

Contemporary Health Research: A Cautionary Tale

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We are on the verge of realizing the enormous promises of recent developments in health research. Simultaneously, however, we are also on the verge of realizing enormous harms. In this paper, I will explore this paradoxical state of affairs.

Consider first the benefits of health research. Health research enables us to determine whether widely accepted treatments actually work. While it is well known that research can confirm therapeutic effect, research can also show that widely accepted standards of care are actually harmful. For example, chloramphenicol was widely accepted as prophylactic treatment for bacterial sepsis in premature infants. Then, through a randomized controlled trial, Burns *et al.* discovered that the drug was causing rather than preventing death.¹

Health research also leads to new and better methods of prevention and health promotion, diagnosis, and treatment. As a result of research, we now know that folic acid supplementation during pregnancy helps to prevent neural tube defects.² We also have ingestible pill-sized cameras that can relay images of the inside of a patient's intestinal tract to guide treatment of Crohn's disease.³ The mortality rates for childhood cancer have declined by more than 50% since the early 1950s.⁴

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¹As discussed in R. Poland, Letter to the Editor "Randomized Clinical Trials" (1991) 325 *New Engl. J. Med.* 1513 at 1513:

[I]n the 1950s, many respected physicians believed that chloramphenicol, in doses analogous to those given to adults, was the best hope for premature infants who were dying apparently of bacterial sepsis. Chloramphenicol was accepted as prophylaxis for premature infants until Burns and associates, who also believed in chloramphenicol, found in a randomized controlled trial that the antibiotic was a cause of death rather than a cure.

²A. Milunsky *et al.*, "Multivitamin/folic acid supplementation in early pregnancy reduces the prevalence of neural tube defects" (1989) 262 *J. Am. Med. A* 2847.

³"Scoping Out New Ways to Check the Plumbing" *The Globe and Mail* (2 January 2001) R6.

⁴As discussed in National Cancer Institute of Canada, "Canadian Cancer Statistics 2001", online: National Cancer Institute of Canada <<http://66.59.133.166/stats/childe.htm>>:

Since the early 1950s, mortality rates for childhood cancer have declined by more than 50% with most of the improvement occurring after 1970. Improved survival has been particularly dramatic for the most common childhood neoplasm, acute lymphocytic leukemia, as well as for lymphomas and kidney cancer. Although essentially no one survived childhood leukemia 40 years ago, currently, approximately 80% of Canadian children and teenagers with acute lymphoblastic leukemia are alive five years after diagnosis.

Enormous strides have also been made in the diagnosis and treatment of cystic fibrosis.⁵

As a result of a number of recent changes in the way research is done, health research is becoming even more effective. For example, we have witnessed the development of new methodologies (e.g., qualitative instead of just quantitative research);⁶ the welcoming of old disciplines to the health research tent (e.g., the new Canadian Institutes of Health Research has an objective to support not just traditional basic and clinical sciences but also the social sciences and humanities);⁷ and the turning of attention to evidence-based practice with its concomitant requirement of supportive research.⁸ In addition, more research now focuses on the needs of discrete populations (e.g., women and aboriginal people).⁹ When research attends to the differences in groups participating in studies and attends to conditions that strike only or predominantly specific groups, treatment decisions need no longer be extrapolated from knowledge derived from and about white males. Health care providers can then better address the health needs of these frequently disadvantaged groups.¹⁰

Finally, new attention to knowledge transfer is yielding better uptake of research results in policy and practice and, hence (we hope), better health.¹¹ The attention to knowledge transfer also feeds the shift in the delivery of health care to evidence-based practice which in turn also leads to better health.¹²

Footnote 12
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⁵ D.J. Halvorson, "Cystic Fibrosis: an update for the otolaryngologist" (1999) 120:4 Otolaryngology – Head & Neck Surgery 502.

⁶ See e.g. Janice M. Morse, Janice M. Swanson, & Anton J. Kuzel, eds., *The Nature of Qualitative Evidence* (Thousand Oaks: Sage Publications, 2001); Otto D. Payton, *Research: The Validation of Clinical Practice*, 3rd ed. (Philadelphia: F.A. Davis Co., 1994) at c. 5; Stephen Polgar & Shane A. Thomas, *Introduction to Research in the Health Sciences*, 4th ed. (Edinburgh: Churchill Livingstone, 2000) at c. 8.

⁷ *Canadian Institutes of Health Research Act*, S.C. 2000, c. 6, ss. 4(c)-(e).

⁸ See e.g. K.J. Ottenbacher & S.R. Hinderer, "Evidence-Based Practice: Methods to Evaluate Patient Improvement" (2001) 80:10 Am. J. Physical Med. & Rehab. 786; B. Ritter, "Considering Evidence-Based Practice" (2001) 26:5 Nurse Practitioner 63 at 64; R. Grol "Successes and Failures in the Implementation of Evidence-Based Guidelines for Clinical Practice" (2001) 39:8 (2d Supp.) Medical Care 1146.

⁹ Note, for example, the creation of the Institute for Gender and Health and the Institute for Aboriginal Health as two of the original institutes making up the Canadian Institutes of Health Research [CIHR]. For details on these institutes, see Institute for Aboriginal Health, online: CIHR <http://www.cihr-irsc.gc.ca/institutes/iaph/index_e.shtml> and Institute for Gender and Health, online: CIHR <http://www.cihr-irsc.gc.ca/institutes/igh/index_e.shtml>.

¹⁰ See R. Dresser, "Wanted: Single, White Male for Medical Research" (1992) 22 Hastings Center Report 24; Françoise Baylis, Jocelyn Downie & Susan Sherwin, "Reframing Research Involving Humans" in *The Feminist Health Care Ethics Research Network & Susan Sherwin, eds., The Politics of Women's Health* (Philadelphia: Temple University Press, 1998) 234.

¹¹ With respect to the importance of knowledge transfer see the statements of the CIHR, "Knowledge Translation", online: CIHR

<http://www.cihr.ca/about_cihr/organization/knowledge_translation/index_e.shtml>; and the mission statement of the Canadian Health Services Research Foundation [CHSRF], "Statement of Institutional Purpose", online: CHSRF <http://www.chsrf.ca/about/mission_e.shtml>.

