

# The Governance of Health Research Involving Human Subjects (HRIHS)

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Ce document est également disponible en français sous le titre "Gouvernance de la recherche en santé avec des sujets humains".



# PREFACE AND ACKNOWLEDGEMENTS

The Law Commission of Canada commissioned this study of the governance of health research involving humans in late 1998. For the past eighteen months, the research team has worked on producing the first comprehensive and in-depth study of Canadian governance for health research involving human subjects.

Most of the members of the research team have been intimately involved in the area of research involving humans not only as academics studying the area, but also practically in terms of policy-making and membership on Research Ethics Boards. Looking at this area through the lens of governance has provided for us new ways of understanding the moral and legal complexities of ethical research involving human subjects. In particular, it has allowed us to examine and reflect upon the integrity and effectiveness of Canadian arrangements for the promotion of research and the protection of human subjects. While we all knew beforehand that research ethics was not simply a matter of codes and policy statements, we were surprised to see how substantial the gaps were between the ideals expressed in policy and the ground arrangements for accountability, effectiveness and other criteria for good governance.

Serious reform is clearly in order. However in order for serious reform to take place, it is essential that policy discussions be informed by ethically sensitive and empirically grounded research on the governance of this area. For far too long, debate in this area has been either abstract and *a priori* or unsystematic and anecdotal. We hope that we have made a contribution to a much better informed and focussed discussion of this complex and controversial area.

There are many people to thank for their support and contributions to this study. First, on behalf of the research team, I wish to express our appreciation for the support of the Law Commission of Canada for this study. The Commission's willingness to look at familiar topics in unfamiliar ways was exemplified in their commissioning of this study of the governance of health research involving human subjects. We wish to thank the President of the LCC, Roderick Macdonald, and one of the Commissioners, Natalie Des Rosiers, for their personal participation in the study panel that advised the research team and the Commission. We especially wish to thank the Commission's Director of Research, Susan Zimmerman, for her unfailing support, enthusiasm and patience.

We wish to express our appreciation to the study panel whose members are listed in Appendix G-3. Their expert advice was very helpful. We appreciate their willingness to take time from their busy schedules to read draft sections of the study and to attend two meetings with members of the research team.

We are very appreciative of all those who participated in interviews. These members of REBs and national groups involved in the governance of health research involving humans are the unsung heroes of the research ethics enterprise. Their willingness to share their vast experience with us and, through this project, with their fellow citizens was very generous. We hope that an important result of this project will be to improve their ability to carry out their significant roles.

As Principal Investigator, I wish to personally express my gratitude to members of the research team. Sometimes coaches talk about their “dream team.” For this project, the members constituted my “dream team” – in terms of expertise, industry and focus.

I also wish to express my gratitude to the graduate research assistants who have worked on this project: Chris Macdonald who helped early in the project on research, Sangeeta Mishra who provided research and copy-editing, and particularly Bryn Williams-Jones for his invaluable assistance in research, copy-editing and formatting. And finally, on a personal note, I express my gratitude to Maria, my wife of thirty-five years and companion in everything.

Michael McDonald  
Principal Investigator  
May 2000

# EXECUTIVE SUMMARY

This is a multi-authored study of the governance of health research involving human subjects (HRIHS).<sup>1</sup> Health research “includes biomedical research as well as other types of research relevant to health, e.g., sociological studies of health, health law and bioethics.” The Law Commission of Canada (Contract #98-09-01) commissioned this study under its governance relationships theme. The Commission selected HRIHS as an example of “an area of activity that highlights the diversity of principles and mechanisms or processes that may be employed in the regulation of human conduct.”<sup>2</sup>

Governance is a complex notion but can be summarised as being: “... about the processes by which human organizations, whether private, public or civic, steer themselves.”<sup>3</sup> Governance issues also arise in regard to the interactions of the many organizations and groups involved in HRIHS: public and private research institutions, research sponsors, research regulators, researchers, research subjects and the general public. An area of special concern for governance is the management of “agency risk,” i.e., the tendency of agents to pursue their own agendas rather than those mandated by or for their organizations. Thus, an important issue is whether current governance processes, incentives and structures for HRIHS function to advance the goals of research at the expense of the protection of human subjects.

The particular focus of this study is the *ethical* governance of HRIHS. The ethics of HRIHS has three main objectives:

1. The **promotion** of socially beneficial research;
2. **Respect** for the dignity and rights of research subjects; and
3. As an overarching aim, the maintenance of **trust** between the research community and society as a whole.

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<sup>1</sup> Human subjects are also referred to as “research subjects” or “research participants”.

<sup>2</sup> From the LCC’s Request for Proposals (98-09-01)

<sup>3</sup> University of Ottawa Centre on Governance <[http://www.governance.uottawa.ca/english/overview/o\\_defi.htm](http://www.governance.uottawa.ca/english/overview/o_defi.htm)>

# I. RESEARCH QUESTIONS

This study addresses two major questions:

1. How is Canadian HRIHS governed in terms of “ensuring ethical research processes?”<sup>4</sup>
2. How effective are these governance relationships in terms of “consistently achieving effective governance of ethical research?”

## A. Question One

Section B of the study provides a broad overview of current Canadian governance mechanisms for HRIHS. In Section C, the focus is on central aspects of the complex multi-layered legal arrangements for HRIHS. Bernard Dickens argues that in Canada “law applies almost inadvertently to biomedical research.” The result is that a complex and uncoordinated mix of federal criminal and provincial civil law governs HRIHS. Bartha Knoppers says that while “biomedical research is governed by law, ethics, and emerging professional norms, (t)he increasingly international and multi-centred nature of such research creates concomitant levels of complexity, and of contradiction if not confusion.”

Section D contains a series of subject specific studies that probe important areas or aspects of HRIHS. Each of the papers in this section shows very significant gaps in the current governance régime for HRIHS. In Section D-1, Michael Burgess and Fern Brunger explore the ethical complexities of research involving groups or collectivities – issues “(that) are particularly vexing because they cannot be managed through individual informed consent...”. They propose “a different ethical mechanism than group informed consent,” namely, “collective acceptability” that takes into account “different types of risk for different types of groups.” In Section D-2, Jean Joly examines the important, but often ignored area, of public health research; he concludes, “In the end, in public health research, no one knows who governs what.” In Section D-3, T. Douglas Kinsella raises serious questions about the adequacy of professional oversight for human subjects research conducted outside of medical faculties. He proposes as a model the Research Ethics Board (REB) established by the Alberta College of Physicians and Surgeons.

## B. Question Two

Question (2) involves an assessment of how well Canada's current governance relationships "consistently achieve effective governance of ethical research." This is mainly addressed in Section E through a qualitative analysis of the in-depth interviews conducted with members of REBs at five Canadian universities that are heavily engaged in HRIHS and with representatives of national organizations who play important governance roles in the area. In Section E-1, Brenda Beagan analyses the results of the more than fifty interviews conducted in English. In Section E-2, Marcelo Otero offers an analysis of the several interviews conducted in French. Beagan notes in her conclusions, "Foremost, while there appears to be strong consensus about the goals of research ethics review, it is also amply apparent that most members of the research ethics community do not have strong empirical bases for believing they are dealing with ethics review effectively."

## II. MAJOR FINDINGS

### A. The Complexity of Canadian Governance Arrangements for HRIHS Poses Major Ethical Challenges

Canada's complex, decentralised, multi-sourced arrangements for governing HRIHS pose major ethical challenges in terms of consistency, transparency and accountability. In part, this is due to the complexity of health research itself and to the complicated ways in which socially constructed norms around scholarship and ethics affect the research process. Moreover, the research process is very much affected by four pervasive international factors:

- Rapid scientific and technological innovation and advances
- Multiple disciplinary and interdisciplinary research modalities
- Commercialization and privatization
- Globalization and harmonization

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<sup>4</sup> *Ibid.*

In addition, factors specific to Canada significantly shape the context of governance for HRIHS. These include the process of creating a new Tri-Council research policy for HRIHS (the *Tri-Council Policy Statement on Research Involving Human Subjects*), proposed federal regulatory changes for clinical trials, deregulation and the complex legal arrangements discussed above.

## B. Ethical Tunnel Vision

When we compare the broad ethical objectives of HRIHS (the promotion of beneficial research, the protection of human subjects and the generation of trust) with what actually takes place, we see a narrowing of concerns that results in a kind of ethical tunnel vision. Sight is lost of central ethical objectives and attention is given to more narrowly bureaucratic concerns involving REB processing of research project proposals. In turn, REBs mainly focus on the approval of consent forms. The result is that the REB approval and informed consent processes bear far more moral weight than they can possibly sustain.

## C. Missing Links: Evidence, Effectiveness and Learning

Our current system places primary responsibility for oversight on the REB. But the REB has limited knowledge of what happens after it approves a research protocol. Rarely is there independent monitoring of the conduct of research. Where there is such monitoring, it is more likely to be by foreign research sponsors than by research institutions or domestic research sponsors (other than pharmaceutical sponsors of research). Most Canadian research institutions and sponsors have a far better idea of what happens to research funds than what happens to research subjects. Research institutions are on the whole reactive rather than proactive with regard to the concerns and interests of research subjects.



### Missing Links

1. Good governance requires virtuous learning loops so all the actors can learn from their successes and failures.
2. Virtuous learning loops should be based on evidence-based standards.
3. Thus, there is an urgent need for research on what happens to human subjects in research.
4. Such research requires resources from sponsors and research institutions; it also requires a commitment to use the research results in improving governance.
5. Failure to establish evidence-based learning loops represents a serious failure in governance for which research institutions, sponsors and standard setters should be held accountable.

We also saw no evidence at the institutional or sponsor levels of systematic and comparative information gathering, assessment and dissemination across the broad range of research they house or sponsor. This means that at best there is anecdotal information about research conduct in regard to harms and benefits for subjects and for third parties. While there is a great deal of emphasis on consent and consent forms, there are no processes in place for determining whether ethical criteria for consent are being met either on a project specific basis or on a systemic basis.

What is lacking are “**virtuous learning loops**”– that is learning loops that lead to improved ethical performance. Or in more familiar terms, missing are the information gathering, learning and accountability processes necessary for quality assurance (QA) and quality improvement (QI).

## D. Missing Subjects

Research subjects have no mandated role in the governance of HRIHS. Subjects appear in the administrative process as signatories on consent forms and occasionally as complainants. We see profound differences in practice and principle between a system in which the stress is on accountability *for* the treatment of certain people and one that adds a significant degree of accountability *to* those people. Two missing “accountabilities *to*” subjects are prominent. First in the conduct of research, our current system for dealing with actual and potential concerns of

subjects is entirely too passive and reactive. Second there is a lack of representative participation in governance on the part of research subjects. At the moment we have a system of governance that is, so to speak, almost completely producer-driven. A more consumer-driven model has much to offer a system of governance. It would be a smarter and more robust system in terms of maintaining and enhancing public trust.

## E. Involvement, Independence and Innovation

To address the many gaps in accountability and effectiveness of governance for HRIHS, we see the need for “three I’s” -- a mixture of (1) greater **involvement** on the part of major actors; (2) more **independence** in specific areas for ethical oversight, monitoring and standard-setting; and (3) much more **innovation** in terms of experimentation with alternative forms of governance and much more research on the effects of research on human subjects.

### 1. Involvement

There are many areas where major actors including research subjects ought to be much more involved in the governance of HRIHS. Research sponsors, research institutions and individual researchers should take greater ownership of the larger responsibilities for ethical research. Virtuous learning loops are needed within the institutions that house and sponsor health research. For example, research institutions like universities, health centres and pharmaceutical companies should carefully assess their own research activities for areas in which there are significant gaps in knowledge about what happens to research subjects. The education and training of researchers on relevant issues in research ethics should be a high priority but such an educational effort must have enough intellectual credibility to engage researchers.

**Creating a research ethics culture** is one of our most important recommendations, but one of the hardest to implement. It is an area that readily invites window-dressing and stalling. Yet it is only through continuous and concerted activities of research communities, research institutions, research sponsors and regulators that research ethics will become a central part of the culture of research. Both private and public sector research sponsors should encourage innovative teaching and research on ethical issues in HRIHS. Academic leaders should be playing a leadership role in putting ethics on their particular research community’s agenda.

Centres for bioethics and health law are important resources that could be utilised to much greater advantage by research institutions.

There also needs to be greater *inter*-institutional involvement of the many organizations that have a stake in HRIHS. For example, we see the need for better communication between research institutions and sponsors about appropriate accountabilities in HRIHS that go well beyond the REB ethics approval process by including quality assurance and quality improvement. It is essential to design accountability relationships that are responsive, effective and not overly bureaucratic. To initiate inter-institutional initiatives, a number of bodies need to work together. This includes organizations such as CIHR, private sector research sponsors, the National Council on the Ethics of Human Research (NCEHR), health charities, deans of medicine and other health related faculties and, related academic groups.

**Research subjects** have had little involvement in the governance of HRIHS. This contrasts markedly with the significant and beneficial role that animal welfare advocates play in the governance of research involving animals. People who have had experience as research subjects, especially in higher risk areas of health research (e.g., cancer therapy trials) would likely bring an important new perspective to the governance of this area, e.g., as members of REBs, NCEHR, ethics secretariats for research sponsors and ethics advisory groups for directors of research. Representatives of human research subjects should be sought from groups whose members are frequently studied in health research involving humans, e.g., from the communities of those living with AIDS, cancer survivors, ethnocultural groups and disability groups.

## 2. Independence

Counter-balancing our recommendation for greater involvement in HRIHS by all parties is our recommendation for greater *independence* in key areas where it is essential to avoid conflict of interest or its appearance. This study shows that those with vested interests in its outcomes – researchers, research institutions and research sponsors, dominate the research process and its governance. While a strong interest in generating valuable knowledge through research is a highly laudable interest, current governance arrangements are such that the governance process appears heavily weighted in favour of the interests of the research community. It is not, we think, enough for researchers, research institutions and research sponsors to ask research subjects and the general public to blindly trust that all is well. In this respect, we agree with the U.S. OIG recommendation for “insulating IRBs from conflicts that can

compromise their mission in protecting human subjects” by adopting a **“trust but verify approach”**.<sup>5</sup>

To be frank, we see the pressures on the independence of Canadian REBs as much greater in Canada than the US. In Canada we lack the strong counterbalance provided in the US by independent federal governance of research ethics approval and by the significant level of research support provided by NIH and other US agencies. Moreover, American institutions of higher learning – especially the most highly productive research institutions – enjoy much greater public and private support than do their Canadian counterparts. This makes Canadian institutions more vulnerable to the need to compete for scarce research funding.

Given this vulnerability, Canadian research institutions, sponsors, federal and provincial governments, and researchers should take greater steps than their U.S. and foreign counterparts to insulate REBs and parallel bodies (e.g., data safety monitoring boards) from pressures that potentially compromise their independence. For instance, it is crucial for substantive reasons and for the sake of appearances that REBs not report to or be appointed by offices of research.

There is also a basic need for more resources for REBs. In summing up the results of interviews, Beagan says:

The need for an infusion of resources cannot be overstated. At the various sites across the country the story is the same: overburdened REB members are stretched to the breaking point. These are well-intentioned volunteers doing the best they can to address extraordinarily complex issues under severe time constraints with severely limited resources. As the work becomes increasingly complicated with globalization, technology and commercialization, REBs are struggling to find committee chairs or even members.

At the national level, we would make a parallel recommendation for greater resources and status. The National Council on the Ethics of Human Research (NCEHR) should enjoy the same status as CCAC and a proportionately equivalent degree of support. We believe that the Canadian public would be distressed to learn that the current situation is one in which national oversight of research involving animals is far more effective, better resourced and independent than that for research involving humans. The Tri-Council group and the other sponsors of NCEHR do not do themselves, research sponsors generally, research institutions or the

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<sup>5</sup> OIG Office of the Inspector-General, *Institutional Review Boards: A Time for Reform* (Department of Health and Human Services (U.S.), June 1998) at 17.

research community any favours in maintaining their current proprietary and managerial relationship to NCEHR and in regard to policy setting, interpretation and enforcement. To maintain and deserve public trust, it is essential that there be an appropriate distance between the arms of government that promote research and those that protect human subjects. Moreover, the arm that protects human subjects must be in a position to verify the effectiveness of its efforts.

If, however, NCEHR is to be a credible and knowledgeable national oversight body for REBs, then it will need a membership that is representative of and knowledgeable about its stakeholders' interests: sponsors, research institutions, researchers, and, most crucially, research subjects. NCEHR also needs a firm base of funding for an enhanced professional and support staff. Ideally it should enjoy a broad base of financial support from both public and private research sponsors. There also should be a clear and effective mechanism for periodic review of NCEHR's effectiveness and direction. Like CCAC, NCEHR faces the challenge of working as a standard setter with limited powers of enforcement due in large part to the complex constitutional division of powers in Canada. So it will have to lead largely by persuasion, public advocacy and reputation.

### 3. Innovation

Under the heading of **innovation** we include both experimentation and research. Both are needed to fill gaps in knowledge, e.g., on appropriate standards for performance-focussed review. There is an urgent need for empirically informed and ethically sensitive research on the effects of research on human subjects as well as on the effectiveness of governance procedures. There is little point in experimentation (e.g., in different forms of monitoring) without careful research-based assessments of processes and results. Likewise research on the governance of HRIHS without experimentation is unlikely to provide a sufficiently wide range of plausible policy options – especially given the general trend towards devolution in regulation.

There is also an urgent need for well-grounded research on the tensions between having standards of performance, monitoring, accreditation and processes that are sensitive to the needs, concerns and rights of research subjects and those that stimulate and facilitate research. Insofar as there are tensions between the promotion of beneficial research and the protection of human subjects, these tensions need to be identified, studied and addressed. For too long in this country, these fundamental questions have been debated in an *a priori* manner or simply by resort to anecdotal evidence.

## F. General Conclusion

We urge a return to the fundamental concerns that motivate health research involving human subjects – the desire for socially beneficial research and the concern for the protection of human subjects. It is our conviction that these cannot be posed as an “either-or” choice. It is a “both-and” choice. Our society needs both socially beneficial research and the protection of human subjects. Without these two together, there is the serious risk of undermining the fundamental trust relations underwriting health research – the public’s trust in researchers, research institutions and sponsors and more specifically, the trust of research subjects whose continuing participation in research is essential not only to health research but also to health care. Governance is about maintaining, enhancing and, where necessary, restoring trust in transparent, accountable and effective ways. It is around this goal of trust that this study of governance for HRIHS has been oriented.

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by Delphine Roigt

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# SECTION A-1

## INTRODUCTION AND OVERVIEW

Michael McDonald, Principal Investigator

The subject of this study is the governance of health research involving human subjects. “Human subjects” are also commonly known as “research subjects” or “research participants.” “Health research” includes but is not limited to biomedical research and includes other types of research relevant to health, e.g., sociological studies of health, health law and bioethics. The abbreviation HRIHS is used to designate “health research involving human subjects”. “Governance” is a complex notion that will be explored in detail below but can be summarised as being: “... about the processes by which human organizations, whether private, public or civic, steer themselves.”<sup>6</sup>

### I. AN OVERVIEW OF THE STUDY

The study is divided into five main sections followed by conclusions.

In **Section A** an overview of the study is provided with a detailed explanation of the origins of the study, methodologies used and its scope and limits.

**Section B** provides an overview of the main aspects of the study: governance (B-1), the health research process (B-2), and the current context of health research involving human subjects (B-3). Section B-2 is especially recommended for those who are unfamiliar with the various procedures and processes used in the initiation, approval, conduct and completion of health research involving human subjects. Michael McDonald, the study’s Principal Investigator, wrote this section.

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<sup>6</sup> University of Ottawa Centre on Governance. [http://www.governance.uottawa.ca/english/overview/o\\_defi.htm](http://www.governance.uottawa.ca/english/overview/o_defi.htm)

**Section C** involves an examination of current legal issues relevant to HRIHS. It begins in Section C-1 with Bernard Dickens' wide-ranging discussion of important issues arising in both federal and provincial law with respect to HRIHS. In Section C-2, Bartha Knoppers considers the complexities posed by the complex interweave of international, federal, provincial and professional norms with respect to two areas central to the ethical treatment of research subjects, namely consent and confidentiality.

**Section D** involves a series of papers designed to probe important areas or aspects of HRIHS. Each of the papers in this section shows very significant gaps in the governance regime for HRIHS. The section begins with an article (Section D-1) by Michael Burgess and Fern Brunger exploring the ethical complexities of research involving groups or collectivities. As noted in Section B-3, the ethics of research involving collectivities has been an especially contentious issue in Canada. The Burgess and Brunger article offers a useful analytical framework and case study for exploring and, perhaps, removing some of the contentiousness from this area. In Section D-2, Jean Joly's paper centres on the important, but often ignored area, of public health research. In Section D-3, T. Douglas Kinsella raises serious questions about the adequacy of professional oversight for HRIHS using the case of the Canadian medical profession as an example.

**Section E** has two papers based on extensive in-depth interviews conducted in person at multiple sites across Canada. A primary concern in these interviews was the effectiveness of the Canadian system of governance for HRIHS as seen by experts in the area – members of Research Ethics Boards (REBs) and representatives of national organizations that play important governance roles in HRIHS. In Section E-1, Brenda Beagan analyses the results of the more than fifty interviews conducted in English. In Section E-2, Marcelo Otero offers an analysis of the several interviews conducted in French.

In **Section F** Michael McDonald presents the research team's considered conclusions. These point to pervasive and fundamental weaknesses in the Canadian system of governance for HRIHS. The weaknesses identified are structural and not personal. These shortcomings include: conflicting incentive structures; lack of co-ordination and cooperation amongst the many institutions with governance responsibilities; major deficiencies in accountability and transparency and, bureaucratization and over-reliance on inadequate mechanisms. These are weaknesses we identified despite the evident good will and hard work of those involved in the

administration of governance for HRIHS in Canada. A number of proposals, some very concrete and specific and others more abstract and general, are made for improvement of the system.

**General appendices** following the study include a reference article on various legal norms (G-1), a list of abbreviations (G-2), members of the Study Panel (G-3) that assisted our work and biographical statements (G-4) from members of the research team.

## II. AUDIENCES FOR THIS STUDY

We recognise that there are many audiences for this report with different interests. Some, for example, will read this report with a strong health research orientation. These include those who are involved in or affected by the governance of this area, e.g., members of Research Ethics Boards (REB), research administrators, sponsors of research and research participants. Other readers' primary interest will be in the ethics of research involving humans, e.g., bioethicists and specialists in health law. Some will be mainly concerned with practical and theoretical issues regarding governance. Other readers will have more specialized concerns with various topics that are touched upon by this report, e.g., professional self-regulation, public health and research involving collectivities.

We very much hope this study will be of interest to those with governance responsibilities for research involving human subjects generally and health research involving human subjects specifically. We also believe that this report will be of interest to those with oversight responsibilities – such as, federal and provincial auditors general, freedom of information and privacy commissioners and ministers of health. Since some of the principal observations and lessons are general, we also think that the study should be of interest to those with governance responsibilities in HRIHS outside Canada.

Needless to say, we cannot address every concern from each of these diverse perspectives. Nonetheless, we believe that this study will have been successful if it contributes to a better understanding of the governance of research involving human subjects. Our aim has not been to have the final word on this complex and controversial area rather, we wish to contribute to a more informed and inclusive dialogue – a dialogue that includes research participants and the general public as well as members of the research community (researchers, research administrators and research sponsors).

### III. TERMS OF REFERENCE FOR THIS STUDY

#### A. The Law Commission's Request for Proposals

In September 1998, the Law Commission of Canada (LCC) issued a request for proposals (RFP Contract #98-09-1) under its governance relationships research theme. Governance relationships are one of the LCC's "four broad research themes: personal relationships, social relationships, governance relationships and economic relationships."<sup>7</sup> The RFP was framed in terms of "three interrelated enquiries":

- What different principles of social ordering are currently deployed in Canada to structure governance and what are their various applications and limitations?
- What conceptions of law, what types of legal instruments, and what kinds of institutions are best suited to empowering human beings to govern themselves?
- How can competing understandings of governance through law held by different groups in society be reconciled, and where appropriate, be legitimated?<sup>8</sup>

The first is descriptive -- what is and could be the case? The second and third are normative – how can the ideal of self-governance be best achieved in a pluralistic society? Our study in content and method are both descriptive and normative.

In the RFP, the LCC explained its selection of research involving human subjects as an area for governance study:

The Commission wishes to examine an area of activity that highlights the diversity of principles and mechanisms or processes that may be employed in the regulation of human conduct. The Commission has selected the subject of research involving humans to illuminate this aspect of its research on governance relationships because it operates at many different layers....

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<sup>7</sup> Law Commission of Canada, LCC *Request for Proposals: Contract # 98-09-01; Governance Relationships* (Ottawa: Law Commission of Canada, September 9, 1998).

<sup>8</sup> *Ibid.*

## B. Focus on Ethical Research Processes

In terms of ‘scope of work,’ the Commission asked for a study “centred on research involving humans, with a focus on biomedical research.” There was a specific request for the identification of “different processes that have been **attempted so far to ensure ethical research processes**” over the life of research projects from origins to completion (our emphasis added). The RFP required additionally an examination and comparison of mechanisms at the “local, regional and national levels” with a view to commenting on “**whether they achieve or are capable of achieving consistently effective governance of ethical research**” (our emphasis added).

Accordingly we would emphasise that the benchmark we have for good governance issues in this report is the promotion of **ethical conduct** with respect to the treatment of humans involved in research. To put this in another way, our study is *not* primarily designed as a study of the political, economic, social or managerial aspects of research involving humans. Rather we try to take such factors into account in seeing how they relate to “effective governance of ethical research.” In this, we take a view of ethics that is basic in current ethical theory and applied ethics work. This view was well-expressed by the renowned Canadian moral theorist Thomas Hurka in a book on the ethics of global warming:

An ethical judgement about climate policy is not just one judgement among many, to be weighed against economic, political, and other judgements in deciding how, all things considered, to act. It is itself an all-things-considered judgement, which takes account of economic and other factors. If a climate policy is right, it is simply right; if it is ethically wrong, it is wrong period.<sup>9</sup>

Although ethical judgements should be “all-things-considered” or integrative judgements, it would be naïve to think that those who specialize in the study of ethical theories and practices should have the final word on ethically controversial matters. Instead, we would suggest that what is needed are ethical judgements integrating relevant factors – economic, legal, social, environmental, etc. A matter of central concern for the governance of this area is who should make such decisions and in what circumstances with respect to the ethical conduct of research involving human subjects.

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<sup>9</sup> T. Hurka, “Ethical Principles” in H. Coward & T. Hurka, eds., *Ethics and Climate Change: The Greenhouse Effect* (Waterloo, Ontario: Wilfrid Laurier University Press, 1993) at 23

## IV. OUR STUDY

In response to the Commission's request for proposals, Michael McDonald formed a twelve-member research team with expertise in three overlapping areas: ethics, law and the social sciences. Team members were chosen based on their practical experience in terms of policy formation and policy implementation in the area of research involving humans, e.g., in the creation of international, national and provincial policies and laws and, as chairs and members of research ethics boards or as members of bodies charged with oversight in these areas.<sup>10</sup>

Our study is unique in three respects. First, while there has been a considerable amount of work on the ethics and law of human subjects research, there have been few previous studies on the governance of such research. Second, the main governance studies in this area have primarily focussed on ethics approval processes and the role of ethics review boards -- REBs in Canada, Institutional Review Boards (IRBs) in the U.S., Institutional Ethics Committees (IECs) in Australia, etc. -- or national oversight bodies.<sup>11</sup> Third, the focus of our study is on Canada. We are of course indebted to a number of previous studies that have illuminated various areas of concern. In particular, we mention the 1995 NCBHR study of biomedical REBs in Canadian universities with medical faculties, Parizeau's 1999 report on Quebec REBs, and the recent U.S. studies on the functioning of U.S. IRBs.<sup>12</sup> We also point out the Ottawa governance study of NCEHR that was released in March 2000 just as our study was being completed.<sup>13</sup>

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<sup>10</sup> See Appendix F-4 for the research team members' biographies.

<sup>11</sup> See for example Law Reform Commission of Canada. LRC, *Toward a Canadian Advisory Council on Biomedical Ethics* (Ottawa: Law Reform Commission of Canada, 1990).

<sup>12</sup> NCBHR, "Protecting and Promoting the Human Research Subject: A Review of the Function of Research Ethics Boards in Canadian Faculties of Medicine" (1995) 6/1 *NCBHR Communique* 32. and OIG Office of the Inspector-General, *Institutional Review Boards: A Time for Reform* (Department of Health and Human Services (U.S.), June 1998).

<sup>13</sup> Centre on Governance Ottawa, *Governance of the Ethical Process for Research Involving Humans* (Ottawa: Centre on Governance, University of Ottawa, March 15, 2000).

## A. Research Questions

In our proposal to the Commission, we identified two issues as central:

1. How is Canadian health research involving humans governed? To address this question, we will identify the processes and groups involved in governance relationships and the bases of their normative relationships (public or private law, professional codes of ethics, guidelines, contractual arrangements, etc.).
2. How effective are these governance relationships for achieving their stated ends? To address this question we propose on-site interviews and an examination of the issues that arise in the multiple governance relationships identified in response to question one.

To address the first research question, we drew on many sources. We looked at the law and judicial precedents internationally, federally and provincially whether directly intended to regulate research or originally intended for other purposes (e.g., freedom of information and privacy acts). We considered relevant Canadian policies (e.g., various guidelines and policy statements of federal research councils) and international policies (e.g., the *International Convention on Harmonisation Guideline for Good Clinical Practice*<sup>14</sup>). Professional standards were another area of concern. In addition, we drew on bioethics and health law literature, our collective experiences in making and applying policy in this area, as well as the interviews conducted for this study.

### 1. First research question: How is HRIHS governed?

As might be expected in such a complex situation, we were better able to explore some areas (e.g., HRIHS under university and hospital auspices) than other areas (e.g., research in private sector organisations). We have indicated areas in which we think further research is urgently needed. Even in better-known areas, there are often considerable differences in practices and standards. Sometimes standards are overlapping and reinforcing yet in other instances they run at cross-purposes and conflict. See for example, Knoppers' paper in Section C-2 on the complexity and confusion of standards applicable in Quebec and Joly's analysis in Section E-2 of public health research. As well, there are significant gaps in standards and

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<sup>14</sup> Also published ICH Topic E6 Guideline for Good Clinical Practice by the European Agency for the Evaluation of Medical Products, Human Medicines Evaluation Unit, ICH Technical Coordination, Step 4 Consolidated Guideline 1.5.96. International Conference on Harmonisation of Technical Requirements for the Registration of Pharmaceuticals for Human Use, *ICH Good Clinical Practice: Consolidated Guidelines, ICH Harmonised Tripartite Guideline* (Ottawa, Ontario: Minister of Health, 1997).

processes; thus, Kinsella in Section D-3 indicates the gaps in professional oversight of research involving humans conducted by professionals in their own offices. Moreover, there are areas where the question of whether to have standards at all is a matter of considerable debate, e.g. whether or not research involving collectivities should be regulated, a concern that Burgess and Brunger address in Section D-1. So our answer to the first research question is complex and multi-faceted.

## 2. Second research question: Effectiveness

Addressing the second question was quite difficult for several reasons.

First, to determine “effectiveness,” one has to determine “effective for what purposes.” Since there are multiple actors with multiple purposes involved in HRIHS, it is unlikely that there would be unanimous agreement about whether current governance arrangements are effective. Our approach here has been to try to identify principal groups of actors and their, albeit sometimes conflicting, goals. As in other areas of human affairs, there are often tensions between official or express goals presented in policy and the actual but tacit objectives expressed in practice.

Second, and closely allied to the first point, a major conclusion of this report is that Canadian governance processes for HRIHS are complex and do not, on an inter-institutional or inter-organisational basis, form a single integrated system. Location matters. Depending on where or under whose auspices HRIHS is conducted governance may vary considerably. For example, the same research conducted by physician-researchers in a university setting would have quite a different oversight than if they had conducted it in their own clinic. Even in institutions of the same type, there may be different standards used to assess the ethics of research. Thus, some universities mainly follow the *Tri-Council Policy Statement on the Ethical Conduct of Research Involving Humans* (TCPS) where others now assess a substantial amount of research according to the *Good Clinical Practice Guideline* (GCP) established as part of the International Convention on Harmonization (ICH) process. Moreover, oversight practices vary from one institution to another, e.g., with respect to monitoring research in progress.

Third, our concern with effectiveness was directed at the ethical conduct of HRIHS. But ethical goals and processes are sometimes in dispute. Even where there is a consensus, there may be profound conflicts over appropriate means of governance.



Fourth, as we shall explain shortly, the governance of RIHS generally (and not just with respect to health research) is in considerable transition. This is in part due to major changes in the practices and environment of HRIHS. However, it also has to do with changes in governance arrangements both in Canada and elsewhere. Judging effectiveness in a period of change is like aiming at a rapidly moving target – or more aptly a set of different targets.

The net result was that our research and findings on question two effectiveness are time-specific, tentative and context sensitive.

## B. Scope and Limits

Our study is directed specifically to Canada although for purposes of comparison we take into account governance practices in other countries. We are interested especially in how Canadian governance arrangements promote the *ethical* conduct of research involving humans. This primary focus on ethics has an important effect on the scope and limits of this report. We can envision and would recommend studies of this area from other perspectives, e.g., a study of the economics and politics of HRIHS.

We have confined our study of governance specifically to *health* research involving humans. Of course, research in this area has to be situated in three larger contexts. First, we considered the factors that shape research generally today regardless of whether or not it involves human subjects. *Inter alia*, we had to locate research involving human subjects in this larger research context. For example, a significant amount of biomedical research involving human subjects is supposed to be preceded by research on animals, cells or computer models. The second context is that of research involving human subjects *per se*. Research subjects are used in many non-health related areas of research, e.g., historical research, experimental psychology and economic research. This context is important not only because there are fuzzy borders between health and other types of research but also because there is a common set of prescriptions for all research involving humans conducted under the aegis of the *Tri-Council Policy Statement* that applies to Canadian universities and hospitals. The third context is that of health care. It would be hard to examine HRIHS without taking into account clinical and other types of health care settings from which many research subjects are recruited and in which many health researchers play a dual role as clinician-researchers. Clearly, too, the governance of health care profoundly intersects the governance of HRIHS.

In terms of the scope of this study, it is important to emphasize that we did not undertake comparisons of governance for HRIHS with governance in very different areas.<sup>15</sup> For example, it was suggested that it would be fruitful to draw comparisons between the governance of health research involving human subjects and the governance of environmental areas, e.g., to compare circumstances in which bottom-up industry-initiated regulation worked far better than top-down rules imposed by regulators.<sup>16</sup> While we agree that such comparisons would likely be potentially illuminating, we must leave it to others to make such comparisons. Our modest hope would be that our report on the governance of HRIHS would be useful for such a comparative analysis.

While we have drawn from some of the extensive literature on governance, we have not made that literature a subject of our enquiry. While our work was informed by relevant academic studies of governance, we used it as a source of generic lessons about the desiderata of good governance for organisations.<sup>17</sup> We are grateful to members of the Law Commission's Study Panel for this project for their helpful suggestions in this area. We also found useful general practical literature on governance in the public, private and not-for-profit sectors. We have been very much influenced by governance as it is examined in our home disciplines – ethics, law and the social sciences.<sup>18</sup>

Even within areas of direct concern, there were areas that we would like to have had the time and resources to examine in more depth. One prominent area is that of private sector research involving humans. While representatives of the Canadian Research Based Pharmaceutical Manufacturers were interviewed, we did not have the time to carry out in-depth interviews of representative individuals in private sector organizations that conduct or sponsor HRIHS. To a considerable extent our perspective on this area is based more on our experiences assessing industry-sponsored research in university or hospital based REBs than on more direct examination of industry practices. A closely related area that we could not investigate is that of private (i.e., for profit) REBs, who are often hired to review HRIHS

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<sup>15</sup> A model of such a crosscutting study is Day and Klein's comparison of governance in five different public services in the UK including health care, water authorities, police, education and social services. P. Day & R. Klein, *Accountabilities: Five Public Services* (London UK: Tavistock Publication, 1987).

<sup>16</sup> D.J. Fiorino, "Strategies for regulatory reform: forward compared to backward mapping" (1997) summer *Policy Studies Journal* 15 <<http://library.northernlight.com/L..wJegZuDmANWwFSXEgEEExZHew8FAM%253D>>.

<sup>17</sup> We have been especially helped by Day and Klein's book, *supra* note 15.

<sup>18</sup> For example, we found quite useful Alan Buchanan's paper. A. Buchanan, "Toward a Theory of the Ethics of Bureaucratic Organizations" (1996) 6/4 *Business Ethics Quarterly* 419.

conducted by private sector organisations and clinical research groups. We would also like to have considered in more depth the role of health charities as research sponsors. Similarly, we would like to have taken a look at the way in which health care professions other than medicine deals with HRIHS. Another area where we have had little to say is about human subjects health research conducted directly by governments.

## V. EMPIRICAL ASPECTS

As called for in the RFP, our project had an empirical aspect. Designing the empirical component was a complicated task. We had several goals in mind for this component.

First and foremost, we wanted to get an idea of the effectiveness of current governance arrangements in terms of whether and to what extent “they achieve or are capable of achieving consistently effective governance of ethical research.”<sup>19</sup> As noted in the important U.S. study *Institutional Review Boards: A Time for Reform*, little attention has been paid to evaluating the effectiveness of ethics review committees known as Institutional Review Boards or IRBs in the US.<sup>20</sup> Moreover, we noted the absence of standards and instruments for measuring effectiveness. Given this, we decided that expert judgement or the judgement of experienced practitioners in the field (e.g., REB members) was a good starting point.

Second, we wanted to get an idea of similarities and differences in governance across the country. To do this, we decided to interview both members of REBs at various sites across Canada and representatives of organisations that have national oversight responsibilities for HRIHS. We were especially interested in how institutional cultures shape practices.

Third, we wanted to get a sense of the richness of different opinions on important issues. So we needed a methodology that let us probe those differences.

While these objectives framed our search for an appropriate empirical study, we also had to be mindful of practical constraints in terms of time and budget.

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<sup>19</sup> *Supra* note 7.

<sup>20</sup> Inspector-General, *supra* note 12 at iii.

We drew on the 1992 survey of Canadian medical faculties concerning the implementation of the 1987 MRC Guidelines conducted by the National Council on the Bioethics of Human Research (NCBHR).<sup>21</sup> The NCBHR study identified significant procedural and substantive problems in ethics review. It also provides some insight into the effectiveness of governance relations at that time. We also drew on the extensive community consultations conducted in 1997 and 1998 by the Tri-Council Working Group on Ethics in the course of preparing its recommendations for a national code for RIIHS.<sup>22</sup> Other relevant studies, both domestic and foreign, were also considered.<sup>23</sup>

## A. Methodology

There was also the question of an appropriate empirical methodology. We did not think that the area was ripe for a quantitative survey instrument. A main reason for this is that for a survey to succeed there must be a good idea of what variables are worth measuring. In our considered opinion, this is not such an area. We saw too much of a danger in a pre-selection bias with respect to issues and variables. Moreover, there is not a good base line here for making comparisons over time. The 1992 NCBHR study reported in 1995 was not a strong survey in regard to statistical measures; the value of the NCBHR study lay in the report of site visits – a more qualitative approach.<sup>24</sup> We also were concerned that there would not be an adequate response to survey instruments. The team also had greater experience with qualitative research methods. We were led then to the qualitative interview approach described in Beagan's paper in Section E-1.

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<sup>21</sup> This survey was conducted in 1992 and published in 1995, NCBHR *supra* note 12.

<sup>22</sup> See Section B-3 in regard to the discussion of the Canadian context of HRIHS.

<sup>23</sup> See for example M.-H. Parizeau, *Rapport d'enquête concernant des comités éthique cliniques et comités de la recherche au Québec* (Québec: Ministère de la Santé et des Services sociaux, September 1998), for a study based on a survey of Quebec REBs, and J. Bell *et al.*, *Final Report: Evaluation of the NIH Implementation of Section 491 of the Public Health Service Act, Mandating a Program of Protections for Research Subjects* (Arlington: James Bell Associates, June 15, 1998) for a survey based study of U.S. IRBs.

<sup>24</sup> NCBHR *supra* note 12.

## B. Interview Participants

In our initial deliberations about who to interview, four main groups were identified:

1. Members of REBs
2. Those setting policy or overseeing its implementation at the national level
3. Research administrators
4. Matched groups of researchers and research participants in several different health research areas

Reflecting on the budget and time available as well as the inherent complexity of the fourth area, we decided that it would not be possible to cover the fourth group in enough detail and with enough range. We still think that it would be highly informative to have studies that take an on-the-ground and in-depth qualitative comparison of the experiences and perceptions of researchers and research subjects. To stay within the constraints just indicated, we confined the interviews to the first three groups.

### 1. Selection of participants and sites

Interviews were conducted with representatives of national organisations involved in various aspects of human subject research governance and with members of REBs at five universities. In the first category were representatives of the following:

- National Council on the Ethics of Human Research (NCEHR)
- Relevant Research Councils (individuals with ethics portfolios or on ethics committees)
- Health Canada
- NHRDP
- Canadian Medical Association (CMA)
- Canadian Research Based Pharmaceutical Manufacturers

In retrospect, we wish we had conducted interviews with representatives of national health charities. These are important funders of health research in Canada and, there is a major effort under way to engage Canadian health charities in a coordinated research effort in partnership with the CIHR.

Members of REBs were interviewed at five universities: Montreal, McGill, Calgary, British Columbia (UBC) and Dalhousie. Both Montreal and McGill operate under Article 21 of the Quebec Civil Code – the only legislation in Canada that provides comprehensive regulation for HRIHS. While Montreal is highly decentralised with REBs at multiple sites (teaching hospitals etc.) McGill has one of its committees designed to meet U.S. standards for IRB's. Calgary has a centralized office for medical research that does an initial screening of protocols through the Office of Biomedical Ethics. UBC has one biomedical REB and one behavioural REB. Dalhousie has several REBs.

Even though we interviewed REB members in several of Canada's regions, we still had to be selective. We did not, for example, carry out interviews in Canada's largest province Ontario. In fact, we made a deliberate choice not to conduct interviews at the University of Toronto for two reasons. The first was a question of practicality due to the number of REBs. The second reason was because the "Oliveri Affair" at Sick Children's Hospital was prominent in the news. We were concerned that this might inhibit individuals from agreeing to be interviewed or colour the interviews thus tainting the picture of the normal state of affairs. We also did not conduct interviews at smaller institutions with medical faculties or at the many Canadian institutions without medical faculties. We did this to economise on the number of sites visited. It was also more convenient to find sites that had both biomedical and behavioural REBs.

At each of the University sites, interviews were conducted with those involved in the University REB and satellite REBs including:

- The Chair or Vice-Chair of the REB
- The jurist or ethicist on the REB
- The University officer to whom the Chair of the REB reports
- Others members of the REB including individuals from the university's centre for bioethics.

The interviews were based on questions developed by Beagan and McDonald. The interviews were open-ended and designed to elicit the interviewee's comments about governance and effectiveness issues.

As a benchmark, we would compare this portion of our work to the much better funded and lengthy process conducted by the US Office of the Inspector General where interviews were held with "many Federal officials and with representatives of 75 IRBs" along with site visits

at 6 academic health centres.<sup>25</sup> Given the constraints on our project, we see our work as reasonably comparable in a number of respects.<sup>26</sup>

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<sup>25</sup> Bell, *supra* note 23.

<sup>26</sup> Inspector-General, *supra* note 7; Bell, *supra* note 23. Two respects in which it was not comparable was that the US OIG attended IRB meetings at the six sites and also “accompanied FDA inspectors on IRB site visits” *Ibid*.





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# SECTION B-1

## ETHICS AND GOVERNANCE

Michael McDonald

In this paper, our main concern is with the governance and ethics of health research involving human subjects (HRIHS). We begin with a discussion of governance.

### I. GOVERNANCE

In answer to the question, “What is governance?” the University of Ottawa’s Centre for Governance provides a useful starting point (see Figure 1 below).

#### FIGURE 1

#### WHAT IS GOVERNANCE?<sup>27</sup>

##### Guiding

Governance is about guiding. It is about the processes by which human organizations, whether private, public or civic, steer themselves.

The study of governance involves:

- examining the distribution of rights, obligations and power that underpin organizations;
- understanding the patterns of coordination that support an organization's diverse activities and that sustain its coherence;

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<sup>27</sup> University of Ottawa Centre on Governance <[http://www.governance.uottawa.ca/english/overview/o\\_defi.htm](http://www.governance.uottawa.ca/english/overview/o_defi.htm)>

- exploring the sources of an organization's dysfunction or lack of fit with its environment that may result in lacklustre performance; and establishing benchmarks, building tools, and
- sharing knowledge to help organizations renew themselves when their governance system demonstrates a need for repair.

## Interacting

Governance pertains not only to organizations, but also to:

- the complex ways in which private, public and social organizations interact and learn from one another;
- the manner in which citizens contribute to the governance system, directly and indirectly, through their collective participation in civil, public and corporate institutions; and
- the instruments, regulations and processes that define the "rules of the game."

## Applications

The knowledge of governance has application not only in determining the appropriate guiding mechanisms for organizations or the evolution of society, but also as:

- a *manière de voir*, or coordination perspective, on the workings of organizations;
- a reference point to clinically probe and repair faltering organizations and to support the development of socio-economic policy;
- an analytical framework providing a language of problem reformulation; and
- a tool to generate alternative *manière de voir* to provide insights into new ways to tackle problems of organizational design and social architecture.

Thus, our study is concerned with the governance of health research involving human subjects (HRIHS) at two levels: (a) the level of particular institutions, organizations and agencies involved in various ways in HRIHS; and (b) the interactions of institutions, organizations and agencies identified at level (a).

As indicated in the Ottawa statement on governance, governance is about "guiding" and "processes by which human organizations ... steer themselves."<sup>28</sup> So governance involves processes by which organizations oversee, govern, regulate or direct their own activities.

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<sup>28</sup> *Ibid.*

Governance structures and processes are ways of affecting changes in human affairs that are themselves subject to change; that is, governance is best understood in dynamic rather than static terms.<sup>29</sup>

In their important work on governance in the public sector, Day and Klein state:

Our starting point is that accountability is all about the construction of an agreed language or currency of discourse about conduct and performance and, the criteria that should be used in assessing them. It is a social and political process. It is about perceptions and power. It can therefore be expected to vary in different contexts, depending on the nature of the policy arena and the power of the different organizational actors.<sup>30</sup>

Accordingly, our concern in this study is with the social structures and processes specific to the governance of health research involving humans, including its “currency of discourse,” “organizational actors,” perceptions and power.”

## A. Criteria for Good Governance

Various criteria for good governance have been proposed. *The Canadian Institutes for Health Research (CIHR) Public Report on Governance* provides a good example of these:

Governance generally refers to the processes and structures that an organization uses to direct and manage its general operations and program activities. An organization without a clear and effective governance structure is unlikely to operate at high levels of efficiency and runs a serious risk that decisions will be made that run counter to the organization’s objectives. It is also unlikely that the organization would have the capacity to adapt readily to change.

A reading of virtually any text or guide on governance would reveal the most fundamental of elements. These include: a clear mission; responsibility; accountability; transparency; stewardship; flexibility; succession; representation; and simplicity. These concepts are the foundation that organizational structures must respect.<sup>31</sup>

<sup>29</sup> In political science, there is discussion of various forms of governance: democracy, autocracy, monarchy, etc. In organizational theory, governance is described in terms of various types of oversight by boards of directors or parallel senior bodies.

The Oxford English Dictionary defines governance as “(1) the action or manner of governing...the fact that a [a person, etc.] governs; (b) control; (c) the state of being governed. (2) The office, function, or power of governing; the governing person or body. (3) Method of management, system of regulations. (4) Mode of living, behaviour, demeanour; (b) wise self-command.

Our main interest is in manners of governing and control (1) and methods of management (3). But we have also identified governing bodies and persons (2). Our concern with good governance has some connection with (4).

<sup>30</sup> See P. Day & R. Klein, *Accountabilities: Five Public Services* (London UK: Tavistock Publication, 1987) at 2.

<sup>31</sup> See D. Zussman, *Proposed Governance Structure for the Canadian Institutes of Health Research* (Ottawa: Public Policy Forum, 1999) at 7 <<http://www.cihr.org/?current=library&page=report#appendix1>>.

This description is in line with our description of governance as a second order function.

McNamee takes a different tack in characterizing corporate governance as an “organization's strategic response to risk.”<sup>32</sup> This is useful because it locates governance in an organization's larger operating environment. However, McNamee's detailed list of corporate governance features overlaps the CIHR list:

- Strategic Planning: Developing plans and objectives to fulfill the organization's purpose.
- Leadership: Communicating the organization's purpose through vision.
- Organization Design: Establishing the structure that defines communication paths.
- Stewardship: Establishing the accountability for preserving the organization's purpose.
- Risk Management: Putting assets at risk to achieve the organization's objectives.
- Assurance: Providing feedback on the efficiency and effectiveness of the governance processes.<sup>33</sup>

Good governance then involves good risk management, oversight and the many other factors listed above.

## B. Conceptualising Governance as Second-Order Oversight

Conceptually we see governance as the way in which organizations –public, private, or not-for-profit– oversee and direct their own activities.<sup>34</sup> Organizations engage in a variety of **first order activities** including the production and sales of goods and services (private sector organizations), education and research (universities), the provision of health services (hospitals) or regulation (government and the professions). With respect to HRIHS, there are private sector organizations like pharmaceutical companies researching, producing and marketing drugs. There are public sector organizations like universities and medical research centres – the

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<sup>32</sup> See D. McNamee, *Corporate Governance, Accountability and Management Control* (25 February 2000), Mc2 Management Consulting, <<http://www.mc2consulting.com/govpage.htm>> (10 April 2000).

<sup>33</sup> *Ibid.*

<sup>34</sup> While the clearest examples of governance are from formally constituted groups, e.g., those established by legislation or associations with a charter, it can also be found in informally constituted groups based on an implicit shared understanding about the nature of the group and its purposes.

former providing research and education and the latter providing health services, health research and health education. In addition, there are public sector research agencies like CIHR, NSERC and SSHRC whose business it is to promote and sponsor Canadian research in various areas. From the not-for-profit sector, health charities like the Heart and Stroke Fund of Canada and the Canadian Kidney Foundation provide health services including education and also sponsor research in their areas.

All these first-order (or first-level) activities need to be managed, directed or guided. Such guidance can be described as a “second-order (or level) activity.” Hence, **governance can be described as an organization’s second-order (or level) activities for controlling, guiding, organizing and in general overseeing its own first-order (or level) activities – whether these are directed internally to the organization’s own members or externally to outside institutions and individuals. Thus, governance represents in organizations a kind of reflexive capacity – a capacity to rationally determine the direction of lower order activities.**<sup>35</sup>

In accord with the preceding discussion of good governance, normal second-order governance activities would include the following:

- Setting, interpreting or changing the mandate, direction and priorities of an organization
- Assigning or reassigning responsibilities with the organization;
- Monitoring and evaluating performance of the organization as a whole, its principal parts, and senior management with special attention to significant opportunities and risks, liabilities and assets
- Ensuring the organization meets its responsibilities to its principal stakeholders (be they stockholders, clients, consumers, the general public, third parties, etc.)<sup>36</sup>

Good governance consists of doing these sorts of things well (e.g., ensuring that there are thorough and timely audits of major risk areas and that these are acted upon). Good

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<sup>35</sup> Typically, senior bodies in an organization – such as a board of directors, the cabinet, or a university senate – undertake governance activities. However, it is quite possible for a given person or group of persons in a social context to occupy both first and second order roles in their organizations (e.g., a physician in a hospital may sit on its board). Our concern in this description of governance is with the function that the Ottawa Centre for Governance describes as “guiding” in Figure 1, “the processes by which human organizations ... steer themselves.” Later in this study, we discuss the “interacting” function, i.e., the interactions of organizations.

<sup>36</sup> See Allen Buchanan’s illuminating discussion of ethical responsibilities of bureaucratic organizations A. Buchanan, “Toward a Theory of the Ethics of Bureaucratic Organizations” (1996) 6/4 *Business Ethics Quarterly* 419. See Appendix A for other examples of criteria for governance.

governance involves steering a middle course between under and over governance (i.e., failing to provide sufficient oversight or providing too much oversight). A good example of too much oversight is that of micro-management. On our view of governance, micro-management involves the needless and even harmful replication of first-level functions.

Our account of governance as a second-level process provides a useful insight into ways in which things can go well or badly at one level without necessarily doing the same at the other level. Thus, a poorly governed corporation might for a period of time be quite profitable despite the ineptness of its CEO and Board. Its doing well despite poor governance could be due to a variety of fortuitous factors such as the high quality and dedication of its employees, the weakness of competitors, protectionist tariffs or, simply by living off its past reputation. Similarly, an organization might be well governed but run into major problems on the ground due to unforeseeable circumstances.<sup>37</sup> Generally speaking though, an organization that performs well on the ground level is likely to be well governed, conversely a well-governed social entity is likely to perform well on the ground over the long run.

Our description of governance as a second-order activity directed to the guidance of first-order activities may create the impression that good governance would involve having second and first order activities carefully aligned with each other. However, such an alignment is at best a necessary, not a sufficient, condition for good governance. There is the possibility of a kind of myopia or even tunnel vision in which the governors of an organization create a situation in which there is good management of a narrow range of first-order activities but other important first-order activities are not overseen or in some cases not even performed. That is, the organization neglects to do many of the things that it ought to do (e.g., according to its mandate or mission statement). But the things that it does do, it does well at both levels. Like individuals, organizations can become practically and even morally blind to their responsibilities at both first and second levels. They can develop a kind of self-deceptive positive feedback loop that ignores major risks and fosters a mistaken sense of complacency and self-satisfaction.

We shall argue that this is the case with respect to the governance of HRIHS by research institutions and sponsors.<sup>38</sup> While they manage research aspects of HRIHS well, there is a general neglect of the ethical aspects of HRIHS. This, we believe, occurs through the

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<sup>37</sup> Of course, there is a part of good governance that has to do with managing in the face of change and so of unexpected circumstances. But such foresight has to be balanced and prudent in that one can over-insure against unexpected calamities.



“bureaucratisation of ethics” (in the REB-approval process). By treating research ethics as equivalent to the REB process, research institutions and sponsors have narrowed the scope of ethical concerns to front-end approvals of research proposals, thus ignoring what happens outside that process. But given that this reduction of research ethics to REB approval, feedback mechanisms in the organization will provide the misleading reassurance that all is well.

### C. “To Govern or Not to Govern”

To paraphrase Hamlet, a primary question is whether (and how much) to govern or not govern. Sometimes it is best to leave matters alone and do without the oversight involved in governance. For example, most of us believe this to be the case for adult etiquette – even though there are a few boors who are readily prepared to behave censoriously in this area. If the governance mechanisms of childhood (parents and teachers) have not done their job, we leave it to peer pressure and Miss Manners to exert their informal and unsystematic pressures on impoliteness and other forms of rudeness. Our reasons for not choosing formalised governance structures in this area are instructive. We worry about

**Moral intrusiveness** – e.g., trampling on rights to privacy

**Effectiveness** – e.g., would a politeness ‘police’ make much of a difference?

**Costs** – e.g., would the costs of second-order oversight be worth the gains?

Some brief comments on each are in order. With respect to moral intrusiveness, we are worried about crossing significant moral boundary lines. We assess effectiveness in systemic terms rather than on an incident-by-incident basis. With respect to costs, we must remember the special weighting that ought to be given to rights. Rights should be seen as “protected interests.” Thus, protecting rights requires active governance in the form of protections for the rights and remedies for their violation.<sup>39</sup> With human rights, the commitment is extensive (all humans) and especially weighty (rights to life, non-discrimination, against torture, etc.).

It is worth noticing that cost and effectiveness are especially germane to the question of “how much governance is appropriate?” But this raises a central issue of whether there are

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<sup>38</sup> See Section F, “Conclusions and Recommendations”.

<sup>39</sup> For a useful philosophical analysis of rights, see C. Wellman, *A theory of rights: persons under laws, institutions, and morals* (Totowa, N.J. : Rowman & Allanheld, 1985) and L.W. Sumner, *The moral foundation of rights* (New York: Oxford University Press, 1987).

situations where good order results without active governance. This is supposed to be the case with Adam Smith's free market, for the market functions essentially as a self-regulating system that brings demand and supply into balance without second-order oversight. Indeed, in the economist's ideal or perfect market, oversight would be redundant and a waste of resources.

The same sort of laissez-faire argument for benign non-governance in well-functioning self-systems has been advanced for freedom of speech generally and academic freedom particularly.<sup>40</sup> Both the poet John Milton and the philosopher John Stuart Mill defend a free market of ideas. Mill does so particularly on the basis of the idea that in such a free market of ideas truth will drive out error and knowledge will vanquish ignorance.<sup>41</sup> As we note in Section B-3, some Canadian academics have recently opposed active governance for research involving human subjects on the grounds that it violates academic freedom and that it is unnecessary because good ethics will drive out bad in an open society.

It is worth noting that while the classical idea of an economic or intellectual free market is only fully exemplified in ideal or perfect markets, most often in real life we deal with imperfect markets that need some degree of regulation and oversight. These imperfect 'mixed' markets are worth considering in regard to the governance of HRIHS. For example, it is worth asking whether reputation effects can serve as a major driver for good behaviour in the partially regulated area of HRIHS. That is, there are important questions about the extent to which various types of governance (e.g., standard setting and monitoring) can be used to reinforce the good tendencies or economic, intellectual or other forms of free markets (concern for long-term reputation), negate bad tendencies (e.g., abuse of research subjects) without being overly costly

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<sup>40</sup> As represented in Lord Broughton's famous dictum from *Queen Caroline's Case*, "An advocate, in the discharge of his duty, knows but one person in all the world and that person is his client", similar arguments have been advanced for legal advocacy in form of total loyalty to a client's interests. M.H. Freeman, "From Lawyers' Ethics in an Adversary Society" in J. Arthur & W. Shaw, eds., *Readings in Philosophy of Law* (Englewood-Cliff: Prentice-Hall, 1984) 488 at 492. For a general discussion of ideal market arguments as ways of ducking moral responsibility for one's own behaviour, see C. Brunk, "Professionalism and Responsibility in the Technological Society" in D. Poff & W.J. Waluchow, eds., Second ed., *Business Ethics in Canada* (Scarborough: Prentice-Hall Canada, 1991) 122 at 130.

<sup>41</sup> See J.R. Lucas, *The Principles of Politics* (Oxford: Clarendon Press, 1966) at 8. Lucas aptly describes the type of society favoured by Milton and Mill as an "Areopagite society". He says, "Areopagites are fallible, and not perfectly informed, but they are possessed by a deep love of truth, and are anxious only to discover the truth, and to establish the rightness of their own views because they are their own. .... And if each Areopagite is liable to some errors of judgement or information, then the more debate and discussion there is, the more errors will be exposed, and the more truth will be established." (*Ibid.*) See also J.S. Mill, "Liberty" in A.D. Lindsay, ed., *Utilitarianism, Liberty, Representative Government*, Everyman Library (London: J.M. Dent & Sons Ltd., 1962).

or counter-productive. This is especially relevant to the various deregulatory steps being taken in regard to health research in Canada.<sup>42</sup>

## D. Governance and Ethics

In a 1996 article entitled “Toward a Theory of the Ethics of Bureaucratic Organizations, Allen Buchanan argues that “bureaucratic organizations” should be seen as “complex webs of principal/agent relationships.”<sup>43</sup> So an adequate theory of ethics for bureaucratic organizations would centre on the reduction of agency risks:

Principals engage agents to perform tasks which they are unable to perform themselves, or which they find too costly or inconvenient to perform themselves. Agency-risks are the risks that are imposed on principals due to the fact that agents have interests that may conflict with those of the principals whom they are supposed to serve. Principal/agent theory describes and in some ways formalizes different types of agency-risks and various techniques for reducing agency-risks. For example, if B serves as A's sales agent for a line of merchandise, Survey B may have incentives to shirk or be less aggressive in seeking sales, unless a special arrangement (typically, reimbursement on a commission basis) is used to reduce this agency-risk.

This bare sketch of the essentials of principal/agent theory should suffice as a basis for formulating the main thesis of the analysis presented here, namely, that much of what is central to, and distinctive of, the ethics of bureaucratic organizations can be understood as responses to agency-risks that are characteristic of such organizations.<sup>44</sup>

Buchanan lists the following as typical risks faced by bureaucratic organizations: “inefficient use of resources,” “outright misappropriation of resources,” “goal substitution” (cases where bureaucrats covertly pursue their own goals ... under the guise of implementing authorized policies), “passive opposition to policies,” “shirking (substituting leisure or the pursuit of other unauthorized activities for compensated work times)” and, “expertise imperialism” (e.g., treating ethical problems as if they were simply economic issues).<sup>45</sup>

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<sup>42</sup> See Section B-3, “The Current Context of HRIHS.”

<sup>43</sup> Buchanan says that bureaucratic organizations have six main features: (i) a hierarchical structure of authority; (ii) a complex division of labour; (iii) professional administrators; (iv) outputs that are the result joint activities; (v) rule or policy based decision-making; and (vi) practices and decision-making based on principal/agent relations. *Supra* note 15 at 419-420.

<sup>44</sup> *Ibid.* at 420.

<sup>45</sup> *Ibid.* at 425-427.

