

The Regulation of Conflicts of Interest in the Canadian Stem Cell Research Environment

Ubaka Ogbogu

Introduction

The ethical dilemmas associated with conflicts of interest (COI) involving biomedical researchers and institutions is a familiar issue in research ethics. There has been a lot of discourse on the subject, and the main points can be summarized as follows. First, COI occur when “professional judgment concerning a primary interest (such as patient welfare or the validity of research) tends to be unduly influenced by a secondary interest (such as financial gain).”¹ Several types of COI exist, depending on the source or nature of the conflicting interest,² although it is generally agreed that financial COI are the most pervasive.³ Second, if not managed or avoided, such conflicts can compromise research integrity, foster negative public perception of the research and jeopardize the welfare of research subjects.⁴ Indeed, several high profile cases of COI in the past few years, including the notorious Olivieri and Healy incidents in Canada, have brought the problems posed by COI to the forefront of research ethics debates.⁵ Third, the establishment of oversight mechanisms to deal with COI is considered imperative, and two key oversight models have been proffered in relevant literature. The first advocates prohibiting interests or situations that could potentially result in COI,⁶ while the second requires management of such conflicts through disclosure and the process of peer review.⁷ Institutional oversight policies are generally based on one or a combination of both models.⁸

Concerns about COI in the biomedical research environment are particularly significant for emerging technologies

like stem cell research. Mere perception of COI involving stem cell researchers and/or other stakeholders could bring adverse public opinion and stifling regulatory scrutiny to the research. Also, as stem cell research moves from the laboratory to the clinical trial stage, it is imperative to eliminate or limit ethical pitfalls that could compromise the safety of research participants, and ultimately jeopardize research continuity.

Many of Canada’s stem cell researchers receive research funds from the Stem Cell Network (SCN or Network), one of Canada’s Networks of Centres of Excellence (NCE).⁹ The SCN’s primary operation is the redistribution of NCE and partner funds to researchers participating in the Network. By virtue of its NCE status, the SCN is responsible for the commercialization of Network-supported research and the management of research portfolios. The SCN is also mandated to maintain close association with private sector interests, both in terms of management and in meeting commercialization objectives.¹⁰ The NCE/SCN funding structure therefore promotes relations between potentially conflicting interests, including academic research, corporate and public interests.

In Part 1, this background paper¹¹ examines actual and potential COI drivers within the stem cell research context, including a consideration of the nature and impact of the NCE program. Much of the discussion in this part examines the potential impact of commercialization in creating opportunities for COI. However, it is important to note that COI is one, and certainly not the only issue associated with



the commercialization of research. Excellent reviews of the issues exist in relevant literature¹² and as such, do not warrant repetition in this paper. Part 2 reviews existing COI oversight policies applicable to the Canadian and international stem cell research context. This part also highlights gaps in COI oversight. In the final part, the paper offers recommendations for addressing identified gaps in oversight and policy.

1. Drivers

a. The NCE Program, Stem Cell Network and the Commercialization Initiative

Canada's NCE program was established in 1989 to steer a "national system of innovation" aimed at linking scientific research with industrial know-how and commercial exploitation.¹³ This was implemented through the creation and funding of nation-wide multi-institutional, multi-disciplinary and multi-sector research networks in areas critical to Canada's economic, scientific and social advancement. The networks are structured as self-governing "institutions without walls," formed by a pool of individual researchers working on mutually related research projects. Networks are expected to redistribute funds received from the NCE program and partner sources to its members through contested research grants available for the pursuit of network-related research. Networks are also required to actively explore avenues for moving scientific research from the laboratory to the market. To better facilitate research exploitation, networks are encouraged to establish commercialization ventures including intellectual property (IP) receptor companies, spin-offs, joint ventures with industry and IP licensing schemes. Also, networks must recognize "industrial partners' contributions to the network...by allowing them access to the commercial exploitation of the intellectual property under terms commensurate with the nature and level of their contributions."¹⁴

It is evident therefore that the strong and unequivocal endorsement of close ties between private interests and the biomedical research community is a cornerstone of the NCE program. Indeed, funding policies encouraging or requiring partnerships between academic researchers and the private sector are now considered routine worldwide.¹⁵ However, unlike other public research funding entities, the linkages promoted through the NCE program extend to the management of the networks. According to the NCE Pro-

gram Guide, "at least half of the membership of the Board of Directors [of funded networks] should be from outside the university community, and the majority of those from industry."¹⁶ Industry representation is also required on each network's research management committee. Arguably therefore, NCEs are the vanguard of the new approach to academy – one that fosters industry connections and encourages direct control of publicly funded research by private interests. While this is not calamitous per se, the shift towards a more direct engagement with private, and often profit-driven, interests may present adverse implications for the altruistic pursuit of scientific knowledge. As noted by Fisher and colleagues,

by promoting industry access to publicly funded research...[NCE] policy recognizes that scientific research is simultaneously fundamental and useful, while skewing the balance in favour of private and commercial science. The NCE offers a major challenge to traditional conceptions of academic autonomy and the public nature of knowledge.¹⁷

Consistent with its mandate as a NCE, the SCN has incorporated a robust commercialization program into its mission and objectives. In 2005, the Network announced a "catalyst" mission focused in part on "translat[ing] research outcomes into clinical applications and commercial products."¹⁸ The Network's strategic research program was also realigned with "three of the most understood routes to the clinic/market: cellular therapies, drug discovery, and tools, reagents and diagnostics."¹⁹ Other strategies employed by the SCN in meeting its commercialization objectives include:

- Support for Principal Investigators (PI) who wish to commercialize their research. Since 2001, Network-supported Intellectual Property (IP) has contributed to the formation and growth of start-up and spin-off companies. Several of these companies are now SCN partners and co-fund Network projects.
- Support for industry partners to ensure they realize commercial value for their investment.
- Research proposals are required to engage public and private partners. Funded projects are encouraged to obtain matching funds from partners. As a result, partner investment in SCN projects amounts to almost 47.7% of total SCN funding, and exceeds SCN investment in certain areas.