Now consider the perils of health research. It is shockingly easy to find examples of research atrocities in Europe, the United States, and here in Canada. In Europe, during the Nazi regime, horrific experiments were conducted on human subjects. These included:

(1) immersion in tanks of cold water of varying temperatures for periods of up to fourteen hours to develop techniques for rapid and complete resuscitation of German pilots downed at sea; (2) simulation of high altitude atmospheric conditions in decompression chambers, with autopsies then performed to study the effect of sudden pressure changes on the body; (3) attempted mass sterilization through castration doses of x-rays, treated diet and intrauterine injections apparently of silver nitrate; (4) mutilation of prisoners as experimental surgical subjects for the training of German surgical students; (5) injection of virulent typhus into prisoners to ensure a ready supply of virus for typhus experiments; (6) infliction of bullet wounds and incisions and introduction of bacteria into the wounds to study and treat infections; (7) shooting of prisoners with poisonous aconite bullets to study the effects of aconite poisoning; (8) forced ingestions of seawater into prisoners to test desalinization processes; (9) experimental bone transplantation; (10) execution and dismemberment of prisoners to furnish “subhuman” skeletal specimens for an anthropological museum; and (11) injection of malaria to test malaria immunity.¹³

In the United States, the Tuskegee Syphilis Study was conducted between 1932 and 1972. Three hundred and ninety nine black men with syphilis were initially enrolled in this study. At first, when there was no effective treatment for syphilis known, the subjects’ well-being was not compromised. However, as new drugs were developed and tested, they were deliberately withheld from the Tuskegee subjects. Even after penicillin had been determined to be an effective treatment for syphilis (by 1951, it was considered standard treatment), the men were kept in the study but were actively denied treatment. This study was not stopped until it was exposed in the press in 1972.¹⁴

In 1939, the Tudor Study (also sometimes known as the “Monster Study”) was conducted on 22 children aged 5-16 resident in the Soldiers and Sailors Orphans’ Home in Iowa. The children were divided into two groups – stutterers and normally fluent. Half of each group was told that they were not stutterers and half was told that they were. Sessions were held with each of the children and the

¹² *Supra* note 8.

¹³ H. Beecher, “Ethics and Clinical Research” (1966) 274 *New Engl. J. Med.* 1354.

¹⁴ See James H. Jones, *Bad Blood: The Tuskegee Syphilis Experiment* (New York: The Free Press, 1993). See also Susan M. Reverby, ed., *Tuskegee’s truths: rethinking the Tuskegee syphilis study* (Chapel Hill, North Carolina: University of North Carolina Press, 2000).

labelling was reinforced through comments on the children's speech. For example, normally fluent children who had been labelled stutterers were told the following:

The staff has come to the conclusion that you have a great deal of trouble with your speech. The type of interruptions which you have are very undesirable. These interruptions indicate stuttering. You have many of the symptoms of a child who is beginning to stutter. You must try to stop yourself immediately. Use your will power. Make up your mind that you are going to speak without a single interruption. It's absolutely necessary that you do this. Do anything to keep from stuttering. Try very hard to speak fluently and evenly. If you have an interruption, stop and begin over. Take a deep breath whenever you feel you are going to stutter. Don't ever speak unless you can do it right. You see how (the name of a child in the institution who stuttered rather severely) stutters, don't you? Well, he undoubtedly started this very same way as you are starting. Watch your speech every minute and try to do something to improve it. Whatever you do, speak fluently and avoid any interruptions whatsoever in your speech.¹⁵

One of the objectives of the study was to determine whether labelling a person a "stutterer" would have any effect on his or her speech fluency. The hypothesis was that "negative reactions to normal speech disfluencies cause stuttering in children."¹⁶ One appalling risk of this study was that participation would permanently turn normally fluent children into stutterers or otherwise interfere with their speech.

In Canada, during the 1950s and 1960s at the Allan Memorial Institute in Montreal, LSD and other hallucinogens were given to at least 80 psychiatric patients without their consent. The results of this research were devastating. Following the study, many subjects did not recognize their families, could no longer read or write, and lost the capacity to perform many core activities of daily living.¹⁷

In addition to these obvious research atrocities involving large numbers of victims, in looking back we also see cases in which single individuals were significantly harmed as a result of participation in research. For example, in the 1960s, a student at the University of Saskatchewan enrolled in a research project but was not told that the drug that was being tested was new or that, as part of the project, a catheter would be inserted into his heart. He had a heart attack and was severely and permanently injured.¹⁸ In the 1980s, a patient in a Quebec teaching

¹⁵ Nicoline Grinager Ambrose & Ehud Yairi, "The Tudor Study: Data and Ethics" (2002) 11:2 *Am. J. Speech-Language Pathology* 190 at 192. See also J. Dryer "Theory improved treatment and understanding of stuttering" *The San Jose Mercury News* (11 June 2001); "Officials apologize for tests on stuttering" *The San Jose Mercury News* (13 June 2001).

¹⁶ Grinager & Yairi, *ibid.* at 190.

¹⁷ Stephen Bindman "Brainwash victims to get compensation" *The Toronto Star* (18 November 1992) A10.

¹⁸ *Halushka v. University of Saskatchewan et al.* (1965), 53 D.L.R. (2d) 436, 52 W.W.R. 608 (Sask. C.A.).

hospital was enrolled in a research project involving the injection of contrast dye for fluoroscein angiography. A physician told him that the associated risks were extremely rare and that he could not recall a single catastrophic reaction occurring in over 12,000 angiograms performed at the hospital. The patient was never told of the risk of death. Following injection of the dye, the patient had a cardiac arrest and died.¹⁹

More recently, James Dent died while enrolled in a gene transfer trial in Toronto. A number of things are troubling about this case. First, an autopsy was conducted 29 hours after his death but the results were not provided to Health Canada until five months later. Days before Dent began the second stage of his gene transfer, a patient died in Indiana during the same experiment yet Dent was not told of this fact. The US regulators were told (it was reported as unexpected and possibly related to the gene transfer) but Health Canada was not. Furthermore, two different consent forms were prepared for the study. One form disclosed that 17 out of 30 patients in a similar trial had suffered serious adverse brain events. James Dent received the other form which did not disclose this.²⁰

In addition to high profile cases, many everyday occurrences are also problematic. For example, research participants are not told all of the objectives of a study, confidentiality clauses in research contracts bar researchers from disclosing risks uncovered during the course of the research to participants, researchers give participants consent forms different from those approved by Research Ethics Boards (REBs), REBs approve research even though methodological flaws mean that no meaningful results will flow from the research, and physicians ask patients to enroll in clinical trials in which the physicians have an undisclosed financial interest.

This paper argues that Canada needs to take steps to ensure adequate governance so that we not only avoid future atrocities but also minimize the more routine problems that undergird the disasters. Governance issues present some of the most threatening challenges for Canadians and also some of the least visible. These issues could be characterized as the 5 C's of concerns about contemporary research: consistency; comprehensiveness; compliance; conflicts of interest; and commercialization. Consider each in turn.

A. Consistency

Research is currently regulated in a haphazard, patchwork manner. Various pieces of provincial legislation and regulations touch, almost in passing, on research (e.g., the Quebec *Civil Code*, mental health acts, and human tissue gift acts).²¹

¹⁹ *Weiss c. Solomon*, [1989] A.Q. no. 312 (C.S. civ.)(QL).

²⁰ As reported by E. Shiff, "In the Service of Science" *The Magazine* (6 March 2000), online: CBC News <www.cbc.ca/national/magazine/gene>.

²¹ See *Civil Code of Quebec*, S.Q. 1991, c.64, ss. 21, 22; *Human Tissues Gift Act*, R.S.B.C. 1996, c. 24, ss. 4(1), 5(1); *Mental Health Act*, R.S.O. 1990, c. M.7, ss. 35(3)(f), 35(4)(a)(b).