Buchanan describes the above as “first-order agency-risks”, but he says that there are also “second-order agency-risks ... in which bureaucrats often engage that serve to thwart the efforts to control first-order risks.”<sup>46</sup> These include:

- A. appeal to authority (“I was just following orders”);
- B. failure to document activities and decisions in such a way as to make accurate evaluation of outcomes and assignment of responsibility possible;
- C. failure to specify duties concretely and assign them unambiguously to particular agents and groups of agents.<sup>47</sup>

To deal with such second-order agency-risk, Buchanan proposes second-order ethical obligations that tie clearly to the criteria for good governance discussed above:

- A. The obligation to see that there are clear lines of authority and responsibility – to see to it that individuals’ roles in the organization and their attendant duties are specified concretely and consistently (so far as possible without impairing needed flexibility and creativity)
- B. The obligation to ensure that performance is monitored and evaluated adequately and that good performance is rewarded and poor performance corrected and/or penalized.

These two second-order obligations stated above have a corollary:

- C. The obligation to provide adequate documentation.<sup>48</sup>

It is relevant to our study of the governance of HRIHS to note that Buchanan’s work on the ethics of bureaucratic organizations arose out of the work he did as a policy advisor on the President’s Advisory Committee on the Human Radiation Experiments, which produced a major study of the abuses of human subjects in medical and other types of research.<sup>49</sup>

It should be emphasized that assessing the governance responsibilities of bureaucrats in ethical terms need not commit one to the view that the only (or the primary) means of addressing agency-risk is through ethical suasion. Often what is needed is attention to institutional design – the use of incentives and disincentives, reporting relationships, auditing

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<sup>46</sup> *Ibid.* at 428.

<sup>47</sup> *Ibid.* at 429.

<sup>48</sup> *Ibid.* at 430-432.

<sup>49</sup> President’s Advisory Committee on Human Radiation Experiments, *The Human Radiation Experiments: Final Report of the President’s Advisory Committee* (New York: Oxford University Press, . at 433.

and other types of control. Hence, in this study, we are very much concerned with the design of various institutions involved in the HRIHS enterprise – in particular with identifying the institutional incentives and governance processes in place for dealing with the ethical challenges posed by HRIHS.

We recognise that while in some areas governance issues are relatively non-contentious in others they are quite contentious. In this regard, Day and Klein usefully contrast “political” with “managerial accountability.” The former they see in terms of “delegated authority being answerable for their actions to the people”. In complex modern societies, they argue political accountability raises difficult questions about “linkages between action and explanation are in place and, if in place, adequate to the task at hand” as well as about openness of processes and the availability of information.<sup>50</sup> By contrast, managerial accountability tends to be around “agreed tasks according to agreed criteria of performance.”<sup>51</sup> Day and Klein argue persuasively that it is a mistake to combine the two models into a “simple hierarchical model.” They argue that

... it is apparent that political processes do not necessarily generate the kind of clear-cut objectives and criteria required if audit is to be a neutral, value-free exercise; the dividing line between political and managerial accountability is, inevitably, blurred as objectives and criteria are generated in all levels of the hierarchy. The results are the demands for opening up the system as a whole to public scrutiny, and creating a more complex (but not necessarily hierarchical) system ... (C)ompounding the arguments both for better links and for a more complex system of accountability, the organizational structure of many public programmes ... is characterized by the fact that some service-deliverers do not fit into a vertical or hierarchical model of accountability; they are an instance of horizontal accountability to peers.<sup>52</sup>

The complications of horizontal accountabilities cutting across vertical accountabilities are especially significant in the strongly peer and professional oriented cultures of HRIHS.<sup>53</sup> But even more important for this study is the point that accountability, particularly political accountability, can be complex and controversial. We recognize then that our assessment of the governance of HRIHS takes us into difficult and sometimes disputed areas. Yet as we shall now argue, there is a surprising amount of consensus around central ethical values for HRIHS.

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<sup>50</sup> P. Day & R. Klein, *Accountabilities: Five Public Services* (London UK: Tavistock Publication, 1987). at 26-27.

<sup>51</sup> *Ibid.*

<sup>52</sup> *Ibid.* at 28.

<sup>53</sup> See especially Kinsella, Section D-3, “Research Involving Humans: Current Regulatory Status of the Canadian Medical Profession”.

## II. THE ETHICS OF HRIHS

To understand the specific objectives of governance for HRIHS, it is necessary to discuss the ethics of research involving human subjects. Our approach in the following is to indicate the values and principles that command a substantial consensus and those that do not. We also highlight specific shortcomings and difficulties in applying consensus standards to human subjects research.

The ethical conduct of research involving humans has contentious areas but, it also has areas in which over time a substantial consensus has developed. That consensus has been greatly shaped by the history of human research particularly since World War II. Whether one dates that history from the infamous Nuremberg Doctors' Trial or the well-documented abuses of vulnerable research subjects in the U.S., Canada and elsewhere – Tuskegee, Willowbrook, the Milgram obedience experiments, the U.S. human radiation experiments, Cameron's CIA and Canadian Government financed psychiatric experiments at McGill, etc. – the history has been extremely important in shaping the dominant national and international norms in this area.<sup>54</sup> That history has led to a significant, albeit evolving, consensus around central norms and processes. In a recent book on international perspectives in bioethics, the well-known bioethicist, Baruch Brody describes that consensus insofar as it is represented in official policies:

A clear-cut consensus has emerged in all of these official policies about the basic conditions of the licitness of research on human subjects. Procedurally, such research needs to be approved in advance by a committee that is independent of the researchers. Substantively, informed voluntary consent of the subject must be obtained, the research must minimise risks and involve a favourable risk-benefit ratio, there should be an equitable non-exploitative selection of subjects, and the privacy of the subjects and, the confidentiality of the data must be protected. These substantive standards are rooted in fundamental moral commitments to respect for persons, to beneficence, and to justice.<sup>55</sup>

With respect to the ethics of HRIHS, the consensus is around three central objectives:

- A. The **promotion** of socially beneficial research
  - a. Meets relevant scholarly standards
  - b. General social benefits outweigh harms

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<sup>54</sup> For useful accounts of this history, see G.E. Pence, *Classic Cases in Medical Ethics* (New York: McGraw Hill Publishing Company, 1990) 397. and D.J. Rothman, *Strangers at the Bedside: A History of How Law and Ethics Transformed Medical Decision Making* (Basic Books, 1991) 303..

<sup>55</sup> B.A. Brody, *The Ethics of Biomedical Research: An International Perspective* (New York: Oxford University Press, 1998) at 36.

- B. **Respect** for the dignity and rights of research subjects
- C. As an overarching aim, the maintenance of **trust** between the research community and society as a whole.<sup>56</sup>

We see (C) as a product of (A) and (B). For (A) to be achieved, there is general agreement, especially in regard to health research, that (A-1) research must meet relevant scholarly standards (e.g., be scientifically valid) and that (A-2) the likely net benefits of the research outweighs harms. With regard to (B), the research must be conducted in a way that respects the dignity and rights of the research subject. These can be summarised in the form of three questions; these are questions that should be asked before, during and after research involving human subjects is initiated.

**Figure 2**

1. Does the research meet relevant scholarly standards, e.g., scientific validity for biomedical research?
2. Is it likely that the net benefits of the research will outweigh its overall harms?
3. Does the research respect the rights of the research subject, including protection from undue harm and informed consent?

## A. Question 1: Scholarly Standards

In regard to question (1), the underlying idea is that research is morally unjustified if it fails to meet relevant standards for research. Two moral arguments are advanced in favour of meeting scholarly standards. The first reason is that badly designed or executed research unnecessarily exposes research subjects to risks since the research is unlikely to produce any useful results. Such risks may be substantial, e.g., death or major trauma due to the bad design of clinical trials of a new drug or exposure to violence by the breach of confidence of a victim of sexual abuse. Or the risk may be low, in which case there is a misuse and abuse of the research subject's time, effort and good will. The second reason focuses on veracity and promise keeping. Through the informed consent process, a researcher implicitly assures

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<sup>56</sup> In Section A-I, we suggested that the maintenance and / or the restoration of "warranted trust" is a crucial criterion for good governance in this area. By "warranted trust", we mean the opposite of "unwarranted trust".

potential subjects that the research is likely to contribute to the advancement of knowledge. Moreover, this is an assurance backed (implicitly, if not explicitly) by the researcher's institution and the sponsors of the research.

### 1. Diverse areas of HRIHS with different scholarly standards for research

Since health research uses a variety of methodologies and approaches, it is essential with respect to question (1) to be sensitive to legitimate differences in scholarly paradigms and standards. In many international documents, scholarly standards are often described narrowly in terms of "scientific validity." While this may have been appropriate when the systematic study of health was conceived in primarily biomedical terms, it is insufficient given the contemporary wider conception of health research.<sup>57</sup> The complexity and variety of scholarly paradigms sometimes gives rise to disputes about what counts as "sound" or "valid" research. However, the problem here is not as intractable in practice as it might initially appear. First, a significant amount of research fits easily within particular paradigms. Thus, a research sponsor or an REB reviewing a proposal for a randomized clinical trial (RCT) would not find the identification of relevant scholarly standards problematic, e.g., statistical validity, stopping rules and clinical equipoise.<sup>58</sup> Second, in new interdisciplinary fields like bioethics and medical sociology, there has been substantial progress in establishing shared scholarly standards. In many cases then it is possible to "operationalise" standards and provide workable ways of addressing the first question. Nevertheless, as we shall now see, addressing the question of overall value has proven much more difficult.

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<sup>57</sup> It is worth noting that in the design of the new Canadian Institutes for Health Research a wide view has been taken of health research including, for example, the study of health determinants, population health issues, and many non-medical factors related to health (economic, social, cultural, legal, etc.). It should also be noted that there were many criticisms of the 1996 draft *Code of Ethical Conduct for Research Involving Humans* for use of the scientific validity standard and for an overly biomedical tone. This was corrected in the 1997 Code.

<sup>58</sup> Freedman describes 'Clinical equipoise': "Clinical equipoise is a situation in which there exists (or is pending) an honest disagreement in the expert clinical community regarding the merits of two or more forms of treatment for a given condition. To be ethical, a controlled trial must begin, and be conducted in a state of clinical equipoise – as between arms of the study – and must, moreover, offer some reasonable hope that the successful conclusion of the trial will disturb the equipoise (that is resolve the controversy in the expert clinical community." B. Freedman, "A Response to a Purported Ethical Difficulty with Randomized Clinical Trials Involving Cancer Patients" in J.D. Arras & B. Steinbock, eds., Fifth ed., *Ethical Issues in Modern Medicine* (Mountainview, CA: Mayfield Publishing Company, 1999) 577 at 578. Also see B. Freedman, "Equipoise and the Ethics of Clinical Research" (1987) 317 *New England Journal of Medicine* 141.



## B. Question 2: Overall Value

### 1. Benefits and beneficiaries

With regard to question (2), the basic idea is that for research involving human subjects to begin and continue, there must be reasonable promise of greater benefits overall than harms in the conduct and results of the research. That is, relevant parties (researchers, research institutions and research sponsors) must have good reasons for believing that the overall net balance of general value is positive rather than negative.<sup>59</sup> But this requires taking a broad perspective with regard to potential benefits and beneficiaries. For example, potential benefits and harms may well be missed if research impacts are assessed solely in terms of biomedical factors like morbidity and mortality. Moreover, even taken in a broad sense, health is only one kind of good humans value.<sup>60</sup> Research involving human subjects (including health research) produces a wide range of other types of goods (and evils): economic (e.g., increased wealth or poverty), social (e.g., positive or negative changes in social status), personal (e.g., self-knowledge or deception), educational (e.g., greater or lesser skills) and myriad other ways in which human welfare is affected for good or ill. As well, the knowledge produced by credible research can be regarded as a good in its own right.

With regard to who benefits, it is again important to take a broad perspective. With respect to health, for example, there is the general health of populations and the health of research subjects themselves. It is important to note that a significant amount of health research has to be described as non-therapeutic, i.e., as highly unlikely to improve the research subject's health.<sup>61</sup> However, there is a body of research that indicates that hopes of health improvement are a significant motivation for individuals to want to participate in research trials even though they have been explicitly told in the informed consent process that the research is non-

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<sup>59</sup> The term 'general value' is used here in a broad sense as including a wide range of 'goods' or things that are generally valued in society. It includes goods valued for their own sake or for the sake of other ends. It includes both non-moral (e.g., happiness and preference satisfaction) as well as moral ends (e.g., greater equity). In other words, we are not committed here to a particular theory of value like those presented in classical or contemporary utilitarian theories or theories of welfare economics.

<sup>60</sup> There has been a debate in the philosophy of medicine and bioethics about the notion of health, and the problems raised by turning 'health' into a surrogate for human welfare. For a discussion of that debate, see M. McDonald, "Health, Health Care and Culture: Diverse Meanings, Shared Agendas" in C. Harold & P. Ratanakul, eds., *A Cross-Cultural Dialogue on Health Care Ethics* (Waterloo, ON: Wilfrid Laurier University Press, 1999) 92.

<sup>61</sup> An important REB concern in reviewing informed consent forms is to make sure that there is due attention to potential harms and that any claims to potential benefits are well-grounded. This moral concern with accuracy and non-manipulation is reinforced by legal liability concerns about ignoring or downplaying potential risks.

therapeutic.<sup>62</sup> As we shall indicate below, this is one of several problems with treating informed consent as a necessary and sufficient condition for research involving humans.

## 2. Criteria and evidence for overall benefits

We have already commented that the second question (overall benefits) is harder to answer than the first question (scholarly standards). One reason is that general answers to (2) sometimes appear to rest on ideologically based claims that are not evidence-based. Some will find it tempting, for example, to address the question of overall benefits on the basis of assuming or denying that the world of research can be modelled as a type of ideal free market in which unfettered competition advances the common good. If one accepts such a free market model then there would be no need to make an explicit determination of a research project's likely overall value; the market will decide whether it is beneficial and, researchers, their sponsors and institutions should be free to enter the market without restriction.<sup>63</sup> Analogously, some defenders of academic freedom in research could, following John Stuart Mill, argue that over the long run unfettered enquiry is maximally productive of truth. As with its economic counterpart, intellectual consumers in the market of ideas will sort out the good from the bad over time. Ideological critics of free markets will claim the opposite, namely that bad research will drive out good. Thus, many university-based health researchers are deeply suspicious of the introduction of the profit motive into the health sector generally and the health research sector particularly. Such underlying ideological orientations certainly colour debates here. In effect then, we wind up with two polarized models of governance with respect to question two – a free market model of passive governance and a command economy model of activist governance.

But ideological models without supporting evidence are unconvincing. They are also unhelpful in that they do not provide sufficient differential information about the overall benefits or harms of particular research projects. After all, what is being proposed, particularly in higher risk research projects are deliberate interventions into the lives of research subjects that may have major ramifications for them and often for others.<sup>64</sup> It seems to be reasonable to ask

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<sup>62</sup> See N.E. Kass *et al.*, "Trust: The Fragile Foundation of Contemporary Biomedical Research" (1996) 26/5 *Hastings Center Report* 25. and Presidential Advisory Commission on Human Radiation Experiments, *The Human Radiation Experiments: Final Report of the President's Advisory Committee* (New York: Oxford University Press, 1996).

<sup>63</sup> Of course a consistent defender of free markets will insist that researchers, sponsors, and institutions respect the right of potential research subjects to freely decide whether they wish to be involved in research.

<sup>64</sup> Consider, for example, the extensive debates around new reproductive technologies (NRTs). Critics of many NRTs argue that they harm the health of women who use them and have socially deleterious effects on the status of

whether such potentially costly interventions into the lives of human subjects are likely to be beneficial or harmful overall.<sup>65</sup> So all the stakeholders in research – from research sponsors to research subjects – need evidence, not just ideology, to address question (2). But it is sometimes difficult to gather sufficient evidence to allow reasonably well-informed predictions of the likely benefit to harm ratio for many research proposals. Especially in new and venturesome areas of research, one cannot amass the powerful evidence that epidemiologists produce through thorough extensive retrospective studies and meta-analyses. The areas in which such evidence is lacking are wider than may generally be believed. Thus, many standard practices in health care are not evidence based. Moreover, in such “soft” but morally crucial areas like quality of life and social effects, research about which effects predominate and matter is really in the early stages.<sup>66</sup>

The net effect of such factors is that question (2) may be difficult to answer and that there may well be a lack of expert consensus on what counts as a good answer. Of course, there will also be clear cases in which on a common sense basis a consensus can be reached on overall value. Still it seems to us that actors in the research system – researchers, research institutions and sponsors and standard-setters – should make a reasonable attempt to address type (2) questions, especially where there appear to be significant consequences for research subjects or society as a whole, e.g., xenotransplantation.<sup>67</sup> Of course, how and from what perspective actors should address question (2) varies from agent to agent. Research institutions and sponsors have different types of obligations concerning the social good, depending crucially, for example, on whether they are in the public (promoting the public interest while respecting private rights) or private sector (advancing the good of stockholders while not harming the public interest).

In any case, we would observe that based on our research and observations, question (2) is much less often addressed than it ought to be. Thus, while research grants are generally

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women overall. It is worth noting that most NRTs have been developed as ‘clinical innovations’ and not as research projects. Hence, they have not been subject to REB approval.

<sup>65</sup> An analogous question can be asked when public money is invested in research – is this from the perspective of the general social good a wise investment of public resources? When they dispense resources for research, health charities have a similar question to answer; namely, in terms of their particular area of concern (e.g., cancer) is investing in this research project or area of research a better use of resources than investing in other areas of research or in, say, direct provision of health care or education?

<sup>66</sup> See the Burgess and Brunger Section D-1, “Negotiating Collective Acceptability of Health Research”.

<sup>67</sup> For potentially high-risk procedures like xenotransplantation, a major social issue is about the placement of the burden of proof. Should it, for example, be set at the level for blood product safety proposed by Krever or does the onus lie on critics of xenotransplantation?

awarded on scholarly grounds (cf. question 1), scant consideration is usually given to the likely overall advantages or disadvantages of particular research projects. It is easy for those awarding research grants to assume that the fact that a particular area is funded means that the sponsors have done a calculation of the expected overall utility for the area of research thus letting the peer review committee off the hook. Similarly research institutions (in the public sector) and REBs may take the fact of external funding as evidence of overall utility. But we wonder whether and to what extent sponsors actually engage in systematic (research-based) assessments of the question of the overall net social value of the research they are funding. All too often relevant parties – sponsors, research competition adjudicators or REBs – fail to address the overall value question in ways that are credible and transparent to the many stakeholders in research. This represents a failure in governance – a lack of accountability to stakeholders. From the research community’s point of view, it is unduly risky. If a line of research turns out to have disastrous results the trustworthiness of researchers will be called into question.

### C. Question 3: Respect for Rights

Question (3) is about respecting the dignity and rights as well as taking into meaningful account the interests of research subjects. These are responsibilities incurred in sponsoring, housing, conducting and approving research. Historically well-founded concerns about the abuse of humans involved in research put this question on the social, political and legal agenda. Here, we can see a historical shift in terms of a general cultural movement from a war-time context in which conscription was taken to be a justifiable social measure to one in which individual and minority human rights come to the fore.<sup>68</sup> In the context of the total war that marked both the First and Second World Wars, each element of society is seen as a part of the national fighting machine – whether as a part of the military, industry or the farm or, naturally as a research subject. In this context, it was easy to rationalize conscripting individuals, particularly populations “under discipline” like army recruits, conscientious objectors or prisoners, to be subjects for research projects that promote the overall war effort, e.g., by reducing infectious diseases in the army or testing new forms of warfare, like exposure to radiation.<sup>69</sup>

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<sup>68</sup> See Radiation Experiments, *supra* note 62, and Rothman, *supra* note 54.

<sup>69</sup> In the Presidential Report on the Human Radiation Experiments, this case is well argued and well documented, though the authors note that in particular areas of moral sensitivity, e.g., experiments around sexually transmitted diseases, even the U.S. Army was very concerned to secure informed consent. *Ibid.* In the 1960’s Canadian prison

In the post war period particularly from the 1960's onwards, there developed a different social ethic that was attuned more to human rights than to collective interests. In many ways, this might be seen as a natural reaction to the horrors of the Second World War – a part of the general move towards the recognition of inherent human rights in various documents, e.g., the UN covenants on human rights, the *Canadian Charter of Rights and Freedoms* and various other human rights acts. What at first sight may be puzzling is that it took so long for this to affect health research, particularly given that the Nazi Doctors' Trials occurred in the immediate post-war period. The historian David Rothman argues that most medical researchers in the Allied countries saw themselves as utterly different than the Nazi doctors, and so little attention at the time was paid to the *Nuremberg Code*.<sup>70</sup> In any case, a much more rights-oriented perspective on the situation of human subjects involved in research came to the fore. This had much in common with the breaking down of racial and gender barriers and increased concerns about other forms of inequality and consumer rights.

Two different kinds of rationale can be urged on behalf of the moral perspective that sees humans generally and research subjects particularly as possessors of rights that ought not to be traded off for the general benefits of research to society as a whole. The first is based on the idea of minimizing agency-risks. Society needs to have in place mechanisms that counter the under-representation or even misrepresentation of research subjects' interests that is likely to occur if researchers, research institutions and sponsors are the only ones in the driver's seat with respect to the governance of HRIHS. The second is based more on an appeal to the intrinsic human rights of research subjects. However, it too argues in favour of accountability and other governance mechanisms over research involving human subjects. For example, steps need to be taken to ensure that the participation of individuals in research is both informed and voluntary. In other words, the arguments reach the same conclusions (rights and remedies to protect the interests of research subjects) but on two different bases: utility and rights.

The first takes the history of research abuse as evidence that researchers, research institutions, research sponsors and governments are not the disinterested judges of overall

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officials offered prisoners as ideal research subjects J. Bronskill and M. Blanchfield, "Experiments in pain: How medical researchers subjected volunteer prisoners to pain, isolation and shocks in 20 years of secretive tests" *The Ottawa Citizen* (Saturday, September 26, 1998) 11 <[www.ottawacitizen.com/national/980926/1637463.html](http://www.ottawacitizen.com/national/980926/1637463.html)>.

<sup>70</sup> Rothman, *supra* note 54.

human welfare that they may purport or even sincerely believe themselves to be.<sup>71</sup> It also takes into account the agency-risks that organizations typically face when employees or managers substitute their own interests for that of the organization.<sup>72</sup> This it might be argued is not based on a jaundiced view of the behaviour of humans generally or researchers particularly but on a realistic assessment of the incentive structures in research organizations. Given the pressures (e.g., to publish, to secure patents, or to be the first in one's field of research), it is easy to see how natural it would be to underestimate the interests of vulnerable populations (e.g., prisoners, institutionalized children or seniors) and over-estimate the expected value of the research. That is, all the major actors here – researchers, research sponsors and research institutions – can be seen as having vested interests in the reputation and resources that flow from potentially successful research. So from a governance perspective, what is needed are barriers that protect research subjects. Informed consent is one such barrier. Another is the independent REB, which because it is independent does not have a vested interest in the research being done. Moreover, it can be argued that REBs are needed to add distinct areas of expertise to the research assessment process – expertise from ethics, law, the community and relevant areas of research.<sup>73</sup> Thus, the REB is justified as a guardian of the rights of research subjects on the pragmatic and utilitarian grounds that an arm's length, knowledgeable third party must be in place to protect the rights of research subjects.

The second rationale for a system of governance that is oriented to the interests of research subjects is based on an appeal to intrinsic human rights. Often such appeals are based on Kant's claim that one should "act in such a way that you always treat humanity, whether in your own person or in the person of any other, never simply as a means but always at the same time as an end." This means that one ought always to treat persons as having an inherent worth in their capacity for autonomous action that gives them a dignity beyond all price.<sup>74</sup> Or, to put it in contemporary terms, the idea is that rights are designed to "trump" social

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<sup>71</sup> The argumentative approach that I am exploring in this paragraph is characteristic of the sort of utilitarian reading of rights that Mill advances on behalf of the presumption in favour of individual liberty in his famous essay, *Mill supra* note 41.

<sup>72</sup> *Supra* note 36.

<sup>73</sup> P. McNeil, *The Ethics and Politics of Human Experimentation* (Cambridge: Cambridge University Press, 1993) at 184. He cites Veatch's argument that there is a tension between an "interdisciplinary professional review model" of the REB and a "jury model", R. Veatch, "Human experimentation committees: professional or representative?" (1975) *October Hastings Center Report* 31. The former emphasizes expertise; whereas, the latter stresses impartiality and community representation. Veatch proposed that the tension should be recognized squarely with two separate ethics review boards – one expert and one lay. McNeill argues for a hybrid model with equal representation from both experts (researchers) and lay people.

<sup>74</sup> I. Kant, *Groundwork of the Metaphysics of Morals*, trans. H.J. Paton (Toronto: HarperCollins Canada, Ltd., 1963).

interests.<sup>75</sup> Such a concern for the basic human rights of research subjects can be extended to support demands for justice or fairness in research – both in terms of non-exploitation of vulnerable research subjects and in terms of equitable distribution of the benefits of research. The latter has been especially important in recent years in regard to traditionally under-researched groups, especially women but also children.<sup>76</sup>

In operational terms, it may be argued that the two rationales give rise to two important standards. The first suggests a concern for **minimising research risks for subjects** (compared to potential gains for them).<sup>77</sup> The second line of argument (based on a Kantian concern for the inherent dignity of persons) especially is reflected in the requirement that research may not proceed with competent persons without their **free and informed consent**. For this study of governance, it is very important to understand that the expert consensus in bioethics is that both standards must be met. So it would not be morally acceptable to impose slight research risks on a competent person without that person's free and informed consent to participate in research. But it is also the case that there are levels of risk that may not be imposed on persons even with their permission.<sup>78</sup>

So question (3) about the protection of research subject rights really requires a two part answer: (a) this research is not likely to impose an impermissible level of harm and (b) research will not proceed unless potential subjects (or in the case of an incompetent subjects, their surrogate decision-makers) have given their free and informed consent. Because both (a) the level of potential risk to the subject and (b) the subject's or the subject's proxy's consent are required, we can see the responsibilities here as fiduciary (due care) rather than as strictly contractual or by agreement (*volenti non fit injuria*). That is the relevant parties in research have

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<sup>75</sup> R. Dworkin, *Taking Rights Seriously* (London: Duckworth, 1977).

<sup>76</sup> One issue is that significant areas of health research have taken the diseases and symptoms of men as species-typical with unfortunate effects on women's and children's health as well as the neglect of research into their health issues.

<sup>77</sup> This justifies riskier research on sicker patients if there is a commensurate increase in benefits. This is part of the ethical rationale for Phase I/II CTs.

<sup>78</sup> The level of harm that is permissible varies depending on the competence of the potential research subject. One can justify imposing higher levels of risk on competent than on incompetent individuals on the grounds that competent individuals can freely and knowingly decide to accept risks to themselves whereas incompetent individuals cannot. We take it that those who have care of incompetent persons have a duty to protect the interests of their wards and so may not beyond the level of minimal or relatively insignificant risk expose their wards to harm. It should be noted that following the *Eve* decision, see *Re Eve*, 31 D.L.R. (4<sup>th</sup>) S.C.C [1987] 2 S.C.R. 388 (S.C.C) determining the level of minimal risk for research involving incompetent persons has been a matter of some dispute. This has generated a fair amount of concern around research involving (incompetent) children and adults.

an obligation to make sure, even with competent subjects, that the “research deal” they offer is reasonable and fair.<sup>79</sup>

However, it should be noted that minimal harm standards can be hard to formulate – when does research cross the line between permissible and impermissible risk?<sup>80</sup> Different researchers and different REBs may have conflicting answers to this question. This is, we suspect, one of the reasons why there are concerns on the part of many REB members about accepting the judgements of other REBs.<sup>81</sup> Moreover, there may be disagreement about the nature or extent of a researcher’s fiduciary responsibilities. On the surface, it looks a lot easier to administer and monitor the informed consent process than that of minimal harm. In fact, informed consent is very easy to monitor if the ethics of HRIHS is reduced to subjects’ signatures on consent forms. However, informed consent is much more than a signed consent form. At best the signed form offers some, though by no means conclusive, evidence of consent at the time. Consent rather is a process of willing and knowing participation over time. Moreover, consent should be seen as only a part, albeit an important part, of the research ethics process. However, as we claim in our conclusions, what has happened is that by and large we have a research ethics system that is operationalised around consent forms and pays little attention either to informed consent as a process or to levels of research risk.

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<sup>79</sup> Similarly in commercial law, there are areas of business where the caveat emptor model does not obtain; rather the vendor must take care to be sure the product is safe and effective. This recognises the imbalance in power that can exist in many types of sales, e.g., telephone sales.

<sup>80</sup> An interesting comparison can be drawn between the way in which minimal risk was formulated in the 1997 draft Code and the 1998 TCPS. The TCPS is much more permissive of harms to subjects than the Code. Tri-Council, *Tri-Council Policy Statement on the Ethical Conduct of Research Involving Humans* (Ottawa: Tri-Council, 1998).

<sup>81</sup> See Beagan, Section E-1.



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## SECTION B-2

# HRIHS: PROCESS AND CONTEXT

Michael McDonald<sup>82</sup>

In this section, we describe the normal processes through which HRIHS is conducted and administered. As indicated in the previous section, we are interested in governance at two levels: (a) the level of particular institutions, organisations and agencies involved in various ways in HRIHS; and (b) the interactions of institutions, organisations and agencies identified at level (a). So we are especially interested in the institutional actors and processes that are central to the governance of HRIHS.

We also intend this section as a useful primer or road map for the reader who is interested in but unfamiliar with this area. For those who are familiar with and who perhaps work or serve within this area (e.g., as researchers, members of Research Ethics Boards (REBs), research sponsors, regulators, or as research subjects), we hope that this introductory part of the study will both 'ring true' with a significant part of their experiences and, also serve to articulate the ways in which the study team's observations and assumptions differ from the readers'.

## I. THE RESEARCH PROCESS

To describe both (a) and (b), we start with a simplified model of the research process (Display 3). We identify four stages:

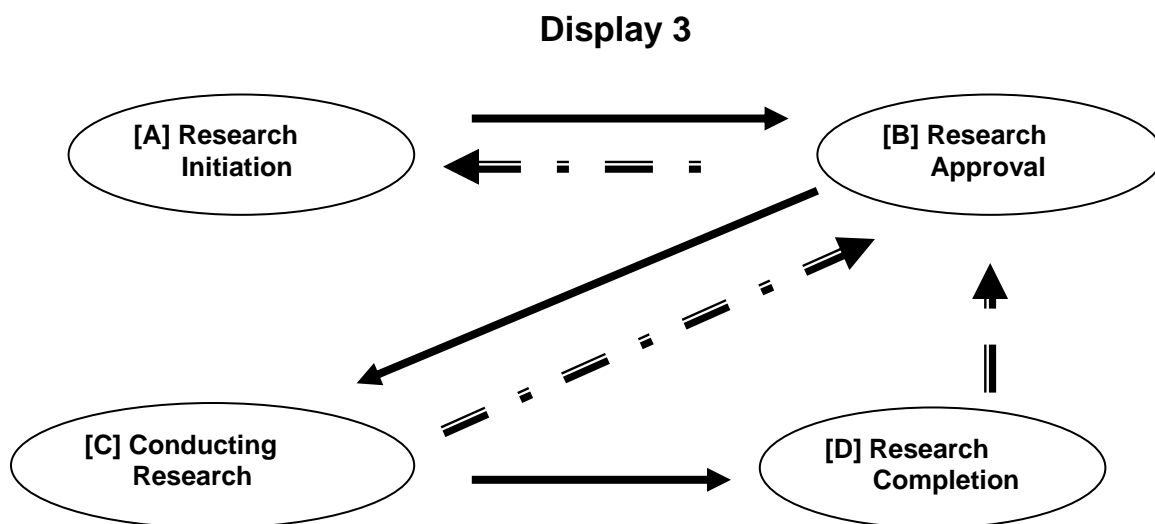
- [A] Research initiation
- [B] Research approval
- [C] Research

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<sup>82</sup> I wish to acknowledge the important role that my colleague Dr. Barbara McGillivray has played in the formation of this section of the study.

[D] Research completion

These are presented as four circles – [A] through [D] – connected by arrows indicating sequences of activities.



The solid arrows represent the normal or usual flow of activities in the research process. The arrows with broken lines represent processes where in some cases research approval of some sort is sought before or after the normal stage of research approval. Thus, when researchers want to do a pilot study involving human subjects they are supposed to seek REB approval. During research, modifications in the protocol or adverse incidents may lead the researcher to return to the REB or even the research sponsor to seek approval or to notify them of such changes. As noted in Joly's paper (Section D-2) on public health research, a public health intervention may result in publishable research; but since many journals now require that the REB have approved the research being reported in the publication, the researcher may seek retrospective REB approval.<sup>83</sup>

<sup>83</sup> For the difference between "retrospective" and "retroactive" rules see M. McDonald, "An Inquiry Into the Ethics of Retroactive Environmental Legislation: the Case of British Columbia's Bill 26" (1995) 29 University of B.C. Law Review 63.

## A. Social Contexts of Research

However, research does not just happen. It occurs in a social context. We identify two types of social context that are directly relevant to the conduct of HRIHS. The first is the social context that sets conditions or boundaries on ethical research involving humans. We see these as determining what counts as (a) acceptable scholarship and (b) respectful treatment of humans involved in research. The second concerns the direction of research – a process that might be broadly referred to as “setting the research agenda”.

### 1. Parameters of research

In Display 4, the outer circle (X) represents the parameters or boundaries of what is regarded as research that is acceptable from a scholarly perspective (Ethics Question 1) and research that is sufficiently respectful of the rights and dignity of humans recruited as research subjects (Ethics Question 3).<sup>84</sup> In the interest of simplicity, both (a) and (b) are represented as a single circle X rather than two only partially congruent circles  $X_a$  and  $X_b$ . The parameters represented by X express what we would describe as an **informed consensus position** on acceptability. The consensus embodies shared social values, yet it also is a morally credible consensus because it commands (or would command, if the question were asked) the agreement of the parties to it. This consensus position could also be described as “minimal” in the sense that the standard and processes represented in it are common across a wide spectrum – a lowest common denominator expression of scholarly acceptability (question 1) and respect for the rights of research subjects (question 3). We note that a consensus does not have to include everyone – there may be outliers. However, the main bodies and their leaders have to generally share values for there to be a consensus.

From a social consensus perspective, research outside these boundaries would be viewed as morally unacceptable by most observers including typical members of the research community, the pool of potential research subjects and the general public. As we have already noted, there are disagreements and uncertainties about where the boundaries are. Values are subject to change here. In terms of Display 4, X might be envisioned as in some places hazy (a fuzzy grey line) and in other places a sharp or precise boundary. Moreover, X would also expand or contract as boundaries of acceptability shift. Without getting into an extended

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<sup>84</sup> See Figure 2, p. 33.

discussion of objectivism and relativism in ethics, we will simply say that the consensus can move in better or worse directions as seen from some historically situated point of view. We certainly do look back in time and criticize the standards applied in previous generations. How much continuity there is in a social consensus over time and whether it is possible to hold previous generations responsible for what are now seen to be serious moral errors is an important question that can be answered meaningfully.<sup>85</sup>

## 2. Setting research directions

In a broad way, we talk about research in various areas having a direction or moving in certain directions. On the classical view of science, the direction of scientific research comes from a process of making empirical hypotheses and testing the hypotheses by observation or experimentation. From a sociological or historical perspective, scientists interacting with each other and the broader population set the direction of science. The groups that significantly influence the directions of future research are listed in box [Y] in the upper left-hand corner of We identify five groups as individually or in combination affecting, influencing and sometimes deliberately setting research directions.

- The scholarly community (which is really an assemblage of many disciplines, sub-disciplines and cross-cutting research groups) through various processes (peer reviewed publications being one of the most salient) establish directions for research.
- Sponsors of research set directions through research funding, especially targeted funding.
- Research institutions, be they public or private, hire and promote researchers, decide on institutional research objectives, build research facilities, etc.
- Government sometimes appears as a research sponsor but the role that we are identifying here is the less direct but nonetheless very important ones that governments have through taxation (e.g., policy on tax deductions for research), regulation (e.g., setting the rules for the approval of new pharmaceuticals<sup>86</sup> and medical devices or the patenting of new inventions) and control (e.g., rules about competency or freedom of information) and,
- Interest groups and the public have an effect upon the above but also are in turn influenced by them.

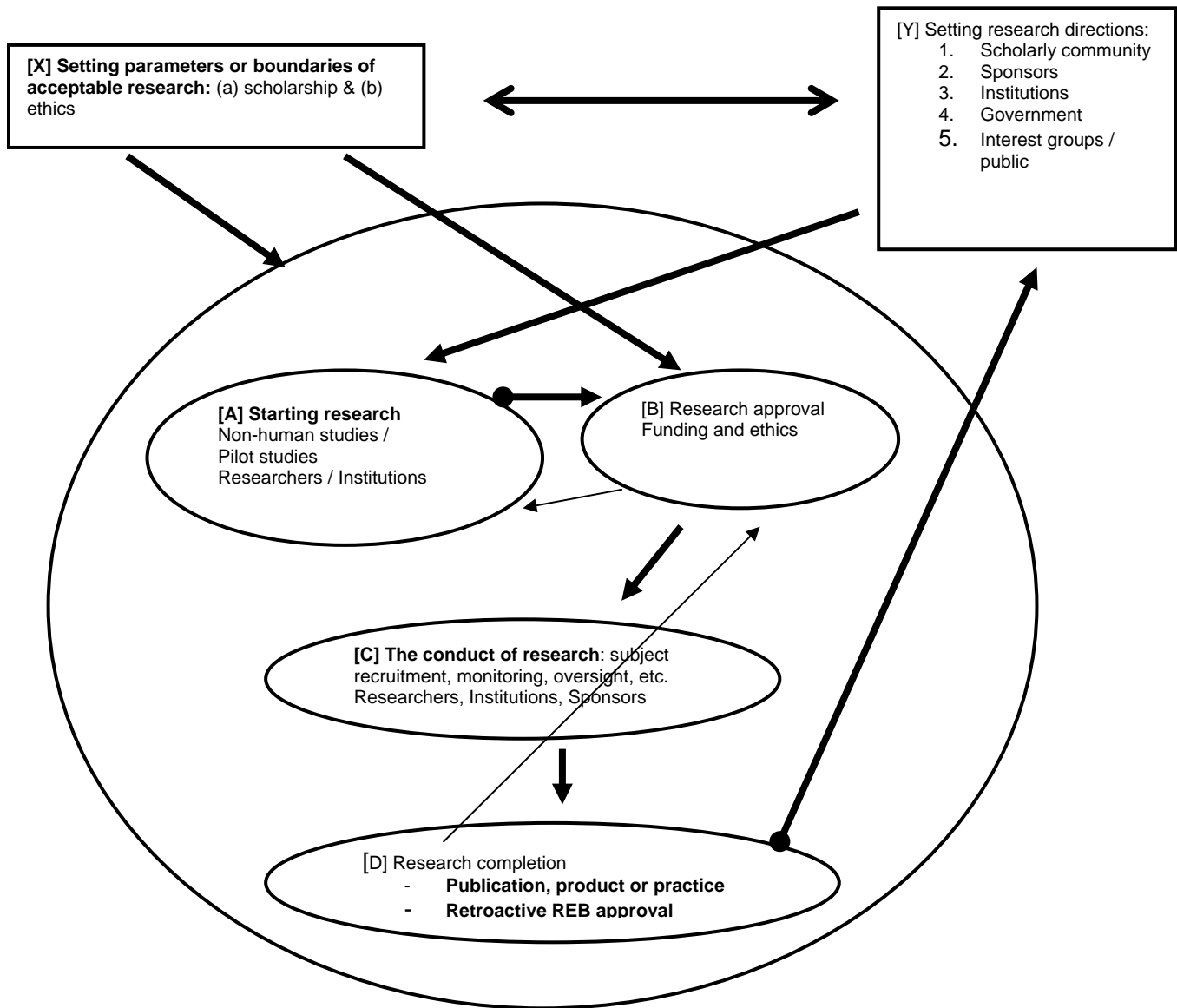
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<sup>85</sup> There is a very good discussion about the conditions in which it is fair to hold previous generations accountable to contemporary moral standards by Alan Buchanan, in the President's Advisory Committee on Human Radiation Experiments, *The Human Radiation Experiments: Final Report of the President's Advisory Committee* (New York: Oxford University Press, 1996) at 113.

<sup>86</sup> See for example the new regulations proposed by the federal government for clinical trials: Department of Health, "Regulations Amending the Food and Drug Regulations (1024 -- Clinical Trials)" Canada Gazette Part 1 (22 January 2000) 227.

In Display 4, we represent the overall picture as follows. Arrows indicate the direction of influences. Broader arrows represent larger influences; narrower arrows represent smaller influences.

Display 4



## B. Agents and Activities

We now develop a more fine-grained analysis of each of the elements in Display 4. We are especially interested in identifying the relevant actors in each stage and their current governance relationship. This allows us to identify a number of areas that are the subject of this study, namely, matters of concern for the ethical governance of HRIHS.

### 1. Scholarly parameters ( $X_a$ )

Meeting acceptable standards for scholarship has been identified as a key issue for ethically appropriate research. We see three groups as pivotal in setting standards:

The first is the broad scholarly community or **community of researchers**. Since there are different forms of scholarly research, it is probably best to think of the scholarly community as a community of overlapping communities that, at the most general level, has shared values regarding acceptable and unacceptable scholarship (e.g., originality and plagiarism). The values are more concrete and unifying in constituent disciplinary communities – e.g., medicine, sociology and law and even more concrete in sub-communities, e.g. paediatrics or medical anthropology. Scholarly standards are conveyed through a variety of mechanisms, such as, education, mentoring, peer review, accreditation and publication. One might take this as best expressed by the American pragmatist philosopher Charles Peirce's notion of science as what scientists accept as science. The standards are both substantive – an accepted body of knowledge, research paradigms and methodologies – and procedural – for example, independent peer review. We see these standards being expressed in a variety of forums: meetings of academic associations, comments on papers submitted for publication, hiring and promotion decisions, and so on. In short, there are very powerful mechanisms at the level of the research community for maintaining scholarly standards.

Second, research institutions – including universities, research and teaching hospitals, pharmaceutical companies, freestanding think tanks and in-house government research departments or agencies, reinforce these mechanisms. However, research institutions should not be regarded simply as extensions of the scholarly community. They usually have other roles, e.g., in education, disease prevention, clinical care, health promotion and regulation. This complicates the scholarly validation processes. Suffice it to say, such institutions have a major role to play in the promotion and maintenance of scholarly standards; they house, hire and



reward researchers through tenure, promotions, honours and the like. They also play an important role in the governance of research through a whole series of processes: certifying researchers (e.g., through granting academic degrees), establishing educational criteria for courses and programmes, quality assurance processes and on-going review of individuals and departments and most importantly, hiring and promotion processes. Research institutions also have other instruments of governance in research, e.g., data and safety monitoring committees, research integrity processes, financial control and oversight of research funds, the establishment or endorsement of ethics approval mechanisms either within the organisation (e.g., an REB in a university or hospital) or outside (e.g., a company using a private REB). Research institutions also make decisions about research priorities based on strategic, fiscal, or safety reasons and sometimes mandate (e.g., a cancer agency or a Roman Catholic health care institution).

Research institutions have significant incentives for ensuring that research involving humans meets appropriate scholarly standards. First, research institutions have a direct stake in the quality of research being conducted by their researchers. The institution's reputation and often its fiscal viability depend on the production of credible research. As well, there may be legal disincentives for not making reasonable efforts to ensure the quality of research in their institutions, e.g., for contract research. Second, many Canadian research institutions have explicit or implied agreements with research sponsors concerning the ways in which research subjects will be treated in their institutions and by their researchers. A leading example of this is the insistence by the Tri-Council group – MRC, NSERC and SSHRC – that makes compliance with the TCPS for all research involving humans conducted at the institution a condition of receiving research funding. Similarly, U.S. agencies like the NIH require compliance with applicable U.S. federal regulations including on-site monitoring for compliance. Other research sponsors have similar requirements. Since the acceptability of scholarship is a consensus condition for the ethical acceptability of research, research institutions have at least on paper 'bought into' these requirements. These requirements, it should be noted, are both substantive and procedural. In particular, relevant ethical guidelines (e.g., TCPS) call for a prior assessment of the scholarship of each proposal for research involving humans before research is begun.

The third group that sets parameters for research scholarship are those that commission and sponsor research – **research sponsors**. Many different types of sponsors sponsor health research in Canada: federal research agencies (MRC), federal regulators (HPB), provincial research agencies (FCAR in Quebec), provincial regulators (public health agencies), private

sector companies (Merck Frost), health charities (Heart and Stroke Fund), etc. In many cases, research institutions also provide internal funding for small-scale research projects, especially pilot studies. Since “he who pays the piper, calls the tune,” research sponsors are in a position to insist that an assessment of scholarship be done before research involving humans is initiated. Like the research community and research institutions, research sponsors have major incentives for ensuring that research meets scholarly standards – the loss of “reputational capital” for not being duly diligent in this regard would be staggering.<sup>87</sup> More importantly, research sponsors justify their existence by the success of their endeavours. They need research credibility to get support from public, private or not-for-profit sector “investors” -- be they shareholders, taxpayers or donors.

These observations about scholarly parameters are summed up in the following display:

<b>Scholarly parameters</b>	
1.	Scholarly / scientific community: peer review, journals, scholarly associations, consensus conferences, etc. <ol style="list-style-type: none"> <li>a. Substantive standards: research paradigms, (e.g., scientific validity) and methodologies</li> <li>b. Procedural: independent peer review</li> </ol>
2.	Research sponsors: <ol style="list-style-type: none"> <li>a. Research award processes</li> <li>b. Scholarly integrity standards</li> <li>c. Research audit processes</li> </ol>
3.	Research institutions <ol style="list-style-type: none"> <li>a. Training and certification of researchers, e.g., degree programs</li> <li>b. Hiring, promotion and tenure decisions</li> <li>c. Areas of permitted research (e.g., safety, corporate focus, religious orientation)</li> </ol>
<b>Display PP-1</b>	

## 2. Ethical parameters ( $X_b$ )

We have already discussed some of the consensus standards on ethical research with human subjects in terms of positive answers to three questions.<sup>88</sup> In additions, there is common agreement about processes. We represent this consensus on ethical parameters (PP-2):

<sup>87</sup> For a discussion of reputational capital in the corporate sector, see L.J. Brooks, “Reputational Capital and Business Ethics” *The Corporate Ethics Monitor* (September-October 1999) 65.

**Consensus ethical standards**

1. Content: 3 issues are basic for review, approval, and conduct of RIHS
  - a. Scientific / scholarly validity
  - b. Overall benefits of research must outweigh potential harms.
  - c. Protection of research subjects' rights and interests
2. Process
  - a. Independent arm's length review by an REB
  - b. Effective monitoring of ethics, safety, academic integrity, etc.

**Display PP-2**

As noted in Section B-1, the minimal consensus is stronger and sharper on some elements than on others. Thus, it is quite strong around the requirement for informed consent and the need for something like prior REB review of research involving humans. But it is weaker and foggier around notions of overall benefit and standards of harm. With respect to standards of harm, there is general agreement in most sectors of health researchers that a minimal harm standard is appropriate; yet, there is considerable uncertainty and disagreement about what counts in practice as “minimal harm” or “a threshold of morally acceptable risk”.<sup>89</sup>

Next we turn to the official sources where ethical and legal standards are expressed. We see three levels: international, Canadian and foreign. In some cases, governments and quasi-governmental bodies set the standards; while in others, associations, e.g., health care professionals, create the standards. Still in other cases, there is a combination of public, private and professional sources (e.g., GCP). In any case, there is with most of the “direct” standards set at the international and national levels a fair amount of consultation amongst various interested parties – professionals, researchers, research institutions and governments; however, these consultations have not extended to research subjects or their representatives. In Canada, we have divided legislative and judicial sources of norms and standards into two kinds: those that are created by a legislature or court expressly for RIHS or, even more particularly, for health research and those that are created for some other purpose (e.g., for protection of the privacy of personal records in government hands) but that have an indirect effect on RIHS.

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<sup>88</sup> See Figure 2 above.

<sup>89</sup> As noted above, this is not an easy concept to state clearly. Further evidence for this is found in the considerable debate around the legal and moral acceptability of minimally harmful research involving infants and (non-competent) children.

### Official sources for ethical/legal standards

#### Standard Setters

1. International
  - a. Intergovernmental, e.g., ICH, UN, WHO
  - b. Associations, e.g., CIOMS, Helsinki
2. Canada
  - a. Legislatively or judicially determined
    - i. Direct intended (e.g., Quebec, HPB regulatory)
    - ii. Indirect unintended (e.g., Bill C-6)
  - b. Research sponsor determined (e.g., TCPS)
  - c. Professional (e.g., CMA Code of Ethics)
  - d. Discipline determined (e.g., epidemiology)
3. Foreign
  - a. Research sponsor (NIH, FDA)
  - b. Site of research (local authorities)

#### Display PP-3

### 3. Governance concerns: Parameter-setting

A major concern of this study is whether the modes of governance prevailing in the area of HRIHS provide “a form of governance that is effective, responsive, transparent and just”.<sup>90</sup> These four characteristics – **effectiveness**, **responsiveness**, **transparency** and **fairness** – form the core of what could in general be described as “ethical governance.” As suggested by the University of Ottawa’s Centre for Governance, governance questions have to be directed at two levels: (a) the level of individual organisations and (b) at the level of the interaction of organisations with each other and with members of the affected population. As illustrated in Display 4, there are many organisations and other types of formal or informal social entities that play roles in HRIHS. The interaction of these social entities is very complex. We are interested in effectiveness, responsiveness, transparency and fairness at both levels. Again in table form, we set out some major areas of concern:

<sup>90</sup> LCC, *Request for Proposals: Contract # 98-09-01; Governance Relationships* (Ottawa: Law Commission of Canada, 1998).

## Ethical governance

### A. Areas of concern

1. What is in place for **quality assurance**: maintaining standards, monitoring for harm, consent, safety and other ethically relevant issues?
2. What is in place for **quality improvement**: learning from our successes and mistakes, e.g., for improving researcher and REB performance?
3. How are **factors underlying ethical or unethical performance** (e.g., knowledge, judgement, attitudes, organisational / professional cultures) addressed?
4. How do those who set standards **assure stakeholders**, especially in the community, that the standards are appropriate and effective?
5. **Who sets the standards?** Who gets a say and who doesn't?

### B. Structural Concerns

1. How is **effectiveness** to be gauged?
2. What are the **processes**?
  - a. Who does what? What role (if any) do **subjects** have?
  - b. **Transparency**? Transparent to whom? How?
  - c. Where is **independence** important?
  - d. Is there **effective feedback** from the field to standard setters, sponsors, etc.?
3. **Who** is accountable for **what to whom? How** are they held accountable?

#### Display PP-4

(A-1) and (A-2) raise concerns about effectiveness. Do research institutions and sponsors have in place the mechanisms for reasonable quality assurance and quality improvement? Of course, this also raises questions about transparency and accountability. Do the research institutions' or sponsors' stakeholders receive a proper accounting of the organisation's performance in these areas?

The same questions arise more acutely at the inter-organisational level, e.g., interactions between research sponsors and institutions. Between institutions things can fall between the cracks. Accountability may become unclear and diffuse; there may well be confusion over who is responsible for what. This is especially the case in the Canadian setting, e.g., with a major federal role in research along with our constitutional separation of powers in health and education. As we shall argue below, this is complicated by the realities of a globalised market place.

(A-3) is meant to raise questions about the cultures of the multiple organisation and social groupings involved in HRIHS. At all the stages and levels of the research process from setting the parameters to research completion, there are many cultures. It is essential to ask if

they are cultures that work effectively, for example, to ensure respect for the dignity and interests of research subjects. From a governance perspective, this concern can be rephrased in terms of whether governors are effectively encouraging and nurturing ethical cultures. This of course leads to many other questions – some at very fundamental levels, like “do ethical cultures just occur naturally or can they be socially engineered?” and others at a very practical level like “Does the institution have a budget and plan for ethics education for REB members and researchers?” Concerning an organisation’s level of commitment it is worth determining if the same degree of concern and commitment is expressed with regard to maintaining an ethical culture in research organisations as is given to maintaining a research culture. Thus while to some extent it is inevitable that good organisational cultures are partially a result of happenstance, we believe that deliberate planning and nurturance have an important role to play.

Concern (A-4) focuses on accountability to stakeholders. This raises a question about who gets counted as a stakeholder. One of our major conclusions is that research subjects are rarely thought of as active stakeholders. By and large the practice at all levels – from standard setting to research governance – has been to treat research subjects as passive stakeholders. In the interviews, very few thought that asking people about their experiences as research subjects had anything to do with judging the effectiveness of REB and researcher performance.

Concern (A-5) is with those who set standards. A penetrating question to ask is who has not been present at the standard-setting table that should be there? Again we observe that it is researchers, research institutions, research sponsors and governments that dominate the area of standard setting. Do these parties ever investigate what research subjects might want and what happens to people involved in research? Are research subjects involved in standard-setting?

Under (B), we raise questions about (1) effectiveness, (2) processes and (3) accountabilities. Two preliminary observations are in order. The first is that at a systemic level these are very difficult issues in the decentralised Canadian context. The second is that given this decentralisation there would seem to be a strong case for individual research institutions and research sponsors to make a concerted effort to ensure they measure up in these areas – not just on their own but working collaboratively with other institutions and groups.

## C. Setting Directions for Research (Y)

In the following five displays (SD 1-5), we map out the main players and issues for box Y in Display 4. In SD 1, our concern is with identifying those who set research directions:

### Who sets / influences directions in research?

1. **Scholarly community** – current and emerging research interests, methods, tools, etc.
2. **Research sponsors** (companies, research councils, health charities, etc.) in strategic planning, grants programmes, etc.
3. **Research institutions** (universities, hospitals, companies, etc.) in hiring, promotions, areas of emphasis, etc.
4. **Researchers** as a talent pool with skill sets, plans etc.
5. **Governments** through regulation, taxation and incentives
6. **Interest groups** and the **public** as investors, consumers, patients, voters, etc.

SD-1

For organisations, there are a number of relevant considerations (SD-2):

### What directions to set?

#### Considerations

- Mission
- People
- Financial resources
- Research opportunities
- State of science / scholarship

#### How to get there?

##### Activities

- Research sponsor targets research or has open competition
- Company makes research investment decisions
- Research teams set directions for future research

SD-2

For these, all the groups identified in SD-1, there are a number of relevant ethical concerns specific to HRIHS (SD-3):

### **ETHICAL CONCERNS**

1. Ensuring that the research directions set meet the sponsor's responsibilities to stakeholders
2. Setting research directions that are compatible with the rights of research subjects
3. Fairness issues addressing public concerns about a non-exploitative and inclusive research agenda

**SD-3**

As with setting the parameters of research, there are a number of ethical governance questions. Those listed in PP-4 are all relevant. But there are some that seem especially apt for setting directions (SD-4):

### **Ethical Governance Issues**

- 1. Internal**
  - a. Responsible use of resources (public or private)
  - b. Transparency and accountability to public / private stakeholders
  - c. Skill sets and organisational cultures: scholarly, ethical, administrative, etc.
- 2. External - co-ordination issues:**
  - a. Who does what?
  - b. Who identifies gaps in research, e.g., research on women's health? Who takes responsibility for filling these gaps?

**SD-4**

## **II. STAGES OF RESEARCH**

We now lay out the four stages of the research process: research initiation, research approval, during research and, research completion.



## A. Research Initiation

Research typically begins with research questions. For many types of medical research, the next step is non-human studies. This may be followed with a pilot study on a small group of patients or subjects. Then researchers are in a position to decide if it is worth proceeding to a

<p><b><u>Research Questions</u></b></p> <ul style="list-style-type: none"> <li>• Observations</li> <li>• Hypotheses</li> <li>• Methodology</li> </ul> <p><b><u>Non-human studies</u></b></p> <ul style="list-style-type: none"> <li>• Literature searches</li> <li>• Cells / computer models</li> <li>• Animal studies (Animal Care approval)</li> </ul> <p><b><u>Local pilot study (human subjects)</u></b></p> <ul style="list-style-type: none"> <li>• Site agreement</li> <li>• REB approval</li> </ul> <p>Design a larger study</p> <p style="text-align: right;"><b>RI-1</b></p>
--

larger scale study.

An example of such a sequence can be taken from an area like cancer research (RI-2):

<p style="text-align: center;"><b>Examples from Cancer Research</b></p> <ol style="list-style-type: none"> <li>1. Non-human studies</li> <li>2. Pilot study on human subjects       <ol style="list-style-type: none"> <li>a. Local study</li> <li>b. Agreement of local site (e.g., hospital)</li> </ol> </li> <li>3. REB Approval</li> <li>4. Results presented to a(n) (inter)national consortium</li> <li>5. Establish expert group if ripe for national / international study,       <ol style="list-style-type: none"> <li>a. Set research questions &amp; methods</li> <li>b. Coordination plan for local studies</li> </ol> </li> <li>6. Apply for funding of a multi-site trial</li> </ol> <p style="text-align: center;"><b>RI-2</b></p>
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Pilot studies raise a number of ethical questions, some of which we have already discussed but others that need to be introduced now, e.g., safety-monitoring and protection of confidential health records.

### **Ethical issues for pilot studies**

#### **General ethical questions**

1. Is this valid / sound research?
2. Do the overall potential benefits of the research outweigh potential harms?
3. Does this research respect the rights and interests of research subjects?
  - a. Harm / benefit issues
  - b. Informed consent issues

#### **Special issues around pilot studies**

1. Blurring clinical treatment / research boundaries
2. Concerns re limited numbers
3. Adequacy of research proposal

#### **Oversight issues**

1. Drug / other intervention monitoring
2. Adherence to professional standards
3. Adherence to scholarly standards
4. Adherence to ethics guidelines, legal rules and regulations

**RI-3**

The research initiation stage raises a number of concerns for ethical governance of HRIHS. These include the following (RI-4):

### **Ethical governance for research initiation**

#### **Areas of concern**

1. Do researchers/REB attempt to assess the effects of projected research on subjects?
2. Selection of topics / areas for research, e.g., avoidance of neglected areas of research / neglected populations and issues
3. Adequacy of non-human models / studies and pilot studies
4. Thoroughness of ethics and site reviews, e.g., is there a lower level of concern for pilot studies than for regular studies?

#### **Types of Concern**

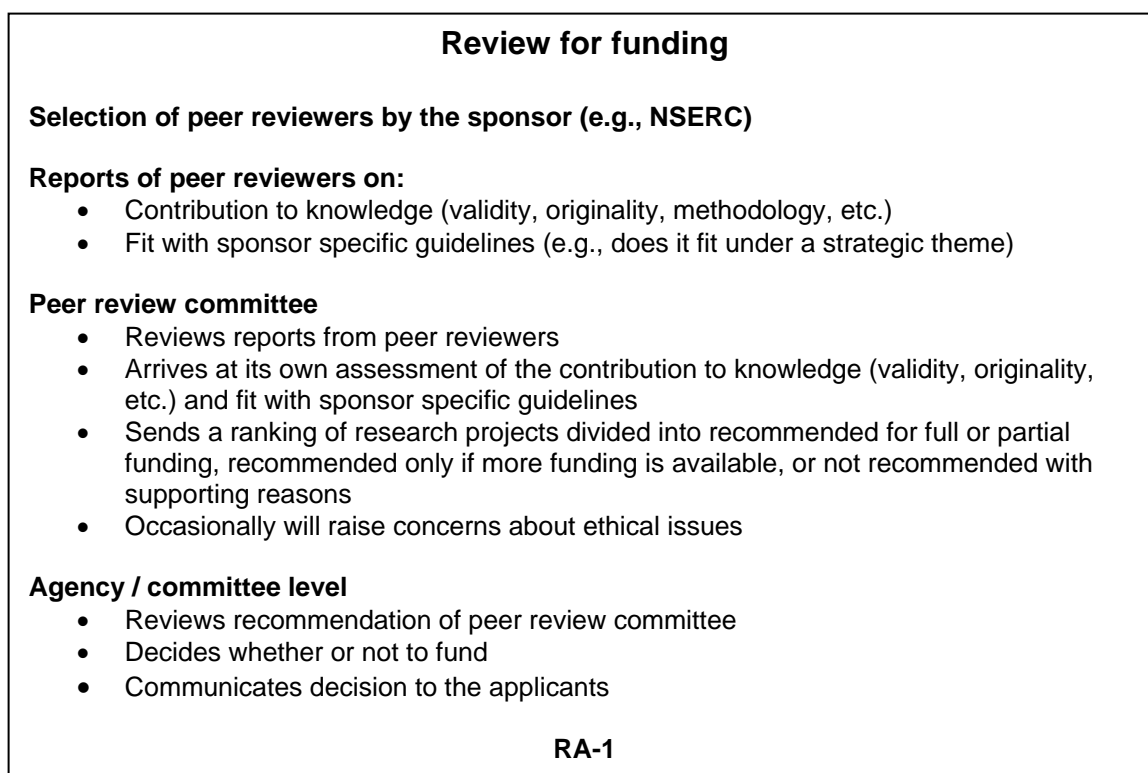
1. Are there any retrospective analyses of good / bad pilot studies?
2. Is the ethics of HRIHS a real concern of all at this stage for researchers and REB members or, is this deferred to the next stage?
3. What slips through the cracks for ethics, safety, confidentiality, clinical responsibility, etc.?

**RI-4**

## B. Research Approval

In our current governance structures, it is at the research approval stage that the most attention is paid to the ethical treatment of human subjects in research. When researchers and research administrators talk about the ethics of research involving humans, this is usually the stage that is the object of discussion – that of REB review of research protocols. Indeed, for most researchers, REB members and in research administrators, this is the sum and substance of the ethics process. At this stage, REBs apply ethical standards (principally the TCPS and GCP and sometimes foreign standards as apply for example to NIH-funded research) to determine if research projects should be approved or modified before acceptance or, rejected.