- In 2002, the SCN created its own biotechnology company called Aggregate Therapeutics (Aggregate). Aggregate is a receptor company for SCN-supported IP and the conduit through which pooled IP can be exploited. Aggregate currently has agreements with eight key Canadian research institutions to serve as an incubator of IP resulting from Network-funded research. The SCN maintains control over Aggregate through a funding agreement and by retaining a “Special Voting Share,” which allows it to appoint two-thirds of the company’s Board of Directors.²⁰

A number of benefits have been linked to the commercialization of biomedical research, including economic growth, job creation, increased research funding and the promotion of strategic and essential public/private partnerships to better facilitate research translation.²¹

These benefits notwithstanding, numerous studies have demonstrated the adverse implications of situating academic research in an environment that supports industry partnerships and control. For example, a seminal 2003 study of all English-language studies in MEDLINE containing original, quantitative data on academy’s financial ties with industry concluded that COI arising from such ties are pervasive, and adversely impact on the research process.²² Some of the negative effects on research identified by the study include the skewing of research results to favour industry perspectives, increased likelihood of publication bias, publication delays and data withholding, and the use in clinical trials of assessment methodologies that “fall short of determining a study’s overall quality.”²³ A recent study focusing on data withholding in the life sciences reveals that having connections with industry, such as owning equity, serving as a consultant, or on a company board, increases the likelihood that researchers in the life sciences would engage in data withholding.²⁴ The authors of the latter study conclude, “one of the main obstacles [to efforts to minimize data withholding] is the growing commercialization of U.S. universities.”²⁵ A similar study on the impact of data withholding on trainees in the life sciences concludes that scientists are less likely to provide their trainees with access to scientific resources when their research is funded by industry.²⁶

A number of benefits have been linked to the commercialization of biomedical research, including economic growth, job creation, increased research funding and the promotion of strategic and essential public/private partnerships to better facilitate research translation.

Concerns have also been raised about the impact of academic-industry partnerships on research publication practices. Indeed, the publication of research results is central to the research endeavor, and to the pharmaceutical industry’s product marketability prospects.²⁷ Academic investigators often have to comply with contractual clauses regulating publication practices as quid pro quo for industry funding. Bodenheimer describes a number of industry-influenced publication practices, including: (1) requiring investigators to co-author industry-authored manuscripts; (2) publication delays resulting from prepublication reviews by the sponsoring company; (3) non-publication of results unfavourable to the sponsoring company; and (4) the “nonwriting author–nonauthor writer” syndrome, whereby clinical investigators appear as authors in publications authored by professional ghostwriters who are not named as authors.²⁸

Even where no adverse effect on publication can be linked to industry support, studies show that such support may have some influence on researchers’ opinions and biases. For example, Stelfox and colleagues have linked financial relationships with pharmaceutical industries to medical literature supporting the safety of calcium-channel antagonists (used for treating cardiovascular diseases).²⁹ Cho and Bero found similar reporting of favorable outcomes for drugs of interest in symposia publications with drug company support.³⁰ Caulfield identifies a “cycle of hype” in the framing of biomedical research results based on a study of newspaper coverage of genetic discoveries in four countries including Canada, which found a bias towards reporting benefits.³¹ He concludes that “genohype” is created by the research community largely in response to “commercial enthusiasm and pressure from public funding agencies”³² to emphasize benefits over risks. The positive message is then transmitted to the public through the media, thus creating a level of public expectation that needs to be satisfied with more hype.³³ This “cycle of hype” could lead to loss of public trust in the science where hyped expectations are not met with promised benefits.³⁴

With or without COI, the commercialized stem cell research environment could also lead to negative public perception of the value of the research.³⁵ As Caulfield rightly notes, “the



mere association with funding entities that have a mandate to commercialize research can produce a perception of bias that might diminish the perceived impartiality of even high quality [research] work.”³⁶ This perception of bias would likely be fostered by the NCE/SCN structure, particularly the involvement of private interests in network and research management. Indeed, a recent Australian study has linked public trust in stem cell researchers to the research context. The study found that there was more public trust in researchers working in public institutions than those working within the private context, and that support for stem cell research is associated with the level of trust for researchers conducting the work.³⁷

Canadian studies have also reached similar conclusions with respect to biotechnology research in general.³⁸ In one study, focus group respondents drawn from the Canadian and US public rated publicly funded university scientists as significantly more credible than their industry-funded and privately employed colleagues.³⁹ Survey respondents also generally agreed that the presence of financial interests raises doubts about the credibility of even the most trusted sources.⁴⁰ In the clinical research context, Kim and colleagues found that potential research participants are less likely to participate in clinical trials run by researchers who own substantial equity in or receive income from sponsoring companies.⁴¹ It appears safe to conclude therefore that involvement of private interests in research may diminish public support of stem cell research. As noted by Caulfield, “Currently, the public believes researchers are motivated by the desire to find cures, not make money.... However, as the line between commerce and research becomes increasingly blurred, the public’s comfort level may diminish.”⁴² A loss of public support would have a profound impact on the continuity of stem cell research, and is likely to result in decreased government support, lack of public interest in clinical trials and applications and/or the imposition of a strict regulatory regime that would frustrate scientists.

Commercialization may also lead to broader conflicts in the policy-making arena, particularly between the innovation and commercialization sectors of the government.

Currently, Canadian health research policies appear to accommodate a number of seemingly conflicting agenda, including: the translation of knowledge, the stimulation of innovation, the promotion of economic growth, the protection of participants’ rights and the improvement of access to health care. The scope of such policy initiatives often necessitates the involvement of various government institutions with differing mandates, priorities and interests. Caulfield

contends that evidence of policy conflicts already exist in recent gene patent controversies and in the human gene patent debate in Canada.⁴³ According to him, “as the products of the genetic revolution begin to reach the marketplace, it is becoming apparent that government commercialization policies have the potential to adversely affect, paradoxically, the very goals of the commercialization agenda, that is, the production and dissemination of innovative genetic technologies.”⁴⁴ While a detailed examination of such conflicts is beyond the scope of this paper, further discussion of

the implications for stem cell research is clearly warranted, given the centrality of innovation and commercialization goals to the research context.

Furthermore, the risks associated with financial COI in general may also be significant in the stem cell research context. These risks include the preferential allocation of institutional resources and research attention to commercially viable projects,⁴⁵ failure to terminate sponsored trials that may adversely affect patient welfare,⁴⁶ failure to comply with clinical trial ethics with respect to recruitment of research subjects⁴⁷ and inordinate focus on fiscal valuation versus ethical and scientific oversight in the review of funded projects. Finally, allowing researchers to handle multiple other responsibilities, such as managing companies and involvement with research oversight, may impact on the quantity or quality of attention paid to basic and clinical research work.

b. Compliance with Logistic Requirements

COI could potentially arise from compliance with logistic requirements associated with SCN funding. One such re-

A recent Australian study has linked public trust in stem cell researchers to the research context. The study found that there was more public trust in researchers working in public institutions than those working within the private context.



quirement is that funded projects identify clear milestones and deliverables from the research. Milestones and deliverables are expected to demonstrate research progress towards social and economic utility. Such a milestone-driven approach appears at odds with the unpredictable nature of the scientific endeavor, especially for novel technologies like stem cell research.