However, these pieces of legislation have only a minimal effect on research, and they are not consistent across the provinces.²² Parts of the federal *Food and Drugs Act* and regulations with respect to drugs, biologics, and devices deal with some, but only some, research.²³ The Tri-Council Policy Statement for Research Involving Humans deals directly and entirely with research but it applies only to researchers funded by the three national funding councils and research conducted at institutions receiving funding from these councils (SSHRC, NSERC, and CIHR).²⁴ The International Conference on Harmonization of Technical Requirements for the Registration of Pharmaceuticals for Human Use—ICH Harmonised Tripartite Guideline deals directly and entirely with research.²⁵ However, it applies only to clinical trials. The Declaration of Helsinki deals directly and entirely with research, but its force and scope in Canada are unclear.²⁶ Finally, international multi-centre trials are subject to the regulations of all of the participating countries (e.g., the U.S. Food and Drug Administration²⁷).

This patchwork leads to substantive inconsistencies. Consider, for example, the issue of placebos in randomized controlled trials. The Declaration of Helsinki prohibits the use of a placebo control when effective therapy exists for the medical condition being studied, except where i) for compelling and scientifically sound methodological reasons its use is necessary to determine the efficacy or safety of a prophylactic, diagnostic or therapeutic method; or ii) where a prophylactic, diagnostic or therapeutic method is being investigated for a minor condition and the patients who receive placebo will not be subject to any additional risk of serious or irreversible harm.²⁸ The *TCPS* says “the use of placebo controls in clinical trials is generally unacceptable when standard therapies or interventions are available for

²² For example, mature minors are treated differently in Quebec, Ontario and Nova Scotia. See *Civil Code of Quebec*, S.Q. 1991, c. 64, ss. 14, 16-18; *Substitute Decisions Act, 1992*, S.O. 1992, c. 30, s. 2(2); whereas Nova Scotia makes no legislative provisions for a mature minor’s consent to treatment, nor has any case law on the matter arisen in Nova Scotia. See also, *Van Mol (Guardian ad litem of) v. Ashmore* (1999), 168 D.L.R. (4th) 637 (B.C.C.A.); leave to appeal to S.C.C. refused, [2000] 1 S.C.R. vi; *Ney v. Canada (Attorney General)* (1993), 79 B.C.L.R. (2d) 47 (S.C.); *Kennett Estate v. Manitoba* (1998), 129 Man. R. (2d) 244, [1999] 1 W.W.R. 639 (C.A.); *C.(J.S.) v. Wren*, [1987] 2 W.W.R. 669 (Alta. C.A.); *Walker (Litigation Guardian of) v. Region 2 Hospital Corp* (1994), 116 D.L.R. (4th) 477 (N.B.C.A.); *Re Y.(A.)* (1993), 111 Nfld. & P.E.I.R. 91 (Nfld. S.C.); *Re K.(L.D.)* (1985), 48 R.F.L. (2d) 164 (Ont. Prov. Ct.); *Re Dueck* (1999), 171 D.L.R. (4th) 761 (Sask. Q.B.); *B.H. (Next Friend of) v. Alberta (Director of Child Welfare)* [2002] A.J. No. 518 (Q.B.)(QL).

²³ See e.g. *Medical Devices Regulations*, S.O.R./98-282, ss. 79-88, *Food and Drug Regulations*, C.R.C., c. 870, ss. G.05.003(5), G.05.002.1-3.

²⁴ CIHR, Natural Sciences and Engineering Research Council of Canada [NSERC] & SSHRC, *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans* (Ottawa: Medical Research Council, 1998) at 1.2, online: NSERC <<http://www.nserc.ca/programs/ethics/english/policy.htm>> [TCPS].

²⁵ International Conference on Harmonisation, *Good Clinical Practice: Consolidated Guidelines* (Ottawa: Therapeutic Products Directorate, Health Canada, 1997) [*Good Clinical Practice*].

²⁶ World Medical Association, “Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects” (Revised October 2000), online: The World Medical Association <<http://www.wma.net/e/policy/b3.htm>> [Declaration of Helsinki].

²⁷ 21 C.F.R. § 50 (1991).

²⁸ Declaration of Helsinki, *supra* note 26 at para. 29 (with clarification added in October 2002).

a particular patient population” and then lists exceptions.²⁹ Guideline E-10 from *Good Clinical Practice* states that “in cases where an available treatment is known to prevent serious harm, such as death or irreversible morbidity in the study population, it is generally inappropriate to use a placebo control.”³⁰ The Therapeutic Products Directorate has made public its opposition to the *TCPS* position on placebos.³¹ Even where there is a standard therapy, placebo-control is recognized by the US FDA as an indicator of the sort of “adequate, well-controlled studies” required for any drug to receive FDA approval.³² Faced with such inconsistency, what are researchers and REBs supposed to do?³³

The regulatory patchwork also leads to inconsistency in application of the standards. Ask almost anyone who has put a multi-centre trial through ethics review how many different sets of comments and criticisms were received and how often mutually incompatible direction was given. Ask almost anyone who has served on an REB how often they have had a researcher respond to a negative review with a statement like: “but six other REBs passed the protocol as it was, why won’t you?”

Thus, in the substance of the standards, we have inconsistency and confusion. In the application of the standards, we have controversy, conflict, and tension.

Clearly, Canadian policy-makers and regulators must send a consistent message about the standards that apply to research in Canada. Furthermore, where multiple inconsistent regulatory mechanisms and standards seem to apply, it must be made clear which govern. In addition, our current and future regulatory mechanisms and standards must be applied consistently.

B. Comprehensiveness

The regulation of research is, quite simply, not comprehensive. A great deal of research is not captured by the *TCPS*.

²⁹ *TCPS*, *supra* note 24, Art. 7.4.

³⁰ *Good Clinical Practice*, *supra* note 25, Guideline E-10.

³¹ Pat Huston, “Placebo Controls in Clinical Trials” (Paper presented to the QEII Health Science Centre, Halifax, Nova Scotia, 24 September 2001) [unpublished].

³² *Applications for FDA Approval to Market a New Drug*, 5 C.F.R. §. 314.126(b)(2)(i) (2002); but see s. 314.126(b)(2)(iv), wherein the regulations also recognize “active control therapy” when, for instance, “the condition treated is such that administration of placebo or no treatment would be contrary to the interests of the patient.” The FDA has decided not to alter its own position with regard to placebo-controlled trials despite the amended position in relation to these trials of the Declaration of Helsinki, *supra* note 26; see “International Agreement Spurs No Change to FDA Placebo Trial Policy” *FDA News.com* (19 March 2001), online: FDA News.com <http://www.fdanews.com/pub/wdl/33_11/fda/3407-1.html>.

³³ It should be noted here that there is a joint CIHR-Health Canada (Therapeutic Products Directorate) initiative “on the use of placebos in clinical trials”; CIHR, “Ethics – Current Initiatives”, online: CIHR <http://www.cihr-irsc.gc.ca/about_cihr/organization/ethics/initiatives_e.shtml>.