Nonetheless, there are other parts of the research approval process that are important. In particular, most studies cannot proceed without funding. In the private sector, this is a corporate decision; while for governmental research agencies, it is a bureaucratic/academic decision following the mandate of the agency (e.g., a DND study of risks of exposure to chemical agents). However, in public sector institutions like universities and health research centres, the pattern is generally that a researcher applies to an external funder or research sponsor – public, private or not-for-profit. The research sponsor has then to make a decision about whether to fund in whole or part the research project (RA 1):



If funding is granted, then the process shifts to the research institution. There may be site-specific approval mechanisms in areas like the following:

<p style="text-align: center;"><b>Site-specific approvals</b></p> <ul style="list-style-type: none"><li>• Safety concerns: biohazards, dangerous materials, contagious diseases, equipment hazards, safety training and qualification of personnel, etc.</li><li>• Concerns re: laboratory space, fiscal concerns (e.g., to collect overhead charges), ensuring that the research is not prohibited for other site-specific reasons (e.g., abortion research in a Catholic or Salvation Army hospital)</li><li>• Adherence to other site related policies (e.g., financial reporting, conflict of interest, etc.), use of clinical records, etc.</li></ul> <p style="text-align: center;"><b>RA-2</b></p>
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Some of the above may be dealt with by the REB, another body or administrator.

Next we move to REB approval. The first thing to consider is where the approval takes place and the information base available to the REB (RA-3):

<p style="text-align: center;"><b>Ethics approval</b></p> <p><b>Where?</b></p> <ul style="list-style-type: none"><li>• If single site, local REB</li><li>• If multi-site, approval at the lead site and all other sites</li></ul> <p><b>Information base</b></p> <ul style="list-style-type: none"><li>• Research protocol</li><li>• Funding decision (if peer reviewed taken as evidence of scholarly / scientific merit)</li><li>• Research budget (sometimes)</li><li>• Ethics review application including informed consent process and forms, and proposals for monitoring (new for TCPS) or adverse incident reporting (mandatory for GCP), stopping rules, etc.</li></ul> <p style="text-align: center;"><b>RA-3</b></p>
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We have already indicated the main issues to be considered by REBs. However, we list them again in RA-4:

**REB needs positive answers to 3 questions**

1. Is this valid / sound research? This is usually based on prior science review by the sponsor; otherwise, see pilot study process.
2. Do the overall potential benefits of the research outweigh potential harms?
3. Does this research respect the rights and interests of research subjects?
  - a. Harm / benefit issues
  - b. Informed consent issues

Plus conformity to other applicable ethical, legal, clinical and institutional standards

**RA-4**

In the following sections, we have much to say about ethical governance issues at the research approval stage. In the interviews (Section E), we found that REB members say that how the REB is perceived focuses on the REBs' role in the approval process. A significant number of participants report that researchers see REBs as either a necessary evil or as another step in a wasteful bureaucratic process. The research community is then very concerned with the REBs' speed and efficiency in approving research. This suggests a high risk of "ethics" being reduced to bureaucratic administration with its attendant demands for paper work.

Further it should be noticed that in terms of the total process from initiation to completion of research, "ethics" is a very small portion. That is, REBs, researchers and research institutions tend to see "ethics in research" as limited to the ethics approval phase – what happens before and after is functionally outside "the research ethics zone." Institutionally who can fault this impression? The only place research institutions invest resources (and scant resources at that) is in the REB process. Canadian standard setters and regulators also are almost exclusively focussed on the REB approval phase. Whether things will change with the TCPS and HPB requirements for monitoring is yet to be seen; however, as can be seen from the interviews, monitoring is for most REBs a large question mark.<sup>91</sup>

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<sup>91</sup> For the HPB proposal, see Department of Health *supra* note 86.

More importantly, when we reflect on the underlying culture of research, we should be asking how much of a concern is there for ethics compared to, particularly, concerns for scholarship and success in research? Recall what was said above about the mechanisms for promoting sound and insightful research in terms of education and training, hiring, promotions, peer adjudication of research proposals and the rest. Then consider by comparison the scant attention paid to education and training of researchers and REB members around the ethical treatment of humans involved in research.

In RA-5, we list multiple governance concerns:

### **Ethical governance issues for the research approval phase**

1. Is there a good fit with other parts of the site-specific approval process? Does the REB have all the information it needs to make its decisions, e.g., does it see full research protocols and budgets?
2. Is the REB an arm's length review body that in substance and appearance is independent and objective in terms of membership, processes, and reporting relationships? Who does the REB report to? Who appoints its membership?
3. Are the interests of prospective research participants adequately represented on the REB? How? Are lay or community representatives effective members of the REB? Do they represent the interests of research subjects?
4. Are there transparent and effective accountability relationships to those who set standards?
5. Who, if anyone, addresses gaps and inconsistencies in standards and processes? How?
6. Does the REB spend the bulk of its time on bureaucratic matters or on substantive ethical concerns? Does it address the full range of ethical issues (cf. the three questions) or is its time mainly spent on consent forms? How does it deal with issues around the likely overall value of a research proposal? How does it deal with issues of minimal harm?
7. Are REBs consistent and fair in their application of standards? How is this shown to relevant stakeholders?
8. Does REB approval improve ethical performance? In particular, does the approval process actually protect research subjects in the way that it is supposed to? Does the REB, research institution, or research sponsor have good means of answering such questions?
9. Where are the mechanisms and measures for quality assurance and quality improvement for the REB approval process? For the researcher application process?
10. Is there ethics training for REB members and researchers? How is adequate expertise on the REB ensured?
11. Is there accreditation and certification for REBs?

**RA-5**

## C. During Research

With REB approval, the research institution will release funds to the researcher to proceed with the human experimentation phase. During research, there are various types of monitoring in place. Many of these vary depending on the nature of the research. For example, as noted in Appendix Two for this paper, clinical trials (CTs) are monitored in ways that other types of research are typically not monitored. Who the research sponsor is also makes a difference. For example, US federal research sponsors require access to all research records, including records of REB meetings, for all the research they fund. US agencies will undertake planned and surprise visits and even random audits, e.g., of REB records. They will issue and enforce (through withdrawal of funding) orders of compliance. Similarly, commercial sponsors of pharmaceutical research regularly monitor research through paper reporting mechanisms (e.g., adverse event reports and regular reports of experimental results), on site visits and, similarly US federal authorities will on occasion audit research they fund. It is worth noting that the federal Tri-Council and other Canadian research sponsors do not use such measures.

Here is a brief overview of some of the monitoring arrangements in place for Canadian HRIHS (DR-1). Others are discussed in the appendix to this article.

### **On-going monitoring and oversight**

#### **1. Financial**

- a. Research institution manages research funds
- b. Research sponsor / funder requires financial reports,

#### **2. Medical**

- a. National / local trial co-ordinators report re clinical trials
- b. Independent health care providers (if any) may report
- c. Sponsors (e.g., pharmaceutical companies, NCIC, FDA) require medical reporting to meet regulatory requirements

#### **3. Other subject relevant concerns** (non-medical harms, consent issues, third party effects)

- a. Dealt with on a reactive basis; no monitoring
- b. REB or its delegate – new TCPS

#### **4. Research quality**

- a. For clinical trials: national trial co-ordinators, sponsors (e.g., pharmaceutical company or NIH)
- b. For other research protocols
  - i. If not NIH or similar body, no monitoring
  - ii. Dealt with on a reactive basis
  - iii. Fraud / plagiarism dealt with on a reactive basis

**DR-1**



The regulatory provisions for monitoring clinical trials are more extensive than for other types of health research. Hence, we provide a display for this area (DR-2):

### **Multi-site clinical trials**

- 1. Local trial coordinators**
  - a. Meet every 6 months
  - b. Feedback local adverse events to national level
  - c. Monitor for adverse effects on health of subjects
- 2. National trial group**
  - a. Deals with randomization and other trial conduct issues
  - b. Compiles adverse incidents and research results
  - c. Decides on continuing, modifying or stopping study
- 3. Ombudsman, office of research, or REB chair receives concerns or complaints from**
  - a. Subjects (telephone number on consent form)
  - b. Nurses, trial co-ordinators or researchers
  - c. And refers these to
    - i. Academic affairs (plagiarism)
    - ii. Equity (harassment)
    - iii. Department heads (academic issues)
    - iv. Financial affairs

**DR-2**

As we have already noted, the ethical treatment of subjects has by and large not been explicitly and systematically addressed outside the research approval phase. This gives rise to a number of ethical governance concerns for the research phase of the process (DR-3):

### **Ethical governance issues**

1. What processes are in place to make sure that subjects are heard during the research phase? Is the system proactive or simply reactive, i.e., requiring subjects to take the initiative to formulate and lodge complaints?
2. How, if at all, are researchers and those charged with the administration of RHIS educated about the likely concerns of research subjects in the types of research being conducted? Are the educational processes grounded in evidence or are they unsystematic and anecdotal?
3. Do monitoring processes, if any, provide effective and reliable quality assurance and quality improvement? In particular, is information gathered during the research process about ethical issues that may arise (e.g., unexpected third party effects, changes in competency, threats to privacy, shifts in the threshold of minimal risk)? Is that information analysed and used to improve future research performance?

i.

**DR-3**

## D. Research Completion

When research is completed, a number of things happen, e.g., reports are filed with sponsors, findings are presented at conferences and in publications and, patents are sought. We summarise these in the following table (RC-1).

<b>Research Completion</b>	
1.	Presentations: local, national and international
2.	Abstract publication
3.	Comments by colleagues
4.	Submission for publication <ol style="list-style-type: none"> <li>a. Blind review for scholarly / scientific merit</li> <li>b. Usually need evidence of REB approval of protocol</li> </ol>
5.	Publication
6.	Implementation, e.g., clinical or professional practice, changes in Q.A. or Q.I.
7.	Submission of product / device for approval <ol style="list-style-type: none"> <li>a. Clinical trial evidence</li> <li>b. REB approval of protocol</li> <li>c. Approval of product/device for marketing</li> </ol>
<b>RC-1</b>	

As will be seen from Joly's discussion in Section D-2 of public health based research, there are cases in which initiatives that started out around ordinary health protection or the ordinary provision of health care can wind up with significant publishable research results. We group these in the following table (RC-2). In addition to public health interventions, this can happen when what at first appeared to be a routine clinical intervention turns up significant research results. Moreover, a distinction is customarily drawn between clinical research and clinical innovations. The former requires REB approval; the latter does not. So the provenance or labelling of a particular procedure as either "research" or "innovation" may mean that at one institution a procedure is treated as one while in a neighbouring institution it is treated as another. For example, many advances in reproductive technologies have never been subject any formalised ethical scrutiny since they were introduced as clinical innovations rather than clinical research.

### **Non-standard research**

1. Arising from clinical practice especially from clinical innovations
  - a. Recognition of research publication or research product potential
  - b. If publication is sought, may seek retrospective REB approval based on paper record (e.g. chart reviews)
2. Public health (e.g., infectious disease)
  - a. Government housed
  - b. Public health act
3. Population health enquiry
  - a. Government initiated call for proposal, e.g., cost-effectiveness of maternal serum triple screen)
  - b. Researcher initiated, e.g., request for access to publicly held records
  - c. Freedom of information and privacy legislation
  - d. Sometimes also REB approval (especially in provinces where REB approval is legally required under freedom of information acts)

### **RC-2**

A number of questions arise concerning ethical governance for this final stage of the research process (RC-3).

### **Ethical governance issues**

- i.
- ii. **In terms of the three questions – scholarly merit, overall benefit and human subjects protection:**
  1. How do sponsors, institutions, REBs, researchers and human subjects know if the completed research met reasonable expectations re: the ethical treatment of human subjects?
  2. Does the research as predicted contribute to the advancement of knowledge? To the greater social good?
  3. How do standard setters (cf. setting parameters) know if prescribed standards and processes are appropriate? Are there retrospective ethical analyses done of completed research projects, e.g., on a random basis? Are subjects ever debriefed?
  4. Is / would this knowledge be used to improve performance?
  5. Is there sufficient transparency and accountability to inspire and deserve the trust of all relevant stakeholders, especially human subjects and the general public?

### **RC-3**



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# APPENDIX ONE

## CURRENT FORMS OF MONITORING

This is a brief overview of current monitoring practices for HRIHS in Canada. Issues regarding monitoring for clinical trials are discussed in the following appendix (Appendix Two) and Section B-2. We start with reports to REBs (Mon-1).

### **Reporting (to REBs)**

1. Annual reports (some, but not all, REBs)
2. Notification of completion or end of study (some, but not all, REBs)
3. Adverse incident reports to sponsors and REBs
4. Protocol revisions
5. Mandated interim reports for higher risk research

**Mon-1**

Next there are fiscal monitoring and reporting regarding the use of research funds.

### **Institutional monitoring of research funds**

1. Institution holds funds until REB approval
2. Institutional financial controls
  - a. To avoid deficit situation
  - b. To assure sponsor funds used for designated purposes
3. Institution reports to research sponsor on a regular basis and on completion of the project regarding the use of sponsor's funds for research.

**Mon-2**

As noted earlier, research sponsors play a role in monitoring (Mon-3):

### **Monitoring by sponsors**

1. Who? Pharmaceutical companies and some foreign sponsors (e.g., FDA, NIH, NCIC)
2. How? Scheduled and sometimes unscheduled on-site visits, sometimes surprise visits, paper audits of researcher and REB records, required compliance plans
3. What? Accuracy of data, reporting issues, allegations of fraud, etc.
4. At stake, continued funding and potential legal liability

#### **Mon-3**

It is important to understand monitoring and other oversight taken by MRC, NSERC, and SSHRC. With the move towards a unified policy on research involving humans, the three Councils moved to have the National Council on Bioethics of Human Research (NCBHR) widen its mandate beyond health research to include other types of research involving humans. NCBHR had been created by MRC, Health Canada and the Royal College of Physicians and Surgeons to provide education in the area of biomedical research involving human subjects and to advise REBs who operated under the MRC Guidelines on Research Involving Human Subjects.<sup>92</sup> Two additional sponsors – NSERC and SSHRC – joined the original sponsors to create the National Council on the Ethics of Human Research (NCEHR). NCEHR's role is described in the following table (Mon-4).

### **NCEHR**

1. Sponsored by MRC, NSERC, SSHRC, Royal College of Physician & Surgeons and Health Canada
2. Educational role re TCPS
3. Site visits voluntary and provides advice to institution
4. Advisory role in policy-making and accreditation; lacks the power to withhold research funds

#### **Mon-4**

NCEHR has a counterpart on the animal research side – the Canadian Council on Animal Care (CCAC). CCAC has a long history and is known internationally for its various guidelines on research involving animals. CCAC has oversight powers with respect to institutional committees for reviewing and approving research involving animals – Animal Care Committees (ACCs). These powers are much more extensive and, in our view, are much more

<sup>92</sup> MRC, *Guidelines on Research Involving Human Subjects* (Ottawa: Medical Research Council of Canada, 1987).



able to demonstrate important positive effects on the welfare of research animals than either NCEHR or its predecessor NCBHR in regard to the rights and interests of human subjects. CCAC is described in the following (Mon-5).

<b>Governance for research involving animals</b>	
<ol style="list-style-type: none"> <li>1. CCAC is funded by MRC and NSERC and some private sponsors (from industry):</li> <li>2. Mandatory site visits</li> <li>3. Institutions must show they are compliant with CCAC Guidelines for all research involving animals within their institution (or develop a plan acceptable to CCAC) to receive non-commercial research funds from MRC and NSERC</li> <li>4. CCAC sets, implements and enforces rules for compliance with TOPS animals</li> <li>5. Non-university agencies conducting research involving animals may for a modest fee be inspected by CCAC and if in compliance with CCAC rules be recognised as such. (In the near future, CCAC will institute a programme of granting Good Animal Practice (GAP) certificates.</li> </ol>	<p style="text-align: center;"><b>Other Tri-Council Efforts</b></p> <ol style="list-style-type: none"> <li><b>Mon-6</b></li> <li><b>Mon-5</b></li> </ol>

Nevertheless, we would also note that in addition to NCEHR the Tri-Council group has other relevant initiatives with respect to research involving humans (Mon-6).



# APPENDIX TWO

## CLINICAL TRIALS

Many of the previous tables centred on HRIHS in the context of university and health research institutions. To close this portion of our overview, it is necessary to look at industry research, particularly at research that is in house. While some of this has been touched on earlier, we draw the material together here in the following tables that centre mainly on pharmaceutically based clinical trials (CT).<sup>93</sup>

### Steps toward human research

#### Cell culture studies

1. Animals (sometimes subcontracted)
2. Safety studies for human exposures
3. Proceed to Phase I

**Ind-1**

### Phase I

1. Required for drug approval
2. Pure Phase I non-therapeutic clinical trials on healthy subjects
  - a. Paid to volunteer
  - b. Sometimes on site or subcontracted
  - c. Acute dosages toxicity / safety
3. Phase I/II Clinical Trials on sick patients,
  - a. To test for toxicities and efficacy
  - b. Also to improve survival or quality of life of subjects
  - c. In hospital, e.g., for cancer – no treatment or failure of 2 attempts at treatment
  - d. Independent access, e.g., AIDS patients
4. Ethics approval by in-house or private (for profit REB)

**Ind-2**

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<sup>93</sup> Issues regarding new federal regulations for CTs are discussed in Section B-3.

**Phase III**

1. Required for drug approval
2. Test for efficacy / short-term toxicities
3. Clinical trials in hospitals
4. On-going monitoring by corporate sponsor or clinical trials subcontractor
5. Limited room for institutional REB to modify proposals

**Ind-4****Phase IV**

1. Post-marketing surveillance studies of long-term efficacy and toxicity of marketed drugs
2. Often in private offices of physicians

**Ind-5**

These give rise to a number of governance concerns.

**Governance concerns**

1. General concerns: sample sizes, data accuracy, stopping rules, inclusiveness, oversight for the broad range of ethical concerns
2. Phase I – independent oversight and monitoring for health, voluntariness, and appropriate compensation
3. Phase I/II – patient vulnerability and consent; harm issues
4. Phase III – monitoring for consent and harm
5. Phase IV – worries re marketing masked as research: researcher qualifications, lack of oversight by professional bodies, potential conflicts of interest on part of participating researchers

**Ind-6**

## SECTION B-3

# THE CURRENT CONTEXT OF HRIHS

Michael McDonald

We now turn to the context of HRIHS. We have divided contextual features into two broad categories. The first includes pervasive general factors shaping contemporary health research around the world. The second includes factors specific to the Canadian context of governance with respect to RIHS.

## I. GLOBAL FEATURES SHAPING HRIHS

We see four major factors shaping contemporary health research:

- **Rapid scientific and technological innovation and advances**
- **Multiple disciplinary and interdisciplinary research modalities**
- **Commercialisation and privatization**
- **Globalisation and harmonisation**

While these are closely related factors that on the whole reinforce each other, the first two can be seen as factors internal to health research and the second two as larger external or, in the broad sense of the word, environmental factors. Genetic research provides a good example of the interplay of these factors.

While genetics had its origins in the late eighteenth century, it is only in the last few decades with Crick and Watson's discoveries that genetics has assumed its modern form. In the early 1970's with the discovery of restriction endonucleases, genetics took off as a major area of research with enormous intellectual, social and economic impacts. There are now major international and national programmes in genetic research, including the Human Genome

Project. There is extensive private sector research and development in genetics including, in directly, health-related areas (pharmaceutical research) and in areas that are potentially health affecting (plant and animal biotechnology). Research in genetics has been typically quite expensive, and its commercial impacts are substantial. As well, research in genetics has global dimensions with major research centres in many countries and (just as important) research on populations around the world, including particularly indigenous peoples. There have been substantial pressures for regulating genetic research both domestically and internationally. In turn, this has prompted multi-disciplinary research into various aspects of genetics – psychological and social impacts, ethical and legal aspects and, economic effects. Moreover the results of research for health, the economy, social well-being and even our very conceptions of ourselves as genetically determined beings are potentially extremely high.

While rapid scientific and technological innovation is particularly apparent in genetics, it is also significant in other areas. For example, computerisation has made possible the accumulation of large databases; these have revolutionized research methods in many areas, such as cancer research and public health. At the same time, these also raise questions about striking the right balance between the potential benefits of such research and concerns for privacy. As noted in the case of genetics, methodologies used in health research have broadened from those used primarily in the natural sciences to include those used in the social sciences and the humanities. In part, this has been prompted by a concern with health behaviours and outcomes (such as healthier life-styles). But it has also been encouraged by a concern with quality of life and ethical issues.

Rapid scientific advancement and new research methodologies have encouraged and been encouraged by commercialisation and globalisation. Thus, the rapid advances in genetic sequencing have created major opportunities for pharmaceutical industries that in turn have created new research opportunities; genetic advances have also reinforced the tendency toward the formation of large multi-national corporations in this sector. Commercialisation, we believe, has created an impetus toward the privatization of legal relationships, i.e., towards making human subject research a matter of private rather than of public law. Similarly, globalisation has created pressures for the harmonisation of various normative régimes, e.g., toward the international harmonisation for pharmaceutical testing.<sup>94</sup>

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<sup>94</sup> This is reflected in the proposed changes in federal regulations for clinical trials Department of Health, "Regulations Amending the Food and Drug Regulations (1024 -- Clinical Trials)" *Canada Gazette Part 1* (22 January 2000) 227.

At the same time, globalisation and commercialisation are part of a larger social and political context that directly affects Canadian health research. For example, the rapid increase in private sector support for health research along with a relative decline in public sector support has changed institutional cultures in Canadian universities and medical research centres. In order to maintain positions supported on ‘soft’ dollars (as opposed to base budgets), Canadian research institutions have felt compelled to scramble for scarce research dollars. This in turn has created pressures on Research Ethics Boards and others involved in the research ethics governance process. In short, these four factors shape the contemporary context of Canadian health research in ways that profoundly affect governance relationships and their effectiveness.

Many of the significant changes that are occurring internationally are usefully summarised in the following chart from the US Office of the Inspector General’s report, *Institutional Review Boards: A Time for Reform* (p. 5). Our main change for the Canadian context would be with the description of the first change mentioned – “Expansion of Managed Care” – which we would replace with “Pressures on Health Care Costs”.

<b>A CHANGING ENVIRONMENT FOR IRBs</b>		
<b>CHANGE</b>	<b>EXPLANATION</b>	<b>KEY IMPLICATIONS FOR IRBs</b>
Expansion of Managed Care	Emphasis on cost control and competition. Squeeze on research support for academic health centers.	<ul style="list-style-type: none"> <li>• Pressures to accommodate research sponsors who can provide research-related revenues for the parent institution.</li> <li>• Increased difficulty in obtaining staff and other resources.</li> <li>• More pressure on staff physicians to generate income with less time available for voluntary commitments to IRBs.</li> </ul>
Increased Commercialization of Research	Heightened industry role in sponsoring research. Sponsor emphasis on rapid product development.	<ul style="list-style-type: none"> <li>• Institutional and sponsor pressures for quick reviews.</li> <li>• Sponsor shopping for customer-focused IRBs.</li> <li>• Added complexity on issues involving liability, academic freedom and, patient disclosure.</li> </ul>
Proliferation of Multi-Center Trials	Proliferation of trials spread across hundreds of sites, even across the world.	<ul style="list-style-type: none"> <li>• Diminished influence of "local" review.</li> <li>• Flood of adverse-event reports to review.</li> <li>• Lack of access to significant information concerning the status of ongoing research.</li> </ul>
New Types of Research	Advances in biomedical research in the areas of gene testing and gene consent and appropriate research. Therapy increased research on mental health issues	<ul style="list-style-type: none"> <li>• Need for new, highly specialized areas of expertise.</li> <li>• Emergence of thorny ethical issues involving informed</li> <li>• Increased importance of having non-institutional board members</li> </ul>

Increased Number of Proposals	Intensified efforts to obtain government funding and to develop new products.	<ul style="list-style-type: none"> <li>• Significant increase in workloads.</li> <li>• Without sufficient increases in staff and/or efficiency, less time is available to review initial protocols and to conduct continuing reviews of approved research.</li> </ul>
Rise of Patient Consumerism	Increased consumer demand for access to research.	<ul style="list-style-type: none"> <li>• Presents major challenges in: Ensuring equitable recruitment of subjects. Ascertaining local attitudes and values. Maintaining distinctions between therapy and research.</li> </ul>

## II. CANADA-SPECIFIC FEATURES SHAPING RIHS

In addition to these four general factors, there are a number of more Canada-specific factors affecting the governance of RIHS. One of the most important of these is the recent introduction of the *Tri-Council Policy Statement (TCPS)* by the MRC, NSERC and SSHRC. A second is the formation of the Canadian Institutes for Health Research (CIHR). The third involves recently proposed changes in federal regulations for clinical trials.<sup>95</sup> Fourth is the impact of private funding on Canadian health research. As well, there are other factors that are discussed in the papers that follow this section – federal and provincial legislative moves in regard to privacy (e.g., Bill C-6) and freedom of information (which Dickens discusses in Section C-1) and some regulation by provincial health professions in regard to RIHS (which Kinsella discusses in Section D-3).

### A. *The Tri-Council Policy Statement (TCPS)*

The TCPS was adopted in 1998 by the three Councils and applies to the conduct of all research carried on by research institutions administering funding provided by the Councils for research purposes. The Councils provide funding to researchers in particular research institutions on condition that *all* research involving human subjects is conducted in accord with the Tri-Council Policy Statement (TCPS) – not just the portion funded by the Councils. In turn, research institutions make following the TCPS a condition of employment for their researchers. In this respect, TCPS continues the arrangements represented in earlier Council policy where

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<sup>95</sup> *Ibid.*



following SSHRC and/or MRC Guidelines for all RIHS was a condition for receiving Council funding.<sup>96</sup>

Where TCPS represents a major change from the former regime governing RIHS at Canadian universities and hospitals is in its creation of a unified set of prescriptions for all research involving humans to replace the previously separate reviews for behavioural research governed by SSHRC Guidelines and biomedical research governed by MRC Guidelines. To explain how the TCPS has changed the Canadian context for HRIHS specifically and RIHS generally, it is useful to briefly review the reasons for the creation of a unified policy statement and the process by which it was developed.

1. NSERC had no guidelines for human subjects' research even though it funded human subjects' research in experimental psychology and biomechanical engineering.
2. In 1993 the three Councils found common moral ground in developing a unified policy on research integrity.
3. Existing guidelines for RIHS were dated -- SSHRC's *Guidelines* were adopted in 1976 and MRC's dated from 1987. Whole new areas of research, especially in health science areas, had developed since the previous guidelines had been adopted, e.g., genetics and reproductive technologies.<sup>97</sup> As well, new research technologies and advances (e.g., genetic sequencing, new reproductive technologies, and even more pervasively computers and electronic databases) had major impacts in such morally sensitive areas as privacy and confidentiality.
4. Interdisciplinary research had come to the fore. Particularly in health research it came to be realised that health results were not simply a function of health technologies or even health care but were related to a large range of health determinants – economic, social and environmental. Having separate behavioural (SSHRC) and biomedical (MRC) guidelines seemed to run contrary to the idea of integrated interdisciplinary health research.
5. In any case, it was generally recognized that there are common moral values which govern all types of research involving humans, e.g., the values found in informed consent and the avoidance of unjustifiable harm.
6. In various areas of research, it was argued that current *Guidelines* were inadequate, in particular, for multi-site clinical trials, research involving human

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<sup>96</sup> Prior to 1998, only two of the Councils had rules for the conduct of RIHS. The MRC had *Guidelines for Research Involving Human Subjects* (1977; revised in 1987), while the SSHRC had *Ethics Guidelines for Research Involving Human Subjects* (1979). NSERC funded researchers carrying out RIHS had their research approved by either a biomedical REB following MRC *Guidelines*, e.g., on biomedical devices, or SSHRC *Guidelines*, e.g., experimental psychology.

<sup>97</sup> See SSHRC, *Ethics Guidelines for Research with Human Subjects* (Ottawa: Social Sciences and Humanities Research Council of Canada, 1979). MRC, *Guidelines on Research Involving Human Subjects* (Ottawa: Medical Research Council of Canada, 1987).

tissues, research involving women, research involving children and research involving collectivities. Some of the impetus for change in these areas came from researchers as well as ethicists and lawyers. But there had also been changes in international, professional and other norms. For example, the 1993 *CIOMS International Guidelines* gave significant recognition to ethical conduct with respect to research in developing countries and part of that recognition was the identification of researcher responsibilities with respect to research involving vulnerable collectivities.<sup>98</sup>

The net result was that in 1994 Presidents of MRC, NSERC and SSHRC formed the Tri-Council Working Group on Ethics with researchers from a number of areas sponsored by the Councils.<sup>99</sup> In 1996, the Tri-Council Working Group completed a draft *Code of Ethical Conduct for Research Involving Humans* and distributed it throughout the Canadian academic community for comment.<sup>100</sup> The Working Group received over 2,000 pages of comments from over 250 respondents – almost all the respondents were from the research community – individual researchers, disciplinary groups, university and hospital administrators, research ethics boards, university departments and research institutions as such. In light of those comments and further discussions, the Working Group produced a final version of the *Code* and submitted it to the Councils in May 1997.<sup>101</sup> At this point, the Tri-Council Working Group was disbanded and played no further part, collectively or individually in the production of the ensuing TCPS.

In late 1997 and early 1998, the Council consulted with various interest or stakeholder groups. As far as we know these consultations were again centred on the research community – researchers and research sponsors particularly – and did not include research participants or their potential advocates. For example, through the Social Sciences and Humanities Federation of Canada, SSHRC conducted extensive consultations with the social science and humanities associations that compose the Federation. There were consultations by MRC with deans of medical faculties and by NSERC with research administrators. As well the Councils used their own internal processes for consultation, e.g., the MRC Standing Committee on Ethics played a

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<sup>98</sup> Council for International Organisations of Medical Sciences Guidelines CIOMS, "International Ethical Guidelines for Biomedical Research Involving Human Subjects," World Health Organization (Geneva: CIOMS, 1993).

<sup>99</sup> Several members of the research team for this project were members of the Tri-Council Working Group – Jean Joly chaired the Working Group, Michael McDonald was deputy chair. Michael Asch, Bernard Dickens, Douglas Kinsella, and Barbara McGillivray were members of the Working Group.

<sup>100</sup> Tri-Council Working-Group, *Code of Conduct for Research Involving Humans* (Ottawa: Medical Research Council of Canada, 1996).

<sup>101</sup> Tri-Council Working-Group, *Code of Ethical Conduct for Research Involving Humans (Final)* (Ottawa: Tri-Council, 1997).

large role in MRC's deliberations. As well the text of the TCPS was given to the Department of Justice for review.

While many researchers viewed the *Code* favourably, some were quite resistant to particular provisions and its overall tone. In particular, there was a strong campaign organized by the Canadian Association of University Teachers around areas of the *Code* that were described as threats to academic freedom. The section on research involving collectivities came under particular fire. The concern expressed in the section on collectivities for vulnerable groups and the desire, where possible, to respectfully negotiate significant differences in moral understandings was seen by many critics as potentially inhibiting research on powerful institutions and public figures. CAUT urged instead that the only legitimate ethical concern for research in this area applied *sui generis* to Aboriginal groups.<sup>102</sup> This ultimately was the approach taken by the three Councils. However, on the recommendation of the Department of Justice, the section of the TCPS on research involving Aboriginal groups has been held in abeyance pending negotiations with indigenous peoples in Canada and abroad.

But there was also considerable controversy about the wisdom of a common approach to the ethics of RIHS on the part of the three Councils, particularly by social scientists in political science, psychology and history. At the extreme, there were suggestions that there should be no prior review of proposed research involving humans – that peer review alone would be a sufficient safeguard against ethical abuse. As well, some claimed that while medical researchers had good reason to be concerned with potential research harms to research subjects, this ought not to be a concern for social scientists and humanists. Some urged this position on the grounds that social science research could never harm research subjects whereas medical research was inherently risky.<sup>103</sup> Others critics argued that informed consent was a sufficient safeguard for research conducted by social scientists so that issues of harm and benefit could be ignored. The separate sets of guidelines for medical and non-medical

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<sup>102</sup> CAUT's defence of a *sui generis* approach to research involving collectivities is out of step with *CIOMS Guidelines* which are designed to apply generally to populations in developing countries and not just indigenous groups. CIOMS, "International Ethical Guidelines for Biomedical Research Involving Human Subjects," World Health Organization (Geneva: CIOMS, 1993). Furthermore, from a moral perspective, there are two major concerns with whether special provisions for indigenous peoples can be justified. The first is that it seems anomalous not to extend concerns to similarly disadvantaged groups. The second is that *sui generis* provisions can be seen as stigmatizing and stereotyping indigenous peoples as uniquely collectivist, that is as being "peoples" unlike non-indigenous who are just plain people (morally significant only as individuals and not as members of groups).

<sup>103</sup> It is worth noting that these critics actually had much in common with the subset of medical researchers who count as significant only physiological and biological harms in that social, psychological and other harms are regarded as insignificant and generally unworthy of any concern.

researchers represented more than two different regulatory processes; they also symbolized two quite different research cultures around research involving humans – a biomedical culture and a non-biomedical/behavioural culture.<sup>104</sup>

Rather less public, but we think no less important, were concerns expressed by research institution administrators about the potential costs of meeting the provisions of the proposed *Code* and also with the difficulties of dealing with reluctant researchers particularly in the social sciences and the humanities. Serious concerns had been articulated about potential competitive disadvantages in attracting research funding if standards were raised especially if other research institutions did not simultaneously raise their standards. One university head ruefully agreed with the description that amongst research institutions there was a potential “race to the bottom.”<sup>105</sup> This was joined with concerns about institutional autonomy and liability. As well some university research directors questioned the legitimacy of Councils imposing policy given the Council declining role in research funding.

The end result of these criticisms was that the three Councils dramatically revised the 1997 draft *Code*. The Councils have been criticized for a behind the doors revision process and a lack of public consultations – especially compared to the very open process used by the Working Group in revising the 1996 draft *Code*.<sup>106</sup> Members of the former Tri-Council Working Group have publicly and privately expressed concerns about the quality and coherence of the revisions made to the 1997 draft *Code*.<sup>107</sup> As well, those involved in research on collectivities have complained about a lack of guidance for research in their area.

Since the Councils adopted the TCPS in 1998, the Councils have asked affected research institutions to prepare a plan for complying with its provisions. By the end of 1999, research institutions had to indicate that they were in compliance with the TCPS or provide a plan for coming into compliance. As evidenced in the interviews, many institutions have had to

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<sup>104</sup> The formation of different sensibilities was a result of many more factors than common guidelines and procedures. There are different factors shaping the two communities. In the case of medical research, there is at the core a set of professional expectations – many biomedical researchers are members of self-governing professions. The idea of professional self-governance is not one that finds many adherents on the social sciences and humanities side where a more *laissez-faire* view prevails. Moreover while incidents of misconduct by medical researchers were widely reported, misconduct by non-medical researchers has been much less publicized. As a result, the first target of regulation in most countries has been medical research with other types of RIHS as a kind of after-thought.

<sup>105</sup> December 1997 conference on research ethics sponsored by the Canadians for Health Research.

<sup>106</sup> F. Baylis *et al.*, “Women and Health Research: From Theory, to Practice, to Policy” in A. Donchin & L. Purdy, eds., *Embodying Bioethics: Recent Feminist Advances* (Lanham: Rowman & Littlefield, 1999) 253..

implement important changes in processes and procedures, e.g., with respect to REB membership, number of REBs in institutions, processes for evaluating student conducted RIHS, and requirements for face to face meetings. The requirement for monitoring research has posed major problems.<sup>108</sup>

We have already noted the advisory and educational role played by NCEHR with respect to the TCPS. As well, there is a Tri-Council Committee working on various changes to the TCPS including achieving harmonisation with the GCP. Both MRC (and likely its successor CIHR) and SSHRC have committees concerned with the ethics of RIHS.

## B. The Formation of the CIHR

While the creation of the TCPS has considerably changed the scene with respect to a substantial part of Canadian RIHS, the formation of the Canadian Institutes for Health Research (scheduled officially for April 2000) and various changes in Canadian health regulation, are also affecting the area especially in regard to health research involving human subjects.

CIHR is not only intended to replace the MRC but it is also supposed to bring about a new and enhanced role for the federal government in sponsoring health research. Part of the enhancement is in the form of increased funding for health research. But another part of the CIHR mission is to produce integrated health research that results in improved health for Canadians. One move is the development of partnerships with other Canadian health research sponsors, e.g., the Heart and Stroke Foundation of Canada and the Canadian Kidney Foundation. There is an emphasis on interdisciplinary research that bridges traditional biomedical sciences and non-biomedical disciplines, like economics, law, ethics and medical anthropology and sociology. SSHRC has been given a significant role in funding such research in the form of an express partnership with CIHR. In the legislation establishing the CIHR, 'ethics' is mentioned four times. There have been several proposals for the integration of ethical processes and just as importantly research in relevant areas of ethics into each of the health institutes being created for CIHR and for the CIHR governing process.<sup>109</sup>

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<sup>107</sup> McDonald and Dickens made this point at the 1998 meeting of the Canadian Bioethics Society.

<sup>108</sup> This requirement originated in the 1996 draft *Code*.

<sup>109</sup> See B. Knoppers, *Report of the Interim Governing Council Subcommittee on Ethics: "Working Paper The Ethics Mandate of the Canadian Institute for Health Research: Implementing a Transformative Vision 1999*, Interim Governing Council, Canadian Institute for Health Research,

## C. Federal Regulatory Changes

Over the past several years, there have been relevant changes in federal regulation of health matters. Most relevant to our concerns have been the following. The first is changes to achieve international harmonisation with respect to pharmaceutical and medical device approvals. The second is very much related to the first. It has to do with increasing reliance on drug and device testing by industry and by university based researchers and much lessened reliance on direct testing by government agencies, e.g., with respect to food and drugs. There are a number of reasons for the devolution of responsibility from government to industry and universities. This can be seen as part of general downsizing on the part of governments in Canada and elsewhere particularly in regard to regulatory bodies. Part of the motivation for this move is to eliminate the duplication of efforts for testing the safety and efficacy of new products. This also has very much to do with enhancing Canada's competitiveness internationally. The most dramatic recent example of this is the forthcoming move by Health Canada (HC) to shorten approval times for some clinical trials.<sup>110</sup> For example, under the new rules a pharmaceutical company would apply to HC for a Phase I Clinical Trial (testing for toxicity) or a Phase I/II trial (testing for short-term efficacy with possibly very ill patients). Unless HC replies in the negative within two working days, the Phase I or I/II trial – the most acute types of CT trials – could be launched immediately.<sup>111</sup> One of the reasons for the proposed change in approval times is to make Canada competitive in attracting CTs from international companies. The Minister has suggested that on an annual basis this could bring nearly one hundred million dollars to Canada – a boon for Canadian researchers and research institutions in its own right and a major boost for Canada's position in drug research.<sup>112</sup>

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<<http://fusion.klickit.com/lee/cihr/file/files/ethicsenglishfinal.PDF2000>>; S. Sherwin et al., *The Ethics Mandate of the Canadian Institutes for Health Research: Integrating Bioethics and Health Law in the CIHR 1999*, Social Sciences and Humanities Research Council of Canada, <<http://www.sshrc.ca/english/programinfo/sherwin.pdf2000>>; and J. Storch et al., *An Institute for the Integration of Ethics, Law, Culture and Health* SSHRC Web Site 1999, Social Sciences and Humanities Research Council of Canada, <<http://www.sshrc.ca/english/programinfo/storch.pdf2000>>. Knoppers chaired the IGC Subcommittee that authored one report and was a member of the team that prepared the Sherwin report. McDonald was a member of all three groups.

<sup>110</sup> See Department of Health, "Regulations Amending the Food and Drug Regulations (1024 -- Clinical Trials)" Canada Gazette Part 1 (22 January 2000) 227.

<sup>111</sup> We would predict that if the accelerated approval times for Phase I and I/II trials are well received default approval times for other phases will also be initiated.

<sup>112</sup> *Supra* note 110.

In some ways the accelerated time schedule and greatly increased responsibilities for REBs can be viewed negatively as potentially weakening mechanisms for research ethics review for Phase I and Phase I/II clinical trials. However, it may have a positive impact in terms of improving the quality of REB review. In the *Regulatory Impact Statement* accompanying the proposed changes, it is argued that:

The proposal would provide federal recognition of the important service provided by REBs. It would improve consistency relating to the roles and responsibilities of these boards by providing a standard for generally accepted principles of GCP. It is hoped that this regulatory requirement will draw attention to the need for to have a formal accreditation system for the REBs. This will promote compliance with generally accepted principles of the GCP. The proposal requires that sponsors obtain their approval prior to conducting trials. This may facilitate new funding mechanisms for these Boards.<sup>113</sup>

Of course, it remains to be seen if consistency of decision-making, accreditation and greater support for REBs result. The new regulations certainly raise the stakes for the credibility of current REB approval processes and place significant strains on scarce resources.

#### D. Impact of Private Funding<sup>114</sup>

In the last twenty years Canadians as well as Americans and Europeans have witnessed major changes in the funding of research projects involving human persons. From an endeavor that was essentially financed by federal and, in some instances provincial governments, research funding is now an activity that is largely financed by for-profit corporations. This is especially true in biomedical research where the recent fiscal constraints had a major impact and led to an ever more present private sector financing.

Parallel to this expansion of private funding in biomedical research, the increasing cost of developing and licensing drugs by health authorities in various countries forced the pharmaceutical industry into cost-containment practices and hence standardization of research practices in different jurisdictions, so that a set of data obtained in one country could be applied in a different country for regulatory purposes. This has spurred the development of internationally accepted *Good Clinical Practice Guidelines* (GCP).<sup>115</sup> These are accepted

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<sup>113</sup> Department of Health, *supra* note 110.

<sup>114</sup> This section was authored by Jean Joly and modified by Michael McDonald.

<sup>115</sup> ICH, *Good Clinical Practice: Consolidated Guidelines, ICH Harmonised Tripartite Guideline* (Ottawa, Ontario: Minister of Health, 1997).

standards of research involving human subjects that are quite detailed and cover a wide range of requirements, from the collection of data to the composition of the REB and various ethical concerns.

These guidelines were developed by a few national governments (United States, Japan and the European Community countries) and the pharmaceutical industry and co-opted by almost all other countries afterwards (including Canada).<sup>116</sup> As mentioned earlier, for the drug industry, the principal motivating factor behind the development of these standards was economic.

Prior to the adoption of these guidelines, Canadian researchers relied heavily on the *Medical Research Council Guidelines* that were first published in the 1960s and updated each decade afterwards. As noted above the last revision made with MRC as the only stakeholder was in 1987, the 1997-99 revision being a joint enterprise of the three Canadian Councils. The guidelines that existed prior to the implementation of the current Canadian guidelines and the *Good Clinical Practice Guidelines* were vague and led to major problems when multi-centre Canadian trials were undertaken: rules adopted in one institution could be quite different from those adopted in a second institution across the street. This led to confusion and loss of information. Data derived from a given center by the pharmaceutical industry could sometimes not be used in their application for drug approval to Health Canada.

A consequence of the development of *Good Clinical Practice Guidelines* is that a researcher or an institution that would not follow them or have requirements that are different from these guidelines (either sub-standard or for whatever reason far above them) would most probably be cut from any private funding from the pharmaceutical industry, especially if the study is for regulatory purposes.

A serious risk of this harmonization of ethical standards across different countries is the imposition of requirements that may be culturally unacceptable or context insensitive. For example, there might be the loss of practices that are appropriate to local cultural circumstances, e.g., oral consent for subjects recruited from oral as opposed to written cultures but, that are deemed to be inferior to international standards for written consent.<sup>117</sup>

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<sup>116</sup> Canada had observer status during the development of these guidelines.

<sup>117</sup> It should be noted that the 1997 draft *Code* was especially sensitive to such issues.



## E. Other Changes

There are then major economic forces driving this devolution, not just on the part of private sector industries but also on the part of Canadian research institutions. As well, there is considerable interest on the part of those seriously affected by major threats to health and their families for beneficial research. Those at risk desire research that significantly improves their health outcomes. Given the absence of attractive therapeutic alternatives, they may well want to participate in clinical trials and/or receive experimental therapies. In some cases, articulate interest groups with strong agendas have formed to lobby for research in areas affecting their health, e.g., people with AIDS or those with or at risk of hereditary forms of breast cancer. This has also complicated the picture we currently have of the ethics of research involving humans, so that it is no longer just a question of protecting research subjects from the potential harms of research (as would have been seen to be a principal task of research ethics processes in the 1970's and 1980's). It introduces then difficult and far-reaching questions about justice or fairness in research -- what types of research get funded, as well as who gets to participate in research trials and under what conditions. More generally, it raises the issue of whose health is deemed significant enough to get on the health research agenda.



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# SECTION C-1

## GOVERNANCE RELATIONS IN BIOMEDICAL RESEARCH

Bernard M. Dickens

### I. INTRODUCTION

Biomedical research involving human subjects remains governed in Canada by law that is primarily directed to other purposes. Law applies almost inadvertently to the enterprise of biomedical research. Not only does legislation pay little regard to biomedical research, but may deliberately exclude it from coverage. In Ontario, for instance, the *Health Care Consent Act* expressly provides that it does not cover health interventions whose primary purpose is research. It therefore remains uncertain whether its detailed provisions on advance medical directives, by which competent persons anticipating future cognitive incapacity can declare what treatments they will accept and which are not to be employed, can authorize research procedures. With the increasing incidence of Alzheimer disease and similar neurological disorders in an aging population, the need for research on subjects incapable of consent is pressing, but research is obstructed by uncertainty concerning the legal validity of advance consent that claims to be given under authority of that Act.

In 1989, the Law Reform Commission of Canada released Working Paper 61, entitled *Biomedical Experimentation Involving Human Subjects*. This recommended, among other developments, that the legality of non-therapeutic biomedical experimentation be recognized in a general federal statute when it involves children and mentally disabled persons, provided that:

- (a) the research is of major scientific importance and cannot be properly conducted using only adult subjects capable of giving consent;
- (b) the research is in close, direct relation to either infantile diseases or pathologies or mental illness or deficiency, as the case may be;

- (c) the research does not involve any serious risks for subjects;
- (d) the consent of a competent adult guardian and of an independent third party (a judge, an ombudsman or a legal representative) is obtained; and
- (e) where possible, the consent of the child or incompetent person is obtained, and the refusal of the child, of whatever age, or of the incompetent person, is always to be respected.

Enactment of such legislation would have to fit within the framework of constitutional distribution of powers between federal and provincial levels of government, and be consistent with guarantees of protection under the *Canadian Charter of Rights and Freedoms*, or be otherwise demonstrably justified in a free and democratic society. As the federal government moves towards the prohibition of some forms of embryo research in the pending return of the former Bill C-47, it may be appropriate to address how federal and provincial legislation may also facilitate the conduct of ethical research involving human subjects and tissues.

## II. FEDERAL LAW ISSUES

### A. Criminal Denial of Informed Consent

In law, touching a person without valid consent, which in most cases is given by that person, constitutes battery in civil law and assault in criminal law. If consent is inadequately informed, it has been held since 1980<sup>118</sup> that it remains valid to neutralize battery or assault. If, however, injury results in consequence of an inadequately informed consent to such a risk that would not have occurred had adequate information been given, for instance because the person would have decided against taking the risk, the person may succeed in an action for negligence. That is, inadequate informing falls within the law of negligence, not assault or battery.

Although negligence tends to be considered a matter of civil (non-criminal) law, crimes exist of criminal negligence causing death and criminal negligence causing bodily harm. These are rarely if ever relevant to scientific research. In September 1998, however, a significant development in understanding occurred, in the Supreme Court of Canada's judgment in the

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<sup>118</sup> *Reibl v. Hughes* (1980), 114 D.L.R. (3d) 1 (S.C.C.).

case of *R. v. Cuerrier*<sup>119</sup>. This concerned a man who knew he was HIV-positive, who had unprotected sexual intercourse with women who consented but from whom he had withheld information of his HIV status. He was later charged with criminal assault. By conventional doctrine, even uninformed consent would have overcome the charge of assault, and the B.C. trial court and B.C. Court of Appeal found that he had committed no crime. The Supreme Court of Canada disagreed, and ruled that, if serious danger to health existed, the man had a duty to inform his prospective partners. Failure to give them that information was fraud in law, which negated the partners' consent. Touching them without their consent, as understood in law, constituted assault. The accused could therefore be convicted of a crime.

This decision imports the legal doctrine of informed consent into criminal law. Its effect is that, if research involves a risk of touching that a court considers a "significant risk of serious harm," failure to give adequate information before the research subject is touched renders the touching non-consensual and so a criminally convictable assault. This raises the stakes on invasive medical and other research that includes a significant risk of serious harm. Further, if failure adequately to inform of risk constitutes fraud, and inadequate information is offered in order to induce consent to studies from which investigators derive payments, charges of obtaining by fraud or false pretence may be applicable.

## B. Theft of Tissue Samples

Although dead bodies have long been considered in law not to be property, the application of craftsmanship or skills to human remains can make them into legal property. These materials can therefore be lawfully owned and possessed, and unlawfully stolen. In *R. v. Kelly* early in 1998<sup>120</sup>, the English Court of Appeal upheld the conviction of a medical technologist when he retained a biological sample (knee and related joints and limb parts) that had been prepared and once used for medical education and research. This clarified status of research tissues makes it necessary for investigators and/or their institutions to determine their legal relationship to the materials they handle, whether for instance ownership (by gift or prior abandonment), possession of others' property (and whose property) or trusteeship for beneficiaries. Improper possession may be convictable as theft.

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<sup>119</sup> (1998), 127 C.C.C. (3d) 1 (S.C.C.).

<sup>120</sup> [1998] 3 All E.R. 741 (C.A.).

## C. Acquisition of Tissue Samples

The Supreme Court of Canada March 1997 judgment in *R. v. Stillman*<sup>121</sup> concerned a criminal suspect who spent several successive hours under questioning in police custody. During this time he refused to give tissue samples for DNA testing, as he was entitled to do. He was offered cigarettes, however, placing the butts in an ashtray that was made available. He was also tearful and distressed, and took a tissue to blow his nose and compose himself, and threw the tissue containing mucous into a garbage can. The police recovered the butts and tissue, and conducted DNA tests on the saliva and mucus samples they contained, in order to make comparisons or contrasts with DNA of tissues left on a victim of crime. The Court held that, since the suspect had been offered the cigarettes after he refused to give a bodily sample, police recovery of the butts for DNA testing constituted unlawful search and seizure. However, significantly for researchers, it was held that the suspect had freely abandoned the tissue, and the police were entitled to recover the mucous for DNA testing.

If police can recover these abandoned bodily materials for incriminating evidence, it seems that a scientific investigator can recover them for purposes of research. The Tri-Council Policy Statement is relevant to the ethics of acquisition of bodily materials for research, but the law may provide a more direct route to acquisition. The law may show the investigator who gains possession of abandoned bodily materials to be the owner. Whether the investigator conducts research on them is an ethical concern, but the legality of the investigator's control can be established. Further, in *R. v. Stillman*, the police obviously knew the identity of the person whose abandoned sample they lawfully possessed. This suggests that the scientific investigator may equally be entitled to use knowledge of the identity of the source of the materials the investigator owns, and be able to apply that knowledge for scientific purposes.

## D. Access to and Protection of Research Data

Investigators may employ legal rights of access to governmental data under freedom of information legislation. This may deny access to identifiable health records, but allow access for instance to aggregated health and other data (see IV, below). As against this, investigators' data, including identifiable health information, may be liable to subpoena in judicial and

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<sup>121</sup> (1997), 113 C.C.C. (3d) 321 (S.C.C.).



administrative proceedings, compelling production under fear of sanctions against investigators for contempt of court. Data may also be vulnerable to search warrants, defiance of which is criminally punishable.

A March 1999 judgment of the Supreme Court of Canada<sup>122</sup> considered the discretion that may arise when information is acquired of an identified individual's dangerous propensity. The case concerned a psychiatrist who, on request of a criminal defendant's lawyer for an expert opinion, examined the defendant, and found him to be seriously planning serial murders. The defendant pleaded guilty, so no evidence of the offence charged was called, and the psychiatrist was not called as a witness at the sentence hearing. The psychiatrist recognized the offence as merely preparatory to the planned serial murders, and feared that on release from his relatively mild sentence the offender would implement his murderous plans. The psychiatrist initiated a judicial inquiry of whether he was legally free to inform the police of his finding regarding the offender.

The legal issue concerned not doctor-patient confidentiality, since the psychiatrist had no therapeutic responsibility for the offender, but lawyer-client confidentiality, since the lawyer who requested the examination had such responsibilities to the defendant. The Supreme Court ruled that danger of a particularly serious and imminent nature might excuse breach of confidential relationships. The conditions are that:

1. There is clear risk to an identified person or group of persons;
2. The risk is of serious bodily harm, including serious psychological harm, or of death; and
3. The danger is imminent.

There may be few scenarios of threatened violence in which a medical investigator would satisfy these conditions, but they seem to excuse disclosure, despite assurances of confidentiality given in good faith, to public health, police or comparable protective and preventive agencies of serious danger an identified research subject is found to pose. Disclosure would have to be as limited as possible to achieve the protective purpose. It would include the discretion of disclosure to a Medical Officer of Health of a communicable or otherwise notifiable disease when, in the investigator-subject relationship, reporting is not mandatory by statute.

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<sup>122</sup> *Smith v. Jones* (1999), 169 D.L.R. (4<sup>th</sup>) 385 (S.C.C.).

### III. PROVINCIAL LAW ISSUES

#### A. Generally

Criminal liability outlined above has many parallels in civil (non-criminal) liability under provincial law. Lack of informed consent leading to injury may be actionable as negligence. Theft may be pursued provincially as civil trespass to property and conversion of property. Civil liability under provincial law exceeds criminal liability in that crimes usually require proof, beyond reasonable doubt, of a defendant's criminal intention as well as of a criminal act, but civil liability arises from proof, on a mere balance of probabilities, of a wrongful handling of property, even with only negligence or with innocence and good faith. That is, the civil wrongs may be strict liability or unintentional wrongs.

Similarly, provincial laws on freedom of information may make non-identifiable health information in the hands of governmental agencies, such as provincial health plan authorities, available to investigators. However, private litigants such as product manufacturers may be able to gain access to biomedical investigators' non-identifiable data, and even to identifiable data. In the U.S., for instance, tobacco companies have achieved access to identities of research subjects whose medical circumstances were claimed to have arisen from, or been aggravated by, tobacco use, in order to undertake the companies' own investigations. Demands have been made not only against adversaries in litigation, but also against independent investigators whose studies adversaries have funded, or simply cited. In judicial, including coroners' inquiries, and quasi-judicial proceedings, investigators' data may be open to disclosure under subpoena.

#### B. Provincial Enforcement of Research Codes

Biomedical research ethics codes, guidelines and policy statements usually lack means of direct legal enforcement; that is, disregard of their requirements for submission of proposals to independent ethical review, constitution and functioning of review boards and, for instance, for prohibition of practices considered unethical, such as creation of human embryos solely for purposes of destructive research, is not in itself directly legally actionable. However, if a research funding agency makes due observance of a code, guideline or policy statement a

contractual condition of an award of funding, breach is enforceable by legal action against a party to the agreement for breach of contract. The same is true when, for instance, a university, hospital or other research centre engages research staff and supervisors with an express condition in their contracts of research employment that research will be conducted and supervised in accordance with relevant codes, guidelines and/or policy statements.

If an employment contract does not specifically refer to a condition of compliance with a code, etc. of conduct, legal enforcement of an implied contract is less clear. Investigators' claims in university employment to academic freedom enjoy strong legal protection. However, while freedom regarding *what* to study and publicize is recognized, there is no comparable freedom regarding *how* studies may be conducted. Clearly, investigators' academic freedom gives them no claim of non-consensual access to another's body or confidences. Investigators may have no claim to conduct research attributed to their university appointment by unethical means, or to immunity from independent institutional ethical review.

Whether any purely implied term, in an investigator's research or employment contract, of observance of an ethical code, etc. is enforceable by, for instance, a subject of study or a university or hospital, is unclear. A court of law may find observance a necessarily implied term. However, in February 1999 the Alberta Court of Appeal held that defendants in a case involving professional engineering services did not owe a duty to plaintiffs who contracted with them for such services to comply with the defendants' code of professional ethics.<sup>123</sup> The Court found that the defendant's compliance with its code of professional ethical conduct was not an implied term of its contract with the plaintiff, whose "remedy does not lie with the court. It lies with the disciplinary bodies and procedures set up by the governing body of the profession".<sup>124</sup> Accordingly, failures to observe a code etc. of ethical conduct may expose investigators to lawful discipline by professional licensing authorities governing them, but when they are not under such governance no sanction for unethical conduct or for breach of an implied term of a contract may be legally imposable by employing universities, hospitals, etc.

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<sup>123</sup> *Terra Energy v. Kilborn Engineering Alberta Ltd.* (1999), 170 D.L.R. (4<sup>th</sup>) 405 (Alta. C.A.).

<sup>124</sup> *Ibid.* at 421-2.

## C. Public Health Research – Individual or Democratic Consent

Because modern biomedical research ethics have been built on principles of clinical medicine and reactions to outrages that resulted in the *Nuremberg Code* of 1947, it has been axiomatic that necessary consent must be obtained from individuals whose bodies, or health care records, are intended to be investigated. In public health or epidemiological research, protection of individuals' confidences remains an important value, and in principle their consent should be sought and obtained before their records are inspected in order to acquire data that will be aggregated, for instance to determine prevalence levels of particular infections or disorders. Provincial legislation on privacy may reinforce barriers against easy access to identifiable records, particularly where health conditions may be disclosed.

Where individual consent is feasible to request, there is an ethical argument that investigators should have to seek it, and be barred from inspection of individually identifiable health records in its absence. Precedents exist, however, for access to individuals' records without their individual consent, and even over their express refusal, where the public interest justifies studies and those who receive information without consent, and perhaps over opposition, are obliged to maintain confidentiality. Hospitals' and other health facilities' Quality Assurance programmes require them to survey recipients of their care to monitor its safety and efficacy. This act of conscientious self-evaluation does not depend on patients' individual consent, and is not liable to their veto. Further, provinces have legislated that some infections are subject to mandatory reporting to public health authorities, and that conditions such as cancer are similarly reportable to research units. They may follow individual patients' health status, and contact patients for follow-up information, when their family physicians had not informed them that their health data had been sent to the unit for registration and monitoring.

This is not non-consensual research, even though individuals subjected to it have not given their individual consent. It is based on consent, given by a democratically constituted legislature. It is not necessarily ethical to employ a legal power, and investigators who are asked why they do not propose to seek individuals' consent would not give an ethically satisfactory answer to say that they do not need to because legislation authorizes their access without such consent. Nevertheless, where a study offers a significant benefit to public health, it may be ethically satisfactory to accept consent to the study at the legislated or democratic level if obtaining the consent of individuals whose identifiable health records would be inspected is not

practically feasible, and recipients of information from such records owe enforceable duties of confidentiality. Legislation accommodating investigators' inspection of identifiable health records without patients' consent would be liable to scrutiny under the *Charter*. It might be found not to constitute unreasonable search or seizure under section 8, nor to violate for instance liberty or security of the person under section 7. If violation of these or another provision was shown, furthermore, it might be defensible under section 1 as demonstrably justified in a free and democratic society.

## D. Confidentiality and Secondary Use of Data

The principle that patients' or other persons' information voluntarily given to others should not be used for a purpose the donor has not authorized, by free and informed consent, has ethical substance as an attribute of confidentiality. The principle sustains the ethical objection to health care providers receiving finders' fees for informing investigators of patients they know who meet a study's inclusion criteria. Ethical circumstances are recognized, however, for instance in the *Tri-Council Policy Statement*, for secondary use of persons' data that they have not authorized (see Section 3C). A question has arisen of whether this is lawful in light of a May 1999 judgment in the English Queen's Bench Division.<sup>125</sup> The judgment was successfully appealed in January 2000<sup>126</sup>, and in any event did not directly address breach of confidentiality for *bona fide* research conducted in the public interest (see C above). Nevertheless, it discussed access to confidential data for purposes of research, and could indicate potential secondary legal liability, for instance for breach of contract or breach of fiduciary duty.<sup>127</sup>

In *R. v. Department of Health ex p. Source Informatics Ltd.*, the trial judge upheld a departmental policy document that claimed that "under common law ... principles, the general rule is that information given in confidence may not be disclosed without the consent of the provider of the information." The case involved a data collecting company seeking to persuade physicians and pharmacists to allow them to collect data, regarding physicians' prescribing habits, consisting of physicians' names and the identity and quantity of the drugs prescribed, but nothing that could identify any patient. The trial judge held, however, that information in

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<sup>125</sup> *R. v. Department of Health, ex p. Source Informatics* [1991] Lloyd's Law Reports 264.

<sup>126</sup> Unreported to date.

