

**RESEARCH ETHICS BOARD (REB)  
GUIDELINES  
FOR ASSESSING CONFLICT OF INTEREST (COI)**

**1) Why are these Guidelines being developed?**

Over the last several years the Hospital for Sick Children (Sick Kids) REB has reviewed applications which include a variety of declared COI statements. The REB has addressed these declarations on a case by case basis but now proposes a set of guidelines to facilitate a consistency in approach by the REB to determine if there is a COI and how to address it. However, it is acknowledged that dealing with COI can be a grey area, and there does need to be a case by case review of these situations. Some recent examples of COI which came before the REB are set out in Appendix “A”.

These Guidelines also provide assistance to researchers when making application to the REB. These Guidelines are complementary to and do not detract or diminish from the requirement to adhere to Sick Kids policies and any external funding requirements. These Guidelines also signal to the broader community the REB’s commitment to minimizing COI.

The Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS) which governs human clinical research at Sick Kids addresses COI specifically in Section 4, Article 4.1. The TCPS requires researchers and REB members to “disclose actual, perceived or potential conflicts of interest to the REB”. It further requires REBs to develop mechanisms to address and resolve COI declared by investigators by obtaining full information on the COI; assessing the likelihood that their judgement may be influenced; and assessing the seriousness of harm that is likely to result. See Appendix “B” for the complete text of the TCPS section.

In addition to REB COI review, researchers who have an appointment to the Research Institute (RI) must also sign a yearly statement that they have disclosed all conflicts of interest throughout that particular year, and that they are in compliance with Sick Kids policies. The focus of the RI review is from an institutional perspective and complements the REB review. Both processes may inform the other.

**2) To whom do these Guidelines apply?**

These Guidelines apply to principal investigators, co-investigators, and any other person affiliated with Sick Kids who participates in the design, conduct or reporting of the research project. It applies to these people when they apply to the REB for review and approval.

**3) Legislative/regulatory/policy context**

In addition to the TCPS, several Sick Kids policies establish or reference COI related requirements. Appendix “C” includes a list of these policies, as at the date of these Guidelines.

The key policies are referenced below:

- 1.2.03 Conflict of Interest
- E.01 Supplementary Conflict of Interest Policy: Research Institute
- 4.02 Industry-Sponsored Research Grants and Research Contracts
- 4.05 Finders’ Fees and Assessment Fees in the Recruitment of Research Subjects

In particular, Policy E.01 requires that researchers make full disclosure of relevant COIs to the REB, the source of any funding for studies. Full disclosure of any COI must also be included in the corresponding consent form for subjects.

External regulatory organizations are also developing COI guidance documents. The US National Institutes of Health has issued a draft guidance document on financial conflicts of interest (March 2003) replacing an earlier 2001 Draft Interim Guidance document. Once finalized, this NIH guidance document, along with any other external regulatory guidance documents, will be reviewed on an ongoing basis with our REB Guidelines to ensure consistency.

#### **4) Principles underlying these Guidelines**

Consistent with the TCPS, other inter/national guidance documents, and other Sick Kids policies, the following principles underpin the REB Conflict of Interest Guidelines:

##### **a) Rights and Safety of Research Subjects**

- the rights and safety of the research subject are paramount
- there must be full disclosure of all aspects of research on the consent form (risks, benefits and COI) to enable subjects to make a fully informed decision

##### **b) Trust in Research**

- an overriding commitment to objectivity in research
- adherence to the highest standards of science
- unprejudiced reporting of results

##### **c) Trust in Sick Kids**

- the doctor/patient relationship is the foundation for trust in the hospital
- support from the community stems from consistently practising good medicine and engaging in ethical and scientifically rigorous research

##### **d) Fairness and Transparency in REB Review**

- openness, transparency and consistency by the REB in the review of research
- fairness and timely response
- a proportionate approach to the management of declared conflicts of interest

#### **5) Guidelines**

##### **(a) COI Definition**

*REB Definition of Conflict of Interest*

*A conflict of interest exists in any situation where there is a potential divergence between the private interests of a researcher or a "Related Person" (being the spouse, domestic partner, immediate family member or close acquaintance of the researcher) and the researcher's obligations to the research subject, such that an independent observer would reasonably question whether the researcher's behaviour or decisions are in any way motivated by considerations of personal gain, financial or otherwise, rather than solely by concern for the rights and welfare of the research subject.*