According to its own statement of its scope, the *TCPS* governs only research funded by, or conducted at institutions that receive funding from, the three funding councils.³⁴ This leaves research conducted at all other institutions largely unregulated. For example, the research being conducted in private physicians' offices, community-based organizations, charitable organizations, industry, and government departments is largely free of regulation. In 2001, only 60% of research conducted in Canada was conducted in universities and hospitals³⁵ (the institutions largely captured by the *TCPS*). Therefore, the *TCPS* does not apply to 40% of research conducted in Canada.

Furthermore, the *TCPS* has significant gaps. For example, when the stem cell controversy broke open in the United States, one might reasonably have thought to check the *TCPS* for the Canadian position. One would have found something on embryo research and fetal tissue research but nothing referring explicitly to stem cell research.³⁶ The issue could clearly have been anticipated by the drafters of the *TCPS* as there is reference to stem cell research in the Royal Commission Report on New Reproductive Technologies published in 1993.³⁷ Similarly, there is no guidance on such important issues as control of personal information about third parties in the context of genetics research, testing children for untreatable late onset genetic disorders, or the role of community consent in research focusing on people from identifiable communities.³⁸

Clearly, we need a regulatory framework that governs **all** research involving humans conducted in Canada. We need standards that give concrete guidance on the issues that are known to us **now**. We also need mechanisms to efficiently and responsibly introduce new standards on issues that **come upon us**.

C. Compliance

There are at least three serious problems with compliance with the standards in Canada (in particular, the *TCPS*). The first problem is that some institutions treat the *TCPS* as an aspirational rather than a prescriptive document. They view the *TCPS* as merely optional "guidelines". These institutions, which receive Council funding, have decided that they do not need to comply with the *TCPS*.

³⁴*TCPS*, *supra* note 24 at i.1: "The Councils will consider funding (or continued funding) only to individuals and institutions which certify compliance with this policy regarding research involving human subjects"; see also *TCPS*, *ibid.* at 1.2: "As a condition of funding, we require, as a minimum, that researchers and their institutions apply the ethical principles and the articles of this policy [the *TCPS*]".

³⁵ Statistics Canada, "Estimates of Total Expenditures on Research and Development in the Health Fields in Canada, 1988 to 2001", online: Statistics Canada

<<http://www.statcan.ca/english/research/88F0006XIE/88F0006XIE2002007.pdf>>

³⁶*TCPS*, *supra* note 24 at 8.5, 9.

³⁷ Canada, Royal Commission on New Reproductive Technologies, *Proceed with Care: The Final Report of the Royal Commission on New Reproductive Technologies*, vol. 1 (Ottawa: The Commission, 1993) at 618 (Chair: Patricia Baird).

³⁸*TCPS*, *supra* note 24 at 4, 5, 6.

The second problem is that no clear message is being sent that researchers and research institutions must comply with the regulations. Allegations of non-compliance are not being adequately dealt with. For example, a major research institution in Canada was significantly in breach of the *TCPS*. Health Canada and CIHR were told of the breach but CIHR did not withdraw its funding to the institution (despite the fact that conformity with the *TCPS* is an explicit condition of funding from the Councils).³⁹ Indeed, “to date the councils have failed to caution or suspend funding to any institution for failing to adhere to the *Tri-Council Policy Statement*.”⁴⁰ Health Canada has also failed to enforce compliance with its own regulations in the case of a set of Children’s Oncology Group protocols.⁴¹ In March 2002, Health Canada became aware of eight clinical trials that had not received approval as required by the regulations.⁴² They advised the principal investigator that he was required to seek approval and set deadlines for the submission of the applications (four weeks for new investigational drugs and eight weeks for approved drugs). These deadlines were not met. An extension of sixty days was sought and granted. The new deadline was not met. In September 2002, seven of the eight clinical trials received Health Canada approval. One remained unapproved due to the lack of required information. In October 2002, a child died while on this unapproved protocol. Health Canada could have enforced compliance and shut down the trials in March 2002 when it first became aware of them. It could have shut them down in April and May when the first deadlines were not met. It could have shut them down in July when the extended deadline was not met. It could have shut down the remaining unapproved trial when it approved the other seven. It did not.

Third, there are problems with the CIHR policies on compliance. These include weaknesses in the policies themselves as well as inadequacies in the implementation of the policies. For example, compliance with the *TCPS* is ensured through a Memorandum of Understanding (MOU) between the CIHR and each institution receiving funding. Compliance is dealt with in Schedules 2 and 8 of the MOU. Under Schedule 2, institutions agree to investigate allegations of individual non-compliance “in accordance with established procedures; for example, by following the process described in institutional policies on integrity in research and scholarship, and by taking appropriate follow-up measures, including reporting to the appropriate Agency or Agencies, as required.” However, it is not clear when reporting to the Agency or Agencies is “required”. Under Schedule 8, instances of non-compliance are referred to as “minor”, “serious”, and “particularly serious or

³⁹ See *TCPS* statements in “Introduction” and “Mandate of the Councils”, *supra* note 24 at i.1, i.2. It might be argued that the statement made in the Introduction could be interpreted to allow ongoing funding in the presence of a breach of the *TCPS* as long as the institution had certified compliance. However, this is an indefensible interpretation of the statement. A known breach at an institution would surely vitiate any certification of compliance from that institution.

⁴⁰ Charles Weijer, “Placebo Trials and Tribulations” (2002) 166 *Can. Med. A. J.* 603.

⁴¹ For further information on these cases, see “Tragic Trials”, online: CBC <www.ottawa.cbc.ca/regional/servlet/View?filename=ot_cartycheotrials>.

⁴² *Food and Drug Regulations*, *supra* note 23, Division 5.

sensitive” with different responses associated with these different categories. Unfortunately, the document provides no criteria for determining which category (and associated responses) applies to any particular instance. “Particularly serious or sensitive breaches” prompt **possible** temporary suspension of funding to specific projects. For breaches deemed “unremediable”, “the President(s) of the Agency or Agencies **may** consider the Institution or all or any portion of its faculty to be ineligible to continue receiving funds from the Agency or Agencies.”⁴³ Arguably, Schedules 2 and 8 are too vague and toothless for such a serious matter.

Further problems with compliance are illustrated through a consideration of the development and implementation of the CIHR stem cell research guidelines. On March 4, 2002, the CIHR released “Human Pluripotent Stem Cell Research: Guidelines for CIHR-Funded Research.”⁴⁴ Section 4 of these Guidelines called for the establishment of a Stem Cell Oversight Committee. At the time of writing, more than a year later, this Committee has still not been established. Indeed, from a review of the CIHR website, it would appear that no steps have been taken to establish the Committee. There has been no call for nominations, no publication of a process for appointment of members, no action at all.⁴⁵ The failure to establish the Oversight Committee is a compliance issue because without the Committee, no researcher funded by the CIHR or working at an institution receiving CIHR funding could conduct human embryonic stem cell research and be compliant with the March 2002 Guidelines (because compliance requires approval by the Committee).