Another requirement is the submission of periodic progress reports by all funded projects for review by the Network's Research Management Committee (RMC). Following RMC review, the Network could continue funding for a project or restructure funding to align with research progress. An unfavourable review could result in the withdrawal or reduction of project funds. The pressure created by expectations of returns could lead researchers to falsify progress reports in order to maintain their funding. Indeed, some commentators on the recent Korean stem cell research publication fraud scandal have noted that the "inordinate pressure created by expectations of returns for such large sums [in government funding]"⁴⁸ played a considerable role in the events that transpired. The pressure to manipulate research results could also arise from the process of obtaining matching funds from funding partners. Caulfield rightly notes, "matching funds are often associated with a desire to achieve a particular research result" and "[a]s such, matching funds can create real and perceived conflicts of interest."⁴⁹

c. Conflicts of Conscience and Funding Hype

Another source of COI could lie in "conflicts of conscience" that can occur where "personal beliefs influence objectivity in research."⁵⁰ This is especially significant for the ELSI research environment where debates over research ethics issues are usually reflective of each proponent's views or inclinations regarding the propriety of stem cell research. Given that the peer-review system is central to research integrity and authenticity, a particular view on stem cells could impact on the scientific merit of studies conducted in the area.

Similar concerns and questions could be raised about the scientific peer review process. For example, will the emphasis on translating research outcomes skew research focus and funding in favour of applied over basic science? If this happens, will the resulting methodological divide among scientists impact the peer review of applied research? Will

funding and hype envy lead to biased critiques of the stem cell research? It is possible that the scientific peer-review process could be obscured by disagreements over scientific methods and the propriety of the research.

2. Conflict of Interest Policies

There is no federal or provincial legislation in Canada regulating COI in the research context. However, several federal and provincial legislative provisions are informed by concerns associated with COI. For example, various provinces have enacted legislation that provides a statutory framework for the disclosure, investigation and management of COI involving members of the Legislative Assembly and Executive Council (see e.g. British Columbia, Ontario, and New Brunswick's *Members' Conflict of Interest Act*).⁵¹ COI provisions have also been applied in the context of health information legislation. Alberta's *Health Information Act*,⁵² for example, allows the Lieutenant Governor-in-Council to reassign the review power of the Information and Privacy Commissioner to a judge of the Court of Queen's Bench where the Commissioner has an apparent, potential or actual COI in a complaint under review.⁵³ A COI exists where the Commissioner is a former employee or member of a custodian of health information.⁵⁴

COI concerns have also resulted in the exclusion of stem cell researchers from oversight and advisory boards. For example, the *Assisted Human Reproduction Act*⁵⁵ precludes persons licensed to conduct hESC research, or potential licensees, from being on the Board of Directors of the Assisted Human Reproduction Agency, the regulatory authority charged with implementing the Act.⁵⁶ Researchers affiliated with SCN cannot be members of the Stem Cell Oversight Committee (SCOC), the national stem cell research ethics board.⁵⁷ The Canadian rules appear to be unique in this regard, as most other jurisdictions allow for relevant expertise on stem cell research oversight/advisory boards, subject to COI management strategies such as disclosure, divestment of financial interests, and exclusion of experts from leadership roles.⁵⁸

COI oversight is mainly handled at an institutional level, and varies among institutions. In practice, some institutional policies apply to a broad range of persons and interests. For example, the Tri-Council Policy Statement (TCPS),⁵⁹ which provides ethical guidelines for research funded by Canada's three main funding councils, applies to a majority



of the researchers in Canada. Also, many university policies are either based on or adopt the provisions of the TCPS. In effect, uniform trends exist in the oversight of investigator COI by virtue of the TCPS.

SCN's COI policy adopts the TCPS and the NCE Conflict of Interest Policy. There is also a Network-specific oversight method referred to as the "Points to Consider" approach.⁶⁰ This is essentially a case-by-case approach to dealing with COI, and not a set of predetermined rules. Therefore, to understand the COI rules that apply in the stem cell research context, one must look to the TCPS and NCE Conflict of Interest Policy.

a. Tri-Council Policy

Article 4.1 of the TCPS contains the provisions dealing with COI involving researchers and institutional Research Ethics Boards (REB). The provision *merely* requires the disclosure of "actual, perceived or potential" COI to the REB. REBs are also responsible for developing oversight mechanisms. Specific guidance for developing such mechanisms is provided in the explanatory notes accompanying the section. Matters covered in the guidance notes include approaches for identifying and managing COI, specific instances of COI involving researchers and REB members, and the parent institution's role in ensuring the independence of its REB.

Other provisions dealing with COI can be found in various sections of the TCPS. Article 2.4(e) requires researchers to disclose potential or actual COI, including conflicts involving their institutions or sponsors, during the process of obtaining informed consent from research subjects. The same section also requires disclosure of the possibility of commercialization of research discoveries. Article 8.7 similarly requires the disclosure of potential for commercial use of genetic material and the data derived from its use. Article 7.3 authorizes REBs to examine the budget of clinical trials to "assure that ethical duties concerning COI are respected."

Within the SCN context, the TCPS applies only to COI on the part of Network-funded researchers, and is ineffectual for conflicts involving SCN officers and the Board, even

where such conflicts are adverse to researchers' interests or tend to jeopardize research integrity. Also, since oversight depends on each researcher's institution and REB, there is a great deal of variance in the rules applicable to investigator COI. This creates an opportunity for diverging approaches to the management of COI, and could result in differing standards of regulation for researchers working on common projects within the SCN virtual network. However, creating an SCN-specific oversight process for researcher COI would have no effect on the application of the TCPS, as the latter policy applies to institutions receiving Tri-Council funds,

including NCEs. Also, many universities require REB review based on policies emulating the TCPS for all protocols their researchers are involved in.

There is a great deal of variance in the rules applicable to investigator COI. This creates an opportunity for diverging approaches to the management of COI, and could result in differing standards of regulation for researchers working on common projects within the SCN virtual network.

b. NCE COI Policy

The NCE COI Policy Framework is contained in Appendix A of the NCE *Program Guide*.⁶¹ Unlike the TCPS, NCE COI Policy applies to all individuals/institutions participating in the networks, including the mem-

bers of the Board of Directors, universities, researchers and network-employees. The responsibility for oversight and implementation of the policy is vested in each network's Board of Directors. Paragraph 1.0 of the Policy defines COI as "a situation where, to the detriment or potential detriment of the network, an individual is, or may be, in a position to use research knowledge, authority or influence for personal or family gain (financial or other) or to benefit others."⁶² Persons wishing to invoke the application of the Policy would therefore have to establish the minimum threshold of potential detriment to the Network. This may prove to be a difficult or restrictive standard, particularly where the detriment is to the researcher or funded research.⁶³ Also, the definition appears to exclude COI that are not detrimental to the Network or its affiliates, for example, where Network officials use their influence to control the research process in the implementation of a Network's commercialization goals.

Similar to the TCPS, the NCE Policy requires the disclosure of financial interests and positions of influence that result in COI. In the event of failure to disclose, the Board can require the defaulter to account for the benefit arising from the conflicting interest, to withdraw from the action



or network or take any other appropriate action. Network members with apparent or actual COI are excluded from participating in network decisions.⁶⁴

c. CIHR Human Pluripotent Stem Cell Research Guidelines (CIHR Guidelines)

The CIHR Guidelines⁶⁵ apply to research on human pluripotent stem cells funded by the Tri-Council or conducted under the auspices of institutions receiving any Tri-Council funding. Although not expressly mentioned in SCN policy documents, the COI provisions in the CIHR Guidelines apply to the SCN and its members by virtue of NCE status. The said provisions are directed towards the oversight of financial institutional COI. Researchers and their institutions are mandated to disclose all commercial interests in the outcome of stem cell research, including income from and equity owned in companies supporting their research. Such disclosure must be made to the SCOC, local REB and prospective research participants.