*A conflict of interest may be actual, apparent, perceived or potential. A conflict of interest does not necessarily imply wrongdoing as a conflict of interest depends upon the circumstances, and not on the character of a researcher.*

The REB definition of Conflict of Interest builds upon the Sick Kids Definition of Conflict of Interest which is set out in the footnote below.<sup>1</sup>

Section 4 of the TCPS indicates that a conflict of interest:

- Can be “real” or “apparent”
- Is something that may compromise independence, objectivity or ethical duties of loyalty
- Is a private or personal interest that may influence or appear to influence the researcher’s judgement
- Can result from competing interests that may arise from family relationships, financial partnerships or other economic interests

#### **(b) Types of COI**

It is difficult to classify the kinds of conflict of interest. The categories are fluid and in some senses, arbitrary. The same situation of conflict often falls into more than one category.

In order to flesh out the definition of COI, four categories or types of COI have been identified: Financial; Direct Status Benefit; Undue Influence; and Competitive Interest. These categories provide a framework for thinking about which situations may give rise to a conflict of interest.

##### **(i) Financial**

This is the most obvious form of COI. If the researcher or Related Person stands to gain financially in the undertaking or outcome of research, there will likely be a financial conflict of interest.

The following are examples of financial conflicts of interest:

---

<sup>1</sup> *A conflict of interest exists in any situation where there is a potential divergence between a staff member's private interests and his or her obligations to the hospital such that an independent observer would reasonably question whether the staff member's behaviour or decisions are in any way motivated by considerations of personal gain, financial or otherwise, from a source other than the hospital. A conflict of interest may be actual, apparent, perceived or potential. A conflict of interest does not necessarily imply wrongdoing as a conflict of interest depends upon the circumstances, and not on the character of a staff member.*

- The researcher or a Related Person owns shares in the sponsor of the study
- The researcher stands to gain from the research in terms of gifts, favours or gratuities
- The researcher will receive a bonus for positive test results
- If the researcher achieves interesting results, s/he will be sent to a conference in a desirable location

**(ii) Direct Status Benefit**

If the researcher or Related Person stands to gain through direct rewards in respect of his or her status (for example career status) in the undertaking or outcome of research, there will likely be a direct status benefit conflict of interest.

The following are examples of direct status conflicts of interest:

- The researcher stands to gain from the research in terms of promotions or other special considerations
- The researcher will be promoted or hired by the sponsor if his or her research is successful

While it is recognized that undertaking research will usually be viewed positively in terms of enhancing career advancement, the question is whether the link between the career enhancement and the outcome of the research is so strong as to bring into question the objectivity of the research process and outcome.

**(iii) Undue Influence**

This category refers to situations in which the position of the researcher is such that the researcher may exert an undue influence over the research, because of his or her position or the vulnerability of other persons involved in the research as subjects. This influence may be due to a personal or professional relationship between the affected individuals.

The following are some examples of situations in which undue influence may constitute a COI:

- The researcher has a sick child who could benefit from a drug being tested, if the drug were approved.
- Recognizing the particular challenges of conducting research in small subspecialties, if the researcher recruits his/her subjects from among his/her patients, the researcher may exert an undue influence on their patients' consent to participate.
- If the researcher recruits subjects from among his/her employees, students, or immediate colleagues, the researcher may exert an undue influence on potential subjects based on the employment relationship.

**(iv) Competing Interest**

This category of COI refers to situations in which the researcher may be influenced to draw conclusions against the interest of the sponsor or another interested party to the study because the researcher or a Related Person has an adversity in interest related to the research.

The following are some examples of a competing interest which may constitute a COI:

- The researcher is a party to legal suit against the research company or sponsor.
- The researcher may have a financial interest in another treatment or product which is used to treat the same medical condition as the subject matter of the research.

Some activities have clearly been identified by Sick Kids as impermissible, because of the likelihood of COI and others have been identified as permissible. These activities are set out in Appendix “D”.

#### **6) REB Procedures for Dealing with COI**

- a) The Principal Investigator is required to make a full COI Declaration to the REB (on behalf of themselves and the research team) as part of their application for REB approval. The Declaration of the Principal Investigator is attached as Appendix E.
- b) If there is a conflict or potential conflict of interest, the Principal Investigator is to propose strategies to mitigate the COI on the COI form.
- c) REB review of the COI declaration may include consulting with experts and with the Chief of Research, especially when sizable financial amounts are involved.
- d) The REB will need to make two determinations: Is there a conflict of interest? If there is, can it be managed and how?