<sup>127</sup> See *McInerney v. MacDonald*, [1992] 2 S.C.R. 138.

prescriptions given to pharmacists was confidential, that for pharmacists or physicians to give even non-identifying, aggregated data about patients was a breach of patients' confidentiality if patients had not given prior consent, and that there is a public interest in ensuring that confidences are kept. The judge left open whether patients can be taken to give implied consent to use of their data for research. He observed that:

it is impossible to escape the logic ... that the proposal involves the unauthorised use by the pharmacist of confidential information ... what is proposed will result in a clear breach of confidence unless the patient gives consent, which is not part of the proposal at present. Nor is it suggested that the patient can be said to have given implied consent. This may be the position where doctors and the Health Service itself use anonymous material for the purpose of research, medical advancement or the proper administration of the Service. That is not, however, a matter on which I have heard sufficient evidence or argument to enable me to come to any conclusion; nor is it necessary for me to do so for the purposes of these proceedings.<sup>128</sup>

The Court of Appeal reversed the trial judge, ruling that communicating anonymized information about a patient for a purpose for which the patient did not give it, without the patient's prior consent, is not in itself a breach of confidentiality. The departmental policy document was held to be incorrect in its statement of the common law principles. Left unresolved is the legal issue of whether patients can be considered in law to have given consent, by implication, to communication of identifying information for purposes of research approved by a Research Ethics Board. Until it is determined by law that consent is implied by patients, or until provincial legislation creates a presumption in favour of implied consent that a patient can expressly rebut, or creates an entitlement to communicate identifying data for research without consent, ethical approval of secondary use of data in accordance with the *Tri-Council Policy Statement* may afford investigators no legal protection against liability for breach of confidentiality.

## E. Compensation for Research-related Injuries

There is considerable uncertainty and variance in practice about whether and, if so, how potential subjects of research can be informed of entitlements to medical care and/or compensation if a study causes them injury. Excluding cases of actionable negligence, a subject who gives adequately informed consent to take a risk of injury assumes that risk, and has no cause of action or entitlement to care or compensation if the injury occurs. Accordingly, unless

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<sup>128</sup> *Supra* note 125, at 268.

an investigator or study sponsor wants to exceed legally imposed responsibility, there is no information that has to be disclosed beyond the irreducible minimum risk of non-negligent injury. Canadian acceptance of information documents prepared by U.S. sponsors of studies that guarantee medical care for injured research subjects is varied. Some REBs disallow them entirely since they appear an inducement, and may offer no more than provincial health insurance plans provide to covered persons in an event, namely medically necessary care. Others allow them since they may offer services that exceed those afforded by provincial health plans. Some REBs allow them even if they offer no more than the provincial health plan offers because, should the plan incur costs treating a research-related injury, the provincial health insurance plan may invoke rights of subrogation and require the subject's name and collaboration in legal proceedings the plan directs to establish the sponsor's or investigator's legal liability, and recover compensation to reimburse the plan for its expenditures.

The urge of provincial health insurance plans to recover expenses they have incurred due to a research-related injury is not uniform, but is perhaps understandable. If a company investing many millions of dollars in product development to promote its commercial profits is responsible for injury to a study subject, but can escape paying for medical costs because they are absorbed by the provincial health insurance plan, the plan and the taxpayers who contribute to its funds may appear to be subsidizing the sponsor's research costs. If the sponsoring company should pay the costs it causes in promoting its profits and market share through research, its liability to repay the provincial health insurance plan's costs of treating injured research subjects through the plan's practice of subrogation, seems just.

An opposite approach is that provincial plans cover costs of medically necessary care for persons injured in recreational, hobby and comparable pursuits, and should do no less for the conscientious research subject who altruistically takes risks to advance medical science and patients' care. Further, since liability may not arise in the absence of negligence, and liability for negligence is not excluded by compensation clauses that research subjects accept, such clauses have no bearing on provincial health insurance plans' subrogation rights, should the plans choose to exercise them. Accordingly, REBs have no interest in serving their province's health insurance policies in insisting upon, accepting or excluding compensation clauses in sponsor-subject consent documents.

An issue of policy rather than of existing legal entitlement is whether commercial sponsors of studies should undertake to cover the costs of subjects' research-related injuries on

a basis of strict (“no fault”) liability. The (Krever) Commission of Inquiry on the Blood System in Canada, 1997, recommended compensation for the recipients of contaminated blood and blood products on this basis, and the 1990 Prichard Report<sup>129</sup> recommended that plaintiffs be able to receive compensation for losses on this basis as an alternative to pursuing claims through ordinary adversarial litigation. Provincial legislation or judicial initiatives imposing strict liability on sponsors of drug and comparable research for research-related injuries might have the appeal of seeming to make them pay the costs they cause. However, apart from liability to *Charter* challenges, such legislation and initiatives might deter pharmaceutical and other sponsors of studies from funding research in a province or in Canada, contrary to governmental policies of attracting such private-sector investment in provincial and Canadian universities and health care facilities. Accordingly, policies of allocating responsibility for costs of research-related injuries fit into a wider setting than achieving justice between study sponsors and research subjects.

## IV. GOVERNMENTAL APPROACHES TO RESEARCH REVIEW

Legislation in some provinces aims to facilitate and encourage research activities involving human subjects. For instance, the *Manitoba Health Research Council Act* establishes a council to promote and assist basic, clinical and applied research in the health sciences, and to receive governmental and other grants for these purposes. In Alberta, the *Health Care Insurance Act* allows disclosure of health insurance information for the purpose of health-related research, including names of individuals provided that investigators who receive identifying names not reveal or identify them to others unless the individuals concerned consent. The title of the *Alberta Heritage Foundation For Medical Research Act* shows its purpose, and the provincial *Public Health Act* authorizes the Chief Medical Officer to require submission of information that permits the conduct of research into communicable diseases. Similarly, in Ontario, the *Cancer Act* requires the collection of individually identifying information on cancer that can be amenable to research studies. It may be presumed that such provincial support of research requires that it be subject to ethical review.

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<sup>129</sup> A Report to the Conference of Deputy Ministers of Health of the Federal/Provincial/ Territorial Review on Liability and Compensation Issues in Health Care, *Liability and Compensation in Health Care*.



The federal government proposes to go considerably further. On January 22, 2000, the *Canada Gazette*<sup>130</sup> published the Department of Health's proposed amended Regulations (1024 – Clinical Trials) under the *Food and Drugs Act*. All human drug clinical trials, Phase I to IV, would be subject to an assessment by the Therapeutic Products Programme (TPP) which would provide federal recognition of the role of REBs. The proposed Regulations might include accreditation of REBs, and a requirement of evidence of REB approval before a submission for product approval can be made to the TPP, or at least before TPP approval may be given. REBs might accordingly need to be constituted and to function in accordance not only with the *Tri-Council Policy Statement*, but also the drug industry's *International Conference on Harmonization (ICH) Guidelines*, for instance for Good Clinical Practice, which the TPP requires drug manufacturers and REBs to observe.

Bringing REBs more formally into the regulatory system for drug approval has far-reaching legal consequences. Their satisfaction of the conditions of accreditation or approval might create delictual, contractual, fiduciary or analogous legal duties to study sponsors, investigators and governmental agencies, as well as to subjects of research. In addition, their influence over prospective investigators' work and careers might give investigators legal rights or legitimate expectations of their proper constitution and functioning, concerning, for instance, adequate records of their deliberations, avoidance or disclosure of members' conflicts of interest, and affording investigators opportunities to make representations before negative decisions are finalized. REBs might have to show, in short, that they are unbiased and disinterested tribunals that meet the criteria of fairness, historically though inadequately described as the rules of Natural Justice. They might also have to be aware of their liability to judicial review as in an English case.<sup>131</sup>

It must be questioned whether REBs have the secretarial infrastructure and membership capacity to act quasi-judicially. It must also be questioned from where they may acquire the resources, including the funds and personnel, to discharge the role the federal Regulations and TPP proposes for them, and whether some potential sources of financial and other support may influence or distort their functions, according to criteria of public perception, professional credibility, and legal propriety. Accordingly, future principles for governance of biomedical research may have to be addressed at governmental, legislative and judicial levels.

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<sup>130</sup> See 227-260.

<sup>131</sup> *R. v. Ethical Committee of St. Mary's Hospital, Manchester, ex parte Harriot*, [1988] 1 F.L.R. 512.



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*Smith v. Jones* (1999), 169 D.L.R. (4<sup>th</sup>) 385 (S.C.C.).

*Terra Energy v. Kilborn Engineering Alberta Ltd.* (1999), 170 D.L.R. (4<sup>th</sup>) 405 (Alta. C.A.).



## SECTION C-2

# ETHICS AND HUMAN RESEARCH: COMPLEXITY OR CONFUSION?

Bartha Maria Knoppers

## I. ABSTRACT

Biomedical research is governed by law, ethics and emerging professional norms. The increasingly international and multi-centred nature of such research creates concomitant levels of complexity, and of contradiction if not confusion. A federal system such as Canada's only further serves to complicate the issue of normative clarity. Two ethical prerequisites - consent and confidentiality - serve to illustrate this situation. At a minimum, Canada should provide REB's with an ongoing "watching brief" of developments in the ethical norms governing biomedical research as well as contribute to international harmonization.

## II. INTRODUCTION

Biomedical research involving humans remains governed in Canada by law that is primarily directed to purposes other than research [See text: Dickens]. Except for Quebec<sup>132</sup>, no province has specific legislation on research involving humans. In fact, Ontario's *Health Care Consent Act*<sup>133</sup> expressly excludes research. Yet, Ontario like most provinces allows advance directives which presumably, though with no legal certainty, may include research.

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<sup>132</sup> *Civil Code of Quebec*, L.Q. 1991, c.64, arts. 20, 21, 24, 25.

<sup>133</sup> *Health Care Consent Act*, S.O. 1996, c.2, sch.A, s.6.

In 1997, Canada's Minister of Health endorsed the *ICH Harmonized Tripartite Guideline of "Good Clinical Practice in Pharmaceutical Trials"*<sup>134</sup> (hereinafter, *Guideline*). Thus, the ICH Guideline, together with the *Tri-Council Policy Statement (1998)*<sup>135</sup> and provincial legislation in Quebec<sup>136</sup> (or indirectly health legislation in other provinces), to say nothing of general medical codes of ethics, professional norms, and case law, form the ethico-legal, regulatory background which governs REB's and researchers. Indeed, positive law, ethics, and professional standards are part of the social structures, processes and relationships that form the normative background governing the diverse endeavours of human research.

Against this national background looms the very real fact of the increase in the number of multi-centred if not multi-national trials bringing to bear on research ethics boards (REB's) and researchers a myriad of often conflicting directives, laws and cultural norms. To illustrate this complex framework and by way of example, we examined four international sources of ethical normativity: the *Helsinki Declaration*<sup>137</sup>, the *International Ethical Guidelines for Biomedical Research Involving Human Subjects* of the Council for the International Organization of the Medical Sciences (CIOMS)<sup>138</sup>, the ICH Guideline<sup>139</sup>, and the *European Convention for Human Rights and Biomedicine*<sup>140</sup> with respect to the norms governing consent and confidentiality.

Research on these issues was also directed at the national level and included Canada, the United Kingdom, the U.S.A., Australia and France. At both the international and national

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<sup>134</sup> International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, *ICH Harmonized Tripartite Guideline for Good Clinical Practice*, (Having reached Step 4 of the ICH Process at the ICH Steering Committee meeting on 1 May 1996, this guideline is recommended for adoption to the three regulatory parties to ICH) <<http://www.ich.org/pdf/fpma/e6.pdf>>.

<sup>135</sup> Medical Research Council (MRC), Natural Sciences and Engineering Research Council (NSERC), Social Sciences and Humanities Research Council (SSHRC), *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans*, Ottawa, 1998.

<sup>136</sup> *Supra* note 132.

<sup>137</sup> World Medical Association, *Helsinki Declaration*, Adopted by 18th World Medical Assembly (Helsinki, Finland, 1964), and revised by 29th World Medical Assembly (Tokyo, Japan, 1975).

<sup>138</sup> Council for the International Organization of the Medical Sciences (CIOMS), *International Ethical Guidelines for Biomedical Research Involving Human Subjects* (Geneva, 1993).

<sup>139</sup> *Supra* note 134.

<sup>140</sup> *Convention on Human Rights and Biomedicine*, April 4 1997, ETS No 164, <<http://www.coe.fr/eng/legaltxt/164e.htm>> (access date: November 24<sup>th</sup> 1999), [hereinafter *Convention on Biomedicine*].

levels, the principles of consent and confidentiality<sup>141</sup> and more particularly, the more recent exceptions of research in the emergency setting (1) and of a breach of confidentiality where third parties are at risk (2) were examined.

## A. Emergency

Research in the emergency setting is an example of conflicting and contradictory approaches under both law and ethics. Indeed, in June 1998, the Quebec Government added to its article 21 on research in its *Civil Code*, the following section on research in the emergency setting:

Consent to experimentation may be given, in the case of a minor, by the person having parental authority or the tutor and, in the case of a person of full age incapable in giving consent, by the mandatory, tutor or curator. Where a person of full age suddenly becomes incapable of consent and the experiment, insofar as it must be undertaken promptly after the appearance of the condition giving rise to it, does not permit, for lack of time, the designation of a legal representative, consent may be given by the person authorized to consent to any care the person requires; it is incumbent upon the competent ethics committee to determine, when examining the research project, whether the experiment meets that condition.

The result of this legislative change is that incompetent adults in Quebec (otherwise excluded from research in the absence of a legally appointed tutor, mandatory or curator), can now be included in the emergency research setting with the simple consent of those authorized to give consent to medical care such as a spouse, family member, partner or other interested person. Furthermore, it should also be noted that on the basis of this consent and the authorization of a duly recognized research ethics board (REB), Quebec also allows the inclusion of incompetent adults (in research) even though the benefit may only be for other persons in the same category or having the same disease or handicap. Thus, research on Alzheimer disease or other neurological disorders in an aging population in Quebec excludes those who have not had the legal foresight and financial wherewithal to foresee the need for appointing legal representation with a research mandate while still competent, but includes those who are incompetent within research in the emergency setting.

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<sup>141</sup> We wish to thank Delphine Roigt for her preparation of the background reference document: "Biomedical Research Ethics: Convergence and Divergence of National and International Standards" (1999). [See Section G-1].

This contrasts with art. 2.8 of the *Tri-Council Statement* which requires a real possibility of direct benefit for the inclusion of incompetent persons in the emergency setting. Furthermore, the *Statement* maintains that if the “authorized” third party cannot be found, then sole REB approval is temporarily sufficient. While the Tri-Council approach of sole REB approval is similar to the ICH *Guideline* (art. 4.8.15), the ICH *Guideline* does not require proof of direct benefit. Thus, the ICH like Quebec does not require direct benefit, but Quebec, contrary to both the ICH and the Tri-Council, requires both REB approval *and* third party authorization. Which norms prevail?

Obviously, for researchers in Quebec, the norms of the *Civil Code* are paramount. The nature of international clinical trials however, makes such conflicts unmanageable in that while requiring third party authorization may simply be more cumbersome (i.e., additional communication and written authorization) in countries where this is the norm, the difference between direct and indirect benefit is a fundamental barrier to inclusion.

## B. Duty to Warn

More comforting in terms of certainty and uniformity of approach, is the duty to maintain confidentiality and protect privacy of research subjects. Indeed, the *Tri-Council Statement* reinforces the rule of no access by third parties and like the European *Convention on Biomedicine* which contains the right not to know (art. 10), states in art. 8.1 in the specific context of genetics, that genetic results should only be reported if the individual so desires. In other words, not only is the individual protected from third parties but potentially from him/herself.

In the area of human research however, there is a need to be cognizant of emerging legal and professional norms on issues not directly addressed by international ethics or by national statements such as that of the Tri-Council. In our study of the multiple and complex norms governing research, the duty to maintain confidentiality did not contain exceptions other than REB approval for access to medical records or to archived tissue samples by researchers.



Yet, as mentioned in our introduction, both local legislation, case law, and emerging professional norms must be considered. Quebec's *Code of Ethics*<sup>142</sup> for physicians (a regulation pursuant to law), provides for discretionary leeway. Indeed, a physician can bypass the refusal of a patient to warn third parties at risk if "there is a just and imperative motive related to the health of the patient or the welfare of others" (art. 3.04). This *Code of Ethics* was adopted pursuant to legislation and so has force of law.<sup>143</sup> Quebec's health legislation also contains a right of access to genetic and pertinent family information by family members where the person has refused to communicate such information, but only after that person's death.<sup>144</sup>

Furthermore, across Canada, the 1998 *Cuerrier*<sup>145</sup> decision of the Supreme Court of Canada held that if serious danger to health exists, there is a duty to warn (HIV-prospective partner) [See text: Dickens]. Likewise in 1999, that Court in the *Jones*<sup>146</sup> case would allow a breach of solicitor-client privilege where the risk of serious bodily harm to another was clear and imminent. Interestingly, this decision [which involved a psychiatrist also under a duty of confidentiality warning the solicitor of the intentions of his client (a sexual rapist)], considered a similar 1975 American case.<sup>147</sup> That case formed the basis for the 1983 Presidential Commission of the United States recommending medical discretion to warn where the person refused to communicate genetic information to identifiable, at-risk family members where prevention or treatment was available.<sup>148</sup> This approach favouring a limited exception to confidentiality has been adopted not only by the American Society of Human Genetics<sup>149</sup> but by several European countries<sup>150</sup> and the WHO as well.<sup>151</sup> In other words, legislation, case law

<sup>142</sup> *Code of Ethics of Physicians*, R.R.Q., c. M-9, r.4, [Hereinafter *Code of Ethics*].

<sup>143</sup> *Professional Code*, L.R.Q., c. C-26, s.87.

<sup>144</sup> *An act respecting health services and social services*, L.R.Q., c. S-4.2, s.23.

<sup>145</sup> *R. v. Cuerrier*, [1998] 2 S.C.R. 371.

<sup>146</sup> *Smith v. Jones*, [1999] 1 S.C.R. 455.

<sup>147</sup> *Tarasoff v. The Regents of the University of California*, 131 Cal. Rptr. 14 (Sup. Ct. 1976).

<sup>148</sup> *Screening and Counseling for Genetic Conditions* (Washington: Government Printing Office, 1983).

<sup>149</sup> American Society of Human Genetics, "ASHG Statement: Professional Disclosure of Familial Genetic Information" (1998) 62 *Am. J. Hum. Genet.* 474.

<sup>150</sup> Council of Europe (Committee of ministers), *Recommendation No. R (97) 5 of the Committee of Ministers to Member States on the Protection of Medical Data*, (1997) <<http://www.coe.fr/cm/ta/rec/1997/97r5.html>> (Nov. 1, 1999); European Commission, Working Group on the Ethical, Social and Legal Aspects of Human Genome Analysis, "Report of 31 December 1991 (WG-ESLA)", (June 1993) *Bull. Med. Eth.* 19; Council of Europe, Committee of Ministers (470th meeting), "Recommendation No. R(92) 3 on Genetic Testing and Screening for Health Care Purposes", (1992) 43 *Int. Dig. Hlth. Leg.* 284; Council of Europe (Committee of Ministers), "Recommendation R (90) 13 on Prenatal Genetic Screening, Prenatal Genetic Diagnosis and Associated Genetic Counselling", (1990) 41:4 *Int. Dig. Hlth. Leg.* 615.

and professional norms cannot be ignored in terms of evaluating the ethical obligations of researchers and of REB oversight.

These exceptions to consent and confidentiality are but two examples of the difficulties and pitfalls facing researchers and REB's. Where ethics committees are not aware of legal and professional norms or of contradictions between them, efficiency and comprehensiveness in the protection of human rights are undermined. While no one would argue for total standardization of such norms, ethics norms not being the equivalent of standard operating procedures (SOP's), and while diversity respects cultural differences between countries, one would expect governmental bodies to be cognizant of conflicting guidelines within the same country and if choosing to differ – at a minimum explaining why. As to differences between international guidelines and provincial and national legislation as well as with emerging ethical and professional norms, we can hope not only for a minimum of harmonization and international awareness, but also for local vigilance and continuing education. In the absence of such harmonization and education, our *Tri-Council Statement* will not become a truly living document in the sense of being both principled, applicable, and current, and thus, good governance will be impossible.

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<sup>151</sup> World Medical Association, "Declaration on the Human Genome Project (Marbella, Spain, September 1992)", (1993) 44:1 *Int. Dig. Hlth. Leg.* 150; World Health Organization, WHO Meeting on Ethical Issues in Medical Genetics, *Proposed International Guidelines on Ethical Issues in Medical Genetics and Genetic Services* (Geneva, December 15 and 16, 1997) <<http://www.who.int/ncd/hgn/hgnethic.htm>> (Aug. 6, 1999); World Health Organization, *Statement of WHO Expert Advisory Group on Ethical Issues in Medical Genetics* (Geneva: December 15 and 16, 1997); World Health Organization, *Guidelines on Ethical Issues in Medical Genetics and the Provision of Genetic Services*, (Geneva, 1995).

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## SECTION D-1

# NEGOTIATING COLLECTIVE ACCEPTABILITY OF HEALTH RESEARCH

Michael Burgess and Fern Brunger, with  
collaboration from Asch and McDonald

The effects of research on groups pose peculiar problems for the governance of research ethics. Ethical issues arising from the effects of research on groups broader than those who participate in research are perhaps best known in relation to the stigmatization from research involving First Nations' communities<sup>152</sup> or ethnic populations<sup>153</sup>. But the simple identification of a social risk factor such as sexual preference or workplace hazards can stimulate effects on non-participants. Typically issues of balancing risks of research with the benefits are managed by informed consent. But the issues related to aggregates or collectives are particularly vexing because they cannot be managed through individual informed consent,

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<sup>152</sup> Association of Canadian Universities for Northern Studies, *Ethical principles for the conduct of research in the North*, (Ottawa: Assoc. of Canadian Universities for Northern Studies, 1982); Canada Royal Commission on Aboriginal Peoples, "Ethical guidelines for research" in *Integrated Research Plan. Appendix B*, (Ottawa: Royal Commission on Aboriginal Peoples, 1993); Interagency Arctic Research Policy Committee, "Principles for the conduct of research in the Arctic" (1995) 9 Arctic Res 56; A.C. Maccaulay, *et al.*, "Participatory research with native community of Kahnawake creates innovative code of research ethics" (1998) 89 Can J Public Health 105; I Maddocks, "Ethics in aboriginal research: a model for minorities or for all?" (1992) 157 Med. J. Aust. 553; K. Scott and O. Receveur, "Ethics for working with communities of Indigenous Peoples" (1995) 73 Can. J. Physiol. Pharmacol 751.

<sup>153</sup> A.M. Brandt, "Racism and research: the case of the Tuskegee syphilis study" (1978) 8:6 Hastings Center Report 21; Caplan, "Handle with care: race, class and genetics", in T. Murphy, M. Lappe, M., eds., *Justice and the Human Genome Project* (Berkeley: University of California Press, Berkeley, 1994) 30; House of Commons Science and Technology Committee, *Third report on human genetics: the science and its consequences* (London: HMSO, 1995); J.H. Jones, "The Tuskegee legacy: AIDS and the Black community" (1992) 22:6 Hastings Center Report 38; J.H. Jones, *Bad Blood: The Tuskegee Syphilis Experiment* (New York: Free Press, 1993); P.A. King, "The past as prologue: race, class, and gene discrimination", in G.J. Annas and S. Elias, eds., *Gene mapping: using law and ethics as guides* (Oxford University Press, Oxford, 1992) 95; T.L. Savitt, "The use of Blacks for medical experimentation and demonstration in the old South" (1982) 48:3 *J of Southern History* 331; E.K. Watson, E.S. Mayall, J. Lamb, J. Chapple, and R. Williamson, "Psychological and social consequences of community carrier screening for cystic fibrosis" (1992) 340:8813 Lancet, 217; C. Weijer, G. Goldsand and E.J., Emanuel, "Protecting communities in research: current guidelines and limits of extrapolation" (1999) 23 Nature Genetics, 275; C. Weijer, "Protecting communities in research: Philosophical and pragmatic challenges" (1999) 8 Cam Q Health Ethics 501.

and relate to the general acceptability of the research to the public, as well as to the accountability of researchers and research review. Health charities represent one form of negotiation of the collective acceptability of research and researchers to a broader set of interests than research participants.

Informed consent is the cornerstone of contemporary research ethics with its historical roots in Western scientific medicine and liberal theory.<sup>154</sup> In this tradition, the collective good that is likely to follow medical research cannot alone justify the risks to individual participants. Rather, individual participants must knowingly accept the risks to them of participation in specific research projects.<sup>155</sup> Informed consent is the focus of most ethical review and discourse, and the ethical validity of informed consent rests on two stages. First, current clinical and scientific knowledge must establish and describe the effects on the individual subjects of participation in the research. Secondly, the information about effects of the research, and reasonable alternatives, must be presented to potential participants in a manner that optimizes their understanding of the effects of participation on them, and produces a decision about participation that is an expression of the individual's personal values.

This section will clarify the relevant range of research effects and consider a different ethical mechanism than group informed consent.<sup>156</sup> First, the range of collective effects will be summarised. It is important to be relatively exhaustive in this cataloguing, so we have divided human experience into the categories of physical, emotional, and social/financial. Then the range of types of groups involved in research will be described. We will consider what would be an ethically justifiable management of the different types of risks for different types of groups. Finally, we will discuss various strategies for negotiating what we will term the "collective

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<sup>154</sup> T.L. Beauchamp and R.R. Faden, "Informed consent: II. Meaning and elements of informed consent", in W.T. Reich, R.R. Faden and T.L. Beauchamp, eds., *A History and Theory of informed Consent* (New York: Oxford University Press, 1986).

<sup>155</sup> National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (April 18, 1979) *The Belmont Report: ethical principles and guidelines for the protection of human subjects of research*, OPRR [Office for Protection from Research Risks] Reports; R.J. Levine, *Ethics and regulation of clinical research*, (New Haven (CT): Yale University Press, 1988); World Medical Association, "Declaration of Helsinki", [1964, rev 1975, 1983, 1989], In W.T. Reich, ed., *Encyclopedia of bioethics*. rev ed. (New York: Simon & Schuster MacMillan 1995) 2765; "Nuremberg Code" [1947], In: W.T. Reich, editor, *Encyclopedia of bioethics*. rev ed., (New York: Simon & Schuster MacMillan, 1995), at 2763-4; "General Assembly of the United Nations: International covenant on civil and political rights" [1958], in W.T. Reich, editor, *Encyclopedia of bioethics*. rev ed. (New York: Simon & Schuster MacMillan, 1995), at 2765; Office for Protection from Research Risk, *Protecting human subjects: Institutional review board guidebook* ( Washington: The Office, 1993).

<sup>156</sup> C. Weijer, G. Goldsand and E.J. Emanuel, "Protecting communities in research: current guidelines and limits of extrapolation", (1999) 23 *Nature Genetics* 275; C. Weijer, "Protecting communities in research: Philosophical and pragmatic challenges" (1999) 8 *Cambridge Quarterly of Healthcare Ethics* 501.

acceptability” of research effects, including problems with informed consent and REB reviews. Genetic testing for hereditary disease will be used as an example.

## I. RANGE OF RESEARCH EFFECTS ON INDIVIDUAL PARTICIPANTS AND COLLECTIVES

Here we consider the relevant range of research effects on individual participants and collectives. Genetic testing for hereditary disease will be used as an example, and the fictitious case of “Nessa” will be used to illustrate the range of research effects.

Nessa has been invited to be a participant in a study on hereditary breast cancer, where she will be tested to see if she has the mutation. Nessa’s mother and aunt both died of breast cancer in their early 30s. She is 26 years old, has two small daughters, is married, and is the primary income earner. She is an English teacher in a high school and is being considered for the Vice Principalship. She has 2 sisters and a brother who are encouraging her to have the test. Nessa decides to be tested, because she worries about dying young and leaving her two children; she is concerned about her daughters’ risk status; she wants to know whether it is wise for her to accept the vice-principalship; and one of her sisters who has 3 daughters is particularly anxious to know if their family does carry a mutation for hereditary breast cancer. She is also interested in doing whatever she can to help other women in her ethnic community, since it seems like there is a higher rate of cancer for them, and the research will evaluate whether there is a founder effect on genetic risk.

The following chart exemplifies the effects of research that Nessa, as an individual research participant, is encouraged to evaluate through informed consent and genetic counselling.

<b>Table 1: Types Of Effects on Individual Participant</b>		
<b>DIRECT: what having the test does to participant</b>		
Physical	Emotional	Social/Financial
<ul style="list-style-type: none"> <li>• Pain of needle</li> <li>• Closer symptomatic monitoring</li> </ul>	<ul style="list-style-type: none"> <li>• Pre- and post-test anxiety</li> <li>• Relief</li> <li>• anxiety to make changes</li> <li>• anxiety about informing others</li> <li>• distraction from other anxieties</li> </ul>	<ul style="list-style-type: none"> <li>• personal costs of testing (sitter; time off, parking)</li> <li>• absence from work/home</li> </ul>
<b>RESPONSIVE: what participant does in response to the test</b>		
Physical	Emotional	Social/Financial
<ul style="list-style-type: none"> <li>• suicide or self-harm</li> <li>• physical exhaustion from the relief of finally knowing results</li> </ul>	<ul style="list-style-type: none"> <li>• Depression</li> <li>• Elation</li> <li>• “Survivor’s guilt”</li> </ul>	<ul style="list-style-type: none"> <li>• quit job</li> <li>• retirement plans</li> <li>• feel discrimination</li> <li>• privacy challenged or more carefully protected</li> </ul>

<b>INDIRECT: what others do to participant because s/he had the test or in response to participant's responses</b>		
Physical	Emotional	Social/Financial
<ul style="list-style-type: none"> <li>• abuse</li> <li>• physical affection</li> </ul>	<ul style="list-style-type: none"> <li>• anger</li> <li>• avoidance</li> <li>• admiration</li> <li>• support</li> <li>• affection</li> </ul>	<ul style="list-style-type: none"> <li>• stigmatization</li> <li>• intra-familial tension</li> <li>• insurance discrimination</li> <li>• employment discrimination</li> <li>• health care discrimination</li> </ul>

Genetic counselling encourages Nessa to think beyond the obvious physical effects and usefulness of the information. She is asked to consider how she and her family might respond to each possible test result, who she might tell about the test results, how she would tell certain people and how they might respond. Since this is predictive testing, Nessa is likely to be told to consider whether she might want to purchase insurance that might be more difficult if she receives a test result confirming an increased risk. Concerns about non-directive counselling have been expressed, but on the whole, informed consent supplemented by genetic counselling seems a reasonable manner in which to anticipate and negotiate these research effects on the participating individual.<sup>157</sup>

Informed consent is typically considered an ethically adequate model to manage effects on individuals because the risks and benefits evaluated are specifically the direct effects of research on the individual. Disclosure of the effects of research participation and voluntary participation is thought to grant the individual full control over their exposure to risks and benefits. In the case of genetic testing (and HIV testing), this model of ethical decision making has been supplemented with counselling due to the difficulty people have predicting their own responses to the test as well as that of family members and others. Counselling is to supplement disclosure of information with support to help participants consider their own and others' responses. Then the acceptance of the direct and "responsive" effects of participating in research is presumed to be sufficiently voluntary.

The main problems with informed consent come from the lack of predictability of the more complex effects. For Nessa, the direct effects of the research were relatively predictable

<sup>157</sup> R. Rapp, "Chromosomes and communication: the discourse of genetic counselling" (1988) 2 *Med Anthropol* Q 143; A. Lippman, "Prenatal diagnosis: Reproductive choice? Reproductive control?" in C. Overall, ed., *The future of human reproduction* (Toronto: The Women's Press, 1989) 182; M.M. Burgess, C.M. Laberge and B.M. Knoppers, "Bioethics for clinicians 14. Ethics and genetics in medicine" (1988) 158 *Canadian Medical Association Journal* 1309.



and minor. These included pain from the bloodletting, worry about what the results would be, and the cost of taking a half-day off work. Predictability decreases with the responsive effects, which included physical exhaustion from the relief of finding out she was not a carrier, as well as guilt and worry because she believes that if she is not a carrier then one of her sisters must be. Some responses are less predictable due to how Nessa integrates the information into her life circumstances, as with a loss of income when she decides to cut work back to half time in order to enjoy time with her children while they are young. Other responses are unpredictable because of the role others and social circumstances have, as illustrated by Nessa emotionally distancing from her sisters as a way of dealing with guilt caused by believing that her not being a carrier means they might be carriers.

Indirect effects stimulated but not caused by the research are often even less predictable. Nessa's sisters are angry with her for "acting weird" around them and not returning their calls, and her husband has been arguing with her since he is feeling the strain of her loss of income. Nessa and her children see less of her husband because he has increased his work hours to make up for her loss of income. Although Nessa has no difficulty qualifying for life insurance, the bank has refused her a loan because there is not sufficient income with her reduced hours at work.

There are two reasons why informed consent is inadequate for non-direct effects of research participation, as illustrated in Nessa's story. Responsive effects are the participants' responses to participation, and these effects are not wholly within participants' control. Reactions such as depression, elation, and anger are not rationally controlled by individuals and are strongly influenced by social circumstances. Further, responsive effects are influenced by the responses of others to both the direct and responsive effects on the participant. While counselling might increase the predictability and provide support for responsive effects, they remain unpredictable and influenced by the responses of others, particularly family members.<sup>158</sup>

Obviously, to be affected by a participant's responses requires a relationship with that person, unless those responses lead to effects on a group of which one is a member, as in ethnic stigmatization due to Nessa being public about her test and ethnicity. Effects on non-participants that follow directly from Nessa's participation are minimal, limited primarily to her absences when she is attending research activities. In extreme cases, physical effects will

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<sup>158</sup> C.V. Hayes, "Genetic testing for Huntington's disease — a family issue [editorial comment]" (1992) 327 N Engl J Med 1449; S. Kessler and M. Bloch, "Social system responses to Huntington disease" (1989) 28 Fam Procs 59.

include abuse as a response to participation, but most often participant responses will have primarily emotional and social effects on non-participants. For example, stigmatization of a family might depend on the participation of an individual and the perception that the person and therefore the family members are at risk of a genetic disease. These are one set of effects on groups of participation in research; both the individual and their social circle must cope with complex and interactive responses. The direct and responsive effects of individuals' participation in genetic testing have been extensively discussed in terms of the "duty to warn".<sup>159</sup>

The second kind of research effects that accrue to groups overlap with responsive, but their causation is located in how information related to or produced by the research is used by individuals and groups. Examples are insurance practices, stigmatization<sup>160</sup> and changes in family relations.<sup>161</sup> These effects of research on groups can be demonstrated by returning to the example of Nessa. The research project in which Nessa is a participant focuses only on Ashkenazi Jewish families at risk for inheriting breast cancer. The effects of the test go beyond Nessa and her family, to include her ethnic community.

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<sup>159</sup> *Final recommendations of Ontario's Medical Expert Panel on the Duty to Inform*, (Toronto: Institute for Clinical Evaluative Sciences in Ontario A285-97, 1996); *Duty to warn: report from council members' dialogue* (Toronto: College of Physicians and Surgeons of Ontario, 1996) 21; American Society of Human Genetics Social Issues Committee, "Points to consider: Professional Duty to Inform of Familial genetic information" (1997) 61 *American Journal of Human Genetics*; *H.(R.) v. Hunter* (1997) 32 C.C.L.T. (2d) 44 (Ont. Court of Justice). *Arndt v. Smith* (1997) 148 D.L.R. (4<sup>TH</sup>) 48 (SCC); T. Caulfield and G. Robertson, "Eugenic policies in Alberta: From the systematic to the systemic?" (1996) *Alberta Law Review* XXXV 59; M.M. Burgess, C.M. Laberge and B.M. Knoppers, "Bioethics for clinicians: 14. Ethics and genetics in medicine" (1998) 158 *Canadian Medical Association Journal* 1309.

<sup>160</sup> NIH-DOE Working Group on Ethical, Legal, and Social Implications of Human Genome Research, *Genetic information and health insurance* (Washington, D.C: Human Genome Project, HIH Pub. No. 93-3686, 1993); T. Lemmens and P. Bahamin, "Genetics in life, disability and additional health insurance in Canada: a legal and ethical analysis", in B.M. Knoppers, ed., *Socio-Ethical Issues in Human Genetics* (Les Editions Yvons-Blais Inc., 1998) 15; H.T. Greely, "Health insurance, employment discrimination and the genetics revolution", in D.J. Kelves and L. Hood eds, *The code of codes: Scientific and social issues in the human genome project* (Cambridge: Harvard University Press, 1992) 274.

<sup>161</sup> Hayes, *supra* note 158; S. Kessler and M. Bloch "Social system responses to Huntington disease" (1989) 28 *Fam Process* 59; M.M. Burgess, M.R. Hayden, "Patients' rights to laboratory data: trinucleotide repeat length in Huntington disease" [editorial] (1996) 162 *Am J Med Gene* 6; K. Quaid, M.K. Wesson, "Exploration of the effects of predictive testing for Huntington disease on intimate relationships" (1995) 57 *Am J Med Genet* at 46.

<b>Table 2: Types Of Effects on Non-Participants</b>		
<b>DIRECT: what Nessa's participation (not her responses) does to non-participants</b>		
Physical Effects on others of Nessa's participation	Emotional Effects on others of Nessa's participation	Social/Financial Effects on others of Nessa's participation
<ul style="list-style-type: none"> <li>Nessa's absences from work or home affects family and co-workers</li> </ul>	<ul style="list-style-type: none"> <li>Those in immediate social context have concern about Nessa's welfare; relief that she is doing something about anxiety</li> <li>Related non-participants may have increased anxiety about their risk</li> </ul>	<ul style="list-style-type: none"> <li>Reorganizing schedules and finances to accommodate Nessa's participation</li> </ul>
<b>RESPONSIVE: What non-participants do in response to Nessa having the test</b>		
Non-participant physical acts	Non-participant emotional responses	Effects on others of Nessa's test
<ul style="list-style-type: none"> <li>None likely</li> <li>Possible physical responses such as abuse</li> </ul>	<ul style="list-style-type: none"> <li>Group anxiety up in reaction to Nessa</li> <li>Dealing with emotions from Nessa</li> <li>Worry about stigmatization of family members or ethnicity</li> </ul>	<ul style="list-style-type: none"> <li>Coping with Nessa's decisions</li> <li>Family adjustment to financial and social responses</li> <li>Others' perceptions of family or ethnic group due to Nessa's responses</li> </ul>
<b>INDIRECT: What others do to non-participants because of Nessa's (and other's) test</b>		
Physical	Emotional	Social/Financial
<ul style="list-style-type: none"> <li>None directly</li> <li>Health and social policy may promote services with physical effects, such as screening and early detection of disease</li> </ul>	<ul style="list-style-type: none"> <li>felt stigmatization for family or ethnic groups</li> <li>felt pressure related to testing</li> </ul>	<ul style="list-style-type: none"> <li>money for info sessions and community support groups</li> <li>increased group solidarity</li> <li>sense of unity with other stigmatized groups</li> <li>insurance companies raise premiums</li> <li>employers block access</li> <li>stigmatize group</li> <li>implications for marriage-ability from within or outside the group</li> <li>group relations strained and anger at those who had the test</li> </ul>

Nessa's example illustrates how effects of research on groups are not necessarily linked to any individual's participation, but characterize the effect on groups of the research itself. For instance, stigmatization of an ethnicity does not require the participation of any specific individual, only that a visible ethnicity is perceived to be at increased risk for a genetic disease. This points to the inadequacies of the notion of informed consent for managing research effects on groups.

Informed consent is inadequate to justify research effects on groups because participants' agreement to participate cannot authorize the acceptability of the effects of

research on other persons. Individual research participants cannot authorize the acceptability of their time away from work or home or the stigmatizing effects of genetic knowledge on their families or ethnicity. Often, this limitation of informed consent is either ignored, or any method of managing these effects is dismissed as too onerous, depriving groups of the benefits of medical research and denying potential participants their right to participate.

It is superficially tempting to suggest a notion of collective consent that involves all people potentially affected by the research in a kind of informed consent to manage the evaluation and authorization of the effects of research on non-participants. For instance, family-wide consent might seem to justify accepting the responsive and indirect effects of the participation of one or more family members in genetic testing. Or perhaps acceptance of the risk of stigmatization of ethnicity in Iceland can be construed as a sort of collective informed consent based on a belief that the resulting medical benefits are worth the risk. As in the case of Nessa and the Ashkenazi Jewish community, it would appear that collective consent might be arranged through a group's authorities, the negotiation of contracts with groups or by consensus among participants.

In fact, in the past decade, questions around how to best protect "communities" (that is, a specific subset of what we call "collectives") have generally been addressed in terms of this idea of expanding individual consent to include community consent for research, with the recommendation that communities are to be consulted about the harms and benefits of research and that the consultation should be along the line of a partnership.<sup>162</sup> Most recently, Weijer has pointed to the need for a more thorough understanding of how the term "community" is used, and emphasises that guidelines developed for one type of community cannot be applied directly to another type. Weijer is speaking about "communities" in a sense that is much narrower than our term "collectives" (that is, it does not include non-cohesive types of collectives such as health charities and other aggregates), even within that narrower definition, his problematizing of the notion of "community" begins to illustrate the inadequacies of the notion of informed consent for managing the effects of research on groups.

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<sup>162</sup> Council for International Organizations of Medical Sciences (CIOMS) *International Ethical Guidelines for Biomedical Research Involving Human Subjects* (Geneva: CIOMS, 1993); R.J. Levine, "Informed consent: some challenges to the universal validity of the Western model" (1991) 19 *Journal of Law, Medicine and Health Care* 207; K.C. Glass, C. Weijer, T. Lemmens, R.M. Palmour and S.H. Shapiro, "Structuring the review of human genetics protocols part II: diagnostic and screening studies" (1997) 19 (3,4) *IRB: A Review of Human Subjects Research* 1; C. Weijer, G. Goldsand and E.J. Emanuel, "Protecting communities in research: current guidelines and limits of extrapolation" (1999) 23 *Nature Genetics* 275; C. Weijer, "Protecting communities in research: Philosophical and pragmatic challenges" (1999) 8 *Cambridge Quarterly of Healthcare Ethics* 501.

The notion of individual autonomy that is presumed by the ethical justification of informed consent is challenged by research that demonstrates how values are socially constructed and enforced by institutional structures such as health care delivery settings. But there are serious restrictions to the notion of informed consent for managing the effects of research on groups even within the model of autonomy and informed consent.

The notion of collective consent fails on two of the primary justifications for individual informed consent. First, individual informed consent must be very specific about the nature and probability of effects (risks and benefits) and the manner of how they will be produced. This predictability is the basis of the claim that individuals can understand and authorize the procedure. Responsive and indirect effects of research are more causally complex, influenced by social context and interaction of people and social forces. Although the reality of these effects is undeniable, their prediction is far more difficult.

Second, the notion of collective consent suggests that the research authorized by the group can proceed. But that mistakes the general acceptability of the objectives and effects of the research to a group with individual authorization of direct, responsive and indirect effects. But no matter what a group decides, the notion of informed consent requires that no individual can be required to accept a groups' assessment of the acceptability of research.

The negotiation of responsive and indirect effects of research requires a mechanism that seeks group evaluation of the effects based on some reasonable attempt to predict these effects, but without any constraint on an individual's freedom to decline participation. This is based on the moral assumption that no one can be required to submit to risks when the benefits of the research are by definition "experimental" (i.e., the results are not yet guaranteed or reproducible). Finally, any negotiation of group evaluation and agreement must also assure reasonable representation of opinion and values within typically heterogeneous groups. In other words, the collective acceptability of research is a negotiation of the public acceptability and accountability with the segment of the public most directly affected by the research. We will refer to the process of seeking group evaluation of the effects of research as negotiating "*collective acceptability*" of research effects.



e.g., all people with breast cancer	e.g., Ashkenazi Jewish community
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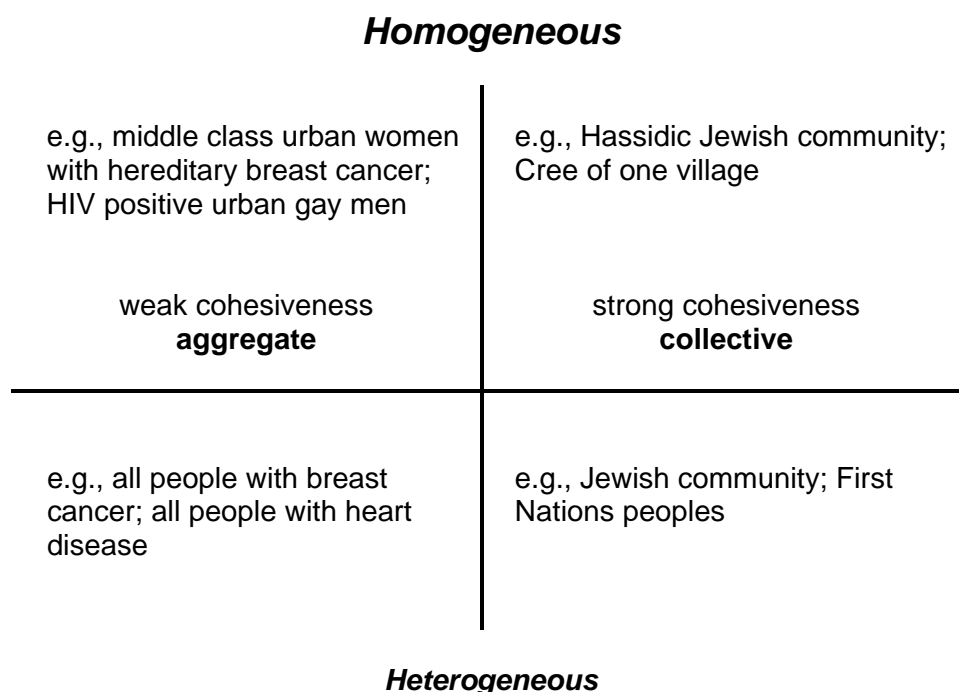
An aggregate is a group of individuals with a very weak sense of collective identity. One example of an aggregate type of collective would be all individuals who have tested positive for a risk of hereditary breast cancer, some of whom are Ashkenazi. The set of all people at risk for hereditary breast cancer is not an obvious collective; its members only have their disease and research participation in common, but are otherwise geographically and socially disparate. However, depending on the individuals, the disease, or the research strategy, the research process can lead an aggregate to have collective interests. Most obviously, this would happen if the research process focuses attention on the disease; and, over time, the individuals identify themselves as a collective, organizing as a group, appointing media spokespeople, lobbying for increased research funding, and gaining a sense of themselves as a collective. Health charities that are now organized to raise and distribute research funds and shape health and research policy are the most obvious of disease-based collectives. The extent to which those organized around diseases have some other identifier in common (gender, ethnicity, class), will influence the degree of cohesiveness developed in the collective.

A less obvious way that an aggregate becomes a more cohesive collective occurs when the research process itself (re)creates membership in a collective that had not previously been important to the identity of its members. (For example, if genetic research links a specific mutation to a group of people who all trace their ancestry to one geographical region, which had previously not been a marker of group identity, or subdivides those who were previously unified). When predicting harms of research, attention must be paid to the possibility that the research process might create or call into question a collective sense of identity, in which case individual consent may not be sufficient.

## B. Homogeneity

A second continuum important for understanding the range of types of groups affected by research is that of homogeneity / heterogeneity. It is important to recognise that for some collectives, the diversity of values or beliefs around risks and benefits of a particular research project may be as great within the group as between groups. The extent to which individuals in a group are homogeneous in the values and beliefs they hold when evaluating the relative risks and benefits of a particular research project is independent of cohesiveness. It is important to

recognize that genetic homogeneity does not necessarily correspond to homogeneity of values and beliefs. For example, while Ashkenazi Jews may be genetically homogeneous, within any one community of Ashkenazi Jews there may be great heterogeneity of beliefs and values. By contrast, in the Hassidic Jewish community there will likely be greater homogeneity of beliefs and values. Similarly, health charities will vary in the extent to which they tolerate heterogeneity of beliefs and values, or limit their representativeness according to certain core beliefs (e.g., relative importance of cure over care in the distribution of research funds).



### III. NEGOTIATING COLLECTIVE ACCEPTABILITY

This section will consider the negotiation of collective acceptability of research in terms of practical goals for researchers and REBs. Categories of research are broadly described using a continuum from “homogeneous collective” to “heterogeneous collective” to “aggregate”. It will be emphasized that cohesiveness is a critical consideration and that there may be diversity even within highly cohesive collectives. Understanding the effects of research on a group, and decisions about whether research is acceptable to a group, must therefore be based on a carefully negotiated understanding of the actual values of affected groups. This means bringing to the forefront of the ethics review process an awareness of relations of power, as well as



diversity of values, between researchers and communities, and between and within communities.

Collective acceptability of research will often require that researchers and REBs consider more than respect for individual autonomy in recruitment and informed consent. Generally, the responsibility to assure collective acceptability increases in proportion to the cohesiveness of the research population for two reasons. Cohesiveness increases the probability of effects on the group as a group, and improves the ease with which a collective acceptability can be easily negotiated and representative of the larger group.

In what follows, the practical recommendations are intended to shape research to better represent collective acceptability of research. The recommendations are sometimes controversial or provocative, as is appropriate for one of the most contentious areas of ethics in human subject research. What duties do researchers and REBs have to assure collective acceptability of research objectives, effects and methods?

## A. Defining Collective Acceptability

Collective acceptability of research is an ideal state where:

- Researcher and research population have equal knowledge about the research and community concerns
- Researcher and research population agree that:
  1. The research goals are appropriate
  2. Effects on group are acceptable (i.e., harms acceptable or justified by potential benefits)
  3. Methods are respectful
- Trust between the researcher and the population assure good recruitment, respect of the group and individual, successful research with results viewed as important by both researcher and research population

In order to assure accountability to research subjects for collective acceptability, researchers and REBs should collaborate to determine how to manage the following concerns:

- Initial acceptability and ongoing review to research population
- Relative power of population and researcher (i.e., can population express or articulate their concerns, or is advocacy required; can researcher maintain reasonable control over intellectual property)
- Informed consent for access to private information or individuals (only in rare cases will collective acceptability be a substitute for individual consent)

## B. Researcher and REB Responsibilities for Collective Acceptability of Research in a Homogeneous Collective

Researcher (including industry)-initiated research on a small or very cohesive community will produce knowledge that is highly generalizable to that community. Effects of this kind of research are very specific to the population, so potential harms to non-participating members cannot be justified through individual informed consent. Sometimes the potential harms considered unacceptable to some group members (e.g., speculative loss of prestige) will be insufficient to justify depriving consenting members from participation and benefits from accruing to the general group (e.g., preventive measures related to disease). Nevertheless, even this harm-benefit calculation cannot be engaged in apart from discussion with such a small or cohesive group.

The presence or absence of obvious group leadership will be an important consideration in negotiating collective acceptability. Groups that are highly cohesive and homogeneous are those that will be most likely to also have appointed group leaders, who will be the first point of entry into negotiating collective acceptability. Negotiating collective acceptability in groups that are highly cohesive and homogeneous with representative leadership will involve discussions with groups' authorities of the relative risks and benefits of the research and discussion of the related objectives that the leaders consider important. Once the group leaders have agreed that the effects of the research on their group are acceptable, then individual participants can be approached for their consent regarding the research effects on each as an individual.

Caution should be exercised not to confuse strong or vocal leadership with good representation of homogeneity within a group. (Issues related to power and representation will be discussed in greater detail in Section III-E below.) Leaders should be asked to identify any controversial points related to the research, and who might be a good resource to explain the range of views within the community. Informed consent might also identify that there is a difference between the leadership's positions and the specific beliefs of members. Good monitoring of informed consent by researchers or an REB should identify where there is a difference between the collective acceptability and actual consent, and assess whether collective assent might be further negotiated to facilitate better representation of the range of values in the group, better participation in research, and improved application of research outcomes.

**Example 1: An agreement between health researchers and the Apache community of Oklahoma for community-based genetic research on diabetes mellitus**

Health researchers negotiated an agreement with the Apache Tribe of Oklahoma to obtain biological samples for genetic research on diabetes mellitus.<sup>164</sup> They began by identifying the culturally appropriate public and private social units within which community members are accustomed to make decisions about health. They report that members of the Apache community were themselves very aware of the question of representativeness and were able to guide the researchers in including specific social units for consultation. In the Apache community, the major public unit is a five-person Apache Business Committee that is elected by tribal members, and is recognized as having public authority to make formal decisions about matters affecting the well-being of the community as a whole. However, everyday private life is ordered by five major extended families, which are the private units within which information about such matters as individual health status is confidential. The Apache Business Committee sponsored a series of public meetings, open to all tribal members, in which researchers explained their research goals. As a result of that initial dialogue, the researchers modified their goals to take account of communal priorities. They then sought grant support for their research, as well as to support the collaboration of the Apache Business Council, which appointed a committee to evaluate the research proposal. This community review board evaluated the research project for its implications for the Apache community and then explained those implications to and negotiated them with researchers. The community review board then held conversations about the proposed study within the five community social units. Agreement was reached that defined the scope of the research, provided options for naming the population in publications, and addressed the distribution of royalties from intellectual property, the future use of archival samples, and specific cultural concerns.

**Example 2: The Icelandic Health Sector Database**

The Icelandic Health Sector Database is a project to collect genetic material from individuals in Iceland for the purpose of studying human disease in a specific population.<sup>165</sup> The project integrates medical information with genealogy and molecular genetic data. The stated

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<sup>164</sup> M.W. Foster, D. Berensten, T.H. Carter, "A model agreement for genetic research in socially identifiable populations" (1988) 63 Am J of Human Genetics 696.

<sup>165</sup> L. Nielsen, "The Icelandic Health Sector Database: Legal and Ethical Considerations", in T. Caulfield & B. Williams-Jones, eds., *The Commercialization of Genetic Research: Ethical, Legal and Policy Issues* (New York: Kluwer Academic/Plenum Publishers, 1999) 111.

purpose is to use the new genetics to create knowledge about disease and help determine the usefulness of this technology in medicine. An Icelandic company is conducting the project, deCode Genetics, in cooperation with a pharmaceutical company, Roche. deCode Genetics is an Icelandic company; of the 270 scientists, statisticians, and informatics specialists involved, 90% are Icelandic. Iceland has a small and very genetically homogeneous population. Therefore, results of this research will have strong implications for all Icelanders.

deCode Genetics obtained a form of “collective acceptability” to carry out the research. The Icelandic Parliament and the Health Ministry (which oversee the health care system in Iceland) agreed to allow irreversibly encrypted medical data to be transferred to the database without explicit informed consent by individuals in Iceland. Collective acceptability of the research risks and benefits took the form of a government bill, introduced by the Minister of Health at the initiative of deCode Genetics. It entitles the Icelandic Ministry of Health the right to grant a license to a company to build a database containing medical records of all Icelanders that could be linked to genetic and genealogical information.

deCode Genetics did not also obtain individual consent from participants; instead, individuals were given the choice to opt out of the database at any time before any data are actually transferred. Individual consent is obtained for generating genetic data and for linking it to the medical information in the database, at the time of blood collection from Icelandic volunteers.

Many ethical concerns have been voiced about the database, within and outside of Iceland. Those concerns revolve around issues related to privacy and confidentiality (given the small population, it would be possible to link information back to specific individuals); autonomy and consent (problems arising from the “opt out” aspect of the system); ethical review and scientific openness (in particular, problems with the Roche pharmaceutical company involvement meaning blocked access to the data by other scientists; and lack of a strongly independent ethics review board to monitor the research); and commercialisation (the Act does not require deCode to share with Icelanders any of the profits it might make off their medical and genetic histories or any money it might make from a public offering of its stock).

However, these ethical concerns do not mean that collective acceptability should not have been obtained, nor that parliament was the not best means of gaining collective agreement by the nation. Iceland is relatively homogeneous and it is cohesive. Prior to passing

the Bill, there was wide-ranging debate among politicians, ethicists, scientists, and health care professionals as well as in the general public. Gallup and other polls consistently showed that at least three quarters of the population supported the database, and parliament passed the Bill in December 1998 by the same margin.

Therefore, this method of negotiating collective acceptability seems to be right for Iceland. Ethical problems arising from the lack of individual consent are important; but they do not mean that collective acceptability was inappropriate, just that it is insufficient.

While this means of negotiating collective acceptability was appropriate for Iceland, the same process of negotiating collective acceptability for a collective that is equally homogeneous and cohesive (for example, another small nation) may NOT always be appropriate. This is most obvious in nations that are not founded on democracy. “Research for Iceland by Icelanders on Icelanders” works because there is general agreement that the society is founded on the principles of individual choice and freedom (it is a working democracy). However, such an appeal to nationhood may lead to coercion in a society that is not democratic or that is characterized by government oppression of some or all segments of the population.

### **Summary, negotiating collective acceptability in homogeneous collective**

REBs must ensure that researchers have provided:

- Evidence of negotiated collective acceptability, or of genuine discord within the community; i.e., explicitly address incompatible concerns
- Description of the group’s homogeneity and diversity, with diversity accommodated
- non-participating collective members have been identified; evidence of supplemental discussion of collective acceptability by outlying or dissenting members
- Evidence of use of population’s own authority or participatory models, such as councils, town-hall meetings, private social units, elders, etc.

### C. Researcher and REB Responsibilities for Collective Acceptability of Research in a Heterogeneous Collective

Most of the documented examples of formal community-based ethics reviews have been of collectives that are relatively homogeneous. However, collectives that are highly heterogeneous (for example, a collective comprised of two or more cultural subgroups) are more common. Negotiating acceptability in a large collective that encompasses diverse subgroups, or in a small homogeneous community that is “nested” within a large heterogeneous collective, poses challenges that are markedly different from those of homogeneous collectives.

Researcher-initiated research on a large diverse collective will produce knowledge that may or may not have consistent effects on all members, and that is more likely not valued in similar ways. Methods acceptable to some may not be acceptable to others. For example, initial discussions with representatives of the Roman Catholic Church in Canada related to birth control practices cannot be presumed to reflect the diversity of views geographically or individually. Local diocese discussions and informed consent are vital to assure local collective acceptability, although the national collective acceptability is also important.

Groups that are cohesive but heterogeneous may have more than one leader if organized subgroups exist within the collective. Collective acceptability by an authority of the broader collective is not sufficient for authorizing or predicting potential harms and benefits of research on a subpopulation of the collective (e.g., a subgroup of First Nations’ peoples suspected to be at increased risk for a particular hereditary disorder). Therefore, in cases where research is being done only on a subpopulation of a larger group, collective acceptability must be sought from representatives of the subpopulation as well. This is particularly necessary when the cultural subgroups may have interests that may be additional to or different from those represented by the community at large, or when one more powerful subgroup attempts to control or shape the values of the broadest collective.

It should be noted that this may lead to group conflict where research may have risks for the subgroup but benefits to the larger group, or vice versa. Dissent and diversity within a collective will be more easily understood and managed when subpopulations within the collective have clear leadership. In the absence of clear leadership of a collective or of

subpopulations within a collective, researchers or other facilitators of collective acceptability must be careful to involve the widest range of perspectives in negotiating acceptability.

The issue of managing dissent between subsections of a collective is not easily resolved; there are no simple formulas or solutions. At a bare minimum, even when dissent is evident and the researcher perceives no likelihood that the two (or more) subsections will come to an agreement over the acceptability of research, the researcher must have held sufficient discussions with various dissenting opinions in order to be as informed as possible about the nature of the dissent (including an awareness of power relationships within the dissenting subpopulations). One way this may be done, for example, is through open invitations to participate in community-wide and sub-community-wide meetings to discuss potential research effects. That is, it may be necessary use several different forums to assess the various risks to different segments of the collective.

The researchers must clearly describe to the REB how the differences of opinion over risks and benefits within the collective are evaluated and negotiated with both groups. There may be an opportunity for an REB, institution, or other organization to work out a specific process to support the negotiation of collective acceptability with these groups.

It should be noted that comparative research on various subpopulations within a heterogeneous collective will be similar to comparative research across two or more unrelated homogeneous collectives (i.e., that are not part of one larger heterogeneous collective). For example, research across several First Nations' communities might require negotiation with each homogeneous community within the broader collective. In both cases (conducting research on two or more unrelated homogeneous collectives; conducting research on two or more homogeneous collectives that are "nested" within a larger heterogeneous collective), it may be necessary to negotiate collective acceptability with each independent homogeneous collective, and also to establish an advisory bringing together representatives from different communities for the duration of the research.

**Examples: Ethics discussions between health researchers and heterogeneous collectives**

An international workshop on "Ethical Issues in Health Research among Circumpolar Indigenous Peoples", held in Inuvik in 1995, brought together researchers, representatives of aboriginal organizations and First Nations leaders to discuss problems in the current ethical

review process and to develop new frameworks which would increase community participation in the research process.<sup>166</sup>

Hadassah and the Jewish Council for Public Affairs initiated a dialogue between Jewish leaders and genetics researchers to review both the value of genetic research to Jews and ways to minimize potential harms to different segments of the Jewish population.<sup>167</sup>

At the University of Northern BC (UNBC), there is an ongoing formal relationship between representatives of various First Nations groups and the University REB. The collective of “First Nations peoples” is comprised of many different groups, each relatively homogeneous and cohesive within, but with great variation between groups. UNBC researchers negotiate collective acceptability with these community representatives whom they call upon to discuss the benefits and risks of research to the community in question, or, as well, to First Nations peoples as a broader collective.

### **Summary, negotiation of collective acceptability in research on heterogeneous collectives**

REBs must ensure that researchers have demonstrated:

- Evidence that collective acceptability has described (non-) representativeness and how it is managed (e.g., how does the group manage similar disagreements, how will feedback be solicited as actual effects accrue, what is the information disclosed in consent)
- Establishment of ongoing mechanisms to respect heterogeneity of feedback from identifiable and relevant sub-populations

In cases where research is being conducted on more than one subpopulation within a heterogeneous collective, REBs must ensure that researchers have demonstrated:

- Evidence of collective acceptability for each collective as with highly cohesive single collectives
- Exchange of concerns between collectives to facilitate identification of shared concerns and benefits and to design good methods (i.e., consistent across populations)
- Multiple feedback mechanisms to assure ongoing acceptability and explicitly (transparently) manage conflicts

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<sup>166</sup> J. Kaufert, L Comanda, B Elias, R Grey, T Kue Young, B Masazumi (1999) “Evolving participation of Aboriginal communities in health research ethics review: The impact of the Inuvik workshop”, *International Journal of Circumpolar Health* 58 134.