The SCOC and REB are empowered to review project budgets for potential or actual COI. The guidelines also direct the ethics boards to conduct periodic reviews of contracts between researchers, institutions and industry sponsors, to ensure that the researcher's right to publish freely is preserved. Where disclosure is considered inadequate, the SCOC and/or REB could require researchers and/or their institutions "to remedy any possible distortion of proper procedures attributable to such conflicts."⁶⁶ No specific remedial measures are mentioned in the guidelines, thus allowing the oversight bodies the flexibility to craft remedies appropriate to individual cases.

d. Case Law

Outside the realm of legislation and policy, case law principles are likely to play a significant role in addressing COI issues, particularly in the area of tort and fiduciary law. For example, Canadian tort law precedents consider the failure to disclose material risks to patients or medical research subjects a breach of the legal duty of informed consent.⁶⁷

In *Reibl*,⁶⁸ the Supreme Court concluded that material risks were best viewed from a patient's perspective and must include all information that a reasonable person in a patient's position would want to know. Applying the *Reibl* materiality standard, various courts have interpreted material risks widely to include not just matters causing the ultimate damage, but also matters which might influence the judgment upon which consent is based.⁶⁹ It is clear therefore that failure to disclose interests that compete with the altruistic pursuit of knowledge could be viewed as a material breach of informed consent – especially where such failure

is linked to activities that adversely impact on patient welfare or rights. American case law is precise on the legal duty to disclose COI. As noted by the California Court of Appeal in *Moore v. The Regents of the University of California*,⁷⁰

The possibility that an interest extraneous to the patient's health has affected the physician's judgment is something that a reasonable patient would want to know in deciding

whether to consent to a proposed course of treatment. It is material to the patient's decision and, thus, a prerequisite to informed consent.⁷¹

Persons involved in stem cell research who fail to disclose COI to their human research subjects may also be liable for a breach of fiduciary duty. According to Litman, the "gravamen of breach of fiduciary obligation is disloyalty"⁷² by "persons whose loyalty is essential to the efficacy and integrity of important but diverse relational institutions."⁷³ While the existence of fiduciary obligations owed by clinicians to their patients is settled law,⁷⁴ the nature of a researcher's fiduciary duty to research participants is less clear. However, Clamon argues that such a duty exists "from the privilege study participants bestow upon investigators and institutions to conduct human subjects research."⁷⁵ He also notes that fiduciary obligations are founded upon a duty of good faith, trust, confidence and candor – all of which are duties owed by biomedical researchers and institutions to their patients, benefactors, other researchers, the government and the public.⁷⁶

With respect to clinicians, it is important to note that their fiduciary obligations extend to the disclosure of "material

Failure to disclose interests that compete with the altruistic pursuit of knowledge could be viewed as a material breach of informed consent – especially where such failure is linked to activities that adversely impact on patient welfare or rights.



personal interest, such as a research interest or an economic interest related to the patient's course of treatment.⁷⁷ Therefore, IVF clinicians involved in obtaining consent for embryo donation to research, or who merely advise patients of the donation option, may be liable under fiduciary law for failure to disclose *any* connection to a stem cell research protocol. Clinician-researchers who enter into contracts that require non-disclosure of research results without the research sponsor's permission could also be in breach of fiduciary obligations.⁷⁸

Commentators have expressed the view that fiduciary law strictly prohibits COI.⁷⁹ Litman contends that avoiding COI is the threshold duty of the fiduciary obligation. In his words:

First, and perhaps foremost, amongst the proscriptive duties of fiduciaries is the obligation to avoid conflicts of interest. Classically, this means that fiduciaries must avoid situations in which their personal interests, most often, but not always economic interests, might interfere with the duty of loyalty.⁸⁰

It is important to stress that the emphasis here is on "avoidance" and not disclosure. It would appear that the mere appearance of COI could provide the basis for an action for breach of fiduciary duty. Indeed, the Ontario Court of Appeal decision in *Cox v. College of Optometrists of Ontario*⁸¹ is authority for the proposition that unlawful COI exist where there is reasonable apprehension or appearance of COI without a potential or actual conflict. Litman urges, "it would be a mistake to assume...that disclosure by a fiduciary of a conflict of interest *ipso facto* cures or reverses the conflict and thereby frees the fiduciary to pursue self-interest with impunity."⁸² While full and frank disclosure is essential, fiduciaries are under a strict duty to hold the interests of those to whom they owe fiduciary obligations above their personal interests, and to resolve conflicts in favour of this duty. In order to avoid lawsuits for breach of the fiduciary relationship, stem cell investigators who own or are involved in commercialization ventures may therefore have to do more than ensure full and frank disclosure of competing interests.

International Policies

Until recently, the development of stem cell research guidelines and policies in many countries has been overshadowed by debates associated with the moral status of the embryo.⁸³ With the enactment of stem cell legislation restricting or allowing the research, regulatory focus has

shifted to the regulation of research ethics issues relevant to stem cell research. However, many countries do not have COI guidelines applicable specifically to the stem cell research context. Also, COI regulation in many countries is largely unarticulated at a national level. Instead, COI oversight depends on individual institutions and a great deal of institutional variance exists (see Fig. 1).

Where national policies exist, such policies are usually reflective of policy responses to the following three factors: (1) high profile COI cases adversely impacting patient welfare and/or academic freedom; (2) a permissive regulatory environment for academy-industry relationships; and (3) the desire for increased accountability of institutional decision makers. However, most national policies apply only to research funded by public funding institutions, and as such, are limited in effect.⁸⁴ In the US for example, the privatization of the academic research enterprise facilitated by the notorious Bayh-Dole Act of 1980⁸⁵ has been curtailed by COI guidelines issued by The Office of Public Health and Science, Department of Health and Human Services (DHHS), the National Science Foundation, and the US Food and Drug Administration. Also, the fallout from highly publicized COI cases resulting in harm to clinical research subjects, including the paradigmatic Jesse Gelsinger incident,⁸⁶ led to calls for the enactment of strict COI policies for biomedical researchers and institutions.⁸⁷

Outside the national context, a survey of policies on disclosure of COI in US medical schools and other research institutions, journal publishers and federal agencies reports that institutional policies are relaxed, lack clarity and vary greatly across institutions.⁸⁸ The study also found that oversight was mainly intra-institutional, and external accountability was lacking.⁸⁹ Since the publication of the latter study, some journal publishers have taken steps to address the lack of institutional COI policies.⁹⁰