#### **7) REB review considerations**

- the nature and size of the total financial COI e.g., consulting + project funding, in discussion with the Chief of Research and the COI Advisory Committee
- advisory board/scientific advisor appointment parameters e.g., role definition and timeframes, compensation, relationship to those who will be making protocol funding decisions
- the vulnerability of the research subjects and whether they need protection e.g., adults vs. children; therapeutic vs. non-therapeutic research
- the seriousness or level of risk of the study interventions
- the likelihood that the COI will have a direct impact on the research

#### **8) Outcome of Review**

- the REB will decide if the research should proceed, in light of the COI and what measures should be taken (if any) to mitigate any COI.
- the REB response will include recommendations on how to mitigate or eliminate the conflict
- REB approval is withheld until a mutually agreeable arrangement for dealing with the COI has been reached

- compliance oversight may require enhanced monitoring by the REB e.g., post approval level of continuing review may be increased
- any subsequent COI identified following REB approval must be declared and reviewed promptly through the amendment request form process

#### **9) Mechanisms for Approval & Dissemination of these Guidelines**

- Input on the draft Guidelines was solicited from internal stakeholders
- The Guidelines were submitted to the REB for approval (twice)
- The Guidelines were revised in accordance with REB comments
- Following approval by the REB, dissemination of these Guidelines will occur through the Sick Kids REB website, REB member/new member training, and researcher education programs

#### **10) Remedies for Non-Compliance with Guidelines**

- Consistent with existing REB procedures, incomplete information is returned to the Investigator and REB approval is withheld until all required information is submitted and reviewed.
- Non-compliance with the measures to deal with COI determined by the REB will be addressed as a research misconduct issue and will be guided by relevant Sick Kids policies.

## **Appendix A**

### **Recent Sick Kids examples of COI and Mechanisms to Address COI**

1-A Sick Kids investigator was recruited by a sponsor to write and conduct a study at Sick Kids. The separate consents investigator was to be paid for both activities. Because of the proximity of the two activities and the perception that undue influence by the sponsor could result in a protocol written to selectively favour results attractive to the sponsor, the REB required that the two activities (and their funding) be separated.

2-A Sick Kids investigator was approached to join a commercially sponsored national advisory board for which an honorarium would be paid. The board's mandate included reviewing and funding individual projects including a project recently written by the same investigator. The investigator decided not to join the advisory board.

3-A Sick Kids investigator requested REB approval to hire her husband to design the database and conduct the statistical analyses for her study which had already received REB approval. The REB requested more details from the investigator e.g., amount of compensation, support of funding agency, support of co-investigators etc before deciding on a course of action. The investigator decided not to employ her husband on this project.

## Appendix B

### Excerpt from Tri-Council Policy Statement: Ethical Conduct of Research Involving Humans

...

#### Section 4

Researchers hold trust relationships with research subjects, research sponsors, institutions, their professional bodies and society. These trust relationships can be put at risk by conflicts of interest that may compromise independence, objectivity or ethical duties of loyalty. Although the potential for such conflicts has always existed, pressures to commercialize research have led to increased concerns. Researchers, their institutions and REBs should identify and address conflicts of interest -- real or apparent -- to maintain the public confidence and trust, discharge professional obligations and ensure accountability.

**Article 4.1 Researchers and REB members shall disclose actual, perceived or potential conflicts of interest to the REB. REBs should develop mechanisms to address and resolve conflicts of interest.**

#### A. Conflicts of Interest Involving Researchers

The REB should assess the likelihood that the researcher's judgement may be influenced, or appear to be influenced, by private or personal interests, and assess the seriousness of any harm that is likely to result from such influence or from the mere appearance of undue influence. Competing interests may arise from family relationships, financial partnerships or other economic interests.

The appearance of a conflict may in some cases be as damaging as a real conflict. Two approaches can be suggested for assessing the potential implications of apparent or real conflicts of interest. One might ask whether an outside observer would question the ability of the individual to make a proper decision despite possible considerations of private or personal interests; alternatively, one might ask whether the public would believe that the trust relationship between the relevant parties could reasonably be maintained if they had accurate information on the potential sources of conflict of interest.