Furthermore, in June 2002, the Governing Council of the CIHR discussed the issue of compliance with the stem cell research guidelines. According to the Minutes for this June meeting, the Governing Council “agreed with the recommendations of the Standing Committee on Ethics on the issues of non-compliance with CIHR’s stem cell guidelines be dealt with in the context of the Memorandum of Understanding (MOU) for Institutional Compliance with the Tri-Council Policy Statement.”⁴⁶ However, the Standing Committee had also expressed concerns about weaknesses in the MOU and its associated schedules in relation to compliance so the Governing Council agreed “that an ad hoc working committee be struck, comprised of representatives from GC, the SCE, CIHR staff and institution representation to clarify any revisions related to the MOU, specifically in relation to the issue of non-compliance with the Tri-Council Policy Statement (TCPS) and the CIHR stem cell guidelines.”⁴⁷ At the November meeting of the Governing Council,

⁴³ NSERC, SSHRC & CIHR, “Schedule 8: Investigation and Resolution of Breaches of Agency Policies” in *Memorandum of Understanding*, online: NSERC

<http://www.nserc.gc.ca/institution/mou_sch8_e.htm> [emphasis added].

⁴⁴ CIHR, “Human Pluripotent Stem Cell Research: Guidelines for CIHR-Funded Research”, online: CIHR <http://www.cihr-irsc.gc.ca/publications/ethics/stem_cell/stem_cell_guidelines_e.shtml>.

⁴⁵ See generally CIHR, online: CIHR <<http://www.cihr-irsc.gc.ca>>.

⁴⁶ Canadian Institutes of Health Research, “Minutes” (16th Meeting of the Governing Council, 19-20 June 2002), online: CIHR <http://www.cihr-irsc.gc.ca/publications/about_cihr/meeting_minutes/governing_council/council/minutes_16_e.shtml>.

⁴⁷ *Ibid.*

the fact that this committee had not been struck was raised and, “Governing Council agreed that it was important that this committee be created **immediately**.”⁴⁸ At the time of writing, nine months after the commitment to strengthen the compliance aspects of the MOU was made and five months after the commitment to “immediate” action was made, this committee has also not yet been established.⁴⁹

These extraordinary examples of ongoing inaction undermine the public’s confidence in the CIHR’s commitment to enforcing compliance with its own guidelines.⁵⁰

In order to adequately protect research participants, we need standards with which compliance is indisputably required. We also need a system that vigorously enforces compliance with these standards. Currently, we have neither.

D. Conflicts of interest

There are good reasons to be seriously concerned about conflicts of interest involving REBs, universities and hospitals, research funders, and industry.

First, consider conflicts of interest and REBs. REBs are largely staffed by members of the very same institution as researchers who submit their proposals to the REB. Most REB members work with the researchers, their departmental budgets may be affected by the research being proposed, and the overall institutional financial well-being is most certainly affected by the research under consideration. For these and other reasons, REB members can be subject to significant explicit and implicit pressures to approve protocols placed before them. Also, because REBs have so few resources of their own, they often depend on the institutional Office of Research Services (or similar entity). The Office of Research Services has a clear mandate to promote research, while the REB has a clear mandate to protect research subjects. These mandates may sometimes conflict and such conflicts must be clearly identified and managed.

⁴⁸ Canadian Institutes of Health Research, “Minutes” (18th Meeting of the Governing Council, 20-21 November 2002), online: CIHR

<www.cihr-irsc.gc.ca/publications/aboutus/governing_council/council/minutes_18.e.shtml> [emphasis added].

⁴⁹ See generally CIHR, online: CIHR <<http://www.cihr-irsc.gc.ca>>.

⁵⁰ In June 2002, the Governing Council also stated that:

CIHR will endeavour to ensure that the research community is aware of and understands the content of the stem cell research guidelines. To this end, the guidelines are currently posted on the CIHR website. As well, in the near future, a section on Frequently Asked Questions (FAQs) will be posted on the CIHR website to provide researchers, REBs and institutions with clearer guidance on what is permitted and prohibited by CIHR.

CIHR, “Compliance with Human Pluripotent Stem Cell Research: Guidelines for CIHR-Funded Research” (Governing Council, 20 June 2002), online: CIHR

<http://www.cihr-irsc.gc.ca/publications/ethics/stem_cell/stem_cell_compliance_e.shtml> At the time of writing, eight months after this commitment was made, no FAQs were posted on the CIHR website, see generally CIHR, online: CIHR <<http://www.cihr-irsc.gc.ca>>.

Furthermore, REB members are often appointed and renewed by or at the direction or recommendation of the institution's Vice President of Research – an individual with a mandate to promote research. He or she is frequently judged by the number of projects and the amount of research money flowing into the institution. It is certainly the case that at least some Vice Presidents of Research have attempted to shape their institutions' REBs in ways that promote research (e.g., not renewing members and Chairs who "cause trouble" or not appointing members and Chairs who they think will "cause trouble"). While many Offices of Research Services and Vice Presidents of Research do place the protection of research subjects above the promotion of research, some do not (or do not do so consistently). All of these sorts of conflicts of interest at the REB level threaten the independence of ethics review and, thereby, threaten the capacity of the current system to protect research subjects.

Second, consider conflicts of interest and universities and hospitals. Over the past few years, we have witnessed two significant cases involving such conflicts of interest.

The first case involved Dr. Nancy Olivieri.⁵¹ Dr. Olivieri, a researcher at the Toronto Hospital for Sick Children (HSC) and the University of Toronto, was conducting trials on a new drug for the treatment of thalassemia. The trials were sponsored by Apotex Inc.. When Dr. Olivieri came to believe that she had identified an unforeseen risk of the drug, she alerted the REB and the company and proposed, on instructions from the REB, to inform the research participants. Apotex abruptly cancelled the trials and threatened her with legal action if she disclosed the risks to the participants. Dr. Olivieri sought support from the HSC and the University of Toronto. She did not receive appropriate support from either institution. For the purposes of a discussion of conflict of interest, it is important to note that, at the time this case was unfolding, the University of Toronto was in discussions with Apotex for a \$30 million donation (\$20 million for the University and \$10 million for the University's affiliated hospitals).