Institutional COI have recently come under scrutiny in the US. Alan Bernstein rightly notes that the increased focus is the result of "increased public demand for accountability and transparency" following Enron and other corporate scandals.⁹¹ In order to ensure that commercial or individual interests of public health officials do not influence public health research funding decisions, the DHHS overhauled its conflict of interest guidelines in 2005. The new regulations, which apply to employees of the National Institutes of Health (NIH), contain stringent provisions prohibiting certain property interests and supplementary activities.⁹² The provisions place a monetary ceiling on financial inter-



Figure 1: COI Policies in Other Jurisdictions

Details of Policy	Key Oversight Mechanism(s)	Features
<p>Country: UK Agency: Medical Research Council (MRC) Funding Mandate? Yes Source of Policy: a. Code of Practice for Members of Council and MRC Boards b. MRC Policy on Declarations of Interest 2006 Applies to: All who advise and make judgments on MRC business including members of MRC’s Council and Research Boards, and their families</p>	Disclosure	<ul style="list-style-type: none"> • Major academic collaborations to be disclosed • Scientific reviewers required to disclose perceived, potential and actual conflicts • Declared interests registered and published on MRC website
<p>Source of Policy: MRC Good Research Practice Guidelines Applies to: MRC-funded scientists</p>	General advisory – no specific guidelines	
<p>Country: UK Agency: Biotechnology and Biological Sciences Research Council Funding Mandate? Yes Source of Policy: Code of Practice for Council Members 2005 Applies to: Members of Council and their “related parties” e.g. family members, partners etc.</p>	Disclosure	<ul style="list-style-type: none"> • No policy applicable to researchers • Disclosure of pecuniary and non-pecuniary interests required • Declaration forms compiled in publicly available registers
<p>Country: US Agency: California Institute of Regenerative Medicine Funding Mandate? Yes Source of Policy: a. Conflict of Interest Code b. Independent Citizens’ Oversight Committee (ICOC) Bylaws c. Conflict of Interest Policy for: <ul style="list-style-type: none"> • CIRM Employees • Standard Working Group Members • Facilities Working Group Members • Granting Working Group Members Applies to: ICOC Members, CIRM Employees and Working Group members</p>	Avoidance, Divestiture, and Disclosure	<ul style="list-style-type: none"> • Proactive policy e.g. ICOC members precluded from applying for grants or acting as Principal Investigators; CIRM employees precluded from owning investments greater than \$10,000 in organizations applying for grants and organizations with more than 5% of research budget devoted to stem cell therapy • “COI” extends to family members and anyone with a common financial interest • A public register of ICOC members’ interests exists (http://www.genetics-and-society.org/policies/california/conflicts.html)
<p>Country: US Agency: National Academies Funding Mandate? No Source of Policy: Policy on Committee Composition and Balance and Conflicts of Interest 2003 Applies to: National Academies’ Committee Members</p>	Disclosure, Avoidance	<ul style="list-style-type: none"> • Potential committee members to fill out a disclosure form • Employees of agencies sponsoring study or activity cannot (subject to listed exceptions) be members of committees engaged in that activity



Details of Policy	Key Oversight Mechanism(s)	Features
<p>Country: Australia Agency: National Health and Medical Research Council Funding Mandate? Yes Source of Policy: a. National Statement on Ethical Conduct in Research Involving Humans 1999 b. Human Research Ethics Handbook 2001 Applies to: Institutional Human Ethics Research Committees (HREC) (Australian REBs), Researchers</p>	<p>Disclosure, Avoidance</p>	<ul style="list-style-type: none"> • Research proposals must be approved by the HREC • Budget of clinical trials must be examined by HREC and relevant aspects of the budget to be disclosed to research participants
<p>Country: Australia Agency: Australian Stem Cell Centre Funding Mandate? Yes Source of Policy: a. Principles and Policies of Good Corporate Governance b. Annual Report 2005 Applies to: Directors, officers, employees, and scientists</p>	<p>Disclosure</p>	<ul style="list-style-type: none"> • Employees and investigators complete a disclosure form

ests owned by NIH employees and their families in “substantially affected organizations” i.e., biotechnology or pharmaceutical companies “involved directly or through subsidiaries in the research, development, or manufacture of biotechnological...devices...or products.”⁹³ Employees are also prohibited from engaging in outside activities in the latter-named companies, with research institutions supported by the NIH, with health care providers and insurers, or from providing consultative services for the preparation of documents to be submitted to the DHHS.

The DHHS regulations are perhaps the most extensive policy guidelines regulating institutional COI in the international context today. However, some commentators have pointed out that the regulations are excessive and may inhibit useful partnerships between the academic community and industry.⁹⁴ In any event, it is imperative to monitor the efficacy of the regulations in addressing institutional COI, to see whether it could be a useful template in developing similar guidelines in other jurisdictions.

Lastly, international ethical guidelines for biomedical research and health care delivery also contain standards for disclosure and management of COI, usually as a compo-

nent of the informed consent requirements. For example, the Declaration of Helsinki, which contains ethical guidelines for the conduct of medical research involving human subjects, requires researchers to inform potential research participants of the “aims, methods, sources of funding, *any possible conflicts of interest*, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail.”⁹⁵ The Declaration also requires authors and publishers to disclose sources of funding, institutional affiliations and any possible COI in publications resulting from research on human subjects.⁹⁶ Publishers must refuse publication where reports of experimentation do not comply with the principles contained in the Declaration.⁹⁷ The Council for International Organizations of Medical Sciences (CIOMS), a joint World Health Organization and UNESCO initiative, recommends including information about COI and management mechanisms in research protocols submitted for ethics review.⁹⁸ Similar provisions can be found in other international documents such as the International Society for Stem Cell Research *Guidelines for the Conduct of Human Embryonic Stem Cell Research*,⁹⁹ and the Organisation for Economic Co-operation and Development *Guidelines for the Licensing of Genetic Inventions*.¹⁰⁰ A detailed list of other international



documents containing COI provisions is available on the excellent HumGen International database, an online resource on ethical, legal and social issues in human genetics.¹⁰¹

Conclusion

Despite the growing concern over COI in biomedical research, the Canadian stem cell research environment appears to be developing within a mixed public and private context that may prove fertile for potential, perceived or actual COI. While these developments are reflective of the government-approved trend towards research commercialization, conflict of interest policies need to be strengthened to avoid or mitigate situations that may adversely affect patient welfare, research integrity and public trust in the science. The review of current policies in this paper reveals the following oversight trends in relation to the stem cell research context:

- COI oversight policies are mainly intra-institutional and vary among institutions. The patchwork of policies may result in lack of clarity on the rules applicable in COI situations.
- Existing COI policies are mostly focused on the management of financial COI without much consideration for other potential COI drivers.
- Oversight is dependent on the funding context – the rules apply only to researchers and institutions receiving NCE or federal Tri-Council funds.
- Disclosure is the more prevalent approach to COI oversight. In most instances, the policies do not provide any guidance on penalties for non- or insufficient disclosure of interests. REBs are therefore allowed the latitude to craft remedial measures.