<sup>167</sup> Stolberg, SC (1998) Concern among Jews is heightened as scientists deepen gene studies. *NY Times* April 22, section A, cited in MW Foster, RR Sharp, WL Freeman, M Chino, D Bernsten, and TH Carter (May 4, 1999), *The Role of Community Review in Evaluating the Risks of Human Genetic Variation*, Electronic publication.



REBs must recognize the limits to collective acceptability in large heterogeneous collectives: informed consent taken collectively may be the best possible response.

#### D. Researcher and REB Responsibilities for Collective Acceptability of Research in an Aggregate

Most clinical trials and other medical research are not on collectives but on aggregates of individuals who have little in common other than diagnosis or clinical presentation. When conducting research on an aggregate of individuals, generally only individual consent can be obtained. Collective consent is neither possible nor useful; individuals within the research population have little in common except their participation in a research project.

However, the research process itself may eventually transform a previously unassociated group of individuals into a collective of individuals with some shared interests. For example, AIDS or genetic research may identify lifestyle, geographic, or ethnic community risk factors that will increase possible harms as well as possible benefits to specific identifiable groups. Genetic research will inevitably identify both disease-related and other identifying features of aggregates, increasing what the aggregate has in common in terms of risk and benefits, but without necessarily diminishing heterogeneity. Research on an aggregate of individuals who have little in common except their disease and/or research participation may eventually identify a sub-set as having many other interests or features in common (e.g., ethnicity, socio-economic status, sexual orientation). This may suggest that there is a move from relative heterogeneity to relative homogeneity within the group. Where the group has organized itself politically (i.e., there is a move from low cohesiveness to high cohesiveness) then collective consent is not only desirable, but also necessary.

As research leads some individuals within an aggregate to organize and politicise, cohesiveness and homogeneity may increase. They may develop a consciousness of having membership in a group, and as members mobilize themselves for support and increased funding, they may form community based groups or health charities. For example, when women began to organize themselves politically to focus research attention on breast cancer, there was movement from low cohesiveness to higher cohesiveness within the aggregate – the aggregate was no longer so loosely associated; there was a consciousness of having membership in a

group (women survivors of breast cancer), and the Breast Cancer Foundation represents some of the interests of the group.

Once a movement toward cohesiveness has occurred, negotiating collective acceptability may be both possible and beneficial to the research. Researchers and REBs must consider how to manage collective acceptability as a group becomes more susceptible to group effects of research and some level of collective acceptability is more readily attainable.

In aggregates, negotiating collective acceptability will be more complex, and caution must be exercised. While some aggregates may have clear leadership (for example, health charities), that leadership will not necessarily represent the values and viewpoints of some individual members of the aggregate. While the research process may establish a single common interest around which a group may have cohesiveness (e.g., research on a cure), individuals may remain heterogeneous on demographics and other factors. Apparent acceptability of research by members that appear to be representative of the larger group may neglect important interests that are diverse within the aggregate (e.g., concerns about caregiver support or economic interests outside of health care services). For instance, the Breast Cancer Foundation could provide some initial perspective on collective acceptability for projects on breast cancer funded through other sources. But those who are active in the political movement for breast cancer awareness are mainly white and middle-to-upper class women; they may not be able to be fully aware of, or represent, issues around the impact of research on all women nor on men with breast cancer. In aggregates that may be relatively homogeneous on important values or interests (for example, HIV positive gay males) discussions through open meetings with a wide range of individuals will help to ensure collective acceptability. In aggregates that are relatively heterogeneous (for example, people with heart disease) individual consent remains the best achievable ethical standard.

The issue of representation in collectives emerging out of aggregates is even more complex when only certain segments of the aggregate adhere to membership in a collective (for example, the aggregate of all people with alcoholism compared to those who belong to a particular collective such as Alcoholics Anonymous). This points to the importance of paying close attention to the particular context of how or why the collective *is* a collective (history, political and social structure, etc.) during the process of negotiating collective acceptability, in order to determine when individual consent alone is sufficient or desirable.

As with research in any collective, no matter how homogeneous or heterogeneous, the negotiation of collective acceptability must be done without any constraint on individuals' freedom to decline participation. Therefore, once collective acceptability has been sought, individual consent must also be obtained.<sup>168</sup>

### Summary, research on aggregates

- For research populations with only medical conditions in common, collective acceptability is either irrelevant or reflected by informed consent
- As clinical conditions become associated with other common features of a population or sub-population, the risk to the groups based on those common features increases, and collective acceptability becomes more relevant. When a health charity provides initial perspective on collective acceptability, the ethics review must include assessment of the extent to which the association represents the heterogeneity of the actual research population or affected non-participants
- Opportunity for review of collective (as well as individual) concerns should be designed or raised as relevant in the course of the research.

## E. The Importance of Understanding Representation and Authority in the Context of Unequal Power Relations in all Types of Collectives

The granting of collective acceptability by a group authority or by the authorities of various subgroups within a collective is not sufficient for authorizing the acceptability of research. While the presence of obvious leadership facilitates the task of negotiating collective acceptability, one cannot assume that the views of leaders are always representative of the entire collective. The extent to which one can *assume* that leaders represent the views of the collective depends on where the group is situated on the matrix of cohesiveness and homogeneity. In collectives that are highly cohesive and relatively homogeneous, the granting of collective acceptability by a group authority may lead individuals to be coerced into participating or to feel obliged to participate because of potential benefits to the group despite potential risks to them as individuals. This may compromise the genuineness of individual informed consent.

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<sup>168</sup> This assumes, of course, that the research is being conducted in a social and cultural context in which the notion of individual consent is meaningful. For the purposes of this paper, the issue of whether signed informed consent is always necessary in a cultural context where the implicit assumptions are not meaningful or important, will not be addressed.

However, whether or not it is apparent to researchers that the collective's authorized representative (e.g., band leader) does represent the full range of values or interests of the collective, it is the responsibility of the researcher to negotiate both collective acceptability and also to negotiate acceptability by general members of the collective. Given that in some cases, general members have no authentic authority to represent them, particular attention must be paid to the process of individual consent to ensure that it is valid. For example, in a study of genetic testing in one American First Nations community where researchers were concerned that individuals might be coerced into research participation by community authorities, researchers structured the study location to ensure that even when an individual did not participate, it appeared to others in the community that they had participated. They were given a meeting time, entered the room where blood samples were being drawn, and were given a copy of the consent form as if they had participated.<sup>169</sup> In contrast, for groups that are weak in cohesiveness and relatively heterogeneous, the benefits or risks of the research to the group may be considered less significant when compared to benefits or risks of the research to the individual. Therefore, in those groups that do not have strong leadership, individual consent is more likely to be freely given and therefore genuine.

Similarly, relations of power between the researcher and the collective will have a bearing on the authenticity of the group's collective acceptability of the research risks. A collective's values and beliefs, including explicit ideologies and taken-for-granted assumptions, are shaped by a social context, culture, and history. This context may strongly influence the extent to which the group is able to authentically approve the research project as having acceptable effects on the group.<sup>170</sup> For example, where relations with the researcher's group reflect an imbalance of power, then the group may feel coerced into giving consent or withhold concerns about possible harms to the group.

Although this discussion has focused on medical research, there is a trend toward integrating all human subject research (e.g., the *Tri-Council Code*) and health-related research

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<sup>169</sup> M.W. Foster, D. Berensten, T.H. Carter, "A model agreement for genetic research in socially identifiable populations" (1988) 63 Am J of Human Genetics 696.

<sup>170</sup> W.F. Brazier, "White researchers in Black communities: When solutions become a part of the problem", (1973) 29:1 Journal of Social Issues 41; D.C. DesJarlais, C. Casriel, B. Stepherson, et al., "Expectations of racial prejudice in AIDS research and prevention programs in the United States," in D.G. Fisher, ed., *AIDS and Alcohol/Drug Abuse: Psychosocial Research* (New York: Haworth Press, 1991)1; W. El-Sadr, and L. Capps, "The challenge of minority recruitment in clinical trials for AIDS" (1992) 267:7 Journal of the Am Med Assoc 954; S. Thomas and S. Quinn, "The Tuskegee syphilis study, 1932-1972: Implications for HIV education and AIDS prevention programs in the black community" (1991) 81 Am J Pub Hlth 1498.

often uses methods from other disciplines. One very beneficial aspect of integrating ethical review and standards for all human subject research is that the various disciplinary experiences provide historical experience managing ethical issues that appear new to medical research. For instance, the history of anthropology shows us that a collective that is relatively unempowered may appear to be participating in a proposed research project when participants have either (a) been coerced into participating by authorities within the collective or by authorities of the larger group/nation of which the collective is a part or (b) felt unable to decline because of historical or current relations of power between the researcher's "society" and that of the collective. In these cases, declining to participate can be done overtly by declaring research effects to be unacceptable and declining to participate; or by stating that the research effects on the collective are acceptable and giving individual informed consent but withholding important information or supplying false information.<sup>171</sup> It is therefore in the best interests of the researcher to facilitate open discussion and negotiation of the effects of the research on both the collective and the individual participants.

The ease with which open and honest discussions are held will vary depending on the nature of the research question and methodology. Different methodologies lead to greater or lesser awareness of the internal politics and diverse values within collectives. Research on collectives can be divided into three broad theoretical approaches based on the extent of community involvement:

1. Research "on" a collective: no involvement of participants in planning or implementation; participants seen as "subjects".
2. Collaborative research: implies a joint research effort, with design, implementation, analysis and dissemination being done by researcher and research community.
3. Research consulting: the community asks the question, gets funding, designs the project, and hires a researcher to conduct the research on behalf of the community; the

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<sup>171</sup> A. Akeroyd, "Ethics in Relation to Informants: The Profession and Governments", in R.F. Ellen, ed., *Ethnographic Research: A Guide to General Conduct* (London: Academic Press, 1984)133; American Anthropological Association, *Principles of Professional Responsibility*, Adopted by the Council of the American Anthropological Association May 1971, as amended through October 1990, 1990; G.N. Appell, *Ethical Dilemmas in Anthropological Inquiry: A Case Book* (Waltham, MA: Crossroads Press, 1978); J. Cassell and M.L. Wax, eds, "Ethical Problems of Fieldwork" (1980) 27 *Social Problems* (special issue) 259; J. Cassell and S.E Jacobs, eds., *Handbook on Ethical Issues in Anthropology*, Special publication no. 23, Washington, DC: American Anthropological Association; M. Punch, *The Politics and Ethics of Fieldwork* (Beverly Hills: Sage, 1986); C. Fluehr-Lobban, *Ethics and the Profession of Anthropology: Dialogue for a new era* ( Philadelphia: University of Pennsylvania Press, 1991); P. Marshall, "Research ethics in applied anthropology" (1992) 14:6 *IRB: A Review of Human Subjects Research* 1; M.A. Rynkiewich and J.P. Spradley, eds., *Ethics and Anthropology: Dilemmas in Fieldwork* (New York: John Wiley, 1976);J.E. Sieber, ed., *The Ethics of Social Research: Fieldwork, Regulation, and Publication* (New York: Springer-Verlag, 1982).

university based research is not in control of the design of the study, but is just hired to implement it.

The more the community is involved in planning and implementation of the project, the more they will be in a position to reflect on the potential harms and benefits of the research; similarly, the more the researcher or REB is involved with the community the more they will understand, from the perspective of members of the collective, how the research may affect the collective as a whole.<sup>172</sup>

It is important to recognise that for most medical research being conducted today, the balance of power tends to be in the hands of the research community and not the collective. Therefore, it is the responsibility of the researcher to ensure that open and honest discussion of the potential effects of the research on the collective, from the perspective of members of the collective, is held. In some cases this re-distribution of power will imply that the research project should not go ahead despite advantages to society, where risks to the collective are felt to be greater than the benefits.

Some researchers have expressed concern that in the effort to correct the history of exploitation of certain groups by researchers, researchers are now inappropriately overcompensating in their sensitivity to involving communities in decision-making around research, with the result that research may be impeded.<sup>173</sup> To clarify our position, the process of negotiating collective acceptability of research is not the same as obtaining collective consent.

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<sup>172</sup> S. McBeth, "Myths of objectivity and the collaborative process in life history research", in C.B. Brettell, ed., *When They Read What We Write: The Politics of Ethnography* (Westport, Conn.: Bergin and Garvey, 1993) 145; M.W. Forster, D. Berensten and T.H. Carter, "A model agreement for genetic research in socially identifiable populations" (1998) 63 *Am J of Human Genetics* 696; A. Cornwall and R. Jewkes, "What is participatory research?" (1995) 41 *Soc Sci Med* 1667; J. Hatch, N. Moss, A. Saran, et al., "Community research: Partnership in black communities" (1993) 9 (Supp) *American Journal of Preventive medicine* 27; B.A. Israel, A. Schultz, E.A. Parker, and A.B. Becker, "Review of community-based research: Assessing partnership approaches to improve Public health" (1998) 19 *Annual review of public health* 173; W.T. Osborne, "The ethical symbiosis between anthropologists and the peoples they study" (1993) 34 *Anthropology Newsletter* 1.

<sup>173</sup> For examples of this debate, see P. O'Neill, "Communities, collectivities, and the ethics of research", *Canadian Journal of Community Mental Health* (1998) 17:2 67; A.F. Benjamin, "Contract and covenant in Curacao: Reciprocal relationships in scholarly research", In N.M.P. King, G.E. Henderson, and J. Stein, eds., *Beyond Regulations: Ethics in Human Subjects Research* (Chapel Hill & London: The University of North Carolina Press, 1999); R.C. Fox, "Commentary 1. Contract and Covenant in Ethnographic Research", In N.M.P. King, G.E. Henderson, and J. Stein, eds., *Beyond Regulations: Ethics in Human Subjects Research* (Chapel Hill & London: The University of North Carolina Press, 1999); Estroff, S.E., "Commentary 2. The Gaze of Scholars and Subjects: Roles, relationships, and obligations in ethnographic research." In N.M.P. King, G.E. Henderson, and J. Stein, eds., *Beyond Regulations: Ethics in Human Subjects Research* (Chapel Hill & London: The University of North Carolina Press, 1999).

**Collective consent** implies that once an REB has seen a letter from a community leader welcoming the researchers into the community, then the research has been deemed acceptable to the community. It also implies that without the permission of the community leader, the research cannot proceed. In the model for community research ethics review we present here, consent by a group authority is not sufficient to authorize the acceptability or unacceptability of the research to members of the collective.

**Collective acceptability** means that an REB must obtain documentation detailing the series of meaningful discussions researchers have held with appropriate leaders and non-leader representatives, with diversity and dissent in opinion outlined; and justification for why, based on these community negotiations and from the perspectives of community members, the potential benefits of research are deemed to outweigh the potential harms such that research is acceptable to the community. Unlike collective consent, then, negotiating collective acceptability means the researcher and REB take an explicitly paternalistic stance. In cases where a researcher is unable to hold negotiations in some of the ways suggested in this section, then research may indeed be impeded; but we predict that in the long run any impediment to specific research projects will be overwhelmed by improvements to research methods and outcome. Specifically, negotiating collective acceptability will lead to increased validity and reliability of research, through increased community participation and the assurance that results will be meaningful and applicable to peoples' everyday lives.

#### IV. IMPLICATIONS FOR GOVERNANCE

One of the most vexing problems for research ethics is the role of public participation in the evaluation of research for its respect of participants and whether the benefits of research justify the specific risks. Collective acceptability suggests that elements of public participation in research ethics is best managed by recognizing the "public" is made of overlapping groups who share affinities with varying levels of coherence and diversity. Public participation is easier to motivate when the participants are engaged in evaluating research that will affect them, whether as participants or as a result of the effects of the research on non-participants. Public representation on REBs is inadequate to manage these evaluations because any individual only understands his or her own perspective on the various public interests. A measure of the effectiveness of any form of public participation should be the degree to which public interests

related to specific research projects shape the research. This discussion on collectives proposes a complimentary set of policies, criteria and actors to negotiate the collective acceptability of specific research projects and of research relationships between researchers, REBs, research institutions and groups affected by or participating in research.

The criteria for collective acceptability have been described in ideal form. Individual research projects and programs will have to be evaluated with respect to these criteria, and different actors and policies will be required of different types of research and depending on the nature of the research population. There are some instances where research practices have respected something like a notion of collective acceptability, such as anthropological participant observation, contract research and collaborative research. In such cases policies such as the requirement of informed consent may be inappropriate if the primary effects of research are group benefits and individual involvement is primarily observational (e.g., historical research to describe traditional land use). Further, refusal of participation by individuals upon disclosure of group risks is ineffective protection from the effects of the research as a result of other members' participation. So researcher and REB responsibility for the effects of research might actually be well managed under some methods that negotiate collective acceptability to the research population, and the requirement of individual consent could be either irrelevant, or even deceptive or harmful. But the review board, researchers and the research population should be satisfied that the criteria of collective acceptability have been reasonably fulfilled.

Funding agencies are one of the actors in governance relations. Both public and private funding sources have vested interests that can influence how research is conducted and used. Access to funding is often the privilege of university or industry based researchers, increasing the power asymmetry between researcher and participants. It is typically in the interests of those who fund research that research projects be based on sound but cost effective methods and analysis. As described earlier, the quality and consistency of research participation can be positively affected by the careful negotiation of collective acceptability and informed consent, although this may have significant financial implications. Health charities, and cohesive cultural or political groups may well find it useful to establish mechanisms for the evaluation of collective acceptability, including establishing their own mechanisms for review, negotiation and articulation of diversity of interests within their memberships, and research agreements with particular institutions or researchers.



REBs should add collective acceptability of research to their checklist of ethical issues to which all human subject research is subjected. Researchers should be required to reflect on the group effects of their research, on how readily identifiable the affected persons are, and on how they might establish collective acceptability. The unfortunate under-funding of REBs and bureaucratization of ethics review often leads to superficial examination of the ethical issues related to research, and how research will affect the group may not always be identified. REBs should require a description of how collective acceptability has been managed, and withdraw approval if it is discovered that collective acceptability is a problem during the research. This would encourage pre-emptive consideration of the related issues by researchers and funding agencies. Some legal governance related to collective acceptability is likely to be found in legislation and decisions that are indirectly related to the acceptability of research. For instance, treaty agreements or specific contracts may restrict or direct the negotiation of any collective agreements with a group for purposes of control over land claims or for overtly political purposes. While these mechanisms suggest strong leadership, their ethical validity for establishing the collective acceptability of research must be carefully evaluated.

Market effects will certainly discourage the negotiation of collective acceptability when the costs of negotiation increase the ultimate costs of developing marketable products. But market forces may also have a curious supporting effect. Since the goal of market driven research is to develop products and services that will be purchased by groups, there is some impetus to assure that the research is based on accurate assumptions about the potential consumers. For instance, some post-marketing research re-appraises the actual effectiveness of drugs when used by consumers to be lower than that of the pre-marketing drug trials or modifies the product to better fit consumption habits. The consumer-based economy increases pressure to assess the target consumer groups' actual perceptions of needs and wants prior to design of a commodity, and this may have some effect on research design and collective acceptability. This may be particularly true for boutique or niche markets, where consumers are identified as affinity groups and products are actually designed for them.

Market and regulatory forces are undergoing a move to globalization that also supports some instances of requiring collective acceptability of research. Globalization brings international attention to how nations are managing issues related to aboriginal peoples. While very large markets may dilute the differences in sub-populations, there is some support for compliance with local community standards. REB and researcher efforts to negotiate collective acceptability of research may be supported by this element of globalization. REBs must be

accountable for how they fulfil their function as representatives for community standards, as well as demonstrating their expertise to do so. But in order to serve this role in the governance of research involving humans, REBs and related mechanisms will require considerable investment to adequately provide for public participation and to promote research that is in the interest of diverse publics.

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## SECTION D-2

# PUBLIC HEALTH RESEARCH AND PUBLIC HEALTH NON-RESEARCH: OR WHO GOVERNS WHAT

Jean Joly

### I. INTRODUCTION

From John Snow who, in 1854, had the water pump handle removed from what he thought was the probable source of the London cholera outbreak (and in fact thus ended that epidemic) to the more recent identification of the mad cow disease in humans (variant Creutzfeldt-Jacob disease), public health officials have greatly learned from observations that were made with or without the consent of the public. Many of these observations led to new knowledge and are appropriately recognized as one of if not the major cause of the 20<sup>th</sup> Century accomplishments in health improvements.

The major tools used in these achievements are surveillance, collection and collation of data analysis of this information and reporting. In fact, these activities are of such importance in our society that many legislatures, both in Canada and abroad, have legally mandated public health officials to accomplish these tasks. The boundary between what is within this legal mandate and what is research is quite blurred and what starts as a routine public health inquiry may end up as the acquisition of new knowledge.

It is the purpose of this section to examine these largely ambiguous boundaries and the rules (or lack of) that govern these endeavours.

## II. DEFINITION OF RESEARCH

The recent policy statement of the three research Councils defines research as “a systematic investigation to establish facts, principles or generalizable knowledge;” furthermore, it is stated that this definition “parallels those employed in other research ethics norms in Canada and abroad.”

Numerous variations of this definition have been advanced. A common tenet of these is “the acquisition of new knowledge.” By whichever means it is achieved, be it from casual observation to experimental designs, this notion of “new knowledge” is always central to the definition of research and will thus be the benchmark used in this paper.

### A. Legislation Governing Research Activities

In Canada, with the exception of the Province of Quebec where a few articles of the Civil Code do contain provisions for the conduct of research, there is no specific legislation in the area of research involving human participation. Hence, most of the research activities in health related fields are governed by the recently adopted *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans* or by other internationally adopted standards. Provisions for recruitment, consent conduct, monitoring and reporting of research activities are defined within these or other similar documents.

Although it is not law, the *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans* does contain some provisions that bind researchers and research institutions into adopting these standards.<sup>174</sup> Hence in order to obtain funding from the Councils and the prestige and recognition associated with it, researchers and institutions are bound to this Policy although Councils account for only a small portion of all health research funds in this country.

The current policy statement by the Councils does not address the issue of public health research in the format that was initially proposed in the Code of Conduct for Research Involving Humans, where under the Privacy and Confidentiality Section, it was clearly stated that :

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<sup>174</sup> “The Councils will consider funding (or continued funding) only to individuals and institutions which certify compliance with this policy regarding research involving human subjects” Introduction; *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans*.

Public health officers may be mandated by law to undertake research and in such cases REB approval is not required; this does not, however, exempt public health officers from seeking REB approval when the research is outside their mandate. In such case, REB approval is mandatory and, in all cases, respect for persons must be observed.<sup>175</sup>

This area of research is thus in a grey zone and the nature of the regulations to be applied are almost totally undefined.

### III. DEFINITION OF PUBLIC HEALTH

One of the most basic definitions of public health is provided in one of the standard textbooks in the area, *Public Health Focuses on Health Issues in Populations*.<sup>176</sup> As vague and broad as this definition can be, it is the most comprehensive and the one that is the most easily amenable to changes as the health of a population changes. Hence, 25 years ago, AIDS was not a public health issue; however, nowadays it is at the forefront of many public health challenges as the pandemic continues to progress in the world.

The practice of public health involves numerous activities, many of which are clearly not within the realm of research. However, at least three public health activities – surveillance, emergency response and program evaluation – are sufficiently close to research activities to justify further reflection. All three activities are at the core of the public health officer legal mandate.

**Surveillance** is usually defined as the ongoing, systematic collection, analysis and interpretation of outcome-specific data, closely integrated with the timely dissemination of these data to those responsible for preventing and controlling disease or injury.<sup>177</sup> Another definition that is also generally accepted is the one proposed by the World Health Organization which states that surveillance is “the ongoing systematic collection, collation, analysis and

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<sup>175</sup> Tri-Council Working-Group, Code of Ethical Conduct for Research Involving Humans (Final) (Ottawa: Tri-Council, 1997).

<sup>176</sup> Maxcy-Rosenau-Last, *Public Health and Preventive Medicine* (Appleton & Lange, 1992).

<sup>177</sup> S.B. Thatcher and R.L. Berkelman, “Public health surveillance in the United States” (1988) 10 *Epidemiologic Review* 164.

interpretation of data and the dissemination of information to those who need to know in order that action may be taken.”<sup>178</sup>

In both of these definitions, it is not mentioned whether or not the disease under surveillance is a known or unknown entity, nor is it mentioned whether or not the disease, if known, could be transmitted by a new route, a different mode of transmission or a previously unidentified vector. In either of the latter two cases, the routine surveillance of a given syndrome or disease would entail the acquisition of new knowledge.

**Emergency response** is a public health activity undertaken in an urgent or emergency situation, usually because of an imminent health threat to the population but, sometimes because the public and/or government authorities perceive an imminent threat which demands immediate action. The primary purpose of the activity is to determine the nature and magnitude of a public health problem in the community and to implement appropriate measures to address the problem.<sup>179</sup>

Finally, **program evaluation** is the systematic application of scientific and statistical procedures for measuring program conceptualization, design, implementation and utility, making comparisons based on these measurements and the use of the resulting information to optimize program outcome.<sup>180,181</sup>

Other activities are also part of the public health official mandate but these three are those that are the most susceptible to be conceived as either research or non-research.

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<sup>178</sup> WHO. *Communicable Disease Surveillance and Response* (1999).

<sup>179</sup> A.D. Langmuir, *The Epidemic Intelligence Service of the Center for Disease Control. Public Health Reports* (1980) 95 470.

<sup>180</sup> P.H. Rossi and H.E. Freeman, *Evaluation : A systematic approach* (Newberg Park, California: Sage Publications, Inc., 1993).

<sup>181</sup> A. Fink, *Evaluation Fundamentals*. (Newberg Park, California: Sage Publication, Inc., 1993).

## IV. PUBLIC HEALTH LEGISLATION

### A. In Canada

There is little in Canadian legislation that deals with public health. In fact, the most consistent piece of Canadian legislation on this issue is the *Quarantine Act* which is basically “an act to prevent the introduction into Canada of infectious or contagious diseases.” This is of little surprise given the major role that provinces do play in the health sector.

### B. In Quebec

In the province of Quebec, quite a few laws do address the issue of public health. *The Loi sur la protection de la santé publique*<sup>182</sup> was adopted in 1972 and still governs this general field although it is currently under revision. Adopted in 1991, the *Loi sur les services de santé et les services sociaux* has profoundly modified the organization of public health in Quebec, though it has not touched its basic mandate as defined in 1972. Finally the recent creation of the “Institut national de santé publique”<sup>183</sup> should create a slightly different environment in the future without substantially modifying the 1972 law. Finally the *Loi sur l'accès aux documents des organismes publics et sur la protection des renseignements personnels*<sup>184</sup> also impacts on the notification of reportable diseases and the conservation and handling of data pertinent to numerous health conditions.

## V. PUBLIC HEALTH RESEARCH

The Province of Quebec *Public Health Protection Act* R.S.Q., c. P-35 states that:

The Minister of Health and Social Services shall be entrusted with the application of this Act. His functions shall be:

a) ...

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<sup>182</sup> L.R.Q., Chap P-35

<sup>183</sup> L.R.Q., Chap 42

<sup>184</sup> L.R.Q., Chap A-2.1

b) to participate in the preparation of programs of popular education, training **and research** in the fields of prevention, diagnosis and treatment of diseases, rehabilitation of the sick and public health generally;<sup>185</sup>

In Quebec and in many other Canadian jurisdictions, it is thus mandated by law that the elaboration of research programs be part of the duties of public health officers. Given this legal obligation, how does one reconcile this obligation and those required by the different policies that are in place to protect research subjects? It is this dilemma and that of defining research that are central to the current controversy in this area.

As mentioned above, obtaining and analyzing data are essential to the practice of public health. For many public health activities, data are systematically collected and analyzed making the distinction between research and non-research appear blurry. The very same scientific methodology is used equally in public health practice (non-research) and public health research. Because scientific principles and methodology are applied to both practice and research, knowledge can be generated in both cases. Furthermore, the extent to which that knowledge is generalizable often does not differ in research and non-research. Thus, research and non-research activities cannot be easily defined by the methods they employ.

## VI. THE DISTINCTION BETWEEN PUBLIC HEALTH RESEARCH AND PUBLIC HEALTH NON-RESEARCH

### A. General Considerations

Given the above definition of public health, the tools used in this discipline and the legal mandate imparted to public health officials, the difficulty is then to define the properties of an activity that will identify it as either research or non-research. One could argue that the initial intent (to generate or contribute to generalizable knowledge [research] or to prevent disease or injury and improve health [non-research]) is the defining principle. Should this be the case, identical methods and procedures including potentially harmful activities could be used with or without the review of a Research Ethics Board (REB), the initial interpretation of the exact

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<sup>185</sup>Loi sur la protection de la santé publique. L.R.Q., chapitre P-35, 1996.

nature of the activity and its eventual submission to an REB being left to the public health official.

An argument could also be made that the level of risk (i.e. above the threshold of minimal risk) is the defining principle. This definition could lead to further complications: what would happen to a project that should be implemented in an emergency situation. Some emergencies can be foreseen (e.g. a hurricane) others are just impossible to predict and do require immediate action (e.g. the investigation of the outbreak of pneumonia among Legionnaires in Philadelphia in 1976). To wait for the deliberations of an REB before implementing measures that can result in the protection of the public as well as generalizable knowledge would not fulfill the legal obligations of the public health officer.

Thus the definition of research in public health is blurred by the fact that identical procedures (and possibly none of them experimental) can be used to collect information in order to gather new knowledge or to improve the health of the population or merely to gain access to data that help define the occurrence of a disease or health condition.

## B. The American Situation

In the United States, the distinction between research and non-research...

... is made by examining the intent of the project. What is the primary purpose for which the project was designed?

**General Attributes of Public Health Research** - Intent of the project is to generate generalizable knowledge to improve public health practice; intended benefits of the project may or may not include study participants, but always extend beyond the study participants, usually to society; and data collected exceed requirements for care of the study participants or extend beyond the scope of the activity. Generalizable knowledge means new information that has relevance beyond the population or program from which it was collected, or information that is added to the scientific literature. Knowledge that can be generalized is collected under systematic procedures that reduce bias, allowing the knowledge to be applied to populations and settings different from the ones from which it was collected. Generalizable, for purposes of defining research, does not refer to the statistical concept of population estimation or to the traditional public health method of collecting information from a sample to understand health in the population from which the sample came. Holding public health activities to a standard of studying every case in order to classify an activity as non-research is not practical or reasonable.

**General Attributes of Non-Research** - Intent of the project is to identify and control a health problem or improve a public health program or service; intended benefits of the project are primarily or exclusively for the participants (or clients) or the participants' community; data collected are needed to assess and/or improve the program or

service, the health of the participants or the participants' community; knowledge that is generated does not extend beyond the scope of the activity; and project activities are not experimental.

Other attributes, such as publication of findings, statutory authority (see discussion in next section), methodological design, selection of subjects, and hypothesis testing/generating, do not necessarily differentiate research from non-research because these types of attributes can be shared by both research and non-research projects.

A non-research project may generate generalizable knowledge after the project is undertaken even though generating this knowledge was not part of the original, primary intent. In this case, since the primary intent was not to generate or contribute to generalizable knowledge, the project is not classified as research at the outset. However, if subsequent analysis of identifiable private information is undertaken to generate or contribute to generalizable knowledge, the analysis constitutes human subjects research that requires IRB review.

If a project includes multiple components and at least one of those components is designed to generate generalizable knowledge, then the entire project is classified as research unless the components are separable.<sup>186</sup>

Thus in the USA, the initial intent is the most determining factor in the identification of research or non-research in public health.

## C. The Situation in Canada

To the best of my knowledge, the definition of research or non-research in Canadian public health is left to the goodwill of the investigator and is submitted or not, as he or she feels appropriate, to the REB. This could be an oversimplification of the situation and requires further evaluation with public health officials in other Canadian provinces.

## D. The Situation in Quebec

The provisions for research in the Quebec Civil Code do entail obligations to public health officials when they are in doubt about the nature of the proposed activity. In order to comply with these provisions, most officials would submit their research project to an appropriate REB. The latter would ensure that the legal and ethical requirements are fulfilled by the researchers.

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<sup>186</sup> CDC Associate Director of Science, *Guidelines for Defining Public Health Research and Public Health Non-Research* (Atlanta: 1999).



Although apparently impervious to criticism, the situation in the province of Quebec does create other problems. Hence, projects that are scientifically fully justifiable and are within the domain of good public health practice have been turned down either by the REB or the Privacy Commissioner on the ground that they were not within the boundaries of the law.

Hence a project on risk factors for the acquisition of HIV infection in male homosexuals aged between 16 and 18 years of age (an age group at high risk of acquiring the infection) was turned down because informed consent from the parents was required. Given the population under study, it is unlikely that many of these potential study participants would have accepted full disclosure of the nature of the project to the person that could give informed consent. In this case, prevention strategies based on appropriate knowledge generated with the population at highest risk will not be possible.

## VII. CONCLUSIONS

In the province of Quebec, where legislation on the conduct of research is in place, inconsistencies between the legal obligations of public health officials and other laws do create major problems in the day-to-day practice of public health. In other provinces, the lack of an appropriate legislative framework also prevents public health officials from performing their duties.

For the public health official these inconsistencies are frequently annoyances and occasionally impediments to the improvement of the health of the Canadian public. In the end, in public health research, no one knows who governs what.



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## SECTION D-3

# RESEARCH INVOLVING HUMANS: CURRENT REGULATORY STATUS OF THE CANADIAN MEDICAL PROFESSION

T. Douglas Kinsella

## I. FOREWORD

In this paper the focus is the Canadian medical profession as it relates to the governance or regulation of its members in research involving humans. This focus has been chosen because the medical profession unquestionably is *the* bell-weather constituency engaged in such activity, when measured by the following parameters: numbers of investigators, access to numbers of research subjects/participants, and researchers' ready access to substantial amounts of available funding from voluntary agencies, industry and government. Although other constituencies, particularly other health professions and academic professions, do engage one or two of these same parameters, none in Canada likely engage all three simultaneously. Thus, the research activities of the Canadian medical profession provide a relevant template from which broader issues of governance in research with humans can be examined.

From another perspective, that of the professional ethical guidelines which underlie the regulation of research with humans, the Canadian medical profession's Code of Ethics can also serve as a comparative template for other health and academic professions. Among the latter, the Canadian Psychological Association (CPA) and the Canadian Nurses Association (CNA) can be seen as disciplines, which engage in 'large volume' human research, whereas the Canadian Physiotherapy Association reflects 'lesser volumes' of human research by smaller health care disciplines. Thus, comparison of the codes of ethics of these three disciplines (as representing non-medical researchers) with those of the Canadian Medical Association (CMA)

should be undertaken to ensure that the use of the CMA Code as a template to examine governance issues of human research is appropriate for generalization.

Baylis and Downie (1), in their book “Codes of Ethics: ethics codes, standards and guidelines for professionals working in a health care setting in Canada”, have listed the essential components of the codes of ethics of the CMA, the CPA, the CNA and the Physiotherapy Association. Although each of these agencies articulates discipline-specific requirements in their codes, they also identify three essential principles of relevance to research on humans: the requirement for ethics review committees, the duty to obtain informed consent from potential research participants, and the duty to report colleagues who transgress the relevant code. Given these fundamental similarities in these codes of ethics, and to avoid repetition, the focus for the remainder of this paper shall be the utility of the CMA Code of Ethics as a governance instrument for research on humans. It is presumed that questions and conclusions concerning the CMA Code will be relevant to at least the CNA, CPA and the Physiotherapy Association.

## II. THE CMA CODE OF ETHICS

As noted, the voice of biomedical ethics for the Canadian medical profession is that of the Canadian Medical Association (CMA). The message of this voice is also essentially replicated by each of the provincial affiliates of the CMA (e.g. Alberta Medical Association - AMA, Ontario Medical Association - OMA, etc.). In addition, the same bioethics message is spoken by provincial colleges of physicians and surgeons. The spectrum of biomedical ethics spoken by the CMA for physicians is appropriately broad and does include principled directives concerning research involving humans. Thus, the CMA Code of Ethics should reasonably be heard as the voice of the Canadian medical profession concerning the governance of research involving humans.

In the CMA Code there are, as previously noted, three principles or articles which encapsulate the duties of Canadian physicians who participate in research involving humans. The first of these articulates the duty of physicians to obtain from research ethics committees or boards (REBs) the review and approval of research involving humans. The second articulates the duty of physicians to obtain informed consent from potential research subjects, and, the

third, to report unethical research behavior - including that of their colleagues - to “appropriate authorities”. Given these specific directives it seems appropriate to ask whether or not the ethics of human research by physicians is, in fact, sufficiently or actually regulated by the CMA Code of Ethics.

As noted, the first of the relevant principles, namely, the duty of Canadian physicians to submit research involving humans to REBs, has been replicated by the provincial affiliates of the CMA and by provincial colleges of physicians and surgeons. Given its wide-scale replication it is not unreasonable to expect that those who proclaimed the ethical duty would have ensured that opportunities existed whereby those who were subject to the duty could actually observe that duty - that is, submit research projects involving human subjects or participants to REBs.

Without belabouring the point, it is well-known that, until recently and with one exception in Alberta, the CMA, its provincial affiliates and provincial colleges of physicians and surgeons mandated but did not themselves create REBs so as to enable their members to observe their required duty. In fact, physicians so-engaged in human research were left to their own devices - for example, to try to access REBs at medical schools (which usually declined because of anticipated potential legal liability) or to engage private, for-profit REBs (whose very existence often suggested ethical impropriety).

The one exception in the Canadian medical establishment to which I have referred, namely, the Alberta College of Physicians and Surgeons, several years ago examined its duty to its members in this matter. As a result, the Alberta College created its own REB to provide ethical review of human research conducted by those of its members who lacked access to REBs at the medical schools and the Alberta Cancer Board. The rationale for this commitment by the College derived from its perception that its ethical obligations to the public encompassed the practice of both clinical medicine and research medicine. Creation of the College’s REB required change in the Province’s *Health Professions Act* to emphasize the disciplinary authority of the College in the area of research medicine - including a prohibition for the use of private, for-profit REBs by its members.

By adopting this process, the Alberta College also addressed the second and third principles of the CMA Code of Ethics related to research - namely, the duty of physicians to obtain informed consent from potential research subjects, and to report unethical behavior in research to “appropriate authorities”. In effect, because the College accepted its duty to extend

its disciplinary authority to its members in both clinical medicine and research medicine, it served notice that its members were ethically and legally bound to report to the College unethical behavior by colleagues in both clinical and research practice. Experience with the Alberta REB to date has revealed no significant procedural or ethical differences between it and the other three 'approved' REBs in Alberta. Thus, the Alberta model and experience should be seen as an opportunity whereby the CMA Code of Ethics could be given relevance with respect to governance of research involving humans, if it were applied by its provincial members and affiliates across Canada.

Despite Alberta's successful initiative, there remain fundamental, unanswered questions about the entire process of review of research involving humans in Canada. Among these questions are the following: what is/are the purpose(s) of the review process; who should conduct the process; do REBs serve a substantive ethical role in the protection of research subjects; what should be the relative decisional weights of science, ethics and the law in the REB process; if research on humans is to be regulated, where should the relevant responsibility for regulation lie; if monitored, what should be the purpose(s) and outcome(s) of monitoring; if/when transgressions occur what should be the locus and form of adjudication; and, of fundamental importance, should there be credentialing of competence of researchers?

This raises as well the issue of the profession's role in the accreditation and training of physicians as researchers.<sup>187</sup> Given that clinical practice and research differ in significant regards, a physician who wishes to conduct research in a given area (e.g., a clinical trial for an anti-depressant) should demonstrate that he or she has the requisite skills and training in the area of research (e.g., clinical trials management) and in the ethics of research involving human subjects. Research ethics training is crucial because the ethical dimensions of research involving human subjects differ in major regards from that of clinical practice. Indeed, one of the important ethical boundaries that may well be blurred is when a physician's patients also become subjects for the physician's research.

Our research team has addressed some of the issues relevant to these - and other - questions. What seems to emerge thus-far for private practice research by the medical profession in Canada is that the Alberta model offers replicable and reasonable self-regulation for the short term. From a broader perspective, based on the similarities of the various

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<sup>187</sup> This paragraph was added by McDonald following consultation with the author of this paper.



Canadian professional codes of ethics, it would also seem reasonable to expect health disciplines with 'higher volume' human research to use the Alberta model for their members.



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# SECTION E-1

## ETHICS REVIEW FOR HUMAN SUBJECTS RESEARCH: INTERVIEWS WITH MEMBERS OF RESEARCH ETHICS BOARDS AND NATIONAL ORGANIZATIONS

Brenda L. Beagan

### I. INTRODUCTION

The field of ethics review in biomedical and health research involving human subjects entails extremely complex issues of governance. In this qualitative study we set out to explore how key players in this field engage with this complexity in their day-to-day working lives. We wanted to know how members of Research Ethics Boards (REBs) at hospitals and universities across Canada go about discharging their responsibility to ensure research in this field is conducted ethically. In addition, we hoped to find out to what extent those REB members think this work is being performed effectively and what evidence they have for that belief. We also sought to understand what unresolved tensions, difficulties and struggles they may perceive in their work. Finally, we wanted to know what impact the current context of biomedical research has on their work in local settings, particularly the impact of industrialization, globalization and new highly sophisticated research techniques.

At the same time one of our goals was to examine what members of the national organizations who set the larger policy context thought about these issues. We wanted to know what unresolved tensions and conflicts they perceive in research ethics involving humans, what they think is being done well, what directions they see for the future in this field. Lastly we wanted to know how these national players see the overall governance of research ethics – in short, how well are we doing in Canada?

## II. RESEARCH METHODS AND PARTICIPANTS

Interviews were conducted in the spring and summer of 1999 with a total of 43 participants. The interviews were one to two hours in length, were semi-structured following an interview guide, were held in participants' offices, were tape-recorded and were later transcribed and coded inductively. Using formal individual informed consent processes interviewees gave their consent to reflect on these issues on tape as a contribution to the research. A draft of the full report was circulated to the interviewees for their feedback.

Thirty-one members and chairs of REBs were interviewed at University of British Columbia and its affiliated hospitals (N=6), University of Calgary and its affiliated hospitals (N=6), McGill University and its affiliated hospitals (N=11) and Dalhousie University and its affiliated hospitals (N=8). In addition 12 members of the following national organizations were interviewed: the Social Sciences and Humanities Research Council, the Medical Research Council, the Natural Sciences and Engineering Research Council, the Canadian Medical Association, Health Protection Branch, National Health Research and Development Program, Canada's Research-Based Pharmaceutical Companies (formerly the Pharmaceutical Manufacturers Association of Canada) and, the National Council for Ethics in Human Research. The interview guides are provided in Appendix One. The structures and processes at the various REBs across the country vary widely. Details about the research sites may be found in Appendix Two. Many REBs were in the process of changing their structures when the interviews were being conducted.

Originally, this empirical study was to include interviews with researchers, particularly clinical researchers involved with multisite trials. That would have added an extremely important perspective, indicating how the day-to-day decisions of researchers in the fields reflect, support or conflict with the ethical decision-making at other levels of the research process. Policy makers set guidelines, REBs implement those guidelines and then researchers carry out their research in accordance – presumably – with the directives established by the REB. Research on this final step of doing ethical research is needed. Nonetheless, though the direct voice of researchers is missing from this study, it is important to point out that virtually all of the REB members and many of the national organization members who were interviewed are also researchers or have been in the past. They often spoke about their views as researchers as well as their views as REB members.

When quotes have been used from interviews they are identified by interview number only. Occasionally other identifying information has been altered or removed for confidentiality. In addition, quotes have been “cleaned” prior to their use. Unnecessary words that are inevitably part of oral language – such as “you know,” “Um,” and false starts – have been removed to make the meaning of the text clearer in written format. Finally, quotes from members of national organizations have been denoted as such in the text. Those who are unfamiliar with reading qualitative research may find the presentation of data disconcerting. Readers should be aware that quoted oral speech never looks as polished as other writing does. This in no way reflects upon the thoughtfulness or articulateness of the speakers. Rather it is a feature of oral communication that we work out our thoughts aloud. The richness of qualitative writing is that it affords the reader an opportunity to “listen in” on the thoughts and words of a number of speakers as they struggle with the issues raised in the research.

### III. FINDINGS

The interview data is organized according to eleven major themes: the goals of research ethics review; the perceptions of REBs; thoughts on the effectiveness of ethics review and suggestions for improving effectiveness; debates about the merits of centralized vs decentralized processes; the impact of multiple existing guidelines for ethics review and remaining gaps in those guidelines; the difficulties of dealing with multisite trials; the role of industry, the level of resources committed for ethics review; thoughts on the importance of cultural differences in conducting ethical research; difficulties dealing with genetic research; and concerns about doing research that affects social groups or collectives. The interviewees were extremely thoughtful about the processes and impact of research ethics review, responding openly to questions and raising provocative ideas, concerns and suggestions. These people are the day-to-day experts on the implementation of REB processes. Their thoughts and opinions should be taken very seriously in considering the ethical governance of health research involving human subjects.

## A. Goals of Research Ethics Review

There was a considerable amount of consensus among the interviewees about the goals or objectives of research ethics review, though there were differences in emphasis or priority. Protection of patients / research subjects, the promotion of good research, the protection of the researcher and enhancement of the credibility of research institutions and the research endeavour as a whole were all identified by significant numbers of interviewees. The protection of research subjects from unnecessary harm was key for almost everyone.

- #10: Well I think the goal of ethics review is to protect the participants from harm. No matter where it's carried out it is the same.
- #31: I think that's really the most important task of the REB. In a sense to act quite paternalistically, and to protect research subjects from bad choices. (national organization member)

One participant explained this obligation as formal recognition of an inherent conflict of interests.

- #24: I as a physician, have a very clear fiduciary obligation to the patient, and nobody else. I, as an investigator have a conflict between my obligation to the subject and my obligation to the community for whom I'm gathering data and doing research – because I do it presumably on behalf of the community – and therefore, in the second role, that of an investigator, I have a conflict of interests. . . . Therefore, in my role as an investigator, because of the conflict in the investigator-subject interaction, the research that I do is governed by additional norms. . . . my behaviour toward the subject is subjected to a different set of review processes.

Another participant stressed that the intent that underlies scrutiny of research ethics is the assumption of a power differential between the researcher and the subjects.

When participants highlighted the promotion of good research as the only or the key goal of research ethics review, they almost always did so in the context of explaining that they did *not* see the review process as one of gate-keeping, as one of preventing anyone from doing their research.

- #18: The attitude of the committee is very much one of not hindering research; we want to let people do things.
- #02: There's this balance that you have to meet in not sort of being a policing agent, not being a road block. You want to encourage research at the university, you want to encourage the generation of new knowledge. How can you do that as well as maintain these ethical standards that as a research community we've agreed upon? . . . I mean you could very easily set up some very hard and fast



policies and say no, no, no, no, which would be the road block [approach]. You would be policing . . . Then you would be halting the generation of new knowledge and what an enormous responsibility that would be.

The greatest number of interviewees noted both of these concerns as primary objectives of ethics review: protecting subjects *and* promoting good research.

#12: Our role is not to forbid research it's to make sure that when research is done it can answer the question and that subjects are respected. That it's as safe as it can be.

#05: I think there're several goals. One is that research does carry on, it's obviously important to improving medical care. So I think it's important that research does occur, but does occur in an environment where subjects are respected and not unnecessarily harmed. . . There is going to be harm that does occur with some of the more challenging protocols. . . I think there's also a goal of being sure it's a question that needs to be asked. What I call avoiding junk science, just doing it because.

#21: In the first place well they're there to protect the public, the participants, and they're secondly there to ensure that good science is going on. And they're thirdly there to *encourage* good science. Good science is good for the community. Sometimes I think in the past REBs may have lost sight of that last thing, you know that they're not censors. Their interest first and foremost is protection of the participants but is compatible with encouraging good science. (national organization member)

Some added a goal of educating researchers, or more broadly, developing and creating a research community that is well-informed and thoughtful about ethical issues. Most participants did not see these two primary goals as being particularly in conflict. A few, however, described these as being in inevitable tension. One pointed out that having research funders design research ethics guidelines is itself problematic.

#31: The Councils themselves are fundamentally in a position of conflict of interest. Funding councils have a mandate to ensure that high-quality research is promoted. Protecting human subjects pulls in the other direction. It says sometimes research shouldn't go forward, even research that some people think is good. It is fundamentally inappropriate for Councils to be writing standards for the research that they fund. That's an obligation of government to protect Canadian citizens. . . To have Councils writing the regulations and then dictating to NCEHR, which is funded by those same Councils – it's really not a good relationship. (national organization member)

Another participant suggested the REBs are caught between protecting patients and protecting the sponsors of the research from potential legal liability.

- #28: It's a struggle about who are we protecting? The potential participants in the hospital? Or the companies? I think there's a tension between [those]. . . . Clauses in consent forms that talk about, "for the protection of you and your foetus" . . . . And the interpretation may be that that's done to protect the patient, to protect the foetus. Well, it isn't! It's done to protect the insurer of the company that– Well, I shouldn't say it isn't, I am sure there's a dual role.

She went on to suggest that REB members whose departments are substantially funded by research also face a particular tension. Consequently, she believes, "It tends to be the non-medical members on the Committee that hammer away at the ethical issues, and not the medical people (#28)."

A smaller but still substantial number of people identified the goal of protecting the credibility of research institutes, and of research as a social endeavour, as central to research ethics review.

- #11: Universities require the confidence of the public, and this is frankly not necessarily an exercise to benefit the individual researcher immediately. It's an exercise designed to ensure broader confidence in our research.
- #29: That you are at least in the first instance going to conduct your research according to what is expected, in terms of the public. And, ultimately, that protects the interests of the research community because the last thing you want to have is the public perception that people are conducting kinds of studies to which they object. That is prejudicial to the institution and to the name of research generally.
- #6: There are acceptable ways of conducting research and behaving in research, that the Canadian public can be proud of. Because if mishaps happen, if scandals happen, if it is known that research is not done in an ethically and morally acceptable way, then our support will be cut off very quickly. And it's not to anybody's benefit or advantage to do that. (national organization member)
- #13: I tell them that it's protecting them [researchers], that if they want to continue research at an academic institution the academic institution has to be credible and this reinforces credibility. Then I come back to protecting the subject as the last one if they want that, if they push. From their mind they're already protecting the subject, they're already trained in ethics, they don't want to hear that we're out there to protect the subject okay because they're ethical. So you have to put it in their frame-work.

A member of one national organization pointed out that to fully accomplish the goals of research ethics review, university and hospital REBs must have disciplinary authority over researchers. Finally, one participant suggested, "If the patient is protected then the institution by definition is protected. . . . If you're looking after that person I can't think of anything that would look bad in the headlines of the newspaper the next day (#01)."

## B. Perceptions of Research Ethics Boards

Members of REBs were not the perfect people to ask about the perceptions of the REB at their site. Nonetheless, most of them did have opinions about how they were perceived, and again, many interviewees were researchers as well as REB members. Some described a single dominant view at their institution, but most described what one participant called, “very much a divided campus.” For example:

- #11: A lot of people simply say it is a damned nuisance. . . There are a number of researchers. . . who would like to see our bureaucratic processes streamlined a bit, but fundamentally accept what is going on. . . [One department] on this campus loathes and detests the idea of anyone reviewing their research. . . Some faculties and departments express profound surprise that there’s any review mechanism at all. They just don’t know about it.
- #30: I think probably if you did a survey, you’d get a range of answers there. Some people— one extreme would look upon it as an obstacle, and the other side of the extreme would be people who would see it as a very valuable process for themselves, for protecting patients. So I would say that most people accept that it’s a necessary process, and important – though not necessarily liking it.

About a quarter of the REB participants believed that the members of their local research community see them, the REB, as unnecessary at best, an affront at worst. Or as one person put it bluntly, “They see it as a pain in the ass! (#28)”

- #13: There certainly is a perception by a group – and I can’t say how large the group is – that research ethics review is not needed because people are ethical and they’ve all been trained in ethics.
- #29: In some people’s view, they don’t see the need for it, and have to be convinced. There is a perception in some fields, particularly in the Humanities, that when you are talking about human subjects, you are talking about humans as experimental subjects, and if humans are not being used as essentially high level guinea pigs, they aren’t really human subjects any more. It takes some explanation at times to convince people that interviewing someone is, in fact, involving the person as a human subject, in the research protocol.
- #02: If somebody says “no” to you then it’s almost an affront to your academic credibility.
- #07: I would say that the investigator views it as, “Of course what I’m doing is ethical,” and “I want you to give me the stamp that it is and if you say it isn’t ethical then I’m offended because I’m an ethical person.”

A smaller but substantial number of people believed that at their institution the dominant view of the REB is as a gate-keeper, “the guys that prevent good research from being done (#05).” A

related perception sees the REB as yet another onerous source of bureaucratic red-tape that at best delays researchers from doing their job.

Interviewer: What is the perception of the REB in the local research community?

- #04: It tends to be kind of like the caricature perception of all civil servants: red-tape, getting in the way, people who have nothing better to do with their time, thinking of ways to make other people's lives miserable. . . Most instances of bureaucratic malfeasance really don't happen often. But the negative examples are the ones that stick and of course there's a whole lore, a whole culture of contempt for bureaucracy. . . So the ninety-nine examples to the other side simply don't even get noticed.
- #07: The number one comment is it takes too much time. . . It's just viewed as part of the bureaucracy and if it delays the project (for quite legitimate reasons) then it gets the investigator angry because of the timing. . . It's viewed I think as necessary but another bureaucracy that the investigator has to go through.

As with most forms of bureaucracy, the chief complaint seems to be that of unnecessary delay.

The best some interviewees were able to say was that local researchers see research ethics review as a necessary evil.

- #03: There's an acceptance that it's there and it's something that you have to do and it's better to get it right. I wouldn't go so far as to say that the value is appreciated.
- #18: IRBs in general of course are viewed as yet another hurdle one has to get past in order to get on and do what you really want to do. . . As a researcher one's impression of the IRB is that it's yet another regulatory body that you have to jump through hoops to satisfy . . . The issue is not, "Is this ethical?" it's "Will this pass the committee?" . . . I think it's viewed as sort of a necessary evil.
- #24: I would suspect that the majority still think we're wasting their time. Despite all the effort and all the goodwill and all that, because they kind of see us as a necessary evil.

A few people suggested a major source of the problem lies in the professional cultures of medical/health researchers. Researchers have been socialized through their professional training to see the ethics review process as an antagonistic one, rather than a collegial peer review process.

- #14: [We've come] to a time where ethics not only is suggested but has become mandatory. And so we've had a lot of investigators around who hadn't been brought up in that environment and hadn't been educated about it and why it was necessary in the first place. So that didn't strike a resonant chord with the vast majority of researchers who have been here for ten, fifteen, twenty years. But

now that the new generation is slowly coming in, they arguably are somewhat more socially conscious and I think that's the reason it's changing.

As in the quote above, most of these interviewees also suggested that professional standards are changing to come more into line with research ethics standards. They suggested we are currently in an "interim phase (#16)" as generational shifts introduce a cohort of researchers more aware of and concerned about research ethics. In the meantime, at least some REB members continue to face, in their words, "hostility (#11)" and "a certain amount of mockery (#04)" from their researcher colleagues for the crucial, sensitive, burdensome and difficult work they do on a volunteer basis.

### C. Effectiveness of Research Ethics Review

Obviously one of the central concerns in this research is the extent to which those engaged in the processes of reviewing the ethics of research protocols involving human subjects are in fact doing effective work. As we have seen above, there was considerable agreement on the goals of ethics review: it is about protecting subjects, researchers, institutions, and the credibility of the research endeavour. As we shall see, most REB interviewees believe their committees are meeting those goals effectively, as do many members of national organizations. But as we shall also see, participants were able to offer very little in the way of evidence for this belief. Some typical comments:

#18: Well I think it's pretty effective. . . I think the committee does a good job.

Interviewer: How would you know? Once a protocol has been reviewed, how would you know if ethics continued to be maintained in the research. Or do you know?

#18: Oh that's a good point. I guess we don't really. I mean the only way to do that would be to have yearly reviews but we don't do anything like site visits or explore the labs or, nothing like that happens. No.

#30: I think we do a pretty good job. You never know exactly what is going on out there after the process, after they've been approved.

#36: My personal view is, on balance it's effective. I'm sure there are some things that are not done very well and a lot of things that are done very, very well. On average, as far as I can tell. . . it's not bad, but it could be improved. (national organization member)

It may well be that these interviewees are right, that research ethics review is highly effective and does an exemplary job in meeting the goals of protecting research subjects, ensuring good research and assuring the public. The point here is that *evidence* for this belief is virtually nonexistent. In an era when "evidence-based medicine" is de rigueur, evidence-based standards for ethical review are not yet even a consideration.

The vast majority of those who claimed their REB was doing an effective job offered no empirical basis for that claim whatsoever. They simply put forward a passionate belief that they *must* be doing their job effectively, expressing a gut-level sense that all is as it should be but, unable to point to measurement of that claim.

- #27: I think it would be almost impossible now for something terrible to get through. I think it's doing its job. . . We're probably missing some small things. We're surely not missing terrible things. . . . I don't think anybody's being hurt. And the atrocities you used to hear about, I don't think are happening now. I really don't think so. I think we're talking about some fairly subtle stuff.
- #17: The past president of the [hospital] is a very close friend of mine, and he used to talk to me about this, "How sure are you that things are being done properly, the Board is concerned about this?" . . . I told him that I thought that the studies were being well reviewed . . . and I hope that we did our job here well.
- #22: I think it's a very good committee, obviously I think we could be better, but I think it's a good committee. I think people are very conscientious. There are good people on it.
- #02: I would have to think it's effective since I've been there thirteen years, wouldn't it! It'd be awful to think it's not effective. Yeah I think it's effective.

Others referred to "intuition (#12)" and "feeling pretty good (#03)" as ways of knowing the process is effective. Still others argued that given the volume of research reviewed in Canada, and the scarcity of problem cases, the system must work. One suggested the system works because most protocols are low risk: "It seems to work reasonably well because a lot of protocols are minimum risk, you know, there's not a lot of harm, and things carry on. We seem to do all right." Again, the point is not that these people are naïve, but rather that – as one member of a national organization stated bluntly – we simply do not have the data needed to know if research ethics review is effective.

One of the measures of effectiveness offered by just under half of the REB members interviewed was reputation.

- #19: One of the [local] newspapers had an expose on Research Ethics Boards saying “they’re not doing their job” with one exception – we were singled out as the model committee.

More important than the reputation in the general public, however, was the reputation among local researchers. Several people pointed out that local researchers – who seldom hesitate to complain if they have a complaint – had never had serious quarrels with the review process; some had even appreciated it.

Interviewer: How would you know if your goals were being met effectively?

- #10: I certainly think that the researchers do not hesitate in coming forward if there are concerns.
- #13: When I was Chair of one of the REBs I had comments from people [investigators] who said they had appreciated their reviews.... Because I’ve been Chair for so long, I get phone calls all the time... If people [investigators] were really unhappy I would hear about it.
- #26: We’ve heard from investigators, also from members who sit on . . . different committees, and so on, that have commented that our reviews tend to be quite thorough on ethical issues, and also in an effective manner. I think we have an effective but stringent committee.
- #33: I would think it is very effective. I don’t know. We’ve had retreats where we’ve invited clinicians to come and talk to us about the problems that there might be with REB submissions, and we’ve only had one individual come.

Similar to the absence of complaints from researchers, the absence of complaints from research subjects was offered as evidence that the review process works effectively. Most obviously, if most cynically, there are not many reports of serious harms.

- #11: There are not too many newspaper reports of obvious deaths generated by research. That’s one rather negative measure that hopefully the research ethics process results in some improvement in protocols.

Less drastically, research subjects are routinely given a phone number of a research administrator, a Dean, or someone at the research institute to contact if they have any complaints about their treatment as research subjects. According to the interviewees, research subjects rarely if ever call to complain.

- #03: Have I ever been contacted about genuinely ethical issues? Once or twice. . . But apart from that one – I’m pretty confident that things are going okay.
- #29: I have not yet had an instance in which the public took exception to a protocol that was approved through this office. I’ve never, in other words, had to answer

for an inadequately done ethics review. . . . You might get a call from somebody in the community that was approached by a researcher and say, "Hey! I don't like this person's approach. I don't like being asked what I was asked. How come you said this was okay?" That's never happened.

As several people pointed out, however, the average research subject might well find calling the Vice-President Research, or an equivalent administrator, rather intimidating, and might not bother to call the number they are given. The absence of complaints does not necessarily mean everything is being done perfectly.

- #09: I can count on less than one hand complaints which have come from the public themselves, the patient complaining about what's happening to them because they think it's unethical. . . It's extraordinarily rare. That's a good thing. The other possibility of course is that there are things happening out there that aren't being reported simply because of people feeling uncomfortable without bothering to complain about it.
- #05: Companies that are in business will tell you if you wait and find out what the complaints are you're going to go out of business. You have to find a way of figuring out how do your customers like the service, because they probably won't tell you.

Another empirical measure of effective ethics review offered by a substantial number of participants was the fact that the vast majority of research protocols are revised. That is taken as an indication that REBs are finding and correcting ethical problems in research.

- #12: I think it's very effective... I think it's extremely rare for issues to surface after we've reviewed them and which we haven't identified.
- #20: I don't think in my history that I have seen a protocol going through that I felt was unethical. . . I think our group has done fine. I think we have certainly sent back a number of protocols that were methodologically flawed and would not provide any useful information . . . so I think that we've been effective.

Interviewer: How effective would you say the review process is here?

- #32: ...I think it's pretty good. I think the projects do get carefully scrutinized and I think if there are major concerns with the protocols, they do get revisited and often investigators go back to companies, and on occasion, major projects don't get done here because of concerns of the committee.