⁵¹ This description is based on Jon Thompson, Patricia Baird & Jocelyn Downie, *The Olivieri Report: The complete text of the report of the independent inquiry commissioned by the Canadian Association of University Teachers* (Toronto: J. Lorimer, 2001), online: Dalhousie University <<http://www.dal.ca/committeefinquiry>>. This case is also discussed in: P. Baird, J. Downie & J. Thompson, "Clinical trials and industry" (2002) 297 *Science* 2211; J. Thompson, P. Baird, & J. Downie, "Independent Inquiry" (2002) 167 *Can. Med. A. J.* 12; J.M. Drazen, "Institutions, contracts, and academic freedom" Editorial Comment (2002) 347 *New Engl. J. Med.* 1362; E. Gibson, F. Baylis, & S. Lewis, "Dances with the pharmaceutical industry" (2002) 166 *Can. Med. A. J.* 448; Morris Litman & Lori Sheremeta, "The Report of the Committee of Inquiry on the Case Involving Dr. Nancy Olivieri: A Fiduciary Law Perspective" (2002) 10:2 *Health L. Rev.* 3; D.G. Nathan & D.J. Weatherall, "Academic freedom in clinical research" Comment (2002) 347:17 *New Engl. J. Med.* 1368; C.D. Naylor, "The deferiprone controversy: time to move on" (2002) 166 *Can. Med. A. J.* 452; C.D. Naylor, "Early Toronto experience with new standards for industry-sponsored clinical research: a progress report" (2002) 166 *Can. Med. A. J.* 453; N. Olivieri, "I beg to differ" Letter (2002) 167 *Can. Med. A. J.* 11; M. Shuchman, "The Olivieri dispute: no end in sight?" (2002) 166 *Can. Med. A. J.* 487; Margaret Somerville, "A postmodern modern tale: the ethics of research relationships" (2002) 1 *Nature Reviews Drug Discovery* 316.

The second case involved Dr. David Healy.⁵² Dr. Healy, a Welsh researcher, had accepted a job at the Centre for Addiction and Mental Health (CAMH) in Toronto. He had signed a contract and made preparations to move his family from Wales to Toronto. At a talk at the Centre, however, he criticized the way that psychiatric drugs were developed and marketed. He claimed, among many other things, that Prozac was linked to increased risk of suicide and suicidal ideation in a certain population. Almost immediately thereafter, Dr. Healy was told that there was no job for him at CAMH. There has been no independent report on the facts of this case yet, so it is premature to draw conclusions about who did what, when, and why (although Dr. Healy sued CAMH and the University of Toronto and the case was recently settled). What is relevant to the discussion of conflict of interest is that serious concerns have been raised about the fact that 52% of the funding for the Mood Disorder Clinic he was to head comes from corporate funding, and about the possible influence of Eli Lilly on the decision to withdraw the job. Eli Lilly, the maker of a drug that Dr. Healy criticized in his speech, is a major donor to CAMH and a significant supporter of psychiatric research at CAMH – including a recent \$1.55 million pledge to CAMH. In this context, it may be relevant that Eli Lilly withdrew funding from the Hastings Center Report because of an article written by Dr. Healy and published therein.⁵³

These cases illustrate some of the dangers when universities and hospitals are significantly dependent on industry for financial support (both through research dollars that subsidize operations, and through donations). These cases highlight the risks to academic freedom and research integrity posed by the conflicts of interest generated by institutional/industry collaborations.⁵⁴ None of this should be taken to mean that industry and universities and hospitals should never interact. I hasten to add that sponsored research is not, in principle, wrong nor are donations from industry to these research institutions. However, we do need to first better identify and then better manage all potential conflicts of interest that may arise as a result of these interactions.

⁵²This description is based on the materials reproduced by Bruce Charlton, “The David Healy Affair”, online: Pharmapolitics <www.pharmapolitics.com>.

⁵³C. Elliott, “Pharma buys a conscience” *The American Prospect* 12:17 (24 September - 8 October, 2001) 16; C. Elliott, “Throwing a Bone to the Watchdog” (2001) 31:2 Hastings Center Report 9.

⁵⁴S. Lewis *et al.*, “Dancing with the porcupine: rules for governing the university-industry relationship” (2001) 165 *Can. Med. A. J.* 783; J.E. Bekelman, Y. Li & C.P. Gross, “Scope and Impact of Financial Conflicts of Interest in Biomedical Research: A Systematic Review” (2003) 289 *J. Am. Med. A.* 454; M.K. Cho *et al.*, “Policies on Faculty Conflicts of Interest at US Universities” (2000) 284 *J. Am. Med. A.* 2203; Nathan & Weatherall, “Academic Freedom in Clinical Research”, *supra* note 51; K. Morin *et al.*, “Managing Conflicts of Interest in the Conduct of Clinical Trials” (2002) 287 *J. Am. Med. A.* 78; J.B. Martin, “Academic-Industrial Collaboration: The Good, the Bad, and the Ugly” (2002) 113 *Transactions of the American Clinical & Climatological Association* 227; Joan Lippert, “The Commercialization of University Medical Research” (1998) 18:2 *The College of Physicians and Surgeons of Columbia University Journal*, online: The College of Physicians and Surgeons of Columbia University <http://healthsciences.columbia.edu/news/journal/journal-o/archives/jour_v18no2_0012.html>; David Shenk “Money + Science = ethics problems on campus” *The Nation* 268:11 (22 March 1999) 11.

We must also be concerned about conflicts of interest and research funders. National funding councils currently set the standards for research ethics and are responsible for enforcement of these standards and yet their mandate is the promotion of research. The presidents of the three national funding councils recently named an interagency Panel on Research Ethics (PRE) with responsibility for interpreting and revising the *TCPS*.⁵⁵ Many in the research ethics community called for this responsibility to be given to a group outside the councils rather than one appointed by and reporting to the presidents of the councils. For example, at a meeting of the CIHR Institute Advisory Boards' ethics designates,

...participants expressed concern about the actual or perceived conflict of interest that arises when federal granting agencies set about to promote research and regulate the very research they promote. Participants took issue with the appropriateness of the proposed structure and role of the Panel/Secretariat [PRE] in light of the key recommendation made in Michael McDonald's report on the Governance of Health [Research] Involving Human Subjects commissioned by the Law Commission of Canada.⁵⁶

The designates "requested that their concerns be formally recorded and brought to the Executive Director and President of CIHR."⁵⁷

Consider also the example of Genome Canada. Genome Canada is an Industry Canada initiative. The mandate of Industry Canada is creating jobs and protecting the economic engines that drive the country and its institutions. According to Industry Canada, "[t]he department's mission is to foster a growing competitive, knowledge-based Canadian economy."⁵⁸ Furthermore,

Industry Canada's mandate is to help make Canadians more productive and competitive in the knowledge-based economy, thus improving the standard of living and quality of life in Canada. The Department's policies, programs and services help grow a dynamic and innovative economy that:

- provides more and better-paying jobs for Canadians;

⁵⁵ CIHR, Press Release, "Federal Funding Agencies to Launch New Panel on Ethics in Research Involving Humans", online: CIHR

<http://www.cihr-irsc.gc.ca/news/press_releases/2001/pr-0136_e.shtml>.

⁵⁶ CIHR, "Minutes of Telephone Conference" (22 June 2002), online: CIHR

<http://www.cihr-irsc.gc.ca/publications/archive/meetings_22june2001_e.pdf>.

⁵⁷ *Ibid.*

⁵⁸ Industry Canada, "The Department", online: Industry Canada

<<http://www.ic.gc.ca/cmb/welcomeic.nsf/ICPages/Department>>.