The following recommendations may be considered in addressing the above trends or resolving some of the gaps in policy identified in this paper:

- A uniform pan-Canadian approach to regulation may be necessary to clearly delineate the rules applicable to different types of COI. Such rules should address the various COI drivers and strive to provide a comprehensive, proactive, educational tool for all stakeholders.
- The oversight role of the SCOC in providing external accountability needs to be strengthened. The SCOC's role could be extended to monitoring the management of SCN's commercialization portfolio.

- More research is required on the efficacy of managing COI through the funding process, and on whether it might be better to adopt a regulatory approach applicable irrespective of funding, particularly in the context of managing institutional COI.
- Institutional COI policies may need to be strengthened. This may require mirroring the US DHHS approach and the prohibition of financial interests, rather than mere disclosure and divestment.
- The definition of COI in NCE policy should be revised to include detriment to funded research.
- Clear rules should be established allowing REBs to see all financial agreements so they can assess the degree of conflict.

In conclusion, it is important to observe that these reform measures have been framed as issues for consideration. This is necessary given the purpose of this paper, which is to provide relevant background for discussions at the stem cell research ethics workshop. Whether these measures are met with agreement or not is immaterial to this purpose. More importantly, the discussions should situate the debate on COI within the stem cell research context on the drivers identified in this paper, and whatever reform measures are agreed upon, if at all, must clearly respond to the need to protect patient welfare, preserve research integrity and promote public trust in stem cell research.

Ubaka Ogbogu is a Research Associate with the Health Law Institute, Faculty of Law, University of Alberta.

Acknowledgements

I would like to thank Timothy Caulfield, Michael McDonald, Wendy Thiessen, Erin Nelson, Nina Hawkins and the entire HLI research team for their invaluable research support, the Stem Cell Network for financial support, Alethea Adair for the meticulous editorial work, and Omolara Oladipo and Jane Steblecki for reviewing earlier drafts of this paper. I am also grateful to David Magnus and the participants at the “Stem Cells and Research Ethics: Informing Policy” Workshop for reviewing the paper. Finally, special thanks to Gift, my lovely wife, for allowing me to work on this in lieu of a honeymoon.

1. Dennis F. Thompson, “Understanding Financial Conflicts of Interest” (1993) 329 *New England Journal of Medicine* 573 at 573. It has been argued that the term “Conflict of interest” is value-laden and may im-



mediately imply moral or ethical malfeasance, even in the absence of actual conflicts resulting from competing interests. Some have suggested that the term be re-conceptualized as “competing interests” or a “convergence of interests.” See Paddi O’Hara, *Report on an International Conference on Conflict of Interest: Forum for Institutional Review Boards (IRBs)/Research Ethics Boards (REBs) in Canada and the United States (FOCUS) June 4-5, 2004* (Washington DC: National Council on Ethics in Human Research, 2005) [O’Hara]; Mark R. Simmons, “What You Should Know About Conflicts of Interest,” online: <<http://www.facilitatedcontrols.com/fraud-investigation/coiknow.htm>>. Whatever merits there are in this argument is somewhat diminished when one considers that there is usually a hierarchy of interests in the research context, and some primary interests (e.g., patient welfare) should *never need* to compete or converge with some secondary interests (e.g., financial gain). Therefore, the use of the term could serve to prevent behavior or situations that could potentially bring interests into competition.

2. O’Hara, *ibid.*
3. Justin E. Bekelman *et al.*, “Scope and Impact of Financial Conflicts of Interest in Biomedical Research: A Systematic Review” (2003) 289 *Journal of the American Medical Association* 454.
4. See generally Catherine D. DeAngelis, “Conflicts of Interest and the Public Trust” (2000) 284 *Journal of the American Medical Association* 2237; David Korn, “Conflicts of Interest in Biomedical Research” (2000) 284 *Journal of the American Medical Association* 2234.
5. The Olivieri and Healy incidents have a number of common elements. Both were medical researchers at the University of Toronto who experienced negative consequences, including the loss of their jobs, for disclosing adverse information about drugs tested in their research. At the time of the incidents, the drug manufacturers financially supported the University of Toronto through research funds and donations, a situation that led the university to abandon support for the researchers. For a full account of the Olivieri case, see Adrian M. Viens & Julian Savulescu, “Introduction to the Olivieri Symposium” (2004) 30 *J. Med. Ethics* 1; for the Healy story, see Trudo Lemmens, “Leopards in the Temple: Restoring Scientific Integrity to the Commercialized Research Scene” (2004) 32 *J. Law, Med. & Ethics* 641.
6. Arthur Schafer, “Biomedical Conflicts of Interest: A Defence of the Sequestration Thesis – Learning from the Cases of Nancy Olivieri and David Healy” (2004) 30 *Journal of Medical Ethics* 8; Sheldon Krimsky, “A Conflict of Interest” (2003) 179: 2410 *New Scientist* 21.
7. Sheldon Krimsky & L.S. Rothenberg, “Financial Interest and its Disclosure in Scientific Publications” (1998) 280 *Journal of the American Medical Association* 225; Kevin P. Weinfurt *et al.*, “Policies of Academic Medical Centers for Disclosing Financial Conflicts of Interest to Potential Research Participants” (2006) 81 *Academic Medicine* 113; Council on Scientific Affairs & Council on Ethical and Judicial Affairs, “Conflicts of Interest in Medical Center/Industry Research Relationships” (1990) 263 *Journal of the American Medical Association* 2790.
8. See S. Van McCrary *et al.*, “A National Survey of Policies on Disclosure of Conflicts of Interest in Biomedical Research” (2000) 343 *New England Journal of Medicine* 1621.
9. The NCE program is a federal funding initiative managed jointly by Canada’s three main federal research funding agencies, namely the Canadian Institutes of Health Research (CIHR), Natural Sciences and Engineering Research Council (NSERC) and Social Sciences and Humanities Research Council (SSHRC) (jointly referred to as the “Tri-Council” in this paper), in partnership with Industry Canada. Organizations that meet eligibility requirements for NCE program funding receive funds to establish a network for a 7-year funding cycle, up to a maximum of two funding cycles. An industry consortium may also receive funds to administer a network. There are currently 21 networks receiving funding from the NCE program. See *Networks of Centres of Excellence, Program Guide*, (Ottawa: Networks of Centres of Excellence, 2003), online: <<http://www.nce.gc.ca/comp/programguide.pdf>>.
10. *Ibid.*
11. This is one of five background papers commissioned for a stem cell research ethics workshop held in February 2007 in Montreal, Quebec, Canada, as part of the SCN project *Towards the Clinic? Ethical, Legal and Social Issues (ELSI) Relevant to Emerging Stem Cell Therapies*.
12. See e.g. Timothy Caulfield, “The Commercialization of Human Genetics: A Discussion of Issues Relevant to the Canadian Consumer” (1998) 21 *Journal of Consumer Policy* 483.
13. Donald Fisher, Janet Atkinson-Grosjean & Dawn House, “Changes in Academy/Industry/State Rela-