When a significant real or apparent conflict of interest is brought to its attention, the REB should require the researcher to disclose this conflict to the prospective subjects during the free and informed consent process. In accord with Article 2.4(e), research subjects should be fully informed of a researcher's potential or actual conflict of interest. To identify and address conflicts properly, REBs should be provided with details on the research project, budgets, commercial interests, consultative relationships and other relevant information (see Article 7.3).

REB management of conflicts of interest requires a proportionate approach. Sometimes, the conflict of interest is so pervasive that it is not enough merely to disclose it to the research subjects, the sponsors of research, institutions, relevant professional bodies or the public at large. In such instances, the REB may require that the researcher abandon one of the interests in conflict. A conscientious researcher will, under such circumstances,

either withdraw from the research or allow others to make research-related decisions without being directed to do so. However, in some cases, the REB might conclude that the identified conflict of interest does not warrant specific actions. When significant conflicts of interest are identified, the continuing ethics review process by the REB may also help to manage them (see Section 1). When a conflict of interest is unavoidable, the continuing ethics review process should be made more stringent, to help ensure that conflicts are managed appropriately.

#### B. Conflicts of Interest by REB Members

To maintain the independence and integrity of ethics review, it is of the highest importance that members of the REB avoid real or apparent conflicts of interest (see Article 1.12). For example, REB members are in a clear conflict of interest when their own research projects are under review by their REB or when they have been in direct academic conflict or collaboration with the researcher whose proposal is under review. To manage such conflicts, REB members must withdraw from the committee when such projects are under consideration. In some instances, individual members of the REB may also have a conflict of interest in accepting undue or excessive honoraria for their participation in the REB (e.g., on commercial REBs).

#### C. Institutional Conflicts of Interest

The REB must act independently from the parent organization. Therefore, institutions must respect the autonomy of the REB and ensure that the REB has the appropriate financial and administrative independence to fulfil its primary duties. Situations may arise where the parent organization has a strong interest in seeing a project approved before all ethical questions are resolved. As the body mandated to maintain high ethical standards, however, the public trust and integrity of the research process require that the REB maintain an arms-length relationship with the parent organization and avoid and manage real or apparent conflicts of interest.

## **Appendix C**

### **List of Sick Kids Policies that Reference COI**

- 1.2.03 Conflict of Interest
- E.01 Supplementary Conflict of Interest Policy: Research Institute
- 4.02 Industry-Sponsored Research Grants and Research Contracts
- 4.03 Research Involving Human Subjects
- 4.04 Free and Informed Consent in Research
- 4.05 Finders' Fees and Assessment Fees in the Recruitment of Research Subjects
- D.03 Committees
- 4.01 Ethical Conduct of Research
- Observers
- B.04 Orientation of New Research Institute Staff
- Criteria and Procedures for Reclassification Review of Scientist-Track Investigators
- Criteria and Procedures for Renewal (three-year) Review in the Research Institute
- Criteria and Procedures for Promotion (six-year) Review
- 1.3.30 Confidentiality of Information
- 2.61 Possible Use of Complementary and Alternative Therapies

## **Appendix D**

### **Permissible & Impermissible Research Activities re COI**

#### **Activities which are permitted with approval from the Chief Research**

- A full time researcher may hold a financial interest in a company up to \$25,000 in one calendar year or provide up to 20 days of consulting not to exceed \$25,000 (pro-rated for part time researchers) if the researcher will also receive research funding from the same organization
- Use of Sick Kids facilities for privately undertaken work
- Supervising an employee for consulting activities and regular Sick Kids duties
- Engaging in any commercial benefit with a Related Person

#### **Activities that are not permitted**

- Accepting gifts of more than nominal value
- The use of overhead funds for other than research related purposes
- Payment offered or accepted simply to identify patients who may be appropriate subjects for a research study i.e., finder's fees
- Industry research contracts that include budgets for personal payments or gifts

## Appendix E

### CONFLICT OF INTEREST DECLARATION BY PRINCIPAL INVESTIGATOR (incorporated into November 2006 version of REB application form)

#### EXPLANATION

Researchers hold trust relationships with research subjects, research sponsors, the Hospital for Sick Children (SickKids), their professional bodies and society. Researchers, SickKids and the REB are required to identify and address actual, potential and perceived conflicts of interest (“Conflicts of Interest”) to maintain public confidence and trust, ensure the integrity of research, discharge professional obligations and ensure accountability.