- supports stronger business growth through continued improvements in productivity and innovation performance; and
- gives consumers, businesses and investors confidence that the marketplace is fair, efficient and competitive.⁵⁹

The policies and practices of Genome Canada are thus to be driven by an industry rather than a health agenda, and yet Genome Canada is a major funder of health research in Canada.⁶⁰

Finally, a very different sort of conflict of interest deserves attention. The current serious insufficiency of numbers of people in Canada trained in research ethics is resulting in conflicts of interest that are potentially contaminating the policy-making process. A good example of this problem comes from recent developments in the area of stem cell research. In 1999, the Canadian Biotechnology Advisory Committee was created with a mandate to advise and educate the public. It established a Special Study on the Use of Novel Genetically Based Interventions. On January 15, 2001, the CBAC Advisory Memorandum “Stem Cells: Opportunities and Challenges” was released.⁶¹ At the relevant time, Françoise Baylis, Timothy Caulfield, and Bartha Knoppers were members of CBAC.⁶² The Stem Cell Network (SCN) was established in March 2001, with a 4-year, \$21.1 million dollar grant from the Networks of Centres of Excellence program of the CIHR, NSERC, and SSHRC, and a mandate “to investigate the immense therapeutic potential of stem cells for the treatment of diseases currently incurable by conventional approaches.”⁶³ Françoise Baylis, Timothy Caulfield, Bartha Knoppers, Gregory Korbitt, and Samuel Weiss are all investigators on the SCN. Barbara Beckett was, at the relevant time, staff at the SCN. In the absence of legislation or direction with respect to stem cell research in the *TCPS*, the CIHR formed a Working Group with a mandate to draft guidelines for stem cell research funded by CIHR.⁶⁴ Françoise Baylis, Timothy Caulfield, Gregory Korbitt, Samuel

⁵⁹ Industry Canada, “Mandate”, online: Industry Canada

<<http://www.ic.gc.ca/cmb/welcomeic.nsf/ICPages/Mandate>>.

⁶⁰ See Jason S. Robert, “Genomes, Hormones, and Health”, Review essay of *The Elusive Embryo: How Women and Men Approach New Reproductive Technologies* by Gay Becker, *Generations at Risk: Reproductive Health and the Environment* by Ted Schettler *et al.*, and *Hormonal Chaos: The Scientific and Social Origins of the Environmental Endocrine Hypothesis* by Sheldon Krinsky (2001) 9:4 *Literary Review of Canada* 18.

⁶¹ Canadian Biotechnology Advisory Committee, “Stem Cells: Opportunities and Challenges”, online: Canadian Biotechnology Advisory Committee <[http://cbac-cccba.ca/epic/internet/incbac-cccba.nsf/vwapj/StemCells_Advisory_e.pdf/\\$FILE/StemCells_Advisory_e.pdf](http://cbac-cccba.ca/epic/internet/incbac-cccba.nsf/vwapj/StemCells_Advisory_e.pdf/$FILE/StemCells_Advisory_e.pdf)>.

⁶² Françoise Baylis resigned from CBAC in June 2001, in part to deal with the issue of conflicts of interest. Personal communication F. Baylis, June 2001.

⁶³ The Stem Cell Network, “Overview”, online: The Stem Cell Network <<http://www.stemcellnetwork.ca/aboutus/overview.php>>.

⁶⁴ CIHR, “Human Pluripotent Stem Cell Research: Recommendations for CIHR-Funded Research – Report of the ad hoc Working Group on Stem Cell Research”, online: CIHR <http://www.cihr-irsc.gc.ca/publications/ethics/stem_cell/stem_cell_recommendations_e.shtml>.

Weiss, and four other individuals were the members of the Working Group, with Barbara Beckett as the rapporteur. The Final Report of the Working Group was released in January 2002. Finally, last year, the Standing Committee on Health was charged with reviewing the draft legislation on assisted reproductive technologies and reporting back to Parliament. Françoise Baylis, Timothy Caulfield, and Bartha Knoppers all made representations to this Committee.

There are at least two reasons to be concerned about groups with such distinct mandates having such significant overlapping membership.⁶⁵ First, when the same individuals are involved in crafting organizational positions on a particular issue, there may be a deceptive (albeit unintentional) appearance of agreement among divergent organizations. Normally, agreement may be taken to strengthen the position the organizations share. However, if the organizations are all advised by the same individuals, the agreement is hardly surprising and is substantially less significant. Second, individuals in the process of applying for funding for research in a particular area (here \$21.1 million for the Stem Cell Network) are in a position of conflict of interest if they are concurrently providing advice to policy-makers on whether such research should be permitted and, if so, how it should be regulated.

There are a number of steps that must be taken to reduce the potential harms that can be caused by unrecognized and/or unmanaged conflicts of interest. These include:

- make REBs truly independent. For example, we need to explore taking REBs out of the institutions conducting the research.
- make institutions reveal amounts of donations and research dollars received from industry and establish clear mechanisms for ensuring that the well-being of research subjects is not compromised by conflicts of interest.
- take the establishment of the research ethics policies and standards, accreditation, and education out of the ambit of the research funders.
- ensure that health research on the scale of Genome Canada be administered (or at the very least, overseen) by an entity with a clear **and primary** mandate to protect the public (thus, not Industry Canada).
- insist, at a minimum, that conflicts of interest at all levels be made transparent to the public. When disclosure alone is not sufficient, then other steps to manage the conflicts (e.g., removal from the situation) must be insisted upon.

⁶⁵ These concerns were discussed by Françoise Baylis. Françoise Baylis, "The Public Face of Bioethics: Watchdog or Show Dog?" (Paper presented to the American Society for Bioethics and Humanities, Fifth Annual Meeting, Baltimore, USA, October 2002) [unpublished].

- engage in significant capacity-building initiatives to increase the number of individuals with training in ethics.⁶⁶ The work requiring ethics expertise should not be done by a very limited number of individuals with overlapping roles and responsibilities – conflicts of interest in the policy-making process must be avoided or, where not possible to avoid, made transparent.

E. Commercialization

Research in Canada has become significantly more commercialized. Consider four revealing examples.

First, there has been a dramatic increase in industry-sponsored research and a decrease in government-funded research. According to a recent systematic review of conflicts of interest in biomedical research in the United States, “[i]ndustry’s share of total investment in biomedical research and development grew from approximately 32% in 1980 to 62% in 2000.”⁶⁷ According to Statistics Canada data, in 2001, \$4.2 billion per year was spent on research and development in the health field. Only 16% of this was spent by the federal government (for research performed by universities, teaching hospitals, business enterprises, government labs, and private non-profit organizations).⁶⁸

Second, universities and researchers are now directly financially invested in their own research. According to the systematic review referred to above, “approximately one fourth of investigators have industry affiliations, and roughly two thirds of academic institutions hold equity in start-ups that sponsor research performed at the same institutions.”⁶⁹

Third, the newly-established CIHR emphasizes commercialization of research. Indeed, the *CIHR Act* lists commercialization as one of its objectives:

4. The objective of the CIHR is to excel, according to internationally accepted standards of scientific excellence, in the creation of new knowledge and its translation into improved health for Canadians, more effective health services and products and a strengthened Canadian health care system, by

(i) encouraging innovation, facilitating the commercialization of

⁶⁶ An example of such an initiative is the CIHR Training Program in the Ethics of Health Research and Policy, see online: <<http://www.ethicstraining.ca>>.