- tions in Canada: The Creation and Development of the Networks of Centres of Excellence” (2001) 39 *Minerva* 299.
14. *Supra* note 9 at 9.
 15. See Timothy Caulfield, “The Commercialization of Human Genetics: Future Policy Concerns” (2003) 15 *Medicina Nei Secoli Arte E Scienza* 55; Timothy Caulfield, “Sustainability and the Balancing of the Health Care and Innovation Agendas: The Commercialization of Genetic Research” (2003) 66 *Sask. L. Rev.* 629 [Caulfield, “Sustainability”].
 16. *Supra* note 9 at 7.
 17. *Supra* note 13 at 300.
 18. Stem Cell Network, *Updated Progress Report and Strategic Plan* (Ottawa: Stem Cell Network, 2005) at B1.
 19. *Ibid.* at B14.
 20. *Ibid.*
 21. See generally *supra* note 15; Roy J. Romanow, *Building on Values: The Future of Health Care in Canada – Final Report* (Saskatoon: Commission on the Future of Health Care in Canada, 2002), online: <http://www.cbc.ca/healthcare/final_report.pdf>.
 22. *Supra* note 3.
 23. *Ibid.* at 463.
 24. David Blumenthal *et al.*, “Data Withholding in Genetics and the other Life Sciences: Prevalences and Predictors” (2006) 81 *Academic Medicine* 137.
 25. *Ibid.* at 145.
 26. Christine Vogeli *et al.*, “Data Withholding and the Next Generation of Scientists: Results of a National Survey” (2006) 81 *Academic Medicine* 128.
 27. Thomas Bodenheimer, “Uneasy Alliance: Clinical Investigators and the Pharmaceutical Industry” (2000) 342 *Health Policy Report* 1539.
 28. *Ibid.*
 29. Henry Thomas Stelfox *et al.*, “Conflict of Interest in the Debate over Calcium-Channel Antagonists” (1998) 338 *New England Journal of Medicine* 101.
 30. Mildred K. Cho & Lisa A. Bero, “The Quality of Drug Studies Published in Symposium Proceedings” (1996) 124 *Annals of Internal Medicine* 485.
 31. Timothy Caulfield, “Popular Media, Biotechnology, and the Cycle of Hype” (2004-5) 5 *Houston J. Health L. & Pol’y* 213 at 219.
 32. *Ibid.*
 33. *Ibid.*
 34. *Ibid.*
 35. Timothy Caulfield, “Stem Cell Patents and Social Controversy: A Speculative View from Canada” (2006) 7 *Medical Law International* 219.
 36. Timothy Caulfield, “Commentary: An Independent Voice?: Conflicts of Interest and Research on Ethical, Legal and Social Issues” (2005) 13: 2-3 *Health L. Rev.* 114 at 115.
 37. Christine R. Critchley, “Public Opinion and Trust in Scientists: The Role of the Research Context and the Perceived Motivation of Stem Cell Researchers” *Public Understanding of Science* [forthcoming 2007].
 38. See Canadian Biotechnology Secretariat, Industry Canada, *A Canada-US Public Opinion Research Study on Emerging Technologies: Report of Findings, March 31, 2005* (Toronto: Decima Research Inc., 2005), online: Government of Canada BioPortal <<http://www.biostrategy.gc.ca/CMFiles/E-Wave13FG49REA-5202005-3052.pdf>> [Canadian Biotechnology Secretariat, *A Canada-US Public Opinion Research Study*]; Canada, *Public Opinion Research into Biotechnology Issues: Third Wave, December 2000* (Ottawa: Pollara Research and Earncliffe Research and Communications, 2000), online: <<http://www.biostrategy.gc.ca/english/view.asp?x=551&all=true>>.
 39. Canadian Biotechnology Secretariat, *A Canada-US Public Opinion Research Study, ibid.*
 40. *Ibid.*
 41. Scott Y. Kim *et al.*, “Potential Research Participants’ Views Regarding Researcher and Institutional Financial Conflicts of Interest” (2004) 30 *Journal of Medical Ethics* 73.
 42. Caulfield “Sustainability,” *supra* note 15 at 636.
 43. *Ibid.*; Timothy Caulfield, “Policy Conflicts: Gene Patents and Health Care in Canada” (2005) 8 *Community Genetics* 223.
 44. Caulfield “Sustainability,” *supra* note 15 at 644.
 45. Marcia Angell, “Is Academic Medicine for Sale?” (2000) 342 *New England Journal of Medicine* 1516.
 46. Donna Shalala, “Protecting Research Subjects – What Must Be Done” (2000) 343 *New England Journal of Medicine* 808.
 47. Lemmens, *supra* note 5.
 48. Mildred K. Cho, Glenn McGee & David Magnus, “Research Conduct: Lessons of the Stem Cell Scandal” (2006) 311 *Science* 614 at 614.
 49. *Supra* note 36 at 115.
 50. O’Hara, *supra* note 1 at 3.
 51. R.S.B.C. 1996, c. 287; R.S.O. 1990, c. M-6; S.N.B. 1999, c. M-7.01.
 52. R.S.A. 2000, c. H-5.