A Conflict of Interest does not necessarily imply wrongdoing, as a conflict of interest depends upon the circumstances, not on the character of the staff member.

A Conflict of interest does not mean that the research cannot proceed. Many (but not all) Conflicts of Interest can be managed, but always require identification of the Conflict of Interest, disclosure to research subjects, and if required, other steps to manage the Conflict of Interest. It will be up to the REB to determine if the Conflict of Interest can be managed and if the proposed mitigation measures are adequate.

All Conflicts of Interest must be clearly identified by the Principal Investigator and the Principal Investigator is making this Declaration on behalf of himself/herself and the members of the research team (collectively referred to in the Declaration as “Researcher”)

#### *Categories of Conflict or Potential Conflict of Interest:*

There are many types of Conflict of Interest which may affect the research. The Conflict of Interest may arise in relation to the Researcher or a “Related Person” to the Researcher (eg., spouse, domestic partner, immediate family member or close acquaintance). The categories of Conflicts of Interest include the following:

#### (i) **Financial**

The Researcher or Related Person stands to gain financially in the undertaking or outcome of research (e.g., share ownership in study sponsor, bonus for positive test results) outside the normal compensation of the Researcher.

#### (ii) **Direct Status Benefit**

The Researcher or Related Person stands to gain through direct rewards in respect of his or her status (e.g., career status) in the undertaking or outcome of research (e.g., promise of promotion for successful research). It is recognized that undertaking research will usually be viewed positively in terms of enhancing career advancement. The question is whether the link between the career enhancement and the outcome of the research is so strong as to bring into question the objectivity of the Researcher or the process and outcome of the research.

#### (iii) **Undue Influence**

The position of the Researcher or Related Person is such that the Researcher or Related Person may exert an undue influence over the research or influence or coerce research subjects, because of his or her position or the vulnerability of the research subjects. This influence may be due to a personal or professional relationship between the affected individuals (e.g., physician recruiting his/her own patients, subjects are to be recruited from Researcher's students or employees).

#### (iv) **Competing Interest**

The Researcher may be influenced to draw conclusions against the interest of the sponsor or another interested party to the study because the Researcher or a Related Person has an adversity in interest related to the research (e.g., – Researcher has an interest in a competitor drug or product, Researcher involved in litigation against sponsor).

**DECLARATION – CONFLICT OF INTEREST**

1. I have spoken with members of my research team and hereby declare that neither I nor (to the best of my knowledge) any members of my research team have an actual, potential or perceived conflict of interest (“Conflict of Interest” or “COI”) with respect to the attached Application for Research.

(tick if applicable)

**OR**

I have spoken with members of my research team and have identified a Conflict(s) of Interest with respect to this application for research in the following categories as specified below. (please tick as appropriate and attach a separate sheet describing the conflict of interest in full detail).

(i) Financial:  Yes  No Member with Conflict of Interest \_\_\_\_\_

(ii) Status:  Yes  No Member with Conflict of Interest \_\_\_\_\_

(iii) Undue Influence:  Yes  No Member with Conflict of Interest \_\_\_\_\_

(iv) Competing Interest:  Yes  No Member with Conflict of Interest \_\_\_\_\_

Details of Conflict of Interest: \_\_\_\_\_

2. (If you have checked yes to any of the items in Section 1 above, please complete sections 2 & 3) I intend to manage the Conflict(s) of Interest as set out below (e.g., disclosure in consent form, declining role/position with sponsor, additional monitoring strategies such as monitoring consent). Please note Conflicts of Interest must be disclosed on the consent form.

\_\_\_\_\_

3. I have declared all Conflicts of Interest to the Research Institute. (If you have not disclosed the Conflicts of Interest to the Research Institute or are not obliged to declare, please explain why.) Please attach a copy of the Research Institute approval of the Conflict(s) of Interest.

Yes  No  N/A

\_\_\_\_\_

4. Should a Conflict of Interest arise for me or any member of my research team during the course of the research, I shall declare this in writing to the Research Ethics Board.

Yes  No

I hereby declare that I have read this Declaration, have discuss this Declaration with the members of my research team, and that to the best of my knowledge and belief, my responses are true and correct.

\_\_\_\_\_  
Name of Principal Investigator

\_\_\_\_\_  
Signature of Principal Investigator

\_\_\_\_\_  
Date