In contrast, the fact that REBs are not finding problems in the protocols they review was also offered as evidence that the committees are doing an effective job. If part of the role of the REB is to create a more ethically-informed research community, then evidence of effectiveness would lie in researchers proposing and conducting more ethical research. About half of the REB



interviewees offered as evidence of their effectiveness the fact that the protocols submitted for review are better quality than they used to be.

- #02: When you look at what's happened to the quality of the application . . . there's been so much change in the number that's applying and the quality of the applications and the way in which they consider ethical issues within their research.
- #09: The protocols we are seeing coming in to us are much better written than they've ever been before. When I first came the consent forms were disastrous.
- #04: There has been a heightening of consciousness about the key questions, consent being the most ubiquitous question. There has been a heightening of consciousness on the campus and for the most part the stuff actually flows far more easily than it did say ten years ago.

Others, however, suggested the improved applications simply reflect better skills for getting past the REB.

- #03: They've learned that if they don't have the right answers in the right boxes that they are delayed another month.
- #11: I don't know whether researchers are doing better research. I would certainly say that the protocols themselves are getting a bit less sloppy.

A few people suggested the impact is deeper than simply improved applications, extending to seeing individual researchers come to understand complex ethical issues and, seeing informed consent, "which was rare forty years ago," become "such an accepted part of the culture that no one questions how much it has impacted how studies are done and what's done in studies (#01)." A member of one national organization suggested ethical concerns have become normative in research.

- #40: Whereas 10 or 15 years ago, you'd call in 'the ethicist' for a particular problem, hopefully now people are becoming more aware of this as an intrinsic part of the thing, and in fact, when you are putting your original research question together, you might say, "Is this ethically a question worth asking?"

Along with lack of complaints, revising protocols and improved quality of protocols, another form of evidence offered to indicate the effectiveness of the review process was administrative efficiency.

- #04: I think we've done a good job making it pretty self administering and that's an important objective in the demands of time and so on. So on balance I'm actually quite proud of what we've done.

- #01: There are many ways of measuring effective. First of all, do people fall through the cracks? Well ninety-nine percent of drug-trials that we do involve some funding from somewhere. We have a rule at our hospital that all cheques must be deposited either in a hospital account or in a university account. . . Cheques that come in for deposit where [ethics review has] not been done, go into what is called a suspense account, and it stays there. . . . So there are checks and balances from that point of view.

One person suggested that the danger of ethics committees is that they, “go off and find a whole bunch of things to do.” He suggested his committee is effective because it avoids this, simply administering the policies that are handed “down from on high” in as fair a manner as possible. Lastly, a small number of people thought they were being effective if they could show they were in compliance with existing guidelines for research ethics review.

To be clear, the point here is not that interviewees are misguided about the intent of ethics review, nor that they are disingenuous in their claims that they work effectively. The point is that acceptable measures of effectiveness do not currently exist – nor do the means for measuring effectiveness. In the absence of such measures and processes REBs do the best they can.

## 1. Concerns About Effectiveness

In spite of the faith evinced by many participants, about half the REB members and a quarter of the members of national organizations expressed significant concerns about the effectiveness of research ethics review. They frequently noted that the system is comprised of conscientious people of good will voluntarily doing their best but with inadequate resources, training and expertise and, too many protocols to review in too little time. Two members of different national organizations were particularly harsh in their critiques:

- #35: In my personal view, the research community has not done a hugely wonderful job demonstrating that it can adequately regulate itself. Three years ago I was more optimistic. . . At that time one could say, "Well, let's see what the research community does, and how the research community—" And I don't know that they've demonstrated in the intervening three years that, "Yes, we can do this for ourselves." I haven't seen evidence of it. . . I don't think Ethics Review Boards across the country are adequately prepared to deal with the tremendously complex issues that are on their plates. . . I'm not convinced. . . that people have demonstrated their willingness and ability to ensure the issues are adequately addressed to the benefit and protection of the subjects. (national organization member)
- #31: To be blunt, a lot of REBs have no idea what they are doing. They focus on the consent form. They really don't get at the substantive issues in the protocol. They don't know how to analyze risks and benefits in a conceptually coherent way.

They are not sensitive to justice issues. They are not sensitive to ethical aspects of design issues in clinical trials. . . .I don't think nearly enough ethical issues are flagged in your average review. I don't think people are called on things, like the sort of financial arrangements that they enter into. (national organization member)

The latter participant went on to suggest that the problems are structural, indicating lack of commitment to research ethics on the part of institutions, national organizations and governments.

#31: It's extraordinary, in Canada, that the government... investment in human research subject protection is less than half of its investment in animal protection through CCAC. So in Canada, you are better protected as a lab rat than you are as a human research subject, which I find quite extraordinary. As a researcher, you actually have to be licensed specifically, trained, tested, and then pass that examination to obtain licensure to do research upon animals. There is no such test for doing research on humans. Indeed, I suppose perhaps that's what people who fail the animal tests do! (national organization member)

Another member of a national organization also drew comparisons with animal research and found ethics review for research with humans lacking:

#40: The Canadian Council on Animal Care can tell you right down to the last one, the number of pigeons, chickens, even rats, that were used in animal experimentation in Canada last year. We don't have a clue how many humans were enrolled. I mean there's just an enormous amount of work to be done to bring the human end of things up to at least the equivalent of that for animals. (national organization member)

Yet another participant from a national organization described the failures of the systems as due to structural shortcomings: "People do that on their free time. They are not supported adequately by the administration. They don't always have the power to do what they think they should be doing. They are not totally independent as they should be. (#41)"

These broad, far-reaching critiques came from people who are not necessarily part of the daily work of ethics review or who are not currently REB members. Most of the concerns raised by REB participants were less fundamental, concerning issues such as lack of consistency between committees and the impact of individual committee members on the quality of review.

#05: I think there's quite a variation in how the protocols are reviewed... I do worry about the quality of review. I'm not sure I should be saying this, but you know I really am not convinced.

- #12: I heard from the secretary of another committee that a protocol we approved they didn't. She said, "Oh well you know when the guy presented to us it just rubbed Dr. X the wrong way and he was just a loose cannon..." These things should not happen.
- #01: My concern is more province-wide, and if you want to extrapolate it to nationally, there are no standards. There are guidelines applied sporadically in different jurisdictions, in different ways, and I think we should have national standards.

Several people particularly noted that REBs tend to "lose track of the broader perspective (#25)," concentrating on bureaucratic concerns rather than substantive ethical concerns. The detailed attention given to consent forms came in for particular attack.

- #14: I think the system could be revamped... If you have twenty people read the same protocol you're always going to come up with a T that's not crossed or an I that isn't dotted.
- #24: We waste too much time being editorial talent on our consent forms.
- #31: Of all the issues that REBs are supposed to deal with in terms of looking at the value and validity of the work – looking at justice issues, looking at risk benefit analysis, looking at questions around how the research is actually going to be carried out, questions around honesty and accuracy, looking at the conduct of the research and its ultimate reporting – of all those things, I think informed consent is the last thing they should be considering and the least important of all those things. Unfortunately, most REBs seem to think that consent is the first thing they should be considering, and the most important of all those things. And I think that's just wrong. (national organization member)

A small number of participants raised more substantial concerns about the adequacy of the individual informed consent process as a whole. They suggested that research evidence and the available literature show research subjects have very little understanding of the consent process.

- #09: A perennial [concern] is whether or not all the patients that read these consent forms actually understand what they're signing for or don't care. I think they don't care after they read the first lot of pages, and if they like the doctor and they trust the doctor... Many patients would take it seriously and read every bit, but some won't and I don't know how you safeguard against that.

One participant had been involved in a study interviewing patients who had been in previous research studies about their perceptions of the consent process they had experienced. They found patients did not understand and simply acquiesced with what they thought their doctor wanted. The study was halted by complaints from researchers.

## 2. Monitoring Effectiveness

There is an expressed desire to be able to evaluate effectiveness in research ethics review. Given the absence of solid empirical evidence about effectiveness, many participants considered the possibility of structured mechanisms for monitoring how well their work in fact meets the goals agreed upon by most REBs. About half the interviewees were at least partially in favour of some form of monitoring or at least saw a need for it.

- #16: We spend a hell of a lot of time looking at consent forms and saying change this word and change that word, and this line shouldn't be there, and what about this danger and that danger and then it's passed and everything is fine, and we don't know if anything has been followed or not unless you monitor it. . . . I think that research is monitored inadequately probably everywhere.
- #22: There could be stuff that's going on. It is disconcerting... we should be doing more monitoring that's certain.
- #07: My concern is that I don't see a continuing evaluation. I see that as a real unmet need. It's one thing to approve at the beginning, it's another thing to ensure that the project hasn't changed... I think it's unethical not to monitor... I think it is indefensible on a part of an organization not to monitor compliance in some fashion. The trick is how to do it in such a way that it's acceptable to the investigator and is effective.
- #31: I think monitoring is very important. Right now REBs in Canada pretty much just review paper, and then the researcher goes out and does God knows what! . . . In fact, it turns out it's rather common for researchers to diverge from the protocol, and when they do they tend not to inform the REB. I think REBs in this country have to go beyond reviewing pieces of paper. (national organization member)
- #8: Right now the ethics committee approves stuff and it hasn't got a clue what goes on! Never checking to see if they followed what they said they were going to follow or whether they're using the forms they said they were going to use, whether they're doing it the way they said they were going to do it. It's reliant on the sense of integrity of the researcher. (national organization member)

Although most people were supportive of monitoring in theory, almost everyone expressed concerns about how the resources would be obtained to actually carry it out. This was seen by many as the main reason monitoring is not already routine.

The other main concern participants expressed about monitoring was that it rests on an assumption that researchers are not trustworthy. This is a serious concern, challenging a core value of professional autonomy.

- #13: [The] system has to be based on trust, because we cannot monitor everything going on through this university. We cannot monitor everything in classrooms in

terms of teaching, so we trust that people aren't going to do things in the classroom that they shouldn't be doing. . . . And I want an ethics review process that works on trust... You tell the researcher what is acceptable and isn't acceptable as an institution. You have trust people after that and we do that in every other element of the university life.

- #18: [It's] up to the researcher to maintain the standard that they claim to have set... I think that's the only way it can work, because if you start having surprise visits on people to see if they're being ethical, first of all it's going to create a tremendous environment of distrust and resentment. I couldn't stand it myself as a scientist... You would have to get people basically to surprise their colleagues and spy on them and that would be disaster if anything like that happened. So I think the only way it can work is if people are trusted to uphold the standards that they say they are going to.
- #36: For the most part we have to hope, trust, that things are generally working out all right. Nobody's perfect, and some people are far, far from perfect, but to monitor everything that everybody does, it's just impossible. That's not to say there should be no monitoring at all... But maybe what needs to be done, is look for certain things to trigger a monitoring – like a complaint, for instance. (national organization member)
- #03: I think the system's based on trust... Do we need a police force, do we need to go out and go through people's file drawers to see whether the consent form is the same as the one we approved, do we make sure that everybody signed one? I'd hate to see that happen.

Several participants directly countered this notion that monitoring implies an unwarranted lack of trust, rooting their belief in monitoring in the age-old acceptance of peer review and community evaluation of scholarly merit.

- #24: Investigators somehow think that monitoring is an assumption that they're not trustworthy. And that's a funny thing for people to think, because we've all decided that the gold standard of research is the randomized control trial. Why does it include controls? Because there is such a thing as placebo effect. The presumption of a placebo effect is not a presumption of dishonesty, it's a presumption of human frailty... Investigators think that if I'm going to examine their records that I presume they're cheating. I'm not presuming they are cheating. I'm presuming an error rate. I'm helping them guard against error. I'm presuming that even if they're pristine, not all the people they work with are... If academic freedom is interpreted as the right to do an untrammelled project, unreviewed by anyone, that right does not extend to human subject research.

Finally, in an interesting twist, one person suggested that the best way to ensure research is conducted ethically is not to monitor researchers in any formal sense but, rather to educate everyone in the research community about ethical standards, “responsible-ize as many people as possible in the structure. If everybody feels responsible for what his colleagues are doing (#26),” unethical research is unlikely to occur, or to be tolerated.

One participant suggested the main reason monitoring is not being done more routinely already, “is because it’s not easy! (#07)” Without unduly taxing the already overburdened volunteer REB members, a process must be devised that strikes a balance between protecting subjects and stifling research with an overly regulatory, controlling, “big brother is watching” approach. Because, as he points out, the monitoring process must take into account that in the vast majority of cases there is not a problem. For the most part, researchers are ethical.

Several people suggested aspects they would incorporate into a monitoring system. A system of random audits, “the equivalent of random drug testing for athletes (#14)” is favoured by some. The beauty of a random process is the impact it has on behaviour even among those who are never actually audited. Others suggested monitoring should be done selectively, beginning by identifying particularly high risk protocols. One alternative would be to have all studies report to the REB regularly, with high risk ones reporting more often. Only when those regular reports flag something problematic would the next level of scrutiny be initiated

#23: I don't think that all protocols, from my experience, really would have the same need for close monitoring because of the nature of what they are doing... An alternative would be to get regular reports and look at the reports and if anything seems to be a problem, to then get back to them. Some way of shifting the work burden to the research team without handing over the monitoring function of it would be a worthwhile endeavour.

There was some disagreement about whether the existing policy guidelines require REBs themselves to do monitoring or, simply require the REB to ensure that monitoring is being carried out by the research team or home department – in effect, monitoring the monitors. There was also disagreement about which of these would be most appropriate.

A minority of participants had actually had experience coordinating monitoring processes of some form. Clinical trials sponsored by pharmaceutical companies are subject to multiple levels of auditing, from the company and from government representatives; the process followed could be informative for other types of research.

#15b: During the clinical trials the sponsor will monitor, and the sponsor will audit at selected sites. There's a difference between monitoring – which is the routine double-checking – and auditing – which is usually a one time snap-shot check of the process. So the sponsor does its activities during the study and applies quality control and quality assurance processes during the analysis and the reporting of the study. Then it gets submitted to the regulatory authorities, and when the data are submitted to the FDA for market approval then they may select some investigators to go and inspect well after the study is finished. (national organization member)

Among the REB members interviewed, they had employed processes ranging from annual reporting mechanisms to one-off project monitoring to regular random audits. A few people described unusual occasions in which a very high risk protocol might be monitored by a member of the REB, or through the auspices of the REB.

#17: In one study that we felt was particularly dangerous, we informed the principal investigator that we would be heading a secondary study which was approved by the committee in which there would be a monitor who would visit the patients after they've given consent to determine if they had given a free and appropriate and understanding consent to what was a very dangerous protocol... It was put through the faculty as a research project, to be published in its own rights.

At a few sites researchers are required to report to the REB annually, or more frequently if the trial is high risk, in order to get continued ethical approval. This allows an opportunity for review of the study, at least on paper.

#19: Approval is given for just one year... Eleven months after the review the investigator must fill in a continuing review form that tells us how many they've enrolled, and how many dropped out, and serious adverse events, any publications, and we would then decide whether this study should continue. You know if they've enrolled a hundred and fifty patients and a hundred and forty dropped out something's wrong. Or there are a whole slew of serious adverse events in the study where they weren't expected.

#22: They have to report back, at a minimum yearly. If there's something that seems high risk but we felt the potential benefits were good enough, we may ask for a reporting before that.

#26: We ask for reports which, typically, are annual but occasionally will be based on other aspects, for instance, we may ask to receive a report after a few patients have been recruited, to ensure that there's nothing unexpected, in cases where risk seems more significant or more difficult to evaluate. I'm not saying that it's common but it's happened.... But realistically you only get what people are telling you.

Going beyond what researchers are willing to report, one hospital REB in Halifax has been conducting annual random audits of ongoing research. From the 80-100 protocols they review each year, the REB selects about eight to ten of various types, some generated locally, some multisite trials, some industry-funded, some funded locally, and so on.

#30: We just arbitrarily select a number of ongoing studies, and have them come in with some of the charts and patients' records from their study, to make sure the documentation is complete, and that the processes are being followed correctly...The Chairs do it, along with two or three members from the committee.

#33: We pick ten at random at the end of the year and do a full audit of their protocol, to look at their enrolment procedures, to see if they have the consents on file,



whether all the paperwork is adequately stored on site. We go through all those issues.

This committee has never considered extending the audit beyond the paper trail to seek the input of research subjects enrolled in these studies.

#33: It's an interesting idea. We haven't done that. No. . . It never extends beyond the paper trail. It doesn't extend to the subjects to see what their experience was in a research project.

#30: I don't know if talking to subjects would be necessary or not.

Nonetheless, this committee is ahead of many others in having three or four years' experience with random auditing of research.

Another REB in Halifax has just initiated a similar auditing process. They have hired someone part-time to coordinate the audits, funded through the hospital's research overhead. They plan to implement the process in a step-wise fashion. Assuming that industry-funded research tends to be subject to greater scrutiny already, they will begin by focusing on the non-industry protocols.

#27: They watch it like a hawk afterwards. They come down and do their own auditing, and they audit the entire process, and they really are concerned about being challenged, about things being properly done. The inquiry-based ones, especially the more amateurish ones – the non-contract, people are just doing it – are the ones that you worry more about. So we're going to be auditing them primarily first, and then working out afterwards.

The process will also be step-wise in the sense that they will begin with review of research documentation, then may decide to go further, possibly even contacting patients.

#32: What we're planning to do is, we'll meet with the investigator and the coordinator, review documents with them, and discuss the situation with them, and then our coordinator will go through the case report forms and make sure that all the regulatory, hospital and any other documentation that has been requested has been done. And I think we'll see how that goes. We've discussed whether we should contact patients and find out, or contact attending physicians and find out if they were aware their patients [were enrolled], and stuff like that. We're going to take this in a step-wise fashion...I think if things are going to go awry, you're not going to have to turn over too many stones to find the problems.

In terms of workload, the REB members who are assigned to the auditing team will be relieved of their regular REB duties. Members of two different national organizations spoke strongly in

favour of such a gradation of monitoring processes. They believe REBs should monitor basic processes, stepping up the level of scrutiny as they find reason to do so.

Members of national organizations were far more likely than REB members to talk about a need to measure REB compliance with national standards, perhaps even a need for REB accreditation.

- #37: If you follow due process and make a mistake, you are in less trouble than if you just simply didn't follow due process. Process is critical... Process is the only thing that can be accounted for, can be accredited. (national organization member)
- #40: I think from a bio-medical point of view, a process of accreditation of REB functions is desirable. (national organization member)
- #6: When the [Tri-Council] document was released... we hadn't defined what measures and what the process would be to monitor compliance. The three Councils... have looked at possible monitoring scenarios ranging from as long as you as an institution and grantee tell us that you follow procedures we'll believe you – that's one extreme – and there were extremes going to a very rigorous process of certification. Now I know that the medical community is more advanced in it's thinking along those lines and would go probably for a certification model. But the other communities, our perception is that the other communities are not ready, that they're still just trying to absorb what the policy statement means, and what it means for them as researchers. Going to a very rigorous monitoring process, a compliance monitoring process, would probably create some kind of backlash or very strong reactions at the very least. (national organization member)

There seemed to be consensus among members of national organizations on this last point: that while the medical research community may be ready for a research ethics accreditation system, the other research communities are not at all prepared. But they also agreed that the process need not be introduced to all areas of research at the same time.

- #41: An accreditation system may start in the medical schools, in hospitals, and then be extended to the others two or three years after. (national organization member)

## D. Centralized vs Decentralized Review

One of the themes that emerged as a “hot topic” during the interviews with members of REBs was concern about the degree of centralization that is desirable for research ethics review in health research involving human subjects. Several people spoke favourably of limiting the

number of REBs in a given location to improve the consistency of reviews across disparate sites as well as to speed up the process

- #07: We've attempted to integrate research ethics review with the teaching hospitals at the university, so that we have one set of rules across all of the teaching hospital sites, so that protocols are dealt with in a consistent, uniform fashion. So investigators in one will have the same rules as the investigators in others, because some studies may cross the multiple hospitals. What we've chosen to do is to use the university human ethics review process as the review process for the hospitals.

Some use a centralized process within the larger institution for all of their reviews (e.g. UBC.) others have a central review process only for research being conducted in multiple hospitals within the affiliated system, while research in individual hospitals is reviewed independently (e.g. McGill). Others have no formal links at all between the REBs of various hospitals within a local system (e.g. Dalhousie). The major arguments for maintaining independent review by individual hospital REBs concern liability issues and the need for flexibility to take into account local culture.

- #05: One of the things that I like about the way things have gone in Alberta is limiting the number of research ethics boards, because as long as there's a huge number you're going to get such a variance. . . One province-wide REB I think would be inappropriate. Just because there may well be and there are variations across the province... I think there needs to be certain amount of diversity. So what's the right number to allow some diversity but some degree of uniformity?

In addition, some people suggested the volume of research in some sites would exceed the capacity of any single REB, necessitating some breakdown and division of labour.

The most heated discussion occurred around suggestions that Canada move toward a national centralized research ethics review process. People weighed in strongly on either side of this question. The arguments in favour of a national ethics committee, from about a quarter of the participants, focused on efficiency, consistency and professionalism.

- #01: My real favorite is a national ethics committee... I would prefer the same system they have in France. In France there is one Ethics Committee for the whole country... There is utter consistency, there is a very fast turn-around and there evolves a national policy, based on a national consensus. It works very well. It would please me greatly if we could have a national committee with e-mail or with faxes. There would be no problem sending it in and we're big enough that it would meet daily. And it would be a full-time job for those doing it. So they wouldn't be hobby ethicists, they would be ethicist ethicists. And that could be good too. And for medical input, there are many sixty-five year old physicians with vast clinical experience who would love the intellectual challenge and the income from having this as a full-time job. This is something that I've never heard

discussed by anyone nationally, but I would definitely support the creation of such a structure.

- #10: I think in Canada we stand on our regional differences too much and I don't think those regional differences are so great as to stand in the way of a national research ethics board. I would support any move towards a national standard. It's functioned very well in the UK, has done for many years. That's a country with the twice the population of Canada so it's doable... What about differences between Edmonton and Calgary, I mean how far do we take this? And I'm not sure that those differences are so great as to preclude the national research ethics review process, I'm really not. We're still looking at human beings who are engaged in a process which poses some risk to them. We are dealing with an issue of being able to provide information to these people in a very clear manner so that it is understandable. And we need to ensure that there is no degree of coercion on the participants to participate. That can be done nationally, I don't believe local culture will affect any of those three basic principles.

Some members of national organizations spoke strongly in favour of the British system of national and local review.

- #21: I'm not sure that you need one IRB for the whole country, but I think we should look more closely into the British regionalized system and see what works and what doesn't work. I think some format for having highly professional good review which can cut down the workload on an individual REBs is a good idea. (national organization member)
- #37: To what extent is an institution prepared to accept the views of others, not in any way to cede its responsibility, but to accept the views of others? In England, Local Research Ethics Committees, LRECs, are set up without any sort of ministerial authority, and they do their thing, the same way as our Research Ethics Boards do. The Minister of State for Health (or something) set up a system of MRECs, Multiple Research Ethics Committees, right across the country each of which has authority across the whole country and that meet at various points in time. Any research program that requires four or five or more research centres must go to the next MREC that is meeting for ethics review, before the LREC. The MREC does the ethics review. It negotiates with the company about consent forms, and about the quality of science and all the rest of it, and then says, "OK." That package then goes to the LREC, which then has the right to decide whether or not it wants this research in its own institution, for reasons of its own management. But doesn't have the authority to go back to the company, or the sponsor of the multi-centre clinical trial, and say, "We want to change this or that." . . . So you have a standardized, centralized review mechanism. I'm not sure how well it's working. (national organization member)

There was a particularly strong sentiment that centralized review mechanisms would be appropriate for multisite trials.

Almost half the participants, however, argued strongly that a national review committee would be a particularly bad idea. They fear the potential impersonality and bureaucracy, the loss

of nuance that comes with knowing the researchers and, they resent the imposition of someone else's standards.

- #26: I'm not convinced that the investigators would gain very much in terms of user-friendliness!
- #13: You're headed into full-time delays, you're headed into a bureaucracy... Why would we move to centralization? It's working as a decentralized system why would we shift it...We've developed things that fit our particular researchers, we've got it done in a timely manner, we don't have to worry about the post office or the electronic mail or whatever. This works. I'm a phone call away from anybody who's unhappy, I'm educated, I'm trained in the process, I know about... You have to be really flexible on this stuff.
- #36: One federal body? No! I can't see that for everything. It would take so long. The bureaucracy involved – it would take forever to get anything approved. (national organization member)
- #24: What I don't want is a province-wide committee, a city-wide committee. I don't want a committee that has nothing to do with this institution. I do not believe centralized review is acceptable at that level... Number one: local patients are best mimicked– because one of the functions of an REB is to be a surrogate for local patients. The best surrogate for local patients are local community members... The second reason is, I like to know who my characters are.... If I have an investigator who had slipshod information in the past, then I'll do a different kind of monitoring in the future. So that is another valuable piece of information. Third, I don't mind a more centralized scientific review process. In other words, I do rely on the fact that MRC has approved the grant...but I still want to know locally, because my norms and my mindset and my resources are not the same as UBC's or Toronto's. . . I can see some coordinated activities. But I don't want a committee in Ottawa telling me what to do.

A couple of participants argued that local review ensures the accountability of local REBs to the local patient population. The most common basis for opposition to centralized research ethics review stressed the need for flexibility to meet local needs and to take local cultural differences into account.

- #6: We would have to create such a big bureaucratic structure to manage it that I don't see that happening... Leaving it to the institutions to develop their own procedures that would probably enable them to be more flexible and respond to their needs... I think they know best exactly how to review research done within their walls, and what their values are, what their culture is. (national organization member)
- #18: There are some disadvantages with that [centralization]. One of the major ones is that one of the kinds of ethical considerations that you have to take into account is things like ethnic diversity and minority groups and all that kind of stuff and they differ from one region to another... And these groups differ very much in how they make up the society locally.

- #36: [Variations on national standards] depend on local circumstances, local patient populations, cultural, linguistic, whatever... there is space for flexibility. (national organization member)

In contrast, some participants argued that concerns about local culture being sacrificed to national uniformity was simply parochialism and desire for local control.

- #14: There is no such local flexibility... That's local or parochial... You're saying that moral issues in Calgary are going to be a little bit different than they are in Quebec City? It doesn't make sense. Control is always the issue... The only thing that requires local review is impact on an institute. The ethics and the science for a multicentre trial or research of any kind could be done by one board nationally who has the appropriate representation, the appropriate sensitivity adhering to the Tri-Council document. I can't imagine a reason why that shouldn't work and I would support that a hundred percent.
- #35: The stuff about cultural differences, Newfoundland to Victoria. I'm not sure about that. Some of those arguments, the relativistic arguments, are not terribly persuasive to me. (national organization member)

Alternatively, some participants suggested that while a national review would not relieve local REBs of their legal liability to review a protocol, it might give reassurance and expedite the process. Others suggested that what needs to occur at the national level is pooling of resources and sharing of information.

- #24: If it's a really tough study, I would like under the umbrella of an organization like NCEHR... to say now this study is going to be started in a dozen centres in Canada. It's an unusual disease. I don't have the expertise. Let's all get together for this study, pool our resources, and bring in an expert from Europe or the US . . . I don't have to rely on the expert, but I'd like to have his or her opinion.
- #15a: In terms of the dissemination of information, there is no real national body. I mean NCEHR is not really a national body representing REBs in this country, it's the opposite. It's a national body offering help to REBs, but it has no manner or method of collecting consensus issues, of sounding out what issues are and in rectifying them. (national organization member)
- #32: There has to be some mechanism to share information so that each committee doesn't have to re-invent the wheel with every clinical trial.

A number of participants also urged the development of national standardized mechanisms and forms such as standard consent forms. Members of national organizations noted that this work is already underway. Some stressed that any such national standards must be restricted to particular research fields.

- #07: I think the national standards need to be areas of common national concern. I think you have to recognize that there are whole sets of ethical issues which are unique to certain scientific questions... So with particular age groups or

guardianship, with maternal fetal issues, reproductive biology issues, with certain genetic issues... I think the sets of problems are the same across Canada by type of research. And I think you need to have a mechanism of recognizing unique problems within each target area.

Many of those who rejected any mention of a national centralized review process spoke more favourably of local or regional reciprocity arrangements. Alberta already has such an arrangement underway.

#05: There's now an informal agreement that if it's been approved at— right now there's four research ethics boards in Alberta that doctors can use. One is the Alberta Cancer Board, one is the College REB, one is the Health Authority Board which is with U of A, and then the fourth is the CHREB in Calgary. And so we have an informal agreement – because we've looked at all four systems and there's enough similarities, and I guess trust – that if it's been approved at one of the Alberta committees although we want to see their documentation and what their concerns were, we may give approval simply based on the fact that it's been approved at one of those other sites.

At this point REBs expedite review if a protocol has been approved elsewhere in Alberta. The hope is that one-day only one REB in Alberta will need to review any one protocol.

#10: The intent in Alberta was to have a process which eventually would become “seamless” so that we would develop true reciprocity with the other three research boards in Alberta.

In other locations, there was tentative interest in increased reciprocity among local or regional institutions. Some suggested within Montreal, or within Halifax reciprocity might be achieved over time. Others thought within a single province REBs could come to agreements about accepting one another's reviews. In Nova Scotia it was suggested this might be facilitated by the fact that there is a common insurer for all hospitals. Others proposed regions such as the Maritimes might reach reciprocal agreements, while a few people suggested a national agreement might one-day be possible – and would be desirable.

#34: We could probably do it across the Maritime provinces without too much difficulty. But I don't know if we'd be prepared to trust Alberta about anything!

#07: The alternative to having a single process is having reciprocity... In sequence it would be getting national standards, getting national standards adopted at individual universities or hospital based organizations and then moving to reciprocity with the comfort that you now have an adjudicated national standard, which is providing some evaluation mechanism.

#15a: We've done a large global study that had six hundred sites, it had six hundred ethics reviews. There are eight-seven sites in Canada, eighty-seven ethics

reviews in Canada. Why couldn't we get the eighty-seven centers together and say, "Can we form a consensus on five centers that will make a decision, that will apply everywhere, and we will make sure that the decision is applicable everywhere and the others can get on with other stuff?" (national organization member)

The obvious barrier, aside from the complex question of legal liability, is that REBs do not yet trust one another.

- #23: I think what it requires is a little more confidence in each other's committees, and we're probably getting to that but we're not quite there.
- #34: We're working from a point where faculty A doesn't trust faculty B... I went to a series of meetings a few years ago... [where] there wasn't enough trust around the table that people would accept a review from across the street, let alone from across the country!
- #01: We don't trust the ethics process at other institutions.
- #37: [Somehow we need to] build some kind of consensus. Everybody says, "Can't you do something about multi-centre clinical trial review?" And everybody says, "But we don't trust those other guys!" (national organization member)

To be clear, it did not appear from the interviews that there is significant disparity across these sites about the fundamental principles and standards of research ethics review. There is substantial consensus on the substantive ethical issues. The distrust between research ethics committees seems more connected to differences in procedures. Quite simply, members of one REB do not know how another REB arrives at its decisions and they do not trust that someone else's process would subject a protocol to the same level of intense scrutiny it would meet in their own committee. One interviewee had a valuable suggestion that might facilitate greater trust within the Canadian REB community. He suggested when a protocol is submitted to more than one site, if it is accepted by one REB and not by the other that case be "autopsied" to determine exactly what is happening differently at the two sites.

## E. Impact of Current Guidelines

The context for this research included the recent release of the Tri-Council Policy Statement; all REBS were expected to fully comply with the guidelines contained in that statement within a few months of the completion of these interviews. The Tri-Council guidelines were at the forefront of the minds of many REB members. In the interviews we were particularly



interested in how the implementation of guidelines at the national level was affecting the day-to-day work of REBs at the local level. Responses ranged widely from no impact, through minor changes, to outright hostility at the imposition of the guidelines. One person said he was, “waiting for the dust to settle” after all the recent changes before he assesses the impact the changes will have locally.

About a third of participants said the Tri-Council Policy Statement had little or no impact on the operations of their REB at the local level. In particular those REBs that had members who also participated in the process of drawing up the Tri-Council guidelines thought they would have been kept well-informed, and thought their own local standards and processes had been incorporated into the national ones.

- #01: The national document is very close to what our chair developed here over the past fifteen years. So it has not resulted in substantial change here. I suspect it's been radical change elsewhere in the country.
- #09: [Our chair] was involved in putting that together; we've been informed all the way through.
- #18: From what I can tell those guidelines are all pretty much common sense and in line with what is currently considered to be ethical.
- #16: I don't recall any areas where we are significantly out of line with the guidelines.

Those who felt the Tri-Council guidelines largely reflect what they were already doing welcomed the moral authority and legitimacy accorded them by the national guidelines.

About two-thirds of participants identified at least some minor changes in local REB functioning occasioned by the introduction of the Tri-Council guidelines. The changes can be categorized as structural, compositional and procedural. Structurally, some changes are relatively minor, such as the need to strike a standing appeals committee rather than an ad hoc one. But for sites such as Dalhousie, which formerly operated with a number of small REBs, the guidelines have meant a total restructuring of the committees.

- #31: Since the fall of last year, there's been a committee under the university Vice President of Research, looking at the implementation of the Tri-Council's policy statement here, with a particular eye to a number of things: amalgamating committees where possible, to make sure committees have an adequate work load and so on; rationalizing the conduits for researchers' submitting protocols, in other words to make sure that it's clear for a particular investigator with a particular protocol to which committee does she submit it. . . The decision was made to amalgamate all the health sciences research ethics boards. (national organization member)

According to one national organization member the impact has been equally great at other institutions across the country

- #41: It is a huge impact. Because in a lot of places, research ethics were not structured. They didn't have a policy. They didn't have any kind of reporting... So they've got to organize themselves. They have, in many cases, to restructure their own research ethics system... For a lot of universities it is a lot of changes. (national organization member)

In terms of composition, the guidelines have meant many REBs have to recruit legal representatives and lay members. The lay membership seems to be a particularly vexing issue for most REBs.

- #25: This is a question that we've been confronted with. It's the way we define 'lay people.' ... Sometimes lay people will not have the time, will not have the expertise... I think it is difficult to recruit purely lay persons, patients who once were treated and who are prepared to spend so much time with the responsibilities that come with sitting on an REB... I think what is important is to have people from the outside.
- #35: From what I hear the community reps are not– it's not a level playing field, and that's the problem. In terms of the symmetry of status, knowledge of the culture, so the community reps are not at home in the way that the researchers are. (national organization member)
- #33: There has to be somebody with a law background, somebody with a medical ethics background, and we have this one individual who seems to cover both quite well... In a small community like this, it's hard to find somebody to fit every slot. So, we sort of interpret the guidelines in a flexible manner.
- #11: One of the horrors of the Tri-Council Policy Statement in the medical world is for schools like McMaster and Memorial, where they're told they've got to have lawyers on their medical committee, and they have no law schools.

A major change that appears to have been occasioned procedurally is that a few committees, particularly those who handle behavioural science protocols, will have to begin having regular face-to-face meetings.

- #03: Our behavioral committee has handled its business by mail forever... The issues there tend to be hugely repetitive and the group hasn't really seen the need to sit down and go through the four hundredth consent form for doing a questionnaire... We are being forced to have that committee meet and that's another bureaucratic change... The net effect will probably be an apparent slow down in reaction time.
- #11: It's going to become more demanding when we are fully signed onto the Tri-Council Policy Statement, because any protocol as you appreciate that involves

more than minimal risk is going to have to be reviewed at a face-to-face meeting of the committee.

- #13: I'm not sure why all of a sudden face-to-face is far better than something that I knew worked. But once they put in the idea that you could look at the amount of risk involved I think really cleaned that up, because now that allows us to maintain our old system for research that meets the criteria of minimal risk in the Tri-Council. And we will continue with that system because it's efficient and it works really well.

In addition some REBs have revised their processes, rewritten consent guidelines and, invested considerable effort in checking all their procedures to ensure compliance with the Guidelines. One person noted the major impact for them would be monitoring.

- #14: The major difference I think for us is going to be the monitoring, surveillance issue after a project is approved. Somebody's going to have to do it, monitor, that's a significant incremental cost... Clearly monitoring accountability after a protocol's approved is a key to the Tri-Council document. And so we're going to have to set up a formalized system of tracking and monitoring.

Almost half of the research participants noted that at least some aspects of the Tri-Council guidelines are particularly helpful to them. They were praised as helping to simplify and clarify things, as well as to clearly define key concepts and, formalize and legitimate processes.

- #29: I think some of the things that were less well defined under the SSHRC guidelines, perhaps because they were just generally understood, are now somewhat more clearly defined... My initial read through of it is that it will be a helpful document.
- #27: The Tri-Council guidelines are beautiful. They are so vague at times but they are so much better than the MRC were because they really have that concept of, "Don't sweat the small stuff," and, "Worry about the big stuff." . . . I like them much, much better. Yes. There are major advantages.
- #34: That's been somewhat helpful. Having somebody at least provide some sort of direction about those issues, which weren't really looked after in the prior guidelines. Besides, you see, we had these competing guidelines - MRC, SSHRC, and there was one for children - so we were looking at two or three books, and trying to decide which ones were most appropriate to the issues, so this is a little cleaner.

In contrast, about a quarter of the participants identified serious problems with the guidelines, particularly that they are overly rigid, imposing a worst-case scenario that may be inappropriate and at best, vastly complicating the process of research ethics review.

- #04: What SSHRC or what the Councils should not be doing is saying that here is the process which absolutely ensures that under no circumstances whatsoever even the worst kind of hazard will not be risked. So we're going to require you all to

use the model that's appropriate for the injection of lethal drugs into people with IQs of forty-five... Most of the research is unbelievably innocuous... On the other hand its impact on the subjects is trivial and the consent issues are really very small. So back off! You know, here's a case that really deserves your attention, give it the attention that it deserves; don't waste your time and don't make us waste our time on trivialities. And also while you're at it think harder than you have in the past about the resources that ordinary citizens have to say no... There is a tendency to do standardization at the worse case level... My sense is that the working groups have started with the worst abuses and said well that's the world of human subjects research and let's make sure that these don't happen.

These interviewees argued that the guidelines infringe on researchers' ability to conduct research, demand of REBs considerably more bureaucratic work without providing any of the necessary resources to meet the new demands and, unwisely attempt to address disparate and dissimilar types of research – in the end failing to satisfy anyone.

Finally, there was some concern about how to make the Tri-Council guidelines have the greatest impact on local research review processes. Some interviewees were concerned that implementation not become overly bureaucratic, revolving around paperwork to Ottawa, rather than around substantive ethical issues. And while most participants were satisfied with the “guideline” nature of the Policy Statement, a few people suggested the only way for it to be effective would be as true regulations or legislation. Finally, one person suggested we need a national collection of case resolutions.

#24: The real question is not what do [the Tri-Council guidelines] say, but what kind of jurisprudence flows from it. I'd like to see a centralized database, a collection of cases and conundrums, and the Law Commission could understand that very well because, how is the law constructed? It's the jurisprudence of the regulation. There's almost nothing of that. Almost nothing of the accumulated wisdom of single Committees is captured... I'd like to see more of the sharing of, "How did we handle that tough situation? Here's what we decided." It doesn't mean that it's a binding decision, but it's an interesting heuristic example.

The Tri-Council Policy Statement is by no means the only set of guidelines governing the conduct of research ethics in the health/biomedical field. In an era of globalization and international trade, researchers and REBs are faced with a proliferation of guidelines at the provincial, national and international levels. Some participants had no difficulty navigating amongst multiple sets of potentially-conflicting guidelines; others found the waters exceedingly murky.

Almost a third of participants saw no difficulty reconciling the Canadian national guidelines with those of the US, with international guidelines or, with guidelines promoted by the

pharmaceutical industry. Some REBs appear to focus almost exclusively on whatever set of guidelines is most pertinent to their situation.

- #28: I would say that probably 90% of the Committee members haven't got a clue what the Good Clinical Practice guidelines are. They all know the Tri-Council guidelines. They all are very aware of the Health Protection Branch, and the FDA, and all of that.
- #27: The only ones I really know reasonably well are the FDA ones. They're so similar. There isn't much difference.
- #13: I may be naive here but I think what we've focused on is the Tri-Council because that's what we're responsive to. Now if any of those other guidelines violated or went against the Tri-Council, the Tri-Council would dominate at this point is my reading.

Others were well aware of multiple guidelines but did not see them as conflicting. As one person suggested, it simply means going with the highest standard. If the Tri-Council guidelines exceed those of the NIH, the NIH should not complain; if the NIH are more rigorous, the local REB will follow those for a US-funded study.

Interviewer: Do you run into conflicts between different sets of guidelines?

- #32: No, they're pretty much in sync. The ICH guidelines are the ones that industry wants you to follow, and we basically have to follow those if you want to do contract clinical trials at your institution. There aren't situations where the ICH guidelines say this, and the Tri-Council guidelines say that, and they're conflicting. It's more, another signature is required for this, or the way you do things, there may be a bit more detail required in one than the other. But they are quite compatible and we can get along with the two available... With NIH studies... I don't recall having any problems.

One national organization member stated quite simply that he does not think REBs find conflicts between differing guidelines to be a major problem.

Other participants saw significant conflicts between different sets of guidelines for research ethics review. In particular REBs in Quebec must meet the requirements of the Quebec Civil Code, which is seen as most problematic and most distinct from the Tri-Council guidelines on issues of incompetent subjects. REBs in Quebec seem to hold both of these sets of guidelines as clearly authoritative, and the Civil Code was at least as much at the forefront of consideration for REB members from Quebec as was the Tri-Council Policy Statement. Nonetheless, it is clear that the law takes precedence. Much greater complexity is introduced when American regulations and other international guidelines must also be satisfied.

- #26: I'm sure everybody has told you it's a pain! I'd have to say that the two sets of guidelines that we always keep in sight are the Tri-Council guidelines and the Civil Code of Quebec. Beyond that, I've not yet found any instances where the initial guidelines that have been put forward by the industry— I've always found that if you meet the requirements of the Tri-Council statement, it seemed to me that those requirements are met also... Where it becomes more of a pain is when you have research that is overseen by a US agency and where you have to start to worry about their regulations, which tend to be much more detailed and complicated.
- #31: Certainly there are clear conflicts now between Tri-Council Policy Statement and US regulations, for example. The definition of minimal risk is different in the two documents. Statements around emergency research differ. Statements around waived consent differs. There are other US documents like the NIH guidelines when the inclusion of women and minorities are subjects in clinical trials, or something like that. Those requirements are far more substantial than just the one throw-away line you find in the Tri-Council Policy Statement on that. In terms of the other documents, Helsinki is in such a state of flux right now . . . I'd be hard pressed to say... But sure. Yes. There'll definitely be conflict. (national organization member)
- #10: I suppose a danger with all of this proliferation of standards and guidelines is that if we all have different requirements it's going to be really confusing for the researchers. Again, it would be nice to make sure that our standard if one is developed would also be in alignment with the international standards. I mean the ICH I think is the document of the moment isn't it, it's the gold standard.
- #15b: One of the worries that industry has is that if the ethics committee thinks that they can follow Tri-Council code and then do industry sponsored research, they're wrong, because they're missing a bit. And some of them are working very hard to become compliant with the Tri-Council Policy Statement, and then we have to come back and tell them "sorry you're not done, you have to add these things and GCP's too." (national organization member)

The representatives of the pharmaceutical industry believed very strongly that the ethics review standards delineated in *Good Clinical Practices* are "more stringent, more demanding" than virtually all other guidelines, particularly concerning, "the need for documentation, the need for procedures, written procedures that describe how the Ethics Committee works." They referred to GCP as the highest standard and puzzled over why REBs would want to use a lesser standard when research is not industry-funded. The one place where they described the standards of GCP being exceeded is in regulations concerning the composition of REBs. American regulations require gender diversity among REB members, while the GCP do not.

Almost everyone seemed to agree that the current situation is highly confusing and frustrating for researchers. Consequently there was substantial support for the idea of harmonizing existing guidelines, nationally and internationally.

- #07: I think the perspective of the investigator is, "Give me a break, I can't possibly deal with all of these expectations, simplify this for me."
- #11: There's a lot going on in the Ministry of Health, where frankly different branches of that organization are pulling in somewhat different directions. We're getting a branch of that organization that is connected to the Tri-Council process. We have a branch of that organization that has produced the Good Clinical Practice Guidelines for the clinical trials from the pharmaceutical industry. And those two documents are not harmonious in all respects, in the amount of procedure nor substantively. So I think we could benefit from certain national standards . . . produced by a government that's speaking with one mouth or one voice.
- #03: There's a big role for somebody to play in sitting down and figuring out what the rules are for clinical trials. What the arena is that we're playing in and how FDA fits in with the Health Protection Branch which fits in with whatever ISO 2000 or all these other things, and puts that out on a form that we can all understand. That would be blindingly useful...Tell us what the rules are, how we have to do things in order to comply with all the international things that impact.
- #24: That's something the Law Commission [could do]. . . I do want some group to help construct a coherence. That would help. I'd love to see that. It would be very useful.
- #39b: We are trying to harmonize and I think we will continue to as we develop legislation or programs, I think we always look to international experience to ensure that there are not direct conflicts, and that we are in harmony with efforts in other jurisdictions. (national organization member)

All of the members of national organizations referred to ongoing efforts to revise existing national standards to eliminate discrepancies with other guidelines. In particular CRBPC (formerly PMAC) has been working closely with the MRC to ensure the Tri-Council Policy is consistent with the GCP. Everyone involved believes this will be a straightforward revision process.

One of the most interesting questions concerning the impact of various guidelines on the work of REBs is on what basis is one set of guidelines taken as authoritative – and on what do the proponents of particular guidelines base their claims to authority. According to the *Tri-Council Policy Statement*, research institutes must comply with their guidelines or lose all SSHRC, MRC and NSERC funding. Interviewees stressed that the local perception was, "do this or else (#34)." Members of the Councils noted that processes for assessing compliance were still in the formative stages; nor is it clear what kinds of infractions would be sufficient to constitute "non-compliance." In particular, one Council member wondered whether some failure to comply on the part of a social science REB would shut down research funding at the university's medical school.

Using the potential for funding withdrawal as a basis for imposing guidelines is seriously undermined by the fact that the funding councils actually sponsor a relatively small fraction of research at most sites.

- #13: The Tri-Council has no right to tell us what to do with unfunded research. And I will continue to advise our vice-presidents that you can not tell us what to do with unfunded research. Now having said that okay I want to continue to follow the processes that we've always had for unfunded research, which is more than the Tri-Council provides, but they just have no jurisdiction in our unfunded research. They have no right to do it.
- #03: We reviewed 740 new protocols last year in the clinical committee. MRC sponsored fourteen of them. MRC is a bit player in human research... So when I hear MRC processing around the country pontificating about ethical reviews I'm not just angry I'm apoplectic.
- #11: I'm not totally comfortable with it being done obliquely through the alleged financial clout of the three funding councils. If for no other reason than that those standards can only get into places where Tri-Council goes... There's a limit to which the Feds can use money as the regulatory device... The smaller the proportion that they fund the less their financial clout, and therefore the less they can do that way.
- #6: That's the question: can the Council actually regulate in an area where it doesn't fund, or can we only, is our line of accountability, our line of authority only related to our funds when NSERC or MRC or SSHRC are funding? Or can we say to institutions that all research conducted within their walls or by their researchers have to follow the policy even if it's not funded by the Councils? And that's a question we haven't asked. Well we've asked but we haven't answered yet. It requires legal advice, it also requires a decision by the Councils themselves to define what their area of authority or responsibility is. (national organization member)

The proportion of research funded through the councils varied from site to site, but the consistent picture in biomedical research is that financial sponsorship from the pharmaceutical industry is increasing rapidly and definitely outweighs council funding at all sites.

- #09: Oh I think the majority would be coming from industry, pharmaceutical industry almost certainly...Percentage, I don't know... But the breakdown would be the majority is for drug trials no doubt about that. Industry funded.
- #07: We've gone from 0% industry support five years ago to in excess of 50% industry support in the last year, and my guess this year it will be closer to 60%. So industry support is becoming an increasing financial component of the research on-site... Last year total funding on site amounted to around twelve million and MRC was probably eight hundred thousand to a million. A very small fraction. Fifty percent is industry off the top and then MRC is probably a fifth to a third of the grant agencies.



Interviewer: Do you have a sense of what proportion is industry-funded?

#27: A tremendous proportion. I mean massive. Of the ones I see? Ninety percent.

#18: The number that involve drug companies is probably close to 50%. Most of the others would be funded by the Medical Research Council of Canada or various specialist disease oriented bodies. Some small number are unfunded.

The lowest figure given for proportion of research funded through industry was 30%, at two different sites. The rest talked about a majority. In contrast, the councils were routinely described as funding only a small proportion of research, a fraction. Interestingly, the Tri-Council guidelines, as we have seen, are nonetheless held as an ultimate authority by many REBs. Their authority seems to rest in the fact that they are believed to capture the current societal norms about what constitutes ethical research.

Interviewer: If 90% of your research is industry-funded, what moral suasion, or what authority does the Tri-Council policy guidelines have? Why do they have any authority with you?

#27: Because they basically reflect the position of Canadian society with regard to the ethics of research. . . They're the "gold standard."

The authority of the GCP guidelines, on the other hand, rests in the fact that unless an REB complies with their standards, a pharmaceutical manufacturer will simply not work with that institution – not if the manufacturer wants to eventually submit the drug for federal approval.

#15a: If industry is going to use the results the REB will have to follow GCP... If they're doing any work with industry they will meet the highest, industry will require the higher standard. Otherwise industry will not work with them.

#15b: Yeah they're required by law... When there's a discrepancy between the two policies they have to follow GCPs. (national organization member)

Industry representatives pointed out that where laws were more stringent, the REB would have to comply with the law.

Finally, some participants identified ongoing gaps in the existing guidelines, areas where they felt they were still left to fend for themselves creating their own ethical standards even amidst the proliferation of guidelines. The bulk of these concerns centered around dealing with adverse events, definitions of research vs quality assessment, aspects of conflict of interest especially regarding payment of researchers, payment of research subjects, requirements regarding the inclusion of women in research, some aspects of pediatric research, use of health

information and databases, research conducted by physicians and other health professionals who are not affiliated with hospitals or universities and, difficulties around coercion when the clinician and the investigator are the same person especially in smaller communities. Members of the national organizations made it abundantly clear that the Tri-Council Policy Statement is a “living document” and is already undergoing processes of revision and amplification. They do not see it as a final statement on research ethics; rather, its standards will be continually reviewed, in part through NCEHR’s work with local REBs to convey their concerns and frustrations with the policy statement to the Councils.

## F. Dealing With Multisite Trials

The reality of biomedical and health research today includes multisite clinical trials as a central component. Researchers are engaged in research that is designed by someone elsewhere, usually a drug company, and that is being simultaneously conducted at numerous sites around the world. When a local REB encounters such a protocol the research project may well have already received ethics approval at numerous sites. The impact such prior approval has on REBs varies. About half the REB participants suggested prior approval elsewhere had no impact on their REB whatsoever. They carry on with their usual processes.

- #05: We do our own approval. We’re not disinterested in the fact that it’s approved elsewhere, but don’t necessarily take that as direction.
- #30: We still have to scrutinize them. Because we’ll often find that the standards of other sites are not equivalent in certain areas so we won’t just accept it.

Some noted that knowing a study had been approved elsewhere might lessen the intensity of local review, though it would certainly still be reviewed. Some do an expedited review.

- #01: We do not accept ethics approval anywhere else other than by our own committee. That being the case I would expect that our own committee doesn’t have a great deal of problem approving nine out of ten of these things; it’s probably the fastest thing they do.
- #16: If it’s been approved [elsewhere] it certainly might affect the intensity of the review, but it would not, I don’t think that it has ever been raised that we shouldn’t review it because it has been approved elsewhere. It would not be an automatic–

One person suggested that although his committee maintained the same process whether or not a protocol has received approval elsewhere, he cannot help but think unconscious biases

toward a favourable review are likely. Another interviewee noted that a prior favourable review *should* affect the REB process.

- #02: I'm not saying it should or it has done, but I would think you would have a different opinion of it if it's already come from somebody else, that you would consider to be an ethical body and they've approved it. So whether it's consciously or subconsciously that I would be biased to being favorable if it's had a yes, I would have to say yes.
- #26: It can affect the process and hopefully should affect the process. If the review has been done properly before, and if we are provided with all the necessary documentation which would include, for instance, the minutes and the approvals or any other exchange, then it helps of course, because you are one step ahead when you start the discussion and you can build on what was done. Unfortunately, it's not always done that way.

In contrast, about half of the participants identified serious pressures on the REB when they encountered protocols for multisite trials that had already been approved elsewhere.

- #07: The pressure on the ethics board is, "nine other centers have approved this and you're the tenth, what right have you to go against the will of the other nine?"
- #10: We get the comment frequently from the researchers: "I've been told by the sponsors that if you guys don't get this passed quickly then we're going to go off to some other center."
- #03: I'm very tired of being told that "on this multicenter trial this is the only institution in North America that has demanded A, B, and C and we're not going to be able to take part in the trial all because of you."
- #09: The pressure against review committees like ours, and I suspect other ones as well, is the offer of the money from outside for research. And universities, hospitals, departments, researchers themselves are always hungry for research dollars ... So if a major drug company offers millions of bucks to get on with a protocol and some little hick review group like us is saying we won't give permission for this, but everyone else has because they can see enormous benefits to the research program benefiting. . . It does raise anger on some occasions, who are you to say this is not good science or who are you to stop that.

Participants described this pressure as "veiled threats:" "It is quite a clear threat that if you are unreasonably fussy from their point-of-view that you may not be asked to participate in future studies (#17)." The particular difficulty is that REBs are put in a position of either approving a protocol with no real revisions or, rejecting it entirely. If a trial is already underway at numerous sites, it must be replicated at the local site without alteration. Thus if a local REB wants revisions those changes would have to be made everywhere to maintain comparability of the data.

Consequently, a few people talked about “letting some things go,” things they would change on a local protocol but that were not worth stopping a multisite trial over.

Most participants also spoke with compassion about the terrible bind researchers are placed in when they are faced with a local REB insisting on revisions and a multinational drug company sponsor insisting that no revisions be made. Researchers are also the repository of conflicts concerning turnaround time for ethics review. The local review process takes time but delays could cost them a lucrative research contract. In order to facilitate the process, and reduce delays, several people recommended a centralized review process specifically for dealing with multisite trials.

#07: One of the issues that I think should be discussed at Canadian Institutes of Health Research is the development of a multicentre clinical trial network across Canada in which there may be a central research ethics board for multicentred clinical trials. Such that you can have one-stop shopping for research ethics boards and that the respective university or hospital research ethics boards would accept the view of the central agency if it is established according to guidelines which are acceptable.

Others saw the centralized review not as replacing local review, but as expediting it. They would treat multisite drug trials with considerably less skepticism if they had already had approval by an independent central review body.

#17: I think that if we recognize that it was done nationally I would review the commercial ones with less skepticism because I must say I read them over and the first thing that comes to mind is, “Is this study real science or is this to get the drug approved for sale?”

Members of two national organizations suggested the process for multisite trials should differ from all others. The one site (or a few sites) involved in the trial should be selected through a transparent process to do the ethics review for the study and the only issues addressed locally would concern institutional impact.

A few participants argued that multiple review of multisite trials is beneficial, since it maximizes the probability that any serious problems will be noticed by one of the many REBs scrutinizing the protocol. Finally, several participants rejected the notion of a centralized review but felt strongly that there could be national coordination of multisite trials with considerably more information sharing.

- #26: I've heard other suggestions that, in the case of multicentre study, that investigators and sponsors should designate a primary review centre that would be outside of their interaction, if you want. And this review would serve for the basis of other reviews across the country. Other committees would then be able to build on this and feedback to both the investigators and the primary review site additional comments, concerns, or whatever. And that it would be better if you try to build one review together, rather than doing it in the dark, repeatedly, independently.
- #24: Canadian ethics committees ought to have a mechanism of sharing information. And I would request, would make a recommendation that, in fact, there be [more communication.] And NCEHR, I think, is thinking of setting up a website for Canadian Ethics Chairs.
- #03: I think there's certainly room for information flow... This is a role that I would like to see NCEHR play.
- #32: I think there certainly would be some value to having a mechanism, where there's some real difficult studies that multiple committees are struggling with, if there was some sort of process to share concerns or expertise.

## G. The Role of Industry

A common theme throughout the interviews with REB members was the increased profile of industry-sponsored research in the biomedical field in recent years. Some REBs reported that as much as 60-70% of the research they review is sponsored by pharmaceutical companies. The relationship between research as science, as truth-seeking, and the bottom line of profit-making that drives any industry makes many participants uncomfortable.

- #17: We have more trouble with some of the commercial protocols because we worry that their motives may be different than the motives of a cooperative study group where one hopes that the ethics within the group are very proper.
- #07: In terms of the shift to industry-sponsored research, I see the conflicts of interests that are arising at an exponential rate, I see the legal liability issues which are now becoming a dominant issue in Canada.

Some people worried particularly about the ways industry funding may – unintentionally – corrupt the processes of academic science as well as the objectivity of ethical review.

- #28: There isn't a department in this hospital that doesn't have industry-funded research, and they are paid mega-bucks to accrue patients into those studies. Their departments depend on that so there's a tension around what they're supposed to be doing, and so they're put in very difficult positions when they get on this Committee

- #09: The majority [of our research] would be coming from the pharmaceutical industry. . . Which is important because that's where the drive is coming from you see, and that's the tricky part... A good example would be... the changing face of whose idea is the research and what is the faculty member's role in it other than just a pair of hands that are actually technically doing the work on a contract basis for the company. When the original idea came from the company, when the design of the project was from the company, when the results have been consulted by the company and when the conjoint paper that comes out is being written by colleagues and maybe even gets written by the professional writers that are hired to do this as well... Compared with the guy you know who's struggling for his NSERC or MRC money and writing his own grants, and writing his own papers and doing his own work and funding and it was his idea.

This person was concerned about universities and university hospitals measuring the research productivity of their staff without distinguishing between very different types of research when decisions are made about promotion, tenure and so on. Some participants also expressed concern that the limited resources of the REBs are being spent on industry-funded research – research they implied was of lesser quality and, research the sponsors could afford to have reviewed elsewhere.

- #20: I do not think that Canada needs to worry about ethically reviewing protocols from drug companies; they have money to pay for that. . . I think if you want to have two systems, have one for the industry people and have one for the peer review funding where people go out and write excellent research and get it funded at a national level and it has no benefit at all to the researcher, to the center, nothing. And the pharmaceutical people. . . go get them done privately. That's what they should be doing.... The problem is... the hospital says gee I'm gonna get a lot of money if I approve this grant.

More commonly, however, participants expressed ambivalence about the role of industry in research. They welcome the resources that make research possible, while harbouring concerns about the impact of funding arrangements on the basic integrity of the research arena. They may also acknowledge that industry-sponsored research is not necessarily “bad research.”

- #27: Industry is a mixed game. On the one hand, it's dangerous and worrisome that so much Canadian research is coming from industry rather than from granting councils at this point in time. It's a real problem. It's a real shame that Canada is getting itself into this and it's something that has to be addressed, because most of our major investigators now– there's an awful lot of inquiry-based research now which is being funded by overruns from contract research. Well, that's not great, to be developing a scientific community on that basis. So that's the negative side. The positive side is that most of the contract stuff is pretty responsible and pretty well done, and to be honest the contract research, you very seldom see an industry-generated pharmaceutical protocol coming through where the science isn't good, the sample sizes are well thought out. It's usually excellent. And they watch it like a hawk afterwards.

One member of a national organization described a complex “love-hate relationship with industry:”

- #8: It has to do with the fact that industry is, after all, profit-making and that's somehow anti-scientific. And yes we know we're training the future people for industry, but we're so clean and pure that we don't want to be tainted by them. But if they give us some money well that's okay too. So it's a very complex love-hate relationship. The ultimate industry to hate is the pharmaceutical company and of course they're making drugs for humans so they need to trial them, and we hate them so much because they're so successful and make so much money. (national organization member)

This same respondent went on to note that while there are “some scumballs” in industry, the “good companies have a lot of pride in doing things properly.” They voluntarily developed their own ethics guidelines (GCP) and most companies have “somebody whose job it is to look out for patients.” Bad research risks serious cost to the reputation of a pharmaceutical manufacturer.

Some members of national organizations also pointed out that MRC's industrial partnerships arrangement with industry has established an exchange whereby industry funds the training of scientists while MRC ensures the science of the research is adequate through peer-review. The incentive for industry is industrial pride. This arrangement, they argue, has markedly improved the quality of industry-sponsored research. Recognizing that some REBs are doing the majority of their work with industrial protocols, the MRC has sponsored workshops to bring together industry and academic science. They have established a working group on best practices in industry/academe collaboration. Recognizing the concerns of industry about the cumbersome processes required to initiate research, MRC also worked with Health Canada toward regulatory reform concerning Phase One Trials so that they can “get off the ground quickly” but without compromising effective ethical assessment, formal decision-making and authorization processes. One national organization member noted the increasing importance of speed in the competitive market of pharmaceutical research.

- #37: Rapidity of turn-around is very important for the ability of this country to compete in the phase one clinical trials market... The company goes where the work can be done effectively and efficiently to meet high standards... If the institutions want to do phase one clinical trials, and thereby get the benefits resulting from the those clinical trials, they are going to have to compete in the world market place... Certainly companies can take their money elsewhere – and will!