53. *Ibid.* s. 96(1).
54. *Ibid.*
55. S.C. 2004, c. 2.
56. *Ibid.* s. 26(8).
57. See Canadian Institutes of Health Research, *Stem Cell Oversight Committee (SCOC): SCOC Mandate, Membership and Operations*, online: Canadian Institutes of Health Research <<http://www.cihr-irsc.gc.ca/e/15298.html>>.
58. In California, for example, applicable rules allow for relevant expertise on stem cell research agencies and oversight boards, including the California Institute of Regenerative Medicine (CIRM), the agency that funds and monitors stem cell research in California. Experts participating in such boards cannot apply for CIRM grants or be principal investigators on a grant. See e.g. California Institute of Regenerative Medicine, *Conflict of Interest Policy for Members of the Independent Citizens' Oversight Committee*, online: California Institute of Regenerative Medicine <http://www.cirm.ca.gov/policies/pdf/ICOC_Members.pdf>; California Institute of Regenerative Medicine, *Conflict of Interest Policy for Standards Working Group Members*, online: California Institute of Regenerative Medicine <<http://www.cirm.ca.gov/policies/pdf/StdWG.pdf>>. Similarly, UK legislation allows infertility clinicians and scientists involved in hESC research to serve as members of the Human Embryology and Fertilisation Authority (HFEA), the body responsible for overseeing embryo research. However, clinicians and scientists cannot serve as Chairman or Deputy Chairman of the HFEA, and at least half of the HFEA members must be drawn from outside the hESC research and infertility treatment community. UK *Human Embryology and Fertilisation Act*, 1990, c. 37, Schedule 1, s. 4. A recent published study of IVF patients' perceptions of the UK's embryo research regulator, the HFEA, also found that there is "overwhelming support for doctors to be the most important members of the Authority, followed by researchers working in the area." Thérèse Callus, "Patient Perceptions of the Human Fertilisation and Embryology Authority" (2007) 15:1 *Med. L. Rev.* 62 at 76.
59. Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, Social Sciences and Humanities Research Council of Canada, *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans 1998 (with 2000, 2002, 2005 amendments)* (Ottawa: Interagency Secretariat on Research Ethics, 1998), online: <http://www.pre.ethics.gc.ca/english/pdf/TCPS%20October%202005_E.pdf>.
60. *Supra* note 18.
61. *Supra* note 9.
62. *Ibid.* at 14.
63. The author acknowledges that detriment to a researcher or funded research can be construed as detriment to the Network.
64. *Supra* note 9.
65. Canadian Institutes of Health Research, *Updated Guidelines for Human Pluripotent Stem Cell Research* (Ottawa: CIHR, 2006), online: <<http://www.cihr-irsc.gc.ca/e/31488.html>>.
66. *Ibid.* at para. 8.4.1.
67. See *Reibl v. Hughes*, [1980] 2 S.C.R. 880 [*Reibl*]; *Halushka v. University of Saskatchewan* (1965), 52 W.W.R. 608, 52 D.L.R. (2d) 436 (Sask. C.A.) [*Halushka*]; *Weiss v. Solomon*, [1989] R.J.Q. 731, [1989] R.R.A. 3749 (Québec Superior Court) [*Weiss*].
68. *Ibid.*
69. See *Weiss, Halushka*, *supra* note 67.
70. 51 Cal. 3d 120 (1990).
71. *Ibid.* at 130.
72. Moe M. Litman, "Fiduciary Law and For-Profit and Not-For-Profit Health Care" in Timothy A. Caulfield & Barbara von Tigerstrom, eds., *Health Care Reform and the Law in Canada: Meeting the Challenge* (Edmonton: University of Alberta Press, 2002) 85 at 93.
73. *Ibid.* at 86.
74. *Ibid.*; see also *Norberg v. Wynrib*, [1992] 2 S.C.R. 318; *McInerney v. McDonald*, [1992] 2 S.C.R. 138.
75. Joseph B. Clamon, "The Search for a Cure: Combating the Problem of Conflicts of Interest that Currently Plagues Biomedical Research" (2003-2004) 89 *Iowa L. Rev.* 235 at 249.
76. *Ibid.*
77. *Supra* note 72.
78. Moe M. 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.
79. See e.g. *supra* note 72; Trudo Lemmens & Peter A. Singer, "Bioethics for Clinicians: Conflict of Interest in Research, Education and Patient Care" (1998) 159 *Canadian Medical Association Journal* 960.
80. *Supra* note 72.
81. (1988), 65 O.R. (2d) 461 (Ont. Div. Ct.).
82. *Supra* note 72 at 96.
83. Rosario M. Isasi & Bartha M. Knoppers, "Mind the



- Gap: Policy Approaches to Embryonic Stem Cell and Cloning Research in 50 Countries” (2006) 13 Euro. J. Health L. 9.
84. Michael M.E. Johns, Mark Barnes & Patrik S. Florencio, “Restoring Balance to Industry-Academia Relationships in an Era of Institutional Financial Conflicts of Interest: Promoting Research While Maintaining Trust” (2003) 289 Journal of the American Medical Association 741.
 85. Patent and Trademark Law Amendments Act, U.S. Code 35 U.S.C. (1980) § 200-212.
 86. For an account of the incident, see Sheryl Gay Stolberg, “The Biotech Death of Jesse Gelsinger” *The New York Times* (28 November 1999), online: The New York Times <<http://www.nytimes.com/library/magazine/home/19991128mag-stolberg.html>>; Duff Wilson & David Heath, “Uninformed Consent: Patients Never Knew the Full Dangers of Clinical Trials on Which they Staked their Lives” *The Seattle Times* (11 March 2001), online: The Seattle Times <http://seattletimes.nwsourc.com/uninformed_consent/bloodcancer/story1.html>.
 87. See e.g. Shalala, *supra* note 46.
 88. *Supra* note 8.
 89. *Ibid.*
 90. See Phil B. Fontanarosa, Annette Flanagin & Catherine D. DeAngelis, “Reporting Conflicts of Interest, Financial Aspects of Research, and Role of Sponsors in Funded Studies” (2005) 294 Journal of the American Medical Association 110; Annette Flanagin, Phil B. Fontanarosa & Catherine D. DeAngelis, “Update on JAMA’s Conflict of Interest Policy” (2006) 296 Journal of the American Medical Association 220; International Committee of Medical Journal Editors, *Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication* (February 2006), online: <<http://www.icmje.org/>>.
 91. Alan Bernstein, “New Ethical Requirements at the NIH: Implications for CIHR and Canada” (2005) 173 Canadian Medical Association Journal 353.
 92. *Supplemental Standards of Ethical Conduct for Employees of the Department of Health and Human Services*, 5 C.F.R. s. 5501 (2006) [*Supplemental Standards of Ethical Conduct*]; Ted Agres, “NIH Bans All Consulting” *The Scientist* (2 February 2005), online: The Scientist <<http://www.the-scientist.com/article/display/22586/>>.
 93. *Supplemental Standards of Ethical Conduct*, *ibid.* at s. 5501.109(10)(1).
 94. See David Korn & Susan H. Ehringhaus, “NIH Conflicts Rules are not Right for Universities” (2005) 434 Nature 821; *supra* note 91.
 95. World Medical Association, *Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects (with amendments)* (Ferney-Voltaire, France: World Medical Association, 1964) at para. 22, online: World Medical Association <<http://www.wma.net/e/policy/b3.htm>>.
 96. *Ibid.* at para 27.
 97. *Ibid.*
 98. See Council for International Organizations of Medical Sciences, *International Ethical Guidelines for Biomedical Research Involving Human Subjects* (Geneva: Council for International Organizations of Medical Sciences, 2002), online: Council for International Organizations of Medical Sciences <http://www.cioms.ch/frame_guidelines_nov_2002.htm>.
 99. International Society for Stem Cell Research, *Guidelines for the Conduct of Human Embryonic Stem Cell Research* (Illinois: International Society for Stem Cell Research, 2006), online: International Society for Stem Cell Research <<http://www.isscr.org/guidelines/ISSCRhESCguidelines2006.pdf>>.
 100. Organisation for Economic Co-operation and Development, *Guidelines for the Licensing of Genetic Inventions* (Paris: Organisation for Economic Co-operation and Development, 2006), online: Organisation for Economic Co-operation and Development <www.oecd.org/dataoecd/39/38/36198812.pdf>.
 101. HumGen International Database, online: Centre de Recherche en Droit Public <<http://www.humgen.umontreal.ca/int/>>.

