study, i.e. what is the reason for performing the study. If in the case of a clinical trial the current therapy is inadequate explain why it is inadequate and discuss the number and type of patients who are affected by the disorder.
- 3) Background
 - a) For a clinical trial it will be necessary for the CHEO investigator to provide the relevant background information to educate the Science Sub-Committee about the type of disorder being treated and contrast current therapy with that proposed in the study.
 - b) For a multicenter center study, if the background material is adequately discussed in the multicenter grant application, refer to those portions (pgs) of the proposal.
- 4) Details of the Experimental Design

Briefly describe how the study is to be performed, time course, measurements made, data collected and analyzed. Discuss potential risk factors.
- 5) Investigators

Statement of names of all CHEO investigators involved in the study and their role.
- 6) Patient Recruitment

Indicate source and number of patients to be involved in the study, i.e.; ambulatory clinic, neurology clinic.

7) Inclusion - Exclusion Criteria

Briefly summarize or refer to a page # in the application supplying this information.

8) Risk Factors

Describe known or possible risks and how they will be handled, i.e. what precautions will be taken?

9) Source of Funding

Indicate source of funding and what is covered by these funds. If further support is required from another CHEO investigator who is not a co-applicant or co-investigator, e.g. creatinine measurements - CHEO - Biochemistry - statement from Director of Biochemistry indicating his/her agreement to perform these measurements.

10) Consent Form

Consent form on CHEO letterhead must be presented with the proposal. Describe how it will be presented.



MULTICENTER STUDY/CLINICAL TRIAL CHECK LIST

The following have been dealt with in the proposal:

YES	NO	
—	—	If this is a randomized controlled trial, completed Consort Check List is attached -checklist is available at: http://www.consort-statement.org
—	—	Statement of objective(s)
—	—	Rationale for the study
—	—	Background information
—	—	Description of Experimental Design
—	—	List of CHEO investigators participating
—	—	Source of patient recruitment
—	—	Inclusion - Exclusion Criteria
—	—	Known or possible risks
—	—	Precautions taken to deal with these problems
—	—	Source of funding (what is covered)
—	—	Statement of participation from other individuals who are not co-investigators
—	—	Consent Form

Registering CIHR-funded randomized controlled trials: a global public good

David Moher, Alan Bernstein

β See related article page 735

On July 26, 2004, the Canadian Institutes of Health Research (CIHR), the largest publicly funded granting agency in Canada, announced that all new CIHR-funded randomized controlled trials (RCTs) must be registered with

CIHR's decision to adopt an open trial-registry approach was based in large part on the set of values articulated in the Institutes' strategic plan, *Blueprint 2007*.³ Those values include the public interest, sound ethical principles, excellence, public transparency, accountability and collaboration. CIHR hopes that, among other benefits, trial registration will encourage and increase collaboration among researchers, the private sector and the community, reduce the risk of publication bias, reduce the wasteful duplication of research efforts, and contribute to global efforts to reduce or eliminate disease.

The call for trial registration is not new.³⁴ Trial reporting standards, such as the CONSORT Statement, have strongly encouraged the use of a trial registration numbering system such as the ISRCTN,⁶ and the member journals of the International Committee of Medical Journals Editors will no longer consider unregistered RCTs for publication.⁷

Similarly, trial registries are not new; there are many in disparate forms and various clinical areas.⁴ CIHR's decision will cover the complete spectrum of trials, that is, those on pharmaceuticals, devices and surgical procedures as well as those examining psychosocial and health system interventions. Among the registration schemes available, CIHR has elected to use the ISRCTN. Increasingly, trials are conducted across geographic boundaries, making the ISRCTN a sensible choice, and a genuinely international one. Clearly, it would be desirable to have a single worldwide public database for all RCTs, regardless of funder and country. The ISRCTN was developed by the UK-based Current Controlled Trials, Ltd. (<http://sciencenow.com/>), a private Web-based publishing company that is supportive of transparency in clinical trials reporting. Each trial can be registered for Cdn\$120, a one-time fee to cover the costs of hosting, indexing and permanently displaying the trial record in the ISRCTN register. CIHR will cover the cost of registration for CIHR-funded trials. The registration fee can be waived at the discretion of the company for trials originating in low-income countries.

What are the benefits of trial registration? In a landmark study published nearly 20 years ago, Simes⁸ examined data contained in an oncology clinical trials registry and reported that statistically pooling the results of published trials only, compared with pooling published plus registered trials provided clinicians and patients alike with differing and opposing estimates of the effectiveness of a cancer

an International Standard Randomised Controlled Trial Number (ISRCTN).¹ Basic information about each registered trial will be posted on the public Web site of the ISRCTN register (www.controlled-trials.com), and the ISRCTN will be cited in any subsequent publication of trial results.

intervention. Researchers are known to be more energetic about writing up reports of RCTs when the results are statistically positive.¹⁰ Likewise, journals seem more interested in publishing statistically positive reports.¹¹ Such behaviours result in publication bias, as first reported more than 40 years ago.¹² Although trial registration will not eliminate publication bias, for publicly funded trials it is likely to provide a degree of transparency and accountability not previously seen.

Even when the results of an RCT are statistically positive, some investigators attempt to report this information multiple times and in multiple ways, such as by publishing separately the results of each participating country or geographic region. Duplicate publication gives the unwary reader the impression of a far larger body of evidence pertaining to an intervention than actually exists.¹³ Such acts of duplication are likely to be reduced by the introduction of trial registration.