## H. Resources for Research Ethics Review

The issue of adequate resources for REB activities was a hot topic in the interviews. Although a member of NCEHR said their recent survey of REBs found a surprising number thought they had adequate resources to do the job, in this research almost everyone noted inadequacy of resources as a major barrier to effective ethical review. One REB member was an exception:

#19: I would say that this hospital came through. Until recently it wasn't putting in as much as it should have. . . I had to put pressure on them until they realized and I must say they did come around nicely. So now we have our own cost center, we have money for education, we have a coordinator now that can work full-time... They've given us money for our needs now, not enough but better than before... I think it's coming partly from grant money. You know money that comes as overage on grants, which I think is reasonable. We don't charge companies to review their protocols. I know that some institutions are and we're wrestling with that.

Most participants, however, argued that the political economy of research and health care is such that the overall infrastructure to maintain research is insufficient.

#07: This touches on a whole concern I have with infrastructure funding in Canada. The operating grants are being provided to do the operating side, but the infrastructure of ethics, of monitoring, of maintenance is not in place... In the United States you have indirect overhead on grants. In Canada zero. And the medical school budgets are being cut and the abilities for infrastructures is gone out the window... More and more regulations are being imposed and there's no ability of the system to fund them... Unless infrastructure is considered a normal component of operating grant proposals, but as research shifts to industry and to the disease agencies, or to the hospitals, or philanthropy, none of those organizations would like to pay infrastructure. So I think there's a widening gap between expectations and ability to perform which is not being addressed.

Several people commented that currently industry is bearing the financial burden of research ethics in Canada.

#14: In all truthfulness really industry is subsidizing the system. Okay, they have an invested interest, but I can tell you right now financially we're riding on their shoulders in terms of getting this process done. I think it's unfair to them.

#15a: For quite a long time our industry has been used to the fact that when we do research in institutions that the institution is charging an overhead for the bricks, the mortar, the lights and everything else like that. Well why wasn't a part of that put back into supporting the research infrastructure, including the REBs? We can't tell them where to apply their overhead. (national organization member)



Almost all of the REBs have at least entertained the thought of paying their members for their time. In particular REB Chairs are seen as carrying too heavy a burden for volunteers.

- #21: In general the university heads should find more ways of rewarding their REB and IRB members... That's one of the issues that should be addressed is how do you reward people for this kind of work.
- #12: I think we would like to offer remuneration but since we don't have funding to do that.
- #17: There is becoming a big problem about paying IRBs – Chairs in particular. I figure I spend a full day a week now. I'm retired from the practice of medicine. I have the time now to do it and like to maintain an interest in what's going on, but if I were a practitioner who earned my livelihood practicing medicine as many of the doctors in the hospital are. . . I couldn't have afforded to spend a day a week.
- #26: I don't think that it would be unethical to compensate members for their time and effort, but of course, we'd have to identify the resources... In this institution, for several years now we have asked a fee for review for industry-sponsored research... But the resources that we obtain there would not be sufficient at this point to offer compensation for every member attending the meeting. The Chairs are not even compensated for their time.
- #27: Chairing is a killer job. If I could do it with a day's protected time that would be a different story. It means the hospital pays you for a day... The only complaint I have about the whole system, the... hospitals get a pretty good deal, right?...I don't think it's too much to ask to pay somebody's salary for one day per week so they can do it right. I think the university's got a more difficult problem, because those aren't contracts, and those are all inquiry-based investigators and the grants are always under-funded... Here, the hospitals make a lot of money out of this.
- #28: We can't get people to be Co-Chairs because of the workload, as it's voluntary. So how do you compensate for that? One group wants payment and some of us... are saying, "it's not the money because you can give me a million bucks, it doesn't free up my time, I still have the twenty things I still have to do, and I have to do them." But what if this was something that counted for tenure, that counted for sabbatical, counted for going to educational things around ethics, that there was some recognition of that work that's not a dollar-and-cents issue? That was free time or support, something that just indicates that the institution does, in fact, believe that it is an important committee?

Some people focused on the need to pay community representatives, who are the only REB members who have no commitment to the institution through their employment status.

- #31: Community members with no affiliation with the university; I've argued for a long time that they ought to be paid. They don't have an obligation to that institution. They're not fulfilling an obligation incurred by being an employee of the institution. They are giving up their time and it seems to me if we really want to get high-quality community people, we're simply going to have to reimburse people at some reasonable rate for their time. Clearly, that's beyond the means of most REBs. (national organization member)

- #11: We may get into issues of paying people to sit on committees. Certainly outsiders, I mean I marvel that the medical committee has community representatives who are willing to go through two meetings a month, plus a fair amount of surrounding work, reading protocols, reading summaries, participating on sub-committees addressing various issues. I mean they're both very committed individuals, but I truly marvel at the fact that they are willing to do this as a gift to their community.

A few participants stressed that adequate resources goes well beyond financial compensation for REB members themselves, to the provision of support services that meet the needs of research ethics administration.

- #17: If we were to be told we had to do monitoring or do other things, or to extend our activities more, there isn't a person in our budget to do it. . . You can't pay a filing clerk salary and expect to have a highly qualified administrative assistant with almost paralegal understanding of things.
- #31: Institutions themselves have an obligation to divert some of the research monies that are coming in to make sure that the Research Ethics Board is adequately resourced. And it's not just a question of money. Clearly, many REBs don't have a full-time administrator. They don't have the computer software that they need for tracking protocol. They don't have other time-saving measures, like having someone who is specifically charged with the task of editing the consent forms, and working with the investigator over that. (national organization member)

One of the concerns that accompanies consideration of financial compensation for participation in research ethics review is the potential for conflict of interest. Several people suggested that a standard overhead charged to every protocol, but earmarked for research services, would ensure sufficient distance between reviewers and the source of funding to eliminate ethical concerns. One person still worried that financial pressure could be brought to bear.

- #17: If the committee were to have a lot of requests from a given sponsor so it finally made up say twenty-five percent of the salary of your coordinator could you afford to lose it? You wouldn't be able to pay your coordinator [if that company withdrew its research]... The money would have to go to the university and not be in any direct way related to the committee. So if the money stopped coming in the committee's support staff would be paid anyway by the university and the sponsor's payment would simply help to offset globally the university deficit providing these services.

Lastly, it is noteworthy that almost all members of national organizations noted that lack of adequate resources does not end at the level of REBs – NCEHR was also identified as being vastly under funded for the tasks that are expected of it. Its funding is even more inadequate if it

is ever to take on some of the tasks members of the Canadian research ethics community would *like* to see NCEHR performing.

## I. Dealing With Cultural Differences

One of the specific gaps in existing guidelines that some participants and some members of our research team identified concerns the application of a Western model of individual informed consent to research that involves human subjects from diverse cultural backgrounds. In short, is the individual informed consent model appropriate across cultures? And how are issues of cross-cultural differences handled by REBs? About a third of the participants said issues of cultural differences simply did not arise for their REBs, due largely to the homogeneity of populations in their regions.

- #11: I've not really seen much in the way of cultural requests. This is becoming a much more diverse city and there are some fairly distinctive communities now where English language capability is not that strong. So I'm anticipating we'll see more of this.
- #10: Believe it or not it [the issue of cultural differences] has not yet been raised... Either we're missing some of them (laughter) or I don't know, I really don't. For example we've had no protocols which are looking at specific clinical health issues in the First Nations populations to date.
- #34: I don't think we've really dealt with that at the committee. Probably because this province is fairly unilingual. We're not a cultural melting pot here, or there's not a huge amount of— we have a Black population, and a Native population, but language is not a significant issue here.
- #30: We haven't encountered a lot of that. I'm not sure how individual researchers deal with that issue. It hasn't been raised at a Committee meeting. We don't have, say, consent forms that are designed for different cultural backgrounds, and are written in different languages. And yet there are no exclusion criteria either based on culture, or language. So, we just, I guess it isn't something we've addressed at this point. . . I haven't seen anything like that, that I can remember anyway. There'll be protocols that will be maybe across Canada, multicentre trials, but... I guess they're not seen as, Canada isn't looked upon as a multicultural society.

About half of the participants said the issue of cultural differences *is* one they encounter and that it raises distinct difficulties. In particular, the role of physicians may differ from culture to culture.

- #16: I have elderly Italian patients with Italian born children who come here and don't want me to tell their father with cancer anything or their mother with cancer. They say, "They're not to be told it's going to kill them." Well we do believe it's their right to know and we're living in Canada . . . You want to be respectful of the cultural difference, and yet we are taught ethical principles that at times are at odds with specific cultural beliefs. So how do you accommodate to those two things? With great difficulty.
- #01: It takes much longer to get informed consent from someone who doesn't accept the principle of making their own decisions. And particularly older aged central Europeans and Southern Europeans and older aged Asians do not, in general, like to be involved in a decision relating to their own health. And this is a cultural difference. It's very real. . . We should not think that our view of physician-patient relationships is the dominant global view. Many patients want a dependency relationship not a co-partnership relationship.
- #36: [In some countries] you really do find the issue of individual consent way up in the air, because clearly, the family, or clan, or whatever, is often the position of authority, and not the individual. So how that translates when people from those cultures come to Canada, and how far do you push the individual consent, once you adapt to the cultural requirements--? ... It's an unresolved issue, but I think that's where you can't be too rigid. (national organization member)

In addition some people pointed out that the role of women differs across cultures and informed consent procedures need to accommodate that difference. They also noted that the research community as a whole needs to attend to issues of cultural bias in terms of inclusion criteria for studies. Especially if language ability is excluding whole populations of people that need to be addressed.

- #11: There are what I will loosely call cultural issues that need to be explored in terms of inclusivity. To make sure that the research is in fact embracing diverse communities. So that's one side of it. The other side of it is indeed if we're going to embrace those diverse communities, how do we deal with the issues of recruitment and consent in a culture that doesn't fit our traditional highly individualistic legalistic norms? I have no easy answer to either question.

As one participant said, "it's a very complicated intersection between what we'd like to think are universal human rights with the notion of tolerance and respect for different cultures (#31)."

In response to this complexity, a handful of REB members said the only solution is to apply standard North American ethical guidelines and processes, particularly when the research is based in a Canadian institution. As one national organization member noted, "culture is enslavement. . . the idea that the head man of the village can sign everybody up for whatever because it's all right it's their culture... Culture and religion are not always to be honoured because culture and religion sometimes put people into impossible situations. (#21)"

- #15b: We have found that in some African countries where we're doing research, the consent process is different than what we accept and we're trying to ask them to follow the Good Clinical Practices model of individual consent... That's the only way we can submit the data... South Africa did a real change in their approach to consent, because industry has a lot of research that's done in South Africa and it has asked for this type of a consent process. And they've gone through a major transition in their thinking about consensus. (national organization member)

A few others questioned the appropriateness of imposing *our* cultural norms, assuming they are best.

- #11: Should we be insisting that people comply with our norms? White, middle class, educated, Judeo-Christian, and so on and so on. I've taken the view certainly with quite a number of the social sciences protocols that if someone could document for me that there are cultural structures here that make it appropriate for consent to be handled in a different way that I will sign off on the protocol... I think we have to recognize that perhaps our individualistic urges can be satisfied by a form of negative consent, where there is a cultural environment that is more conducive to collective or authoritarian consent. And how far do you go along that line if you're doing research? ... How we draw these lines I don't know. Where the boundary is between cultural sensitivity and sprinkling holy water on rampant authoritarianism.

In general, however, participants agreed that the notion of individual informed consent was cross-culturally appropriate, they simply entertained alternative ideas about how that consent should be obtained. When researchers proposed any variations on the norms, they were required to provide substantial justification.

In keeping with that tendency, although a couple of people said their REB would seek outside expert opinion about culturally appropriate research ethics, the majority tend to rely on the researchers themselves to identify what would be culturally appropriate.

- #29: We would trust the researcher. People normally don't do that kind of research unless they are already familiar with the area.
- #03: We rely on the applicant to tell us if there are special cultural issues.
- #04: Where written informed consent is not culturally appropriate? Our basic point of view is to acknowledge that and put the onus on the researcher to make a case. And to accommodate... The researcher makes the case.
- #05: We make the assumption that if you're a Sikh or an East-Indian or whatever you are, it'll be up to you whether you can consent or not, who consents for you, and for the researcher to be responsible about that.

Finally, one person suggested the REB should have membership from the culturally relevant group(s); two others suggested only research that substantially involves members of the relevant cultural communities on the research team should be given ethical approval.

## J. Dealing With Research In Genetics

A major area where REBs are seeking direction is in the field of genetic research. Almost all the research participants indicated that they have serious struggles around this. As one person said, “that’s a major area where we are going to need mega help (#28).”

- #24: Here’s a situation which NCEHR and the Law Commission, or whoever else, could develop a consensus conference, and let’s grapple with this. Put the ideas on the table, make some guidelines. We may or may not follow them, but at least the ideas will be put on the table. There’s a great idea... I want some help centrally in making policy options.
- #35: I’ve talked with members of Research Ethics Boards who have told me that they are over their heads with genetics. (national organization member)

Wide ranging concerns were expressed surrounding privacy rights, the use of information, the incidental gathering of information as a by-product of other research, the potential for commercial use of genetic data, and other such issues. The primary concern, however, was how to handle research that proposes the banking of genetic samples for future unspecified research.

- #17: The ramifications for banking tissue have become hugely increased with the power of genetics now. It’s a horrible problem and this is the one area in which we get the most argument in our group because nobody knows what the right answer is.

Three people insisted that such research is enormously valuable and must be allowed to be conducted.

- #12: Some of the ethics community have been taken aback at the request to keep a specimen in case something pops up, but from my point of view I think that’s absolutely essential. I don’t deal with tumors, but apart from leukemia in children all of the other cancers are individually extremely rare. So that this institution would see one those kinds of cancer once a year or every four or five years or whatever, and the only way to do research on that particular type of tumor is to have a tumor bank. It’s in the interest of the children that we have a tumor bank and it’s our responsibility to be safe-guarding.

Two people believed the best policy is to allow no such banking for future unspecified research. Tissue samples can only be collected for specific purposes identified in advance.

- #14: I think the policy is fairly clear you can't do tissue or any kind of banking with a notion that someday you'll do something else with it. The approval to DNA bank or tissue bank is linked to a protocol and outcome, and our established process to review those protocols and evidence.

Three people said their REBs allow samples to be banked but only if they are anonymous.

- #10: We have been making sure that the information is anonymized. That's really as much as we have done, and also making sure that the participant is informed that there will be tissue banking and it's appropriately explained to them what that means. That's as far as we have gone to date.
- #30: I think our main objection is the linkage. So we have insisted upon that, that there's no linkage if they are going to keep the tissue and perhaps use it in some future study. But I don't think we've gone to the extreme of saying that if it's not like the original protocol you can't use it.

If anonymity is ensured, any research is okay. Lastly, a number of REBs are using or developing (or considering) informed consent forms that itemize clearly the range of options for consenting to future use of banked samples. Some require researchers to say explicitly on the form what uses will be made of the samples. The more complex ones, however, provide a checklist of options for consent.

- #33: We want to have it specifically stated whether these are anonymized banks, whether they'd ever be able to get back to the individual, having it specifically laid out in the consent in a check-off style.

Will you have your material tested?                      Yes.    No.

Do you want it banked?                                      Yes.    No.

Do you want to be informed of any  
information that comes up in the future  
regarding this banked material?                      Yes.    No.

We sort of leave it up to the patient to decide. But that, in itself, is not good, because I think a lot of times they really don't understand what the consequences of this might be. . . [But it] gives them a little bit of control.

## K. Addressing Research with Collectives

The issue of research with collectives and the distinct ethical dilemmas it involves, are dealt with in detail elsewhere in this larger report. Thus it will be treated cursorily here. In short,

when asked how they are dealing with research which may have implications beyond the individuals who gave informed consent, research affecting all members of a particular social group, a significant number of participants were unable to grasp the question. This was more true of REB members than members of national organizations but, even in the latter group 2 of the 12 interviewees did not seem to understand the issues.

Of those who understood the questions, the vast majority said they have no way of dealing with this issue, or have simply not begun to address it at all.

Interviewer: [What about] research protocols where every individual may be able to give informed consent on their own behalf, and may fully do so, but the impact of the research will be broader than those individuals . . . How are committees dealing with that?

- #11: On a wing and a prayer, frankly. It certainly is a concern that's raised... What are we doing about it? Nothing very coherent.... All I can say is, yes there is a concern there, I've seen no coherent process or coherent set of standards right now on either the medical or the non-medical side for really addressing those concerns... I just don't know what to do about it.
- #16: These are questions that I don't have any answers for. On the one hand you don't want to impede scientific progress, but on the other hand you also want to make sure that you're not harming a whole segment of people.
- #04: For the most part we've simply averted our gaze from that. I think in truth we for the most part just haven't thought about it.
- #15b: We typically look at the benefits for the individual, and the benefits for society and for the community. But we rarely look at the risks except on the individual level, we don't look at the risks of the community. (national organization member)
- #05: We ask some of those questions, but I don't think we're asking them well or correctly as yet... I don't think anyone's really looked into this adequately. I mean how do we know? ... I really think we're dealing with it extremely badly, to be quite blunt, because it's not in our face so we sort of ignore it.
- #18: We haven't really discussed that although it's sort of been just below the surface in a couple of cases. Again I don't know what you would do.
- #28: I think we'd deal with it the best we could, but we would not understand the collective risk that we might inflict. I don't think that we would understand what potentially could happen.

A significant number of REB members argued that there is no justification for suppression of research; in essence the truth is an objective reality and in the end the truth will out. Thus the ramifications for a collective of telling the truth about their community or social



group should be irrelevant to decision-making about the ethics of the research. (Interestingly this view was not expressed by any of the members of national organizations.)

- #03: I guess you can take the classic academic attitude and say if this is the truth then you don't want to suppress it. This is important information they should know.
- #01: I am uncomfortable with the rights of society taking precedence... Anything objective is good science and you should not shy away from the objective assessment of anything.
- #07: That does raise ethical questions [about] hiding information or providing misleading information, or cultural controls over the scientific agenda of seeking truth and who gets to decide that... Intellectually I say I'm a seeker of truth and therefore, I would respond that if we seek truth then the truth will be where it may lay. Culturally, if I'm speaking culturally then I would have a different opinion, or I *may* have a different opinion. So it is a conflict but it's between the scientific agenda and the cultural ethic, a conflict that may or may not be resolvable.
- #04: I'm generally of the view that the chips should be allowed to fall where they may. As expressed by interviewee #01 above, many participants held grave concerns about the notion of granting any kind of rights to social groups as collectives.
- #25: I, for one, am more oriented towards the individual's right. Rights of the collectivity– for me, rights belong to the individual. That doesn't mean that we should not analyze, or study, the impact on the collectivity and be preoccupied by this. If it leads, let's say, to some kind of discrimination within a community, I think this should be of real concern to those who are looking at a research project. . . We have to look at this broader dimension of research, but I wouldn't talk about the rights of a collectivity.

Several people noted that research with collectives often can be accomplished ethically by adding a layer of collective approval or consent. For example Native Band Councils may be asked to agree to the research on behalf of their entire Band.

- #29: When we see things dealing with communities of interest – a Band Council, for example... then we look for assurance that the community is informed that this kind of work is going on, and that the appropriate representatives of community interests are told, consulted, and asked about it, as well as the individuals who may be asked to participate.
- #03: This often comes out in terms of secondary levels of approval that we require, what we call generically agency approval. So if research is being done with a First Nations Band for example, we would want to see written approval from the Band as part of the approval process. That particular collective would say, "Yes we'll let you come in, but if you come in we're going to put some restrictions on how you deal with the information."
- #23: We really need to go back to the collectivity as well, and say, "You might not have recognized it, but if we ask individual members of your community for consent, this is also going to have an impact on your community so do you have a means of consulting the community about this?" On the basis of what we can tell you, and what we're telling you about the impact is of varying degrees of predictability, so take that as well into consideration. We can't always predict

impact and therefore you may want to say 'No' on the basis of it not being predictable enough for you. Or you may want to say, "That's good enough for us!" But it seems to me we have some obligation to go back to the collectivity as well. If it's an identifiable group.

Some participants suggested that any collective with recognized social standing would have some organized body that would be able to consent for the collective.

#23: It's hard nowadays not to find a group that at least *claims* to be representative. We have some obligation to check that out, of course. But at least if they are representative, or we can be persuaded that they are for that particular collectivity, short of a vote, then I think we ought to do that... It isn't always possible to say what's the community. But on the other hand I think, in some cases, it can be they themselves, or a representative group that undertakes finding that out.

One REB member even suggested that the HIV/AIDS community provides such effective representation for that collective that REBs are afraid to do anything that might meet with their collective disapproval. Others questioned the assumption that all social groups have a representative spokesperson or agency who can give approval to the research on behalf of the collective – interestingly using the AIDS community as an example.

#04: For certain kinds of groups like Indian bands you start with the Band Councils... Similarly where research goes into labor or business organizations it's common to seek permission from the organization... I think that in every case where we do that we may not have thought this through when we did it, but what we found ourselves accidentally doing was identifying places where there was a credible collective or institutional interest which had some sort of right of veto. Does the community of AIDS sufferers– who speaks for the community of AIDS sufferers in some critical way? Well the answer is no one, even though there may be a true collective interest. Where the interest is emergent at this point I'd say there's not much that we can do.

This same participant expressed concerns about the legitimacy of approval-granting bodies, even those that are officially recognized: "I think we simply take for granted the representativeness and the authority of Band Councils... I think we probably over-estimate the extent to which Bands are sort of unitary entities with a consensual culture (#04)."

In an interesting twist on protection of research subjects, a substantial number of participants suggested that members of the collective, the social group, are best positioned to assess the impact of the research on the members of their community. Thus researchers can rely on individual research subjects to make informed consent decisions that protect the members of their larger social group.

- #02: If within the consent form it is well indicated to each individual what the purpose of the research is without deception, why are you engaging in this interview, and then in some instances that puts a bit more responsibility on the individual within the collective to say, "Oh well I see this is going to have a lot of impact upon this group, therefore I'm not going to consent to this."

Some participants also suggested trust in the researcher who works in the particular field is the only way to deal with collective risks in research ethics review.

- #33: It's really up to the researcher again to deal with the information he gets from a study. If he finds a particular ethnic group is more prone to a particular disease, it's really up to him to convey that information in a way it won't stigmatize that population. We do state that. If we see something in a protocol that may be directed towards a specific ethnic group, looking at genetic diseases, say Ashkenazi Jews, we make sure that we state that this research has the potential to stigmatize or to affect how society looks at this one group, that they have to be aware of that and how they present that information. . . I guess we trust the investigator... and the subjects too, to understand how this [might have an impact].
- #15b: It's a complex issue that kind of relies upon the trust in the researcher... that may or may not be warranted depending on the researcher. (national organization member)

One participant noted that even if the researcher can be trusted to report findings appropriately in respected academic journals, that still makes the findings available to the "gutter press." Several REB members suggested possible approaches to dealing with the ethical issues raised by research with collectives. Two suggested not approving the research. One qualified the nature of the problem and suggested altering the recruitment to avoid the issue.

- #02: If that [lack of consent from the collective] is a problem then that's a problem for the research itself. And we could refer that back to a committee and not give consent to it even though the individual consent may be procedurally good, there may be some problem with the overall impact of the research.
- #18: I don't know what you would do. I think our committee, if our committee ever sensed that there really was a real danger of some of something like that happening we would not approve that research.
- #11: I've tended to take the view that we should be cautious about allowing research that will inevitably impact, demonstrably, negatively, on people whose consent is not being sought. Now the key words there are inevitably and demonstrably... I've not, I confess, felt confident enough as Chair of the committee to ban that type of research in a non-medical setting... I try to negotiate a little bit with individual researchers to see if there is any way that a different population can be used or is the research necessarily population specific... A different recruiting pattern . . . would broaden the recruiting base and avoid that problem.

One participant suggested the researcher needs to explain the reasons for doing the research to the satisfaction of the collective.

- #09: You've got to explain to people, "Here's the evidence for thinking you people are at risk because you're carrying this particular gene for a disease. And we'd like to help... but it's your call." You know, we can't just assume it [is okay because] we're interested in that for science's sake.
- #12: We have four ethical principles, but autonomy's a trump card. And I guess we need to rethink whether that should be a trump card and whether the justice of the fourth one should be not just individual but should be community impact and should have a higher priority... But at the moment autonomy trumps everything... North Americans have a big problem with community oriented standards. The only thing that we can do in the meantime is make sure that people are informed.

Another suggested leaders from the community in question must be involved with the research protocol to ensure it is adequate ethically.

Virtually all of the participants from national organizations said dealing with the ethical issues surrounding research with collectives is high on their agenda for revising existing guidelines. Everyone is aware of the problem and concerned about it and, SSHRC is actively leading the process of developing consensus to revise the Tri-Council Policy Statement in this regard. Where there does not yet seem to be agreement is on whether the guidelines should be about research with Aboriginal communities or, more broadly about research with collectives. The national organizations seem to be inclined toward the former, which may well leave the issues relevant to research with other social groups unaddressed.

## IV. CONCLUSIONS

While the research data here do not provide numerical evidence of the scope of these issues, the depth of the qualitative research does allow us to sense the intensity these concerns carry for the research participants. The data also illustrate the matters that REB members and national organization members consider important to their daily work and the lack of consensus on some issues. The extent of consensus across the country would need to be measured using quantitative methods. Here we have heard, in their own words, the concerns that occupy the people who review the ethical considerations of medical and health-related research.

Some important themes emerge. Foremost, while there appears to be strong consensus about the goals of research ethics review, it is also amply apparent that most members of the research ethics community do not have strong empirical bases for believing they are dealing

with ethics review effectively. Most people have, at best, a sense that things are working as they should. Many participants expressed serious concerns about the treatment of research ethics, and particularly the absence of measures of effectiveness. Yet there were mixed feelings about the desirability of monitoring ongoing research, particularly beyond auditing documentation. Nonetheless the national organizations expressed a certain determination to go forward in this direction, favouring a step-wise introduction of monitoring.

There are mixed feelings about the desirability of increased centralization of ethics review. While general consensus on substantive ethical issues would suggest reciprocity arrangements among committees might be likely, simply to lessen workloads and speed up the review process, significant distrust about each other's processes would undoubtedly pose major barriers to such moves. Centralizing review for multisite trials would meet with the most approval. Similarly, although some REBs are not particularly troubled by the multiplicity of guidelines purporting to direct their work, others find this situation extremely confusing. Harmonization of existing guidelines would be welcomed by all.

Multisite trials clearly raise some of the greatest pressures on many REBs, both in their need for fast turnaround and in their refusal to entertain major changes to a trial already underway at other locations. They put local REBs in a difficult position. This is complicated by the fact that industry now funds such a significant proportion of research at some institutions. That situation raises its own concerns for many participants, particularly the inevitable power dynamics entrenched as research institutions become financially beholden to an industry whose ultimate goal is profit rather than pure science and knowledge production. Yet the current political and economic climate seem to lead health research inexorably down that path, as public institutions appear routinely unable to adequately provide for the resource needs of research ethics review. Industry appears to be the only player in the field with the money.

The need for an infusion of resources cannot be overstated. At the various sites across the country the story is the same: overburdened REB members are stretched to the breaking point. These are well-intentioned volunteers doing the best they can to address extraordinarily complex issues under severe time constraints with severely limited resources. As the work becomes increasingly complicated with globalization, technology and commercialization, REBs are struggling to find committee chairs or even members.

Lastly, this research has highlighted the need for continued work on some areas in which there are serious gaps in REBs' understanding of and ability to deal with complex research issues. In particular REB members have barely begun to grapple with the ways in which cultural differences may demand different approaches, particularly to informed consent. They are struggling to keep up with the complexities posed by genetic research, particularly concerning the banking of tissue samples. Finally, many REBs generally seem unable to conceive of research that would address the ethical considerations of collectives rather than individuals. Even the national organizations, whose members *are* beginning to work on the issue of research with collectives, are rarely thinking beyond the narrow framework of Aboriginal communities to encompass other types of social groups. In all of these areas there is tremendous scope for work that will help those who design policy as well as for those who implement it daily.

# APPENDIX ONE

## I. INTERVIEW GUIDE — RESEARCH ETHICS BOARDS

- Tell me about the structure of your REB, and its processes. What can you tell me about its history? (Probe: Science review? Impact? Time lines? Numbers?)
- How do you think members of the local research communities perceive your REB?
- To what extent do you think researchers “on the ground” are influenced by the ethics standards of your REB? (Probe other possible influences: local culture, professional guidelines, etc)
- How do you deal with a multisite trial brought to your REB that has already received ethics approval at other sites? (Probe: what pressures does that add?)
- How effective do you think your review process is? Why do you think that? (What is your evidence? What do you actually measure? What are the goals or objectives of research ethics review?)
- How is the Tri-Council Policy Statement affecting your REB at the local level? What are your concerns? The difficulties you foresee? (Probe: Central vs decentralized review)
- There seem to be a lot of “players” involved right now in the arena of research ethics in biomedicine and health — federal and provincial legislation, Ministry of Health directives, international guidelines, national guidelines, industry standards. . . How does this affect your work here at a local level? (Probe: In the context of multiple guidelines, what do you see as authoritative?)
- Do you see the fairly plentiful research ethics guidelines as a help or a hindrance?
- What impact do you see from globalization and the trend toward international harmonization of standards in research ethics?
- What gaps do you see remaining in terms of guidance for research ethics review?
- How do you deal with the issue of cultural difference regarding informed consent? Is there an effective way to deal with informed consent in a cross-cultural context?
- How does your committee deal with the issue of tissue banking for future unspecified genetic research?

- Some people have commented that it is particularly difficult to address the issue of benefits/risks to collectivities in a framework that centres around individual informed consent. What do you think? Are there effective ways to get at this issue?

## II. INTERVIEW GUIDE — NATIONAL ORGANIZATIONS

- Can you tell me a bit about the structure of (the organization), and its processes. What can you tell me about its history? (Probe: Why did it get set up the way it is? Major changes over time?)
- How do you see the relationship between (the organization) and (other national organizations)?
- How do you see the relationship between your organization and local research ethics boards? Between you and industry?
- To what extent do you think researchers “on the ground” are influenced by the ethics standards of your organization? (Probe other possible influences: local culture, professional guidelines, local REB, accepted publishing standards...)
- How do you see the Tri-Council Policy Statement affecting local REBs? What are your concerns? The difficulties you foresee?
- There seem to be a lot of “players” involved right now in the arena of research ethics in biomedicine and health — federal and provincial legislation, Ministry of Health directives, international guidelines, national guidelines, industry standards... What kinds of impacts does this have on the work of your organization? What advantages and disadvantages are there to the various ways of getting at ethical research?
- Do you see current ways of dealing with research ethics in Canada as effective, overall? Why do you think that?
- What would you say are the goals or objectives of research ethics review, from your perspective? What would “effective” ethics review look like?
- Do you see remaining significant gaps in research ethics guidelines? What directions do you see research ethics taking? Where would you like to see it go?
- How is the issue of cultural difference regarding informed consent being dealt with, from your view? Is there an effective way to deal with informed consent in a cross-cultural context?
- The issue of genetic research and the banking of genetic samples for future research is particularly problematic for some people. What do you think about this?



- Some people have commented that it is particularly difficult to address the issue of benefits/risks to collectivities in a framework that centres around individual informed consent. What do you think? Are there effective ways to get at this issue?



Site	Committee	Responsibilities	Approximate # of protocols reviewed annually	Usual turnaround time	Process
Vancouver*	University of British Columbia Behavioral Sciences REB	All research whose methods are considered non-invasive, regardless of investigator's institutional affiliation.	500-700 About 50% health-related.	6-8 weeks	<ul style="list-style-type: none"> <li>no meetings</li> <li>2 reviewers and one Co-chair read each protocol</li> </ul>
	University of British Columbia Clinical REB	All research whose methods are considered invasive, regardless of investigator's institutional affiliation. Includes research from affiliated hospitals BC Women and Children's, Vancouver General, and BC Cancer Agency.	700	6-8 weeks	<ul style="list-style-type: none"> <li>monthly meetings</li> <li>2 reviewers, lawyer, lay rep, Chair read every protocol. Reviewers may bring to REB for discussion.</li> <li>do own science review (except Cancer agency protocols); may send to external reviewers</li> </ul>
Calgary*	Con-joint Faculties Research Ethics Board	All non-medical, non-educational research at University of Calgary.	250	2-3 weeks	<ul style="list-style-type: none"> <li>no meetings</li> <li>3 reviewers submit responses to Chair who makes decisions</li> </ul>
	Con-joint areas Health Ethics Review Committee	All research that takes place on the premises of Calgary Regional Health Authority plus any research done by any member of U of Calgary Faculty of Medicine.	400+	4-8 weeks	<ul style="list-style-type: none"> <li>meet twice a month</li> <li>science review, facility impact analysis, ethics review done sequentially</li> <li>one main reviewer summarizes to rest of REB</li> </ul>
	Alberta College of Physicians & Surgeons REB	All research done by physicians in Alberta that is not reviewed by the CHREB or by REBs at U of Alberta or Alberta Cancer Agency.	~200	4 weeks	<ul style="list-style-type: none"> <li>monthly meetings</li> <li>two reviewers present to whole committee</li> <li>own science review unless expertise is lacking then seek external review</li> </ul>

\* One UBC affiliated hospital, St. Paul's, does not have its research ethics reviewed through the UBC Clinical committee; it has its own committee. No one from that committee was interviewed.

♦ University of Calgary also had at the time of the interviews a committee reviewing research in education. It was about to amalgamate with the Con-joint Faculties committee. No one from the education committee was interviewed.

Montreal (McGill)*	V.	MCGILL IRB	Any protocols involving more than one McGill-affiliated hospital; other health-related research not done through a hospital.	100	~6 weeks	<ul style="list-style-type: none"> <li>• monthly meetings</li> <li>• one reviewer presents to whole committee</li> <li>• Chair reads all protocols</li> <li>• own science review</li> </ul>
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\* Several other hospitals are affiliated with McGill University, but no one from their research ethics committees was interviewed (Royal Victoria Hospital, Montreal Neurologic Institute, St. Mary's Hospital, Montreal Chest Hospital, Douglas Psychiatric Hospital) due to time constraints. All Chairs of hospital REBs and of McGill IRB are members of the Research Ethics Committee of the Faculty of Medicine, an oversight committee.

## SECTION E-2

# GOVERNANCE RELATIONS IN BIOMEDICAL RESEARCH INVOLVING HUMAN SUBJECTS

(Section E-2 is a translation of the original French version)

Marcelo Otero

## I. INTRODUCTION

Within the scope of this study, this is an examination of the governance relations that regulate scientific activity in the field of biomedical research involving human subjects. Research practices in this field are subject to a series of complex standards and regulations derived from or inspired by a range of sources such as civil and public law, professional codes of ethics, guidelines issued by specific organizations (public, para-public and private), standards set by the pharmaceutical and biomedical industry, the axiological and cultural contexts within which researchers operate, and so on.

In order to better understand how biomedical research involving human subjects is “governed” «governed» today in francophone Quebec, a series of interviews were conducted<sup>188</sup> with members of the research ethics boards (REBs) of the establishments affiliated with the University of Montreal, university administrators with that same institution, and provincial government representatives. The two interview guides (G1 and G2)<sup>189</sup> were designed with one main objective: to identify the structures, processes and trends that “govern” «govern» biomedical research and the effectiveness of all the mechanisms for regulating researchers' activities with respect to research ethics, as perceived, of course, by the individuals interviewed. Besides this overall objective concerning the various governance relations of research ethics, three other specific issues raised explicitly during the interviews generated considerable interest

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<sup>188</sup> Sociologist Pierrette Mulazzi conducted this part of the research.

<sup>189</sup> Reproduced as appendices.

among all the respondents, namely: the ethical dilemmas posed by genetics research, the conflicting interests and legitimacy of the various levels of consent (the individual, society and communities), and the delicate and conflicting relations between the pharmaceutical companies and scientific research activity.

The analysis of the material gleaned from the interviews reveals the views and concrete experiences of a specific group of actors (our respondents) involved in the process of reviewing research projects and in the development of guidelines to provide a framework for and orient both the activity of researchers and the review processes. The conclusions based on the analysis of the interviews should contribute to a better understanding of the specificity, or at least some revealing characteristics, of not only the concrete practices of these actors, but also of their perception of those practices and of the issues they see as related to them.

A better knowledge of the interviewees' experiences, of the significance they ascribe to them, and of their perceptions of what is at stake, is apt to help shed light on the overall issue of the governance relations of biomedical research ethics.

## A. Information About the Interviews and the Respondents

At the start of the study, the plan was to conduct eleven interviews. As one of the people contacted refused to participate and one of the recordings was inaudible, in the end nine interviews were used. These interviews were conducted between September and December 1999 and lasted from one-and-a-half to two hours. The interviewees' co-operation was satisfactory.

For francophone Quebec, five interviews were conducted with five people who sit on the REBs of hospitals and institutions affiliated with the University of Montreal, two administrators of that same university, and two officials of government agencies. The interviewees<sup>190</sup> included doctors, lawyers, researchers and ethicists.

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<sup>190</sup> In order to better respect the anonymity of the persons interviewed, the masculine form is used indiscriminately to refer to both male and female respondents.

## II. STRUCTURE AND FUNCTIONING OF ETHICS BOARDS

### A. REBs and Boards of Directors: Autonomy and Stability

Most of the REBs to which the interviewees for this study are attached have undergone major changes in recent years (in the last two to ten years, depending on the REB). These changes have had to do essentially with their independence vis-à-vis scientific review boards (SRBs), their composition and the stability of their personnel, the operating rules, the increase in the number of normative sources and basic guidelines for reviewing research protocols, and the effectiveness of the mechanisms for controlling scientific research activity.

Today, the REBs of the Quebec hospitals covered by this study are independent from both the hospitals' research centres and the scientific review boards (SRBs) that often constitute (or did constitute, depending on the hospital) sub-committees of the first (#1), (#2), (#3), (#4), (#5). They are attached to the hospitals' Boards of Directors (BDs), which also appoint their members (#1). One interviewee links this major change to the implementation of the Tri-Council «Tri-Council» Policy Statement, one of whose effects seems to have been greater autonomy for REBs and less of a monopoly by physicians of these boards. In effect,

...all research ethics boards have come under the responsibility of the hospital's Board of Directors, rather than under the responsibility of the Medical Staff. This in several hospitals, but not all, because in some this was already the case, but in a lot of hospitals it was a major change that signalled essentially a change in the policies of hospitals, since it is no longer the doctors who control the research ethics boards, it is the BDs, so it is a responsibility of the hospital. So it was of extremely decisive importance, I think, to the restructuring of ethics boards. (#7)

Each hospital in fact has its own local REB that answers directly to the BD. The REB of the CHUM is divided into three teams that sit in each of its hospitals (Notre-Dame, Hôtel Dieu and St. Luc), and they are headed, respectively, by a chair and two vice-chairs (#3) (#4).

The University Ethics Committee (UEC) is appointed by the authorities of the University of Montreal (UofM). The UEC consists of, among others, the sector-based research ethics boards that review the projects of researchers, professors, and master's and doctoral students. While it is true that the research centres and hospitals affiliated with the UofM are required

«under\_Québec\_law» to set up their own REBs (#7), these units seem to retain their «capacity» “status” as university centres and the UofM understands that it in turn has some responsibility towards the REBs of its affiliated units. Both these reasons are cited to explain the UEC's establishment, in 1993, of a liaison committee of the various REBs at the UofM-affiliated hospitals, known as CLERUM (#7). As for “the REB of the Department of Health Sciences” «the», two years ago there was an extensive overhaul of the former multi-faculty health sciences ethics board that reviewed research protocols by means of “ad hoc committee” «ad\_hoc\_committees». Since then, the health sciences REB has acquired a stable, more autonomous structure. (#8)

The ethics board of the BD of the FRSQ<sup>191</sup> is an advisory board that addresses concerns relating to research ethics likely to be raised within the BD (#10). Finally, the provincial ethics board (PEB) has a mandate to review research projects involving incapable persons in institutions where there is no REB appointed by the Minister of Health and Social Services (#10).

## B. REBs and SRBs: Specificity and Overlapping of Their Mandates

The purpose of reducing the formal ties between ethics boards and scientific boards by connecting the first to higher levels of authority, such as BDs, is to ensure a certain independence that is ultimately essential to the effective operation of REBs. The ties that formerly characterized the structures of REBs and SRBs, which were a little too close, even blurred, made it difficult to take certain decisions likely to offend some scientific board members. For example, a member of the REB of one hospital stated that:

... for REBs, the first question that arises is: Is the protocol scientifically acceptable? We feel it is important to be able to say no if necessary ... So if the SRB is dependent on us [as was the case at this hospital 5 years earlier] it is very awkward to refuse ... (#1)

The ties between REBs and SRBs continue, however, to be many and complex in a number of respects. It often seems that some individuals sit simultaneously on both boards, and at times these boards share the services of the same secretary (#2). The interviewee quoted

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<sup>191</sup> It is important to realize that this board does not review research projects to determine whether they are acceptable ethically, but it advises the BD on the policies, standards and norms researchers and research centres are to adhere to in order to meet the requirements of the FRSQ.



above confirmed that three people, including one who represents the director of research, «liaise» regularly “established links” between the SRB and the REB, and act as “rapporteurs” «report» on the review previously done within the SRB (#1) (#2) (#5). Moreover, the ethicist on the REB of one hospital asked to be present during the REB’s meetings” (#1). In the case of the REB of the board of directors of the FRSQ, the FRSQ director of research sits in on meetings regularly (#10).

It seems to be standard procedure for SRBs to review and approve research protocols about two weeks before they are submitted to REBs (#2) (#3) (#5). One of the interviewees stated that the responsibility of SRBs is to do “a kind of pruning to start with... of what is scientifically acceptable or not” and, he went on to say, “if a protocol is not scientifically acceptable it would doubtless be difficult to justify ethically” (#2). In exceptional cases, REBs will adopt a position on a research project before it is reviewed by the SRB,

... for example, in an emergency ... there are projects that pose absolutely no problem from the standpoint of the scientific review, but that may pose huge problems from the ethical standpoint, and vice versa ... (#3)

... generally, the projects looked at undergo a scientific review, but not always; it can happen that it has not been reviewed scientifically ... (#8)

If REBs and SRBs have different structures, the limits of their mandates do not always seem clearly defined, as evidenced by the following accounts of respondents:

... for REBs the first question that arises is: Is the protocol scientifically acceptable? (#1)

... methodologically, it is the scientific board that will solve these problems beforehand ... So the scientific review is done first. We ... nevertheless take a look scientifically ... that is to say, the ethics can't be separated from the science. (#5)

... we want the researcher to demonstrate to us that his project is based, let's say, on science because doing a study without science isn't ethical ... (#8)

... basically, someone who sits on an ethics board has an extremely difficult mandate to carry out because he has to, at the same time, make sure that the broad underlying principles are adhered to and that the activity he approves will also be acceptable scientifically. (#10)

In other cases, the distinction between ethical review and scientific review and the respective roles of REBs and SRBs seems clearer.

... we don't ignore the scientific merit of the project ... but that isn't what we're there for ... we look at the risk-benefit ratio for the [patient], the consent form, etc. ... (3#)

One concrete example given by one of the interviewees attempts to illustrate the specificity of the respective mandates of REBs and SRBs:

... it's possible that for scientific reasons the ideal situation ... for example, when you want to include subjects in a research project, ... would be to make sure that going into it they are cleansed of their previous treatments. And in order to cleanse them, you may decide ... to deprive them of all drug therapy and then if you have, let's say, schizophrenics as subjects, you decide they won't receive treatment for 2 or 3 months, no medication in order to have schizophrenics who are very clean and fresh. Definitely from the scientific standpoint alone, this is the right approach. But it's easy to understand that it's not right to let a schizophrenic function without medication for 2 or 3 months. And so, you have to find a middle ground between the ideal laboratory solution and the completely legitimate concern of someone who says you don't do that. (#10)

Given the degree of specialization of the research projects that are reviewed by the various REBs, the assistance of SRBs often becomes indispensable. In this regard, one interviewee explained that REBs:

... will have projects that involve children, the elderly, heart patients, diabetics, surgeons. Basically, you can't be an expert in all that, which means it's important to have an opinion of a scientific board that says: "Listen, the science is correct, now you can address the problem at another level and tell us if, in a human perspective, it is reasonable to subject or engage the research subject in this "adventure""!Syntax Error, «. (#10).

This state of dependency resulting from scientific specialization seems to have declined in recent years, as the mandate of REBs is becoming clearer and their members are better able to define the aspects of a research project that fall more within the sphere of ethics than within the sphere of the strictly scientific review (#2).

### C. Personnel on REBs: Doctors and "Outside Members" «Outside\_Members»

REBs usually have between nine and thirteen members of varied and complementary training. While in the past these boards seem to have been almost exclusively monopolized by physicians, they have opened up in recent years to "external members" «outside\_members», notably jurists, ethicists, and representatives of the public, the community, patients or users. In the case of one local REB, a respondent reported seeing, over the last six years, the broadening and opening up of this board:

... before it was very professional, if you will, it was very limited, it was a small board, it was very professional [It was made up mainly] of doctors, psychologists, there was a dietitian, a nurse ... There was a good distribution, if you will, professionally, but it was the balance between the internal and the external that wasn't there ... So I really had to go out and win over, if you will, on the one hand, expertise elsewhere ... (#5)

Another interviewee recounted that:

... for the last 10 years ... there have been not just doctors, but also people from the general public, there are lawyers, there are scientists, there are women (sic) ... (#2)

This same respondent, a physician by training, felt that “newcomers” «newcomers» from outside should be given more power within the structure of REBs. In effect,

... the chair shouldn't be in medicine, shouldn't be in pharmacy ... but should really be a lawyer ... and his right arm should be not only the secretary of the REB but also a well-paid ... ethicist. (#2)

The opening up of REBs to “external members” «outside\_members» is not unrelated to the impact of the Tri-Council «Tri-Council» Policy Statement, held responsible for having largely helped break down the resistance of some institutions where REBs were the physicians' prerogative. In effect,

... now there is an obligation to appoint a public representative from the community, something almost no hospitals had, and then no research ethics boards that had representatives of the public in Canada and Quebec, in our region as well. So that too led to a change ... And also some hospitals didn't want anyone, didn't consider it important to have [someone] in ethics or someone in law. So these appointments transformed the ethics boards, because people at both the federal and provincial level who don't conform to this structure of an ethics board can't receive grants. That was extremely important. I personally think these are the two most important changes, because really when it comes to how research ethics is thought about in an institution that changes a whole lot. (#7)

The respondents did not always exactly remember all the members on the REBs or their exact number. It was therefore not unusual, during interviews, to hear phrases such as this: “we are about ten or something like this” «there\_must\_be\_a\_dozen,\_something\_like» (#5). But, roughly speaking, their composition is the same. Here are a few examples:

... twelve people assisted by a half-time secretary: a member appointed by the UofM, a representative of the BD, a representative of the research centre's director of research, a representative of the departments, a representative of the Medical Staff, an ethicist, a jurist, a physician secretary and a users' representative ... (#1)

... the associate director of clinical research who is a statutory member [rapporteur of SRB proceedings], an ethicist [paid with funds from the pharmaceutical industry] who [also] reviews SRB protocols, a patients' representative, a representative of the BD, a jurist, a representative of Nursing, a pharmacist ... (#2)

The REB of the CHUM has 31 or 32 members divided into three teams that sit in each hospital; they do not necessarily decide on the research projects of the respective hospitals, but

on the projects previously selected and grouped by specialty (there are about 40 specialties). Provision is made, however, for some rotation of the members of each board so that they gradually become familiar with all the specialties and “that they don’t even get bored” (#3). Each team of the CHUM that has 10 or 11 members, one of whom serves as chair, is made up of a lawyer, an ethics consultant, a social worker or child protection worker, a nurse, two medical specialists (for example an anaesthetist and a cardiologist), a retired physician (usually very available), a users' representative, a representative of the university (often a physician, but not necessarily) and a «mental\_health» specialist, i.e., a psychiatrist or a psychologist (#3) (#4).

While one of the interviewees said that the presence of the representative of users or the public “is not mandatory”!Syntax Error, « on REBs (#3), another claimed the opposite:

... there must always be a representative of the public and if it gets up to 10 members, there have to be 2 representatives of the public ... if there are 6 it can stay at 1, [moreover] the representatives of the public ... must be present when adopting the review, [which] gives them considerable power ... essentially the ethics boards are obliged to have one person who represents, at least, one person who represents the public. (#7)

Nine people sit on the health sciences REB, including one representative from the five «health\_sciences» faculties “of Health Sciences”, a students' representative, a legal expert, an ethicist, a representative of the public, and one other person whom the respondent could not recall (#8).

Occasionally, some interviewees pointed out the specific skills of the “external members” «outside\_members», usually the jurist and the ethicist, notably in terms of their contribution to resolving numerous problems encountered by REBs during meetings (#10). One respondent, however, said that “ethics is only starting”!Syntax Error, « and that the discourse of many ethicists is “superfluous” «superfluous» in the sense that the role of these professionals seems to be to tell others what they already know, in this case “we have to do good and avoid evil”!Syntax Error, « (#3).

As for the administrative support given REBs, it quite often boils down to a half-time secretary being available once a week (or a month, depending on the REB), sometimes also assigned to the SRB, who looks after opening files and preparing them ahead of time for the review (#2) (#3) (#8).

## D. Functioning of REBs

In the case of REBs responsible for reviewing research protocols, the people interviewed maintained that the meetings follow certain rules of procedure and that the review is carried out according to specific standards and controlled procedures. One respondent attributed the changes related to functioning in recent years to the implementation of the Tri-Council«Tri-Council» Policy Statement. In effect,

... at the level of functioning now, here too there has been a change. Because what has somewhat shaken up the functioning has been the documents of the three Councils ... [our board] also spent a lot of introspective time on processes. (#5)

Another interviewee stated that in his REB “we have established some kind of “Bible”... the process we follow... from beginning to end”!**Syntax Error**, « (#3). In general, REBs meet once a month according to a pre-arranged schedule (#2) (#3) (#4) (#5) (#8) (#7), meetings can last from 4 to 5 hours (#2) and the rules of quorum are adhered to, so that REBs cannot function with fewer than five members present (#2) (#5).

According to one respondent, the meeting time is allocated as follows: “two-thirds for protocol presentation and one-third for a small matters”!**Syntax Error**, « (#2). The REBs review 4 to 7 protocols per meeting, and when there are 10 or 12 protocols, they try and have two meetings in the same month (#2). The REB of the CHUM (the three teams), perhaps the largest in Quebec, if not in Canada according to one interviewee, reviews about 350 research projects involving human subjects each year (#3). Another respondent said that in his REB «about» at the rate of 4 or 5 a month (#8). At times, the fluctuation in the number of projects reviewed each year by a given board was stressed, since

... it varies greatly ... There are years when we've had nearly 40 protocols, and other years when we've had 20 or 25. (#5)

The usual procedure is for the researcher to forward his project to the secretary of the SRB and the REB (sometimes the same person in both cases), who is responsible for making sure certain administrative formalities have been carried out before turning the protocols over to board members (#3). In some REBs, the researcher is required to be present only “when there is important questions” (#2), or “ambiguities or vagueness in the protocol”!**Syntax Error**, « (#4), in which case the researcher is invited to the next meeting. In other REBs, **Syntax Error**, «however, the researcher is no longer required to present his research protocol to the board

members, as seems to have been the case in the past. [The board] limits itself to asking him about specific aspects that pose problems for the approval of the project and “we review with him, line by line, the information and consent form”!Syntax Error, « (#2).

### III. THE REVIEW PROCESS

#### A. Purpose of the Review: Balance Between Protection of the Subjects and the Advancement of Science

The main objective of the research ethics review process is to protect the human subjects involved in the research (#1) (#2) (#3) (#4) (#5) (#7) (#9). In general, the interviewees expressed the desire

... to protect research subjects ... to ensure that the explanations they are given are accurate and are complete, that nothing is being kept from them that would be of a nature to influence their decision ... that the consent covers all aspects of the research including the aspects most difficult to control ... for example, when a trial involves the sending of tissue in data banks ... (#1)

It is therefore hardly surprising that one interviewee said that “95% of our interventions [in the REB’s meetings] are on the consent form” (#3). Still in a timid way, the subject of financial compensation for subjects enrolled in trials is starting to be discussed when reviewing protocols. This interviewee maintained that

... we are starting to look a little at the financial aspect, but this is still in the early stages [for example we’re asking the question] is this an undue incentive? (#3)

Maintaining (or adhering to) an acceptable “risk-benefit”!Syntax Error, « ratio for research projects involving human subjects is also one of the main objectives of the review. In fact, any review should be able to verify that “the risks do not surpass the benefits we expect”!Syntax Error, « (#1). However, the analysis of what constitutes an acceptable risk-benefit ratio seems to be linked to the proposed project’s contribution to “advance knowledge”«the\_advancement\_of\_knowledge» (#7), which reminds us of the overlap of REBs and SRBs (see section 1. 2). In effect,

... an ethics board must be able to determine whether this research project is sufficiently worthwhile and relevant to ultimately advance knowledge to such an extent that it was worth using humans to advance knowledge. Because it seems to me it's always the relationship between advancing knowledge, on the one hand, and being obliged to use humans to advance knowledge. It's this balance between the goal and one of the means to be used for that, so how to achieve that balance. (#7)

One respondent who broached the topic of the side effects of “very strong medication” «powerful\_drugs» (#2) suggested there are several ways to view the question of the relations between scientific progress and the risks run by research subjects, since it is often forgotten that one way of “serving the patient [is also] allowing access to new medication” (#2). In other words, the risks run today are likely to become “clinical benefits” «clinical\_benefits» tomorrow. Most respondents did not consider the regulations governing research ethics an impediment to scientific progress; quite the contrary, they allowed that:

... operations will be done according to what society in general considers to be right, in the broad sense. And I would say that as an individual, if I agree to participate in a research project as a subject, it's comforting for me to know there are people who have studied this from various angles ... (10#)

The potential benefits that give us hope, for example, that a new drug will be developed, should not, however, preclude all possible precautions being taken to protect the subject in an emergency or accident. We should systematically ask ourselves “how are we going to overcome these risks” (#3) and be prepared to change the consent form based on the review of the potential side effects on subjects (#2) (#4), in order to give them additional or more accurate information. For example, one interviewee maintained that

... we're interested in knowing the methods for recruiting subjects, the measures for ensuring confidentiality, for triggering emergency measures if it's a high-risk project ... [Moreover] the subject is also sent a kit ... (#8).

One of the indirect aims of the interventions of REBs that was pointed out was to “educate our researchers and focus their attention on the important things”! **Syntax Error**, « (#1) (#3) (#4) (#5). Also, one interviewee pointed out that researchers should understand that the REB not only protects the interests of the research subjects and those of the community, but also, although indirectly, those of the researcher and those of the institution where the research will be done, both of which are legally liable for any possible mishaps that may occur along the way. In effect,

... we work for the patient but also for the protection of the researcher and the hospital ... it's not my main goal, but indirectly that's what it's for [...] sometimes the [pharmaceutical] companies urge on the researcher who doesn't realize he can be sued ... (#3)

... I think researchers ... would find it hard to say it, if you will. But I believe that intuitively they realize this [intervention of REBs] protects them and avoids real problems. (#5)

## B. Development of Guidelines and Policies Governing Research Ethics

In the context of the REBs of hospitals, the members confine themselves to applying standards and guidelines developed elsewhere; some interviewees are on boards or with institutions whose role it is, at least in part, to develop guidelines and standards intended to provide a framework or to guide research involving human subjects. For example, the advisory committee of the BD of the FRSQ, which includes a chairperson who sits on the BD, the FRSQ director of research, a representative of the College of Physicians, a jurist, an ethicist and someone “who comes from the pharmaceutical industry” «from\_the\_pharmaceutical\_community», has a mandate to:

... propose norms, standards, guidelines for the ethics boards and [for] the scientific integrity of the research centres that deal with the FRSQ ... (#10)

These norms, standards and guidelines are aimed at improving the review process of the units linked to the FQRS. At present, this committee is working on two major projects of drafting documents related to the amendments made to Article 21 of the Civil Code of Quebec. One of these documents will be about the setting of

... minimum standards we hope to see in our centres ... not a document intended to make ethics operations in our centres entirely uniform and homogeneous ... We think there's room there for the local culture ... but there are broad principles that everyone should adopt and that should be respected ... it won't be revolutionary ... but to set what we understand to be the basic standards that should be met. (#10)

Among the principles all researchers should adhere to is, firstly, the obligation to declare any research activity carried out in a unit linked to the FRSQ.



So any researcher who is affiliated with a hospital institution with which the FRSQ has dealings is obliged to declare to his institution all research activity ... researchers who don't do so would clearly be, let's say, outside the institution's legal or judicial or formal framework ... (#10)

The other document the advisory committee is working on is intended essentially to systematize the inevitable processes or operations of the review process.

... it's a guide - it's called the guide for ethics boards - it isn't intended as a recipe or what you might call a checklist or validation list ... but it would make it possible to say to the members of an ethics board: here are the steps you have to take or you have to follow when you want to review a project. What questions you should ask and what answers can reasonably be expected when reviewing a research project from the researcher who submits it ... A series of guidelines that can be presented in the form of a series of operations or questions that a member who wants to do a decent job should ask himself when he has to review a project ... (#10)

Another topic attracting the attention of this advisory committee right now is the improvement of the mechanisms for forwarding and managing complaints “related to the researcher’s conduct” «about\_the\_researcher's\_conduct», from both his colleagues and the subjects participating in the research. The interviewee made a point of referring explicitly, however, to the limitation with respect to a breach of the guidelines set by the committee and the penalties that might result, though he argued that “until now we have never had any difficulties with our centres in that regard” (#10). In his own words,

Someone who wouldn't do that [follow the guidelines of the future guide] would be outside the law within the meaning of the FRSQ and the penalty might be that he loses his grant, that his centre has problems with the FRSQ. (#10)

Another way to help harmonize the various approaches of the local REBs and limit the dispersion of the norms and criteria used to evaluate research protocols is to set up liaison committees. For example, the CLERUM is a liaison committee on which two UEC members sit, including the chair, the chair of the medical faculty's research board, the chair of the health sciences ethics board, the representatives of the affiliated REBs and the “representatives from the university”, notably from health sciences (#7). The specific mandate of the CLERUM is:

... to agree on the policies to be developed, to promote co-operation between the various centres affiliated [with the UofM], to have somewhat similar policies and also to consult each other ... so that they are not all going every which way when it comes to the approval of research projects ... (#7)

The strategic position of this liaison committee seems to have prompted the members of the CLERUM to note the “lack of training and education”!Syntax Error, « (#7) not only of some researchers, but also of some members of the REBs. These deficiencies in the training of many intervenors seem to give rise to “all kinds of interpretations of the documents and the guides”!Syntax Error, « supposed to guide the review (#7). Consequently, one of the tasks the CLERUM has taken on is to “prioritize education of the REB’s members” (#7).

The member of the CLERUM consulted in the context of this study proposed going further and organizing “training days”«training\_days» and “workshops around specific themes”«workshops\_around\_specific\_themes». And he felt it desirable to “work with professors in research methodology since ethics are a part of methodology”, and to help “researchers to prepare their projects... so they are not rejected for omissions” (#7).

While the respondent felt that the CLERUM is strategically positioned to benefit from the exchange between the various local REBs of positive and negative experiences and to formulate recommendations according to this mutually enriching “give and take”, he complained of this liaison committee's lack of autonomy and power. In effect,

... the CLERUM, because it is a creature of the UEC, has no connection with extremely important entities [MSSS, granting agencies, National Assembly]. It must always go through the University ... (#7)

Nor does the CLERUM have any authority over the REBs of the affiliated hospitals, and recommendations formulated within the CLERUM are sent to the UEC, not to the hospitals. In other words, “it would be through the UEC that hospitals are made aware of recommendations” (#7). Similarly, when researchers want to appeal a decision of a local REB, they have to go directly to the UEC, which, according to the interviewee, poses “legal problems under Quebec law” «legal\_problems\_under\_Québec\_law» (#7). While it is true that the CLERUM has no authority as such, it seems to offer at least possible room for agreement to resolve certain jurisdictional conflicts between REBs of the centres affiliated with the UofM. For example, when research is partly done in a hospital setting and partly on campus, the jurisdictions of the hospital's REB and of the health sciences REB are apt to overlap and lead to conflict (#8).

At the provincial level, an MSSS official, interviewed as part of this study, said that major changes have taken place since 1994 in the control mechanisms for research involving human subjects. While the Deschamps Report seems to have found that “the general process [concerning research ethics] was acceptable”!Syntax Error, «, it stressed the importance of

“identifying responsibilities in the context of research activities” «identifying\_responsibilities\_for\_researc» (#9). Following this report, the MSSS held a broad consultation with “all the establishments involved” «all\_system\_institutions», with “research partners” «research\_partners» (CQRS, etc.), and with “MSSS advisory bodies (the Conférence des recteurs des universités, the Canadian Association of “medical industries”, “a series of researchers in ethics,” jurists, and “ethics research group” «research\_ethics\_groups». This consultation resulted in a document called the “**Syntax Error**, «Ministerial Action Plan on Research Ethics and Scientific Integrity”, commonly known as the “Action Plan of the MSSS” (#9).

The Action Plan advocated “the precept of institutional responsibility” «the\_precept\_of\_institutional\_responsibil» while taking into account the amendment to Article 21 of the Civil Code of Quebec governing the protection of persons. In fact, the amendment of this article seems to have allowed the MSSS to establish a chain of responsibility for the approval of research projects that is more realistic than symbolic. Before the amendment, all projects involving human subjects had to be approved by the MSSS, which in actual fact merely ratified decisions taken elsewhere. Henceforth, these projects are to be approved by a REB “designated by the minister” «appointed\_by\_the\_Minister» and consequently, the MSSS “guarantees the work of the ethics committee globally but not the projects it approves” **Syntax Error**, « (#9). At present, the **Syntax Error**, «“law on health and social services in the matters related to access to subjects files in the context of research” is also being amended (#9).