⁶⁷ Bekelmen, Li & Gross, *supra* note 54 at 454.

⁶⁸ *Supra* note 35

⁶⁹ Bekelmen, Li & Gross, *supra* note 54 at 454.

health research in Canada and promoting economic development through health research in Canada;⁷⁰

Fourth, Genome Canada places tremendous emphasis on commercialization. Genome Canada has an explicit commercialization mandate to realize the economic potential of genomics research (“to create and realize economic, industrial and social benefits to Canada”⁷¹). Even more importantly, it also requires matched funds at a rate of 50 cents on the dollar and thereby compels partnerships (and, as they will logically and largely be linked to promises of future potential gain, they are likely to be particular kinds of partnerships).⁷²

The extent of the emphasis on commercialization at Genome Canada is illustrated through a statement made in an interview with *Biotechnology Focus* by Martin Godbout, President of Genome Canada: “Genome Canada is not a granting council; Genome Canada is a corporation that is investing in specific projects. It’s like venture capital, but instead of having equity in the company we sponsor, we invest in projects.”⁷³ In the same interview, Dr. Godbout also said:

Genome Canada is a hybrid of venture capital and granting council... It’s a mix of both, and to create that, instead of being an agency at the federal level, Genome Canada is a not-for-profit corporation. We use the name Genome Canada the same way you have Bell Canada or Air Canada, and it’s a trademark now. And Genome Canada will be used also to open doors at the international level. When you use the words Genome Canada, there’s no doubt in your mind that it’s genomics and it’s in Canada.⁷⁴

There is no doubt that commercialization of research has potential benefits. For example, through commercialization, public institutions can gain access to funds to replace those lost in the recent budget cuts and they can use these to pursue their missions. Efficiencies of public/private partnerships can be realized and therefore more research can potentially be conducted for the same total resources. More research may get done if the public sector sees the potential for income that can be used to subsidize basic operations. Similarly, more research may get done if the private sector sees the potential for profit.

⁷⁰ *Canadian Institutes of Health Research Act*, *supra* note 7, s. 4(i); CIHR, “Final Report of the Working Group on Partnership”, online: CIHR <http://www.cihr-irsc.gc.ca/publications/about_cihr/partner_wrk_grp_report_e.pdf>.

⁷¹ Genome Canada, “Genome Canada at a Glance: Mission and Objectives”, online: Genome Canada <<http://www.genomecanada.ca/fsTemp.asp?l=e>>.

⁷² Genome Canada, “Research Program: Panel Guidelines for Review – Competition II”, online: Genome Canada <<http://www.genomecanada.ca/fsTemp.asp?l=e>>.

⁷³ “Mapping Canada’s Genome: In conversation with Genome Canada’s president, Dr. Martin Godbout” *Biotechnology Focus* 4:5 (July/August 2001), online: Genome Canada <http://www.genomecanada.ca/media/biofocus_july-august2001.pdf>.

⁷⁴ *Ibid.*

However, there are also considerable potential harms. The commercialization of research can have a number of harmful effects by:

- *limiting what gets researched.* With little potential for profit, research into conceptual or philosophical questions, diseases with no profitable markets (e.g., affecting the poor or small numbers of people), inexpensive diagnostic tools or treatments, health protection and promotion, and population health research is less likely to be conducted. These kinds of research are critical to the well-being of Canadians but have little commercial potential.
- *shaping research design.* Cheaper methods and methods designed to increase the likelihood of positive results are likely to be favoured even when the quality of the results may be compromised. For example, recent research has demonstrated that industry-sponsored studies are more likely to use inactive controls than non-industry studies. Placebo or no-treatment studies can be more dangerous than active control studies and can increase the likelihood of positive results.⁷⁵
- *restricting what gets disclosed.* Data and information sharing between researchers will be limited. Limits on publication will be imposed. The 2003 JAMA meta-analysis of the impact of financial conflicts of interest in biomedical research demonstrated an association between industry sponsorship and restrictions on publication and data-sharing.⁷⁶
- *shaping what gets submitted for publication.* The JAMA meta-analysis also demonstrated a statistically significant association between industry sponsorship and pro-industry conclusions.⁷⁷ This should not be surprising, for researchers may be wary of (or prevented from) publishing negative results fearing loss of industry sponsorship for future trials and/or consulting contracts. Furthermore, companies may provide financial support to the researchers for writing up positive results but not for writing up negative results. Sometimes they go even further and commission a ghostwriter (i.e., someone to anonymously write up a study based on the materials provided by the company) and give the text as a “draft” to a physician to submit to journals as the author.⁷⁸

⁷⁵ Bekelmen, Li & Gross, *supra* note 54 at 456-459.

⁷⁶ *Ibid.*

⁷⁷ *Ibid.*

⁷⁸ Melody Petersen “Whistle-Blower Says Marketers Broke the Rules to Push a Drug” *New York Times* (14 March 2002), online: Bennett Law Firm <<http://www.bennettlawfirm.com/NYTimesStory.htm>>; CBC News, Marketplace, “Medical Ghostwriting” (25 March 2003), online: CBC News <<http://www.cbc.ca/consumers/market/files/health/ghostwriting>>; A. Flanagan *et al.*, “Prevalence of Articles with Honorary Authors and Ghost Authors in Peer-Reviewed Medical Journals” (July 15, 1998) 280 *J. Am. Med. A.* 222.

- *limiting access to the benefits of the research.* If investments need to be recouped, the price of the results (e.g., new drugs or vaccines) may be well out of the range of most people in the world.

Clearly, while commercialization is important (and a legitimate goal for some research), the effects of commercialization on research (both the conduct and outcomes) must be carefully studied. There are multiple mandates to manage: protecting research participants; protecting the recipients of the results of research; generating knowledge, goods, and services to benefit the public; generating knowledge for its own sake; creating jobs; and building the economy. However, from a governance perspective, the relationship between these mandates must be explored and conflicting mandates must be managed such that the protection of research participants and the promotion of the public interest are given priority.

Conclusion

Until now, the regulation of research has focussed largely on regulating the relationship between researchers and research subjects. As this paper has demonstrated, however, the focus should now be more on regulating the relationships between institutions: that is, between industry and universities and hospitals and government (in all of the possible permutations). The 5 C's of concerns about contemporary health research (consistency, comprehensiveness, compliance, conflicts of interest, and commercialization) arise within the context of these relationships and must be addressed. In response to these concerns, we must immediately move to develop a new system of governance for research involving humans designed to ensure the proper protection of research participants and the users of research results.