Knowledge of a trial's existence is particularly important to those who conduct systematic reviews. Such reviews are a fundamental building-block in the delivery of evidence-based health care. The results of systematic reviews will more likely produce biased results if they are missing information about the existence of trials and if covert duplicate publication results in double counting. Suboptimal systematic reviews are of little help to clinicians, clinical practice guideline developers, consumers and anyone else who uses them to inform decision-making.

Ultimately, trial registration will succeed only when all funders of randomized trials, including the pharmaceutical industry, come onboard. Pharmaceutical companies fund about 90% of RCTs performed globally. The decisions by GlaxoSmithKline and Eli Lilly to move toward trial registration are steps in the right direction.

Trial registration might also be the impetus for other good clinical trials practice. Chan and colleagues compared the contents of 102 trial protocols approved by the scientific ethics committees for Copenhagen and Frederiksberg, Denmark, during 1994 and 1995 with 122 subsequent publications.¹⁴ They reported that in nearly two thirds of the trials there was a change in at least one primary outcome between the protocol and publication. They also reported that statistically significant outcomes had a higher likelihood of being reported compared with nonsignificant outcomes. Similar results are reported in this issue of *CMAJ*.¹⁵ Taken together, these results suggest that linking the ISRCTN with a publicly available protocol will be another positive step.

The business of RCTs is very large. CenterWatch, a Boston-based publishing and information services company focusing on the clinical trials industry, estimates that at least 41 000 RCTs are currently in progress in North America (www.centerwatch.com).

Trial registration is an important initiative, but it is not a panacea. It will not provide access to trials submitted to regulatory agencies, a major source of trials.¹⁶ It will not in itself be sufficient to stop publication bias, duplicate publication or a plethora of questionable behaviours.

RCTs are central to the development of evidence-based health care. If we are to accelerate the development of cost-effective new interventions, then open and public access to all trials and their outcomes will be key to achieving that goal. Transparency and accountability are important values in the work of the CIHR, and nowhere is that more visible and crucial than in research in which the immediate goal is

to assess the safety and efficacy of a new drug, device, procedure or other intervention.

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References

- 1 Canadian Institutes of Health Research. CIHR joins in the international registration of randomised controlled trials [news release]. Available: www.cihr-irsc.gc.ca/e/news/24107.shtml (accessed 2004 Aug 29).
- 2 Canadian Institutes of Health Research. Investing in Canada's future: CHIR's blueprint for health research and innovation. Available: www.cihrirsc.gc.ca/e/20266.html (accessed 2004 Aug 29).
- 3 Chalmers I, Dickersin K, Chalmers TC. Getting to grips with Archie Cochrane's agenda: all randomised controlled trials should be registered and reported. *BMJ* 1992;305:786-7.
- 4 Dickersin K, Rennie D. Registering clinical trials. *JAMA* 2003;290:516-23.
- 5 Moher D. Clinical-trial registration: a call for its implementation in Canada. *CMAJ* 1993;149:1657-8.
- 6 Moher D, Schulz KF, Altman DG for the CONSORT Group. The CONSORT Statement: revised recommendations for improving the quality of reports of parallel-group randomized trials. *Ann Intern Med* 2001;134:657-62.
- 7 De Angelis D, Drazen JM, Frizelle FA, Haug C, Hoey J, Horton R, et al. Clinical trial registration: a statement from the International Committee of Medical Journal Editors. *CMAJ* 2004;171(6):606-7.
- 8 Easterbrook PJ. Directory of registries of clinical trials. *Stat Med* 1992;11:345-423.
- 9 Simes RJ. Publication bias: the case for an international registry of

clinical tri-als. *J Clin Oncol* 1986;4:1529-41.

10 Dickersin K, Min YI. NIH clinical trials and publication bias. *Online J Curr Clin Trials* 1993; Apr 28(doc 50).

11 Dickersin K, Min YI, Meinert CL. Factors influencing publication of research results: follow-up of applications submitted to two institutional review boards. *JAMA* 1992;267:374-8.

12 Sterling TD. Publication decisions and their possible effects on inferences drawn from tests of significance — or vice versa. *J Am Stat Assoc* 1959;54:30-4.

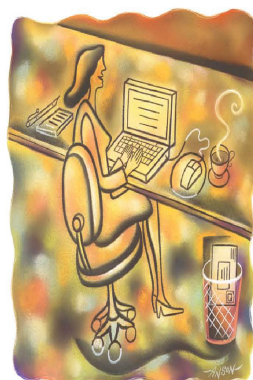
13 Huston P, Moher D. Redundancy, disaggregation, and the integrity of medical research. *Lancet* 1997; 347:1024-6.

14 Chan AW, Hrobjartsson A, Haahr MT, Gøtzsche PC, Altman DG. Empirical evidence for selective reporting of outcomes in randomized trials: comparison of protocols to published articles. *JAMA* 2004;291(20):2457-65.

15 Chan AW, Krole'za-Jeric' K, Schmid I, Altman DG. Outcome reporting bias in randomized trials funded by the Canadian Institutes of Health Research. *CMAJ* 2004;171(7):735-40.

16 MacLean CH, Morton SC, Ofman JJ, Roth E, Shekelle PG. How useful are unpublished data from the Food and Drug Administration in meta-analysis? *J Clin Epidemiol* 2003;56:44-51.

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