The reason cited by the MSSS official to justify this major overhaul at the provincial level is the government's concern to

... maintain a balance between the pursuit of research activities of the highest possible quality and the protection of individuals who lend their support to them. (#9)

Some interviewees nevertheless felt that the Action Plan has not contributed much that is new to the review guidelines, and that its essential aspects are borrowed from the Tri-Council Policy Statement. The Action Plan seems to be somewhat limited to clarifying certain administrative aspects. In effect,

... the action plan is administrative ... there is no broad principle there ... well, it basically repeats the principles of the three Councils. There's nothing new in it ... everything they said we should do has already been done ... (#3)

... I think it [the Action Plan] forced the hospitals that were doing research ... to have a research ethics board that is consistent with the model of the three Councils, since in the Action Plan it's more or less the same thing only some of the words are different ... (#7)

... the Tri-Council Statement claims to speak to research ethics while the policy of the ministry [MSSS] doesn't make that claim, it simply pretends to be involved in ... ethics ... Yet in saying that, the policy of the ministry [MSSS] reaffirms at the outset the protection of subjects, making the protection of subjects the priority. (#5)

## C. Normative Sources and Guidelines: Diversity, Similarities and Differences

The normative sources and guidelines that are supposed to orient and provide a framework for the process of reviewing research projects are appreciably the same for all those interviewed. The interviewees mentioned basically the “Tri-Council Policy Statement” «Tri-Council\_Policy\_Statement» (or “Tri-Council rules” «the\_rules\_of\_the\_three\_Councils»), «Good\_Clinical\_Practice» the “Good clinical practices” and by “policies established” «policies\_established» by the institutions (the University, research centres, hospitals), the Civil Code of Quebec and the MSSS Action Plan. Here are some examples:

... the REB functions according to the rules laid down by the Medical Research Council of Canada, or according to the rules of what are known as the three Councils ... (#2)

[our REB functions according to] the rules of the three Councils, Good Clinical Practice and all of that ... (#4)

... the Tri-Council Statement has been the standard we've been trying for two years to bring our operation a little into step with [and] obviously [the Action Plan] of the ministry of Health and Social Services on ethics boards, I would say it's really those two documents that have served as the basis [for the reorganization of the local REB on which this respondent sits] ... (#5)

... there's a well-established policy [that] of the three Councils and the policy of the UofM ... In fact, we use the Tri-Council Policy Statement a lot with respect to the use of human subjects in research, I myself would say that's probably what we use most, we also ... we also have brief excerpts from the Civil Code of Quebec. (#8)

... the main documents ... it's the Policy Statement [of the three Councils] ... that's really what virtually determines what choices we're going to make. And the Action Plan [of the MSSS] for the hospitals, that's extremely important, for the University it's less important because for the University what affects the University is more the appointed boards ... A third document that's important is the document of [Good] Clinical Practice, which is a federal government document but which also represents an international consensus ... You could say that from day to day these are the documents that have the most influence, without excluding in any case the Civil Code, which is an unavoidable base but ... when there are choices to make about how to do a particular thing, these are the documents that you'll ... (#7)

It clearly emerges from all the interviews that the “Tri-Council Policy Statement” «Tri-Council\_Policy\_Statement», or the so-called “rules of the Tri-Council” «rules\_of\_the\_three\_Councils», rank high among the guidelines for reviewing projects. While it is true it has no force of law as such, adherence to this statement is an essential condition for access to the sources of funding of the main granting agencies. In effect,

... it's not a law here, nor is it a regulation, it's a code we're to adhere to ... we're to adhere to it because if we don't, there won't be any money ... any grant ... but there's no risk of being sued ... (#3)

... that [Tri-Council Policy Statement] is the one that enables us to get grants, quite frankly, that's the one that's most important, practically speaking ... And the University of Montreal, for example, and all the hospitals basically have redone their research policies based on this document. (#7)

Several interviewees pointed out, however, the existence of major weaknesses in the normative sources and guidelines available. Some cited the lack of clarity on specific topics that pose problems for the members of REBs. According to one respondent, there are:

... some issues on which ... the main documents ... of the three Councils are vague, unclear ... for example, the appeal of decisions of REBs by researchers who have been turned down ... [nor] do we have a policy for emergencies, for protocol review in emergencies ... (#1)

Others were critical of the “rules of the Tri-Council” «rules\_of\_the\_three\_Councils» for giving the various intervenors who use them a little too much room for interpretation, even of the overly general nature of the guidelines set out. In this regard, three respondents had this to say:

In some respects, I don't find it [the Tri-Council Policy Statement] clear enough ... [and it is] subject to interpretation and therefore to various interpretations. (#4)

... the rules of the three Councils in some respects are very clear, in some respects they're very vague ... there's a lot of room for interpretation ... I don't need broad guidelines to tell me that ideally a research project shouldn't harm the subject, that it should provide as many benefits as possible ... I could have guessed that ... I want to be informed about specific subjects ... there's little specific technical help ... (#3)

... the ethical review now relies on a kind of ... overall moral relativism because if you look at the Tri-Council Statement, at how the ethical principles are stated, it's anything ... so there's no criterion of morality that emerges from it. So it's left up to the individual subjectivity of each member of the ethics board to determine whether it's ethical or not ... (#5)

The discrepancy between theory and practice, or between the perception of those who formulate the guidelines and the needs of those who operate in the context of local REBs, was also raised by several interviewees:

... I am extremely grateful for these broad guidelines, I think they're helpful, but at times you find there's a certain gap, a certain discrepancy between the reality that's happening every day and these broad guidelines, as though they were 6 months behind ... a dissociation between the true reality and then the broad general principles ... [for example] There are people who talk about genetics and who make rules but who aren't involved in it ... who don't see patients with genetic problems ... I think these 3 Councils are doing a good job but I think the ultimate test is the field ... (#2)

[I'd] like there to be a bank [of documentation] ... a place of expertise, a chair ... for getting clear and concrete solutions ... I think it would be good to have that ... there's no place to turn to ... (#3)

The abundance of normative sources or guidelines governing biomedical research ethics does not seem at first glance to be of too much concern to some interviewees. Comments such as the following were rare:

... I've never come across a conflict between the legal standards applicable here and the international standards...[I don't see the abundance of guidelines] as a nuisance. (#1)

I think they're all made in the same spirit. Personally, I don't see a major discrepancy. Between what I see as the main requirements, which in fact are to protect the patient from abuse. (#4)

I think that when I take the various documents I'm familiar with, but I'm no expert on this subject, the documents that I've seen as a member of the FRSQ board always end up being similar. The Helsinki Declaration, the Tokyo Declaration, are in fact documents that clarify the significance or meaning of earlier texts. When I discuss, with the people who are the drafters of the document of the three Councils, the basic principles or broad laws governing ethics, I think the documents all say pretty much the same thing. (#10)

For others, the potential conflicts between different guidelines seem to be resolved according to the source of funding, since:

... if you're doing research projects subsidized by the Americans, it's no longer our guidelines that are important, it's theirs. So you could say the important guidelines depend on the funding agency. (#7)

In contrast, documents whose guidelines have nothing to do with access to funding sources seem, by all appearances, to have far less real impact. In effect,

... the other extremely important documents like the Helsinki Declaration, the international guidelines, the international guidelines of the CIOMS, they're there ... [but] since the Helsinki Declaration doesn't subsidize anyone, nor do the International Guidelines, they're far off in the landscape. (#7)

Another interviewee claimed to manage the abundance of guidelines by retaining the essentials of each:

... basically, that was sort of the job the board did initially, our board, had to do a kind of synthesis or assessment of what was inescapable, if I can use that term, in the various international, national, provincial documents ... Basically, what's ideal is to try and bring together everything that's essential to be able to claim that the standards of each of these authorities are being met. (#10)

Yet it does not always seem possible to achieve such a synthesis and it would seem to be the researchers who pay the cost, since, in a context of abundant regulations, some of which are contradictory:

... the researcher is in a bit of a bind because if the federal government requires that in future, to receive support at the federal level, researchers must comply with our standards which appear in the report of the three Councils. Then after the fact, we're told: be careful, because in the standards of the 3 Councils, there are little subtleties in a few places where these standards contradicted other standards, well, you'll have to make sure you abide by the provincial standards. There's always, in the reports of the three Councils, a concern for the famous Civil Code of Quebec. If a researcher wants to comply with the federal standards, right now, he can't comply with the provincial standards because of the Civil Code. (#10)

For example, it's easier to use certain tissue samples in the rest of Canada, it's easier to do that without having the person's express consent, whereas in Quebec you're still subject to the Civil Code. (#4)

... [moreover] it should be made clear that in Canada there's very little legislation as such [whereas] in Quebec [it's] the Civil Code that has more specific requirements, and the Criminal Code ... (#3)

... there are distinctions that are made [about the regulation of research ethics]. I'm thinking of the federal perspective and the provincial perspective ... (#5)

Even within the province of Quebec, specific conflicts can arise because of the multiplicity of authorities one can turn to when reviewing certain aspects of a given research project. One interviewee gave a concrete example of this:

I can think, for example, of the rules of confidentiality for access to the record, that, that can vary greatly from one institution to the other, and especially, I think we're far stricter in our rules than the Commission de l'accès à l'information du Québec, and there again, as the ethics chairperson, it's very disturbing to be told by a researcher that he can go and find all that out from the Commission d'accès du Québec, get the list of all the patients who have a particular thing ... you, as the ethics board, how is it that you're ... entitled to deny me that when the Commission d'accès, which is a government agency and all that, gives it to me. (#4)

There is, however, no consensus on a possible unification of normative sources in order to resolve the conflicts between contradictory guidelines. Some were opposed to the setting up of "a large centralized structure that imposes things with a large Scientific Committee" «a\_big\_central\_structure\_that\_imposes\_thi» and preferred to see more latitude given to local

“small ethics committee”! **Syntax Error**, «, apparently in a better position to resolve possible conflicts (#2). Others were in favour of the unification of the various guidelines:

Actually, I think ideally they should be unified, that may be a more important consideration for hospital ethics boards that have to review projects that will be submitted, for example, to the NIH, that therefore have to submit to the concerns, that have to meet the American standards. I think it can easily become problematic to find yourself on a board where you have to discuss, where you have to give the board the green light ... So the abundance of standards, on that level, can be a problem. I think efforts are being made to unify ethical standards. (#8)

## D. The Perception of REBs and Their Influence

There was near unanimity among those interviewed that there is a before and an after for researchers' perceptions of REBs. At the time when ethics boards had less power and autonomy and their duties were not clearly defined, being confused with other agencies, researchers do not seem to have had negative attitudes about an ultimately diffuse, rather unstructured and powerless regulatory mechanism. When this situation changed (over the last two to ten years, according to the interviews), a number of researchers began to see the functioning of REBs as a kind of intrusion or interference in their sphere of competence, giving rise, at least in some cases, to a kind of wrestling match between the members of REBs and some researchers. One interviewee recounted that

... a few years ago ... we changed our attitudes and became far more demanding with respect to research protocols and consent information forms and even drafted a guide for researchers ... This stirred a very negative reaction at first among some researchers [the most experienced] **Syntax Error**, «What are these people after? Surely, they won't come and tell me how we research subjects”... They let the secretary back then, two-and-a-half years ago, know their grievances ... We discussed them ... and we decided we wouldn't change, on the contrary, that we would be even more strict and demanding ... (#1)

While according to this interviewee, it was the most experienced researchers who brought some resistance to the rigorous functioning of REBs, other respondents argued the opposite, that it was the youngest researchers who were the most hard-headed:

... there are still young researchers who don't understand us and we have to start over ... I think that has to be said, I think that especially with researchers who do a lot of research, there's no problem. In fact, mostly precisely because they're used to doing a good job, so obviously there are almost no more corrections to be made to their consent form, it's very well prepared and that makes relationships easier ... It's among the inexperienced ... there are residents who don't understand why they have to change all



their consent forms [however] I establish very good relationships with all the senior researchers. (#4)

Others meet with resistance from both some senior researchers seniors and young ones, notably about the relevance or, frankly, utility of the interventions of REBs in research ethics. In the minds of these researchers, good intentions and the contribution to the advancement of science should be enough to guide their scientific research activities. In effect,

Many young researchers, moreover, and other older ones find that this prevents them from doing the good job they'd like to do because, basically, their research is good, they want to help people, to advance science, humanity, health, etc. and then someone comes along and says: no, no, that's not right, you have to do it this way, and a lot of researchers don't understand what this ethics is all about ... (#7)

Nor is it unusual for REBs to be perceived on both sides as a kind of “ethics police” «ethics\_police» that keep watch over all activities of researchers, perhaps to the point of stopping payment of a grant or terminating a research project that does not adhere to certain ethical standards and guidelines.

... the University's new policy gives us powers we didn't used to have and in fact these powers are quite simply that if the study is done using humans and ethics approval isn't obtained, the researchers won't get their money that comes from a granting agency. So we have a certain power that may be repressive to some extent ... [but] it's for a good cause ... (#8)

... last year I met with a team ... of young researchers ... and they all answered in unison the question: What is research ethics? They all answered that it was the police. It doesn't help them ... there's a very negative image, let's say negative, of research ethics ... but I think that's largely because there hasn't been any initiation to research ethics, there's no understanding of its significance ... (#7)

Another theme that recurs often concerning the perceived role of REBs is that of the time that the ethics review of protocols would add to the already cumbersome process of grant applications, and of the many preliminary procedures for starting up research with other hospital and university bureaucracies. Which in “a universe of competition and high standards, [concedes one of the participant] is a little annoying”! **Syntax Error**, « (#7). However, most of the members of REBs interviewed did not support this analysis of the situation, or at least claimed that the current situation is much better in terms of delays due to the ethics review of protocols. In effect,

... for a long time this was perceived as something cumbersome, tiresome, not very useful, that added delays, paperwork ... But that time has changed, it's over ... the researcher simply answers questions ... before, he was asked to re-explain the protocol ... (#2)

This same interviewee did not hesitate to say that if anyone is responsible for additional delays as a result of the ethics review process, it is the researchers themselves. For,

... the researchers are responsible for the delays because of neglect ... [for example] they haven't written the consent form properly ... they haven't signed all the forms ... in general, it's the researchers' fault if there's a delay ... (#2)

Another respondent who maintained having undertaken consultations with representatives of pharmaceutical companies, reported that these companies hold researchers primarily responsible for delays in the review of protocols.

To our great astonishment, they [the representatives of pharmaceutical companies] told us that in delays ... especially in Quebec, with ethics boards, it's not the board that's responsible. In most cases, it's the researcher. The one who runs the project, who doesn't manage the process properly, who's late submitting the project, who doesn't submit it in acceptable forms, who gives a disorganized, poorly written, badly structured presentation that the ethics boards find difficult to follow. (#10)

Most of the interviewees admitted, however, that the impression researchers have today of REBs has greatly improved after an initial period of some turbulence. The gradual acceptance of the role of REBs in the protocol review process and the changes that seem to be taking place at the level of research ethics practices seem to have helped shape a new image of REBs. Here are some examples of this evolution:

... now the attitude of researchers has apparently become more favourable ... they thank us ... they tell us they always learn something when they come to see us ... we aren't nitpicking, we're trying to protect the subjects ... they've understood that ... (#1)

... as the years go by it's getting easier because this researcher in particular understands ... I think we've made a lot of progress and that the more they understand the reasons behind certain rules, the more they agree they're obvious and have to be applied. (#4)

In five years, I can really see a difference. On the one hand, because it's been made clear to us what's expected, and there have been meetings with the researchers, usually once a year ... (#5)

... they [the researchers] are grateful ... (#3)

While the attitude of understanding, even gratitude, on the part of many researchers vis-à-vis the role of REBs seems increasingly widespread, or at least on the way there according to most interviewees, the fact remains that some researchers still refuse to accept the “interference”«interference» of REB interventions, which they still see as a bureaucratic impediment to the advancement of science. In effect,

... there are still a few implacable ones, we have our share like anyone ... who think that the only criterion should be the advancement of research and that [what we're creating] is a dog's breakfast and that the laws are badly made and it's all foolishness ... but that's the exception ... (#3)

... [they see REBs] as a necessary evil. As a terrible evil. They hate us, I believe ... [they think our role] is just to coddle or nitpick. I think ... I hope ... it's mostly out of ignorance ... (#4)

We're a nuisance, that's clear ... [in our institution], we have a reputation for being very strict, for being difficult, we don't approve just any protocol. (#5)

Most interviewees also believed that, aside from the acceptance—more or less resigned or grateful as the case may be—of the requirements governing research ethics imposed by REBs, there is a real impact on research practices in terms of the education of researchers. The pedagogical impact of REBs is described in these terms:

... they [researchers] end up realizing the importance of certain precautions and procedures and after they take the initiative ... there was a time when we received documents that had to be completely redone from A to Z. It was dreadful. Whereas today we generally receive things we can find little fault with ... researchers have changed a lot ... yes, it's rooted in the practices now ... (#1)

... there's education within this process. They [the researchers] know what parameters are important to us, and so I'm convinced there's a kind of education vis-à-vis researchers ... (#8)

In some hospitals, researchers have at their disposal ad hoc guides for writing research protocols to enable them to better meet the requirements of REBs. In these circumstances, it may then become awkward for the researcher not to comply, since he has been given explicit, detailed instructions. In effect,

... a year and a half ago we came up with a form entitled "verification and attestation"! **Syntax Error**, « which seems very helpful for writing protocols, [now] it accompanies every protocol, so it becomes very awkward to submit a protocol and sign it and then not have it comply with what is written ... (#1)

...before ... evaluators were given a guide that provided some guidance ... the criteria to be considered when applying to a REB for a review ... these documents are still used sometimes, they're given to researchers to help them prepare the application to the REB ... (#8)

Another interviewee felt that the influence of the ethics standards and guidelines promoted by, among others, the members of REBs on research practices is becoming inevitable, firstly, out of constraint. Secondly, researchers are gradually "sensitized" «becoming\_sensitized» to the need to comply with certain standards of research ethics.

... it's that since all research activity must be declared and all research activity must be approved by an ethics board, the norms and standards that will be established in our research centres will become a little constraining, just like the norms and standards we apply when doing the scientific review of projects, it's something that's very constraining and that researchers in the research community can't avoid ... But once they're made aware, because that's one of the objectives of our board, to educate in quotation marks [less constraint will be needed]... (#10)

Another respondent did not seem very convinced of the real ability of REBs to constrain the activities of researchers. He recalled that RBCs are often made up of volunteers, which would lay bare a lack of concrete support on the part of administrators and granting agencies. In fact, according to this respondent,

... basically, ethics boards that aren't very very strong entities, I must say there isn't a lot of support for them, even if it's mandatory to have them. They're people who are, for the most part, volunteers, who do that in addition to their job ... You see they ... find themselves in difficult positions. So I find they're not adequately supported by administrations, whether by their own administrations in the setting or by the granting agencies. (#7)

On the other hand, when it comes, for example, to support from BDs of the sometimes difficult decisions taken by local REBs, those interviewed seemed to be far more satisfied (#4) (#2).

Finally, despite the tools researchers seem to have and the progress made in “their education” «educating\_them» about research ethics, there are still problems with the writing of protocols, which means that, in some cases, approval by REBs is not at all an automatic process.

In fact, it's fairly unusual to grant ethics approval the first time around, it's fairly unusual. The application has to be very very well-structured ... The vast majority of files require a response to our comments and changes to the consent form ... but it [also] happens that no ethics approval is granted ... (#8).

## E. Effectiveness of the Review Process

Not all interviewees gave the question about the effectiveness of the ethics review of research projects the same interpretation. Some of them referred first to the effectiveness of REBs in achieving the overall ethical objectives set by the guidelines and norms mentioned earlier (protection of subjects, acceptable risk-benefit ratio, good clinical practice, etc.). Others

referred first to the effectiveness of the functioning of REBs in processing research protocols within reasonable time periods that do not hamper the activity of researchers. Both, however, felt that REBs are generally fairly effective in both regards, considering the limited resources available to them (#2). The competence and diverse fields of training of REB members were sometimes presented as a variable determining the effectiveness of the review. Here are several accounts of interviewees:

... with the means we have ... I find we're quite good [notably compared to what was done in the past in terms of review] ... we deliver the goods, but only just ... (#3)

It [the review process] is effective, I would say clearly ... (#1)

... I find that ... honestly we're doing a very good job ... I think that ... when I look at it I'm quite proud of the work we've done. (#5)

It is as effective as the board members ... I think it's reasonably effective, I think I know the members and I think we do our job as conscientiously as possible ... (#4).

I think a number of measures [used by the REBs] ... are effective. (#7)

I think it's fairly [effective] I think it's fairly good because in fact we have the opportunity to have experts come from five different units, who have varied experience in research and also ... people with training in law, people with training in ethics, and I think that all of that together, that all these ideas put together, all these people reading the problem, I think it's evidence, let's say, of the effort and competence of the ethics board. (#8)

Lack of resources was mentioned by almost everyone as one of the threats hovering over the quality and effectiveness of the review of research projects within a reasonable time. In fact, mention was often made of

... the excessive workload, far too many projects to analyse, meetings should be held more often, but we can't ask much more of the volunteers ... (#3)

... if you wanted it to be even more effective, you would need, for example, an office, maybe not five days a week, but to have more resources ... with our clerical staff one day a week it's hard, let's say you'd almost have to add a second day. (#8)

... ethics isn't something that hampers research, but we must make sure, too, that it will be done effectively and that it won't become an impediment to the reasonable advancement of research projects ... the problem right now is that ethics boards carry out only part of their overall responsibilities, and it's not out of lack of willingness, or even ignorance, it's a question of resources ... (#10).

Improving the effectiveness of REBs is not, however, only a “question of means” «question\_of\_resources». Several interviewees felt that the training of researchers to better prepare them to meet the requirements of REBs, and possibly requests to modify research protocols, also ensures the effectiveness of the review. These interviewees argued that

... the first thing should really be for all researchers to have basic training in ethics so they can provide us with relevant information. (#4)

... there should be more clerical support for researchers ... they don't have the skills to change a consent form quickly ... (#2)

... there should be more communication with researchers ... (#3)

At least in the minds of the interviewees, the main drawback in the research project review process is without a doubt the non-existence of active follow-up once the research protocol is approved. REBs must in fact make do with the information willingly provided by the researchers themselves:

... there is a kind of passive follow-up, that is, follow-up that's driven by the researcher himself ... we require him to provide an annual report ... they're supposed to submit any change in the protocol to us ... to have sub-studies approved ... but we're driven by the researcher. (#3)

... the researcher is asked, is given the form [for] telling us as soon as there's a problem or a new circumstance arises during his research project ... he's asked to let us know. Now, along with that, we contact him a year after he's given the ethics approval ... (#8).

... for two years now, we've been asking researchers on completion of the research to complete a brief report, a short questionnaire, a few small questions ... it's ... really ... more to force the researcher to notify us that the research is finished, and possibly to see if there are ethical problems the researcher may have forgotten to mention ... (#5)

... it might be much better to be able to have constant monitoring ... because it's fairly passive ... we don't really have the resources to be effective after the fact ... (#1)

... there are things, obviously, that can escape us, especially if they aren't even mentioned. (#4)

Among the ethics problems that can «escape» the control of REBs, some do because of a deliberate action on the part of researchers, and others because of the researchers' lack of training or information. Occasionally, some researchers omit certain aspects of the research, important in the eyes of REB members, from the research protocol, thinking them not worth mentioning. For example,

... one researcher informed us of problems that had arisen twelve months later ... once the protocol had expired ... (#1)

... once, by chance, in talking with the researcher, it was discovered that in fact the patients would be hospitalized for 24 hours, which was mentioned nowhere ... so that's something we found out, there can be things you don't find out ... (#4).

While there was no doubt in the minds of the interviewees as to the need to do effective follow-up, there was no consensus as to the concrete means of achieving that end. According to one respondent:

... a big document was produced [on follow-up], which is very difficult ... there are two concepts of follow-up [active and passive] ... [But] What is the actual ability to do serious follow-up of a research project in their setting?... There's no consensus on how to go about it. (#7)

This interviewee added that the local REBs have neither the training nor the time to attend to active project follow-up, even though, according to the guidelines in effect, it is their responsibility to do so.

So if you look now in the context of the Tri-Council Policy Statement, and the ministerial Action Plan, it's the ethics boards that are responsible for doing follow-up ... [But] I don't think they have the capacity to really do rigorous active follow-up. The members of these boards are people who are already overburdened. (#7)

The respondents nevertheless made several suggestions. According to some, given the real impossibility of doing continuous monitoring, a visiting board should be set up that would visit the different centres and laboratories (#1). Others thought that follow-up should be done according to the nature of the research project, since

... it is important to understand the type of protocol you have and then to understand the type of follow-up that should be done ... [you have to] try and establish levels of priority, that is to say, for many protocols we might think follow-up is important, while for others we aren't going to be the watchdog insofar as our ethics review doesn't turn up *a priori* any ethical problems. So we've said to ourselves, it's important to put the emphasis on a protocol considered risky rather than do broad [follow-up], because we have neither the resources nor the time. (#5)

... where the risk is low, minor follow-up [and] where the risk is high, extensive follow-up ... (#9).

Follow-up “by sampling”«by\_sampling» (#1) seems to have the advantage of acting as a deterrent on the community of researchers as a whole. One interviewee in fact said that:

For it to be effective, I think perhaps mechanisms should be adopted that will ensure that not necessarily all research activities will be checked, that not necessary all research projects will be checked, but that people are informed that any research project could be evaluated, and I think that's already one way of making sure people respect the limits. (#10)

Finally, some suggested creating an ad hoc structure of professionals specialized in doing active follow-up.

... follow-up should be linked by teams that are a little more qualified, made up of people who are a little better trained in the area ... I think that the CLERUM [of which the respondent is a member] could create a pool of people qualified to do this work ... I think that most centres that have stated their position to their research ethics board [on the topic of follow-up] have proven very interested (#7).

Whatever form follow-up takes in practice, some interviewees were sure that the establishment of a follow-up mechanism is not only a necessary trend, but also inevitable given the increasingly complex ethical issues that biomedical research entails today.

At first, they [the research centres] were against follow-up, but I think that, now, the people who have worked since last year on the CLERUM have realized, first of all, that follow-up was becoming inevitable. (#7)

For me, evaluation in the centres, ethics operations that will even go into the field, in what would be called follow-up, is something that's needed. (#10)

... we're [already] considering in the medium term doing active follow-up ... in the field ... (#3)

## F. Multi-centre Research and Globalization

When research protocols are submitted to the REBs of several institutions in the context of multi-centre research, each local REB does its own review that disregards the **Syntax Error**, «ethics certificates» obtained elsewhere (#1) (#2) (#3) (#8). While it seems each multi-centre project is reviewed by each local REB “as if they were not multi-centered” **Syntax Error**, «(#1), this does not mean the inclusion of a favourable review in the file to undergo a further viewed will not occasionally be “well considered” «viewed\_favourably» by the evaluators. Let us hear what one respondent had to say:

... I think it's important to do a review anyway, and of course if a researcher has obtained ethics approval from other institutions it's a good idea to include it in the application, that is, it's a little more, if I can say, if it's included in the application. (#8)

In some cases, a separate local review of multi-centre projects is done pursuant to an internal by-law, for example in the case of the CHUM (#3). In other cases, different reasons are given to justify the additional review of a research project approved elsewhere. These reasons include, firstly, the “obligation” «obligation» to keep the staff at the local centre where part of the research will be done informed, and the “obligation” «obligation» to protect research subjects recruited locally. One interviewee argued that it is necessary to ensure that:



... the doctors, nurses, etc. ... know ... there's the obligation to know exactly what is happening within the hospital ... [and also] there's the obligation to protect our patients with full knowledge of the facts ... (#2)

Another reason for the additional review of a multi-centre research project that often came up in the interviews is the existence of review criteria adapted to the local culture of each REB. In fact, it seems that:

... not all REBs are equal, there are some that take perhaps a closer look than others ... that don't have the same composition ... [in fact] ... at least 3% of the forms already approved elsewhere are changed ... (#2)

The varying criteria of Canadian agencies on the one hand, and of American granting agencies and the pharmaceutical industry on the other, were pointed out by one interviewee who felt the former were more concerned about protecting patients/subjects and the latter more concerned about the legal technicalities.

... we have a great many multi-centre projects that are funded either by the pharmaceutical industry or by American granting agencies ... these agencies are very fussy [even, in some respects] extreme, sometimes they ask us to have a plenary committee approve utterly insignificant changes, which makes no sense at all ... Canadians [seem more inclined to examine issues that are] more fundamental ... (#3)

However, another interviewee who participated in a survey by the MSSS to assess the functioning of ethics boards in Quebec thought that:

... deep down, if you will, from the survey I did at the ministry I would have to say that a majority of research ethics boards are either «oversight» committees or quibble over consent forms, so over form, they don't tackle the real ethical problems ... (#5)

In some cases at least, the divergence of evaluation criteria can run far deeper, to the point of being construed as laxness or negligence. In fact, one respondent said that:

... sometimes we have in our hands documents from somewhere else ... forms telling us it's been approved at a particular hospital ... and our hairs stand on end ... we say to ourselves ... they approved [it] without reading ... (#1)

Another interviewee stressed the split that seems to exist between the approaches of researchers and evaluators who are anglophone (or with an anglophone institution) and those who are francophone, in these terms:

... some important projects have been blocked [one in cardiology, another in anesthesia, a third in neurology, etc. ] ... and [in the case of] some of these projects ... we learned through the grapevine ... other anglophone researchers go ahead with the approval of the ethics board [of their hospitals]. (#3)

The same interviewee who spoke with an anglophone evaluator to find out the reasons why this happened reported the gist of the exchange:

[the evaluator said that] this particular section of the act didn't hold up and in any case it was going to be changed, and that the government was about to make an amendment and in the meantime he approved it ... it's a very Anglo-Saxon way [the interviewee continued] of settling the case ... (#3)

The same respondent, however, gave the example of a project for the treatment of breast cancer which had been favourably reviewed by a hospital in the francophone system, but had been rejected by the REB the respondent sits on “since the risk-benefit ratio was not correct”! **Syntax Error**, « (#3). And another member of an REB at a hospital in the francophone system played down the differences in ethics review criteria between francophone and anglophone institutions, as the latter “have the same questions and objections”! **Syntax Error**, « as their francophone counterparts (#4).

Though more the exception, certain forms of blackmail are used by some researchers whose projects have previously been reviewed and approved by the REBs of another research centre or hospital. In effect,

... we refuse to be told ... since it's already happened, well ... a particular hospital approved it, I don't see why you would be fussier than them ... It's a kind of blackmail we don't give in to ... there's been [in the past] blackmail [on the part of some researchers] when there are multi-centre protocols ... (#1).

... often we don't know that it [the protocol] has been approved by another hospital. Unless the researcher tells us to try and put pressure on, I think there isn't a lot [of that]. Very seldom ... (#4).

The review of the protocol by each centre involved in the multi-centre research sometimes seems to put the researcher in an uncomfortable position, since he must adapt his conduct, at least in some cases, to different, even conflicting, recommendations. According to one interviewee,

... the boards don't necessarily have the same view of the project, in the end the researcher finds himself with recommendations that will at times even be contradictory. And they often find themselves with forms that vary from one centre to another. In fact, it's a complication at the management and logistical level [...] They actually find themselves, in extreme cases, with two consent forms to be signed by the same subject

in a given site. One form for his university, and another for the site. Well, those, I think, are extreme cases we would want to try and avoid. (#10)

The interviewee suggested looking at solutions that have proven somewhat effective elsewhere (in other provinces or in some pharmaceutical companies) to correct such situations. It seems that:

... in British Columbia, for example, they have adopted ... what they call templates, especially for the consent form, but even for the presentation of protocols, too. The pharmaceutical companies and researchers use these templates and it simplifies the operations of the boards because it always comes somewhat in the same format, the same information is found in the same place and that makes it possible, let's say, to be able to process it more efficiently, that also makes it possible to avoid having to rewrite the clauses because the ethics boards, generally, when they have suggestions or changes to make, 9 times out of 10 it's in the consent forms [...] apparently that makes it possible to simplify operations and to have forms that are a little more standard, in any case that, for a given project, are the same even if there are more than one. (#10)

While centralizing projects are not approved unanimously (#2), one of the interviewees suggested setting up an ad hoc board to resolve conflicts related to multi-centre research projects.

... the long-term goal would be to have a somewhat central ethics board for multi-centre projects ... I think the advantage of a national ethics board, especially if it has been divided into several specialties or several very specific disciplines, [is that it] might have access to experts who are even more abreast of that and in this sense it could be valuable. It would also be more independent of pressure groups ... (#4)

Most of the respondents did seem overly concerned, however, about the current trend towards the international harmonization of research ethics standards and guidelines. A number of them had given no thought to this subject (#1). Others saw it not only as an inevitable process, but also as having very positive aspects, such as greater protection for research subjects in countries where there are no effective, even reliable, control mechanisms, and the changes taking place in terms of the quality of the information provided by the pharmaceutical companies. In effect,

[the trend towards the harmonization of research ethics standards] I think that's good ... it's inevitable ... I see it as a certain system of protection ... (#2)

[the trends towards the harmonization of research ethics standards] ... it's not negative in itself. Because research is increasingly multi-centre and multi-country ... I think it [harmonization] is fine for the rules on the whole to be similar, because it's intolerable to be allowed to do anything at all in Zaire and to not be able to do it here. There's no reason why less affluent communities should undergo off-the-wall, let's say, interventions than in our Western societies. (#3)

I think it [harmonization] is excellent because I've seen, for example with pharmaceutical companies, the presentation of projects, the information provided in ten years has improved noticeably. (#4)

In the opinion of another respondent, the harmonization of standards and guidelines would also make the job of researchers and evaluators easier:

On the one hand, I think it would probably make life easier for researchers, it would probably make life easier for the people who have responsibilities on ethics boards and I think it would be desirable ... I hope it can work and I imagine it's the industrialized countries or the more developed countries that will become the advocates ... to promote this cause. (#8)

But the question of which Western country will play the leadership role prompted some reservations among a number of respondents, notably about the possibility that less powerful countries would have less room for discussion and to manoeuvre.

... I have the impression it will be the United States because the research budgets are the largest ... (#3)

... I have the impression it's with the United States that there may well be conflicts ... (#1)

All I hope is that ... it isn't the wealth of some or the power of some that will win out, but that there truly is room for discussion and debate. (#7)

One respondent thought that the process of harmonizing the standards and guidelines is in keeping with a logic of power and profit-seeking imposed by transnational companies and the West in general. In effect,

... I try to show precisely that standardization and globalization is a way for the transnational companies ... to ultimately impose certain ways of doing science and scientific technique under cover of a rhetoric of social utility ... I'm not talking only about the pharmaceutical companies, I'm talking about the West versus the other countries, I mean it's a whole logic when you're talking about globalization, it's the whole planet, so you have to be clear that this maximization of utility doesn't benefit only a very few ... (#5)

Other fears about the process of the globalization of research ethics standards are the increase in the amount of information, and the inability of the poorest countries to implement the regulations proposed by supranational agencies. In effect,

There's almost too much information, globalization can pose this problem because when you're able to approve a side effect or be informed of a side effect ... that occurred in Spain, you don't know the treatment conditions, what do I do? ... Fine, I became aware of it and the usefulness I see in becoming aware of it ... is simply to see if it was done at risk just once, you don't have too much to worry about, if you see it happen two or three times, then, since you have a global view, you can start to worry ... It also makes it a lot

harder to interpret what's going on ... every week we get... [information from everywhere out there] and it makes for a lot more work. (#4)

There's just one small thing I question: will it be possible to apply these standards the same way in the case of countries, of researchers or populations in less developed countries? That's the only thing I question. (#8)

## G. REBs and the Pharmaceutical Companies

The relations between REBs and the pharmaceutical companies were described by a number of respondents as being generally fairly good (notably #10). However, positive and negative aspects of these relationships emerged from the interviews as a whole. First of all, the interviewees noted generally the increased funding from pharmaceutical companies for many research projects being done in hospitals, research centres and universities. One of the interviewees said that:

... we have a lot of multi-centre projects that are funded either by the pharmaceutical industry or by American granting agencies ... (#3)

When talking about funding for research projects by pharmaceutical companies, often no mention was made of the public sector's contribution to private research, which not only translates into better care for the population, but also into bigger profits for the pharmaceutical industry. In fact, there is also public funding for private research, if only at the level of giving pharmaceutical companies access to public institutions (hospitals, research centres, universities), their staff (researchers, support staff), even the public (research subjects). In this regard, one MSSS official explained that

... there is a public-sector contribution ... to the private sector ... if only in that researchers who work in partnership with pharmaceutical companies often use the facilities of the [public] institution ... (#9)

The participation of representatives of pharmaceutical companies on some ethics boards is seen as an asset, notably because of their expertise and strictness on the one hand, and the existence of certain goals common to researchers and the pharmaceutical industry on the other. According to two interviewees:

[the representative of the pharmaceutical community sitting on the board] had a responsibility as manager of research projects to ensure that projects were carried out according to *Good Clinical Practice* ... he had a good knowledge of the standards, of Canadian, Quebec laws, of international norms, treaties and agreements governing

clinical research ... [and later the respondent went on to say that] the board of the FRSQ, basically, is interested in having the enlightenment of these people, their perceptions of the difficulties and accomplishments, basically, in the field of ethics because ideally, what everyone wants, it's so for the pharmaceutical companies, it's so for the researchers, is to eventually have, at the level of the ethics board, effective management that ... will ensure that ethics isn't an obstacle to the development and advancement of research. (#10)

Although we don't always agree with the philosophy of the pharmaceutical companies, we find they're much stricter than our ethics boards and people will tell you that. (#7)

In return, it seems that the representatives of pharmaceutical companies can also be somewhat influenced by the discussions that take place within the context of REBs “since [explained a participant] we want to sensitize them to social problems as perceived by the subject”!Syntax Error, « (#10).

Another controversial issue is the excessive waiting periods for research protocols funded or co-funded by pharmaceutical companies. According to the provincial government official interviewed as part of this study, the representatives of these companies complain regularly of the delays caused by the review process. He claimed “I prefer to live in a country where the constraint is ethics rather than a country where the constraint is corruption” (#9). Another side of the story is provided by a respondent who claims he held a consultation with representatives of pharmaceutical companies. This respondent claimed that “to our amazement” «much\_to\_our\_surprise», it is not the REBs that are held responsible for delays, but “in the majority of cases it is the researcher”!Syntax Error, « who is fingered by the representatives of pharmaceutical companies (#10).

Still, the representatives of pharmaceutical companies would like to see in Quebec some standardization in the presentation of research protocols (#2). For example,

... to have a guideline ... that would say: in future, pharmaceutical companies presenting a project in Quebec must use the following form, the following form so that when a board meets, it knows where to find the researcher's c.v., the protocol, the sample size ... and there's a pattern that's imposed and that there's, let's say, a kind of consent form that would be somewhat standardized ... (#10)

Another problem experienced by the members of REBs is that of «phony» research that does not pursue scientific objectives, but purely commercial objectives, such as when certain pharmaceutical companies propose doing research that is going on elsewhere for better market recognition or, quite simply, for publicity. According to one interviewee, these practices seem to be “systematically rejected” «systematically\_rejected» (#2). Similarly, another member of a hospital REB reported turning down research protocols

... aimed at marketing a product [or] promoting a drug whose effectiveness is proven but they simply want to show it's better than another one ... (#1)

In some institutions, however, research for promotional purposes seems to have its place. In fact, one respondent said that

... there were drug trials, but no phase 3 clinical trials, rather there were promotional phases, phases where the drug was already on the market ... (#5)

The final sore point between the evaluators on REBs and the representatives of pharmaceutical companies that emerged from the interviews, is the inclusion with research protocols of forms or clauses that violate the provisions of the Civil Code of Quebec, notably those limiting the legal liability of institutions, companies or researchers. In fact, some companies

... include on the form phrases about their liability in the event of accident, bodily harm ... whose effect is to deter the subject [from suing the company], for example, *no other compensation will be available* ... we reject these phrases ... [even if] it's pointed out to us that a particular hospital has signed it ... [but in Quebec] under the Civil Code [which states] you can't limit or exclude personal liability, such phrases are worthless ... (#1)

... we don't allow forms ready-made by the pharmaceutical companies ... the consent form is the responsibility of the researcher and of the institution ... (#2).

[phrases such as] I promise not to sue the company, or something like that. For us here in Quebec that wording isn't acceptable. When the protocol is drafted in New York or Amsterdam, often it's a version that will contain elements of that nature. Inevitably, the ethics board says: we can't accept this form. (#10)

One of the interviewees cited the case of a study that was not done in Quebec because of the provisions of the Civil Code of Quebec, **Syntax Error**, «“but most of the time [he claims] things go very well with the pharmaceutical companies” (#2).

## IV. FREE AND INFORMED CONSENT: OF THE INDIVIDUAL, SOCIETY AND COMMUNITIES

### A. Limits of Individual Consent

The question of the consent of subjects to participate in biomedical research raises many issues that cannot be resolved merely through the technical elaboration of the form they

are to sign, however carefully drafted it might be. In some circumstances, and for certain categories of people, psychological, axiological, social and cultural constraints and/or characteristics may limit the free will the subjects have, theoretically, to agree or refuse to take part in a study, and introduce an element of bias as to the truly informed nature of the consent.

One of the interviewees raised the problem of the limits of free choice in the case of elderly people who have a relationship of dependency with certain members of the care staff, or who feel insecure because of their advanced age or their uncertain state of health. These people

... are anxious to have the caregivers remain close to them, don't want to lose them, are always insecure about what will happen to them. If it's their doctor who presents a research project to them, basically, the doctor has special requirements because these people are possibly at greater risk of readily giving consent so as not to lose the doctor. We've seen a lot of things. The same goes for nurses or people who work in the home, who go to the home, visiting nurses for example, because there's a fear of losing the support of these people if they don't consent. So there's no informed consent ... at least there may be informed consent, but it's not very free. (#7)

One respondent analyzed the various ways of obtaining “free and informed”! **Syntax Error**, « consent from the research subject. There seem to be roughly two schools: the first stresses the importance of the exhaustive and detailed description of the characteristics and risks of the research; the second is based on the bond of trust that exists between the sujet/patient and the caregiver responsible for giving them (in understandable form) the relevant information. In effect,

... one school ... wants the consent form to be very explicit, wants a document to be provided that can at times be quite lengthy, consent forms of 10, 12, 15 pages in which all the potential risks are identified, and an attempt made to describe them. And then there's another school that says basically, I think we could perhaps confine ourselves to making a kind of list, as exhaustive as possible, saying: if you have concerns or questions about these elements, don't hesitate to ask the person who is having you sign, if that person is able and qualified to answer all your questions. In other words, one school that says everything has to be put on paper, another school that says you can put a bit of trust in the caregiver who's going to have the form signed, assuming it's someone who would be able to inform, because we're talking about informed consent, to inform the patient. (#10)

The interviewee felt that the second solution is ultimately more realistic than the first because it is likely to take into account the specific context of the consent, which may cause discomfort for or intimidate the subject. Here is what he said:

I myself would be more of the school that puts a bit of trust in the caregivers, because my feeling, and this has often been confirmed to me by people who have told me so, when



you present a consent form that's 12, 15 pages long in a context, let's say, where the person is uncomfortable because they have some illness and you're explaining to them, because it's a word they aren't familiar with, what a placebo is and a randomized clinical trial, and you really don't want to give them a course in epidemiology and you give them a basic lesson on the risks associated with an intervention in a context of a disease like diabetes or oxygen therapy ... people say to me: I signed without asking. (#10)

Another tricky problem is that of the legitimacy of individual consent in the case of research that could potentially affect a whole community that has not been consulted on the matter. At least three interviewees had difficulty right away grasping this problem when asked explicitly about the conflict between individual consent and collective consent (#1) (#2) (#4). One of them set about elaborating on the notion of free and informed consent while giving assurances that “we do nothing without the consent of the subject, or those who have the authority of the subject”! **Syntax Error**, « (#1). The second respondent thought about the question in these terms: “I think we still live in an altruistic society where people like to do things for others” (#2). A third informer said that individual consent always takes precedence, but one always acts on the basis of “the concept of minimal risk, than we try to follow the guidelines which say that the potential benefits must always be greater than the risks”! **Syntax Error**, «. He went on to say that “[if] the risk was completely out of proportion to the possible benefit, than clearly it was not acceptable.” (#4)

When the problem was clearly understood, it was conceded that there are no global or ready-made solutions (#10) (#7) (#3) (#5). One of the interviewees acknowledged that this problem is one of the most complex and fundamental dilemmas facing research ethics (#10). Moreover, the conflicts between individual consent and collective consent seem all the more difficult to raise, as the dominant North American bioethics discourse is centred on respect for the rights of the individual subject. In fact,

... it's the wilderness of ethics thinking. And I don't understand why anthropologists aren't more interested in this issue, because it forces us to rethink the reverse, that is, the limit of individual consent, of the individual subject. There needs to be a rethinking of ante-modern (sic) logic, that is, the familial, tribal reality, ... there's nothing, there's nothing. And for me, that's fundamental. Because I assure you, from having ... done follow-up, I've seen patient records and I've seen information on whole families ... [and] the people don't know that their sister-in-law or their cousin told the story of their life with an illness and the deaths, the legitimate and illegitimate children, that's family histories ... On what authority? To search out a gene ... There are rules of ethics involved, confidentiality, respect for the individual subject ... I mean that the practice completely contradicts the rules of ethics ... this touches precisely on the antithesis of the whole American bioethics discourse that is based on the consent of the individual. (#5)

Another respondent suggested that “the political, spiritual, or “in any case the natural leaders”!**Syntax Error**, « of the collectivities concerned be consulted before going ahead and recruiting subjects, to discuss what is at stake in the study (#3). This is not to ignore the fact that, often, several collectivities are affected by a given project, and it is not always easy to identify the “natural leaders”«natural\_leaders» or the spokespersons. For example, this respondent said that it seems easier to identify and consult the representatives of a community of “Jews of a particular sect”«Jews,\_of\_a\_given\_religious\_faith» than those of the community of “Chicoutimi-Lac-St-Jean”!**Syntax Error**, «. (#3)

Another interviewee felt that this should not be limited to cases of cultural communities, but that the “milieu”«environment» on which the research may have a particular impact should also be taken into account. He thought that:

... on ethics boards there should be people who have a good knowledge of their environment. The environments where the research is going to be done, not just about the knowledge of the individuals ... If you're doing research about underprivileged communities, or ... in tougher schools or if you're doing research, for example, about diseases or situations that affect mostly women, for example breast cancer, in all these situations it can be said [that] objectively it seems ... quite alright, but there are collectivities there, there are communities at stake. (#7)

One of the solutions proposed is the mandatory inclusion of some form of consultation with the communities or collectivities or groups concerned. In this regard,

... should there not be, when you have a project that affects more targeted categories of people, mandatory consultation with the people of these boards to really make sure that this project respects, takes into account and is going to serve this community? ... [we should] consult ... members of these communities and not just people who study these communities. (#7)

Despite the solutions proposed by the interviewees who broached the topic of the conflict between individual consent and collective consent, they seemed to be aware of the fact that, in complex cases where multiple interests are at stake, ethics as a discipline cannot avoid taking a decision at some point, by examining and adapting to the characteristics and the variables of each particular case. There seems to be, in such cases:

... a kind of dilemma that may not be easy to resolve generally, but I think that's the genius of ethics, it's that a decision that's taken in a specific context, on a specific project, in a specific environment, at a specific time and that the same project in another context, in another environment, in another culture, would not necessarily result in the same decision ... So basically the response of an ethics board can't be universal. It is somewhere, in a given place, at a given time, in a given community. (#10)

## B. Cultural Differences

One of the dilemmas the members of REBs occasionally face is that of obtaining! **Syntax Error**, « “free and informed” consent from people belonging to cultural communities whose values differ significantly from those of the host society. Two broad themes captured the interviewees' attention when discussing the topic of cultural differences: the inability of the prospective research subject to speak at least one official language, and the diverse values of the subjects who are recruited. In the first case, two opposing views clash when it comes time to decide whether or not to recruit subjects who speak neither English nor French. Some feel it is alright to go ahead with the recruitment if you have:

... at the minimum, a full translation of the form in the person's language, that could be provided, for example, on cassette tape ... but this person must be able in this way to refer, if not to a text, at least to a [recording] ... (#4).

... some people [of the REB] advocate bringing in an interpreter to interpret everything ... and recording that ... (#3)

[when] we found ourselves with someone was hospitalized and a first-generation immigrant and who ultimately had learned little or no English or French, we usually used a translator, that's something at the hospital that's used ... (#5)

A physician sitting on the same REB as the previous interviewee felt that a prospective subject should not be recruited if he cannot make himself understood or understand the characteristics of the proposed project. In effect,

... when there's someone who doesn't speak French or English ... and I know they can't understand me and I can't understand, I don't enrol them, period ... (#3)

This physician explained that even if the interpreter properly translates the consent form on paper or cassette tape, he probably will not be at the subject's side through all phases of the research, which the subject must understand as it progresses and at all times, in order for the requirements of the protocol approved by the REB to be met. The same problem arises when an emergency occurs during research, in the face of which the subject who speaks neither French nor English is utterly defenceless. For these reasons, the translation of the consent form is not always an adequate guarantee that the protocol will be respected and that the consent will be informed (#3).

The interviewees who broached the topic of the linguistic difference seemed aware of the fact that all solutions proposed in the context of REB discussions involve controversial aspects, ranging from the introduction of a form of systematic language-based discrimination to tolerance of some uncertainty as to the truly informed nature of the subject's consent. In the case of a subject who must go through an intermediary in order to understand the nature of the research in which he will be participating, another respondent expressed a view on the non-recruitment of the subject, citing the subject's protection. In effect,

... researchers, they won't enrol a subject if they have to go through the son to get him to understand, I think they still also have a very lofty sense of their responsibilities and often [it's not possible to respond] to an emergency this way, if it's necessary to go through an intermediary. So of course we don't try to discriminate on the basis of language, but rather it's discrimination on the basis of consent ... to be sure they have clearly understood. (#4)

The problem of different values proves even more tricky and delicate than that of linguistic difference, although the two are often related. The study of each case ("the case by case approach") seems to be the preferred approach of most interviewees when there is a concern to protect the individual subjects and the communities concerned, but also to not subject them to any form of discrimination (#1) (#3) (#4) (#7) (#8) (#10). Three of the respondents cited the importance of respecting cultural differences in these terms:

... there has to be a certain respect for the community ... you can't offend the customs or traditions of that community ... because you can easily sink into ... clichés or value judgments. [Moreover] the people who agree to be the subject of an experiment do so in good faith, they're told that their rights will be respected, that their integrity will be respected, you have to do it and sometimes if they have traditions that are different you mustn't shake them up, you have to take these factors into account in the project review. (#8)

... if you aren't sensitive to these communities, if you do research on natives too, if there's no sensitivity towards these communities, the project will be passed over. (#7)

... we've had a lot of discussions on that issue ... on just how to respect the cultural difference ... We've had very interesting discussions and then basically what came of it was that we should try in all cases to be as attuned as possible to the cultural differences ... (#5)

It was occasionally commented that the members of REBs in the francophone community face the dilemmas posed by multiculturalism less often than those in the anglophone community or in other Canadian provinces (#4). In some cases, where the cultural differences do not seem very pronounced, the ethical dilemma they pose can be overlooked, either because they are not considered significant enough to affect the "free and informed"! **Syntax**

**Error**, « nature of the subject's consent, or because the issue is simply not raised by the members of the REB. In effect,

... I have to admit that we haven't questioned whether, for example, someone of Italian ancestry would react differently to a cardiology project, or someone of French-Canadian ancestry, for example. (#4)

Even those who have never been “confronted with this problem” «faced\_this\_problem» thought it would be appropriate to involve certain members of the community or communities concerned in the process of obtaining the subject's consent, for example, there should be a requirement that “it be people of the same cultural background as the subject... that know their values” (#1) (#3). Several interviewees felt that the participation and involvement of representatives of the community or communities concerned should be encouraged and increased. The inclusion of this “third player” «third\_player» becomes indispensable from the ethical standpoint in the context of multi-country studies or in cases of research projects entailing serious risks for the subject or the community. In effect,

... to get them to give their consent, you have to have worked with people from the community so that these people [can] help the researchers clearly identify the values of this community, is this project consistent with the experience of this community, will it address their needs, not address their needs ... In order for them [the subjects] to feel really free because they understand what this project is about ... And is it not conceivable that in ... projects that are more important or a little riskier, that it be members of the community who also help explain, or that the people at least have the opportunity to call, to contact people from their community to check, to ask questions?... (#7)

I personally think you can't ignore the cultural aspects in ethical issues. For me, ethics is a decision that involves the patient, the caregiver (it may be the doctor, a nurse, a psychologist) and let's say a third player who could be the family or a slightly larger group, a community, and for me the third part of this trio, it's the cultural aspect, so it's the environment in which the patient, the subject of the study and the caregiver are situated ... [in the case] of research that would be, let's say, global, you can't ignore the cultural environment in the decision-making process. (#10)

One interviewee went even further, stating that the representatives of the community or communities affected by a project should participate in the actual process of elaborating the research project, since

... Quebec public health projects on the whole, for example, are all geared to making individuals autonomous. Which is almost the reverse or in contradiction of certain values of cultural communities. So maybe ... it's the same thing for research projects ... How to integrate the communities more so that these communities have a say in the elaboration of research projects? And only then will informed consent mean anything. (#7)

## C. Human Tissue and Genetics

Studies in the area of genetics and those that have to do with the handling, and notably the storage, of human tissue pose many ethical dilemmas. All the interviewees said they are concerned about the complexity of issues raised and about the limited knowledge they have of a field that is experimental, highly specialized and constantly evolving. These interviewees expressed frame of mind that seems widespread among the members of several REBs:

... we're always a bit uncomfortable because we don't yet have much experience ... (#1)

... for us anything having to do with genetics, by definition, there are no fast-track procedures, because it's too much a field that's evolving and for which the rules, for example on protection of confidentiality, are so volatile it's a battle to impose criteria ... it's full of pitfalls ... because ... there are no international guidelines on all the problems ... it's evolving. (#5)

In the case of a research project of genetic screening of the members of one or more families, or even of a local community, one respondent raised a global anthropological issue of specific concern to Western societies. In effect,

Here [in Quebec], since the individual subject has primacy ... we face an internal contradiction when we want to do genetic research because we're obliged to rely precisely on the anthropological considerations of family, group, clan. But there are no longer any rules, because families are broken ... it's the collapse of the consent of the individual subject ... it's the necessary but inadequate condition ... Whereas all discourse is individualistic discourse, discourse that reinforces the autonomy of the capable, responsible subject. (#5)

Some interviewees wanted to point out that, aside from added precautions about the free and informed nature of subjects' consent and the risk-benefit ratio for the community concerned, special attention should be paid to the delicate matter of the communication of results in the case of a genetic screening project (#2) (#4) (#3). One interviewee mentioned a case he was involved in in the following terms:

... the concern we had, was communicating the results ... The problem was mostly at the level of families, because the degree of risk, if we discover a certain genetic mutation, can depend on factors that mean you should disclose what the uncle or the aunt has ... (#4)

Several different situations can arise, however, with regard to the management of the results of a study on genetic mutations, although non-disclosure seems to be the norm when the

results are provisional or not wholly conclusive (#3). In cases where “the importance of the mutation is not known... we are not going to communicate the results to the persons”!**Syntax Error**, «, just as [when] the aim [of the research] is to see the prevalence in this community, the tests will be completely anonymized (sic) (#4). This last respondent mentioned a situation in which a number of people wanted to be informed of the research results, and this disclosure involved a breach of the promise of anonymity to the other subjects involved in the study. In such a case

... we said ... listen, we can't tell you if you're a carrier because that involves having to involve other members of your family who don't necessarily want to know, however, if you personally are worried about it, then in the consent form we had the researcher's assurance that the patient could see a qualified genetic consultant and have the analysis redone from that clinical standpoint ... so give them an alternative to try and protect the confidentiality of the other members. (#4)

Unlike the rather widely held view of those who think that “the benefits are collective and the risks individual”!**Syntax Error**, « (#10), some research projects underscore the considerable risks the community or communities concerned may run. In fact, the inappropriate or hasty public release of the results of some research can lead to forms of stigmatization or social discrimination, or in some cases, to financial hardship. One interviewee felt it must be ensured that:

... the results of the research do not mean that this ethnic group or that community will be socially stigmatized [for example, when it comes to hiring for certain job categories] ... [moreover] ... we must be very cautious ... [because] these people may no longer have any insurance individually or collectively ... that's the big risk that lies in wait for projects of this type right now, and we'll see more and more of it ... (#3)

To ward off such a risk, the interviewee felt it appropriate to clearly inform “chiefs, spoke persons and leaders”!**Syntax Error**, « of every “religious or ethnic community or each tribe”!**Syntax Error**, «, before doing genetic screening and before making the results of the research public (#3). However, the contacts made with the representatives of the communities concerned must be intended not only to protect individual subjects and the community, but also to further understanding of the potential benefits of doing certain genetic screening. In this regard, one respondent said:

... I would be agreeable to discussing with a particular ethnic community, here in Montreal there are many ... to discuss with an ethnic community such as the Indians, the native peoples of Canada, to discuss for example their prevalence of diabetes or things like that ... it's necessary to discuss this with them and tell them we have these things, we are

able to do these tests, we think we could detect everyone, what do you think about it. What do the thinkers of your community think of that? (#2)

This interviewee proposed following the models of Scriver, Knoppers and Laberge when approaching specific communities to explain to them the advantages and disadvantages of a genetic screening research project, as one must not underestimate the fact that **Syntax Error**, «there are advantages to researching frequent or serious diseases in specific communities». (#2) Nevertheless, the ethical dilemmas and conflicts of interest remain between the different parties involved in genetic screening research, namely: the research subjects, the community concerned, society in general, and the researchers. According to one interviewee, the burden of proof rests, for the most part, with the researcher. In effect,

... it's a little up to the researcher to explain to us in his discussion of the ethical aspects, to explain to us the advantages and disadvantages of such an approach, if for genetic reasons there is a higher incidence of this particular anomaly within a population, I think the researcher has the right, and it may be beneficial for society as well, to do it, to go ahead and investigate the targeted population. (#8)

The implications and ethical dilemmas of storing various types of human samples are also many and complex. According to this last interviewee:

... there is a kind of grey area we're into more and more, like it or not, for example with human tissue, with the technologies of molecular biology. That, that raises questions that we come up against and that really aren't easy to answer ... So let's say for that particular field, it's an avenue where a lot of questions are being raised. (#8)

The comments of some interviewees point up the existence of this “grey area” «grey\_area» of research ethics and the lack (or ignorance) of guidelines to steer the conduct of researchers when handling human samples. In effect,

... we must make provision for and even keep samples if we have the means ... but we mustn't keep them for sale or for laboratory tests ... or if they must be sold, the money should be given to the community ... the community from which they come [or to] universities, things like that ... (#2)

While several respondents stressed the “restrictive” «restrictive» or “constraining” «constraining» nature of the provisions of the Civil Code of Quebec on the handling of human samples, two interviewees explained their concern vis-à-vis the real effectiveness of this norm given the current inability to do active follow-up once the consent form has been signed.



... people have to sign a consent form, it's mandatory under the Civil Code, especially if they leave a blood sample or whatever else it might be, human tissue, it's mandatory under Article 20 or 22 of the Civil Code, I don't remember exactly. In this consent form you have to explain ... what's going to be done with the analysis, you have to explain at what point the samples will be destroyed, because it would be a concern for me that this tissue might be kept, for example, for years and years and years, without knowing exactly what tests will be done on these samples, that, that would be a concern ... (#8)

... the Civil Code of Quebec is much more restrictive about the use that can be made of specimens. At the same time, once the patient agrees to a piece of tissue from his tumour being shared among researchers, we clearly specify in the consent form that it can be used only for research purposes, let's say for breast cancer, but it becomes a little like the Internet. It will now depend on the integrity of the researcher, I can no longer follow up far enough, that, that worries me ... Genetics projects also pose a problem because researchers not only want specimens in general from the patient, but also from the family, and that, as you know, that's a whole area that's somewhat evolving, so there, too, there's an attempt to set guidelines, but I think it's harder to have control over that. (#4)

In the opinion of at least one interviewee in the genetic research community, the concerns of scientists about Quebec legislation governing research ethics have more to do with what the law does not allow them to do than with what it cannot regulate effectively.

Right now, let's say researchers who are in the area of genetics consider the Quebec laws to be very very constraining, very restrictive, and ultimately Quebec would not be able to make real contributions to genetic research because the laws governing information of this type, access to information, are very limiting. (#10)

The frustration of some Quebec geneticists is compounded by the fact that Quebec society is also a distinct society in terms of its genetic research potential, as it has specific advantages that very few societies seem to have. In effect,

Quebec is a population with advantages unique in the world in terms of genetic research. That's for historical reasons that make for a population that has been captive and whose marriage and birth records are very extensive ... because the population was very religious ... and that's rather unique in the world ... And so when you're looking for diseases you believe are hereditary, the fact of having records like that, it's an utterly extraordinary asset because you can trace back the genealogy and trace the family tree and see if in fact there are phenomena that are clearly genetic in nature. (#10)

This interviewee gave a concrete example of the difficulties Quebec laws seem to pose in some cases with regard to genetic research:

I'll give you an example; about a year ago, there was a researcher at a research centre in Montreal who developed a test for knowing in advance how a degenerative disease would evolve, but this test, he was able to develop it because he had access to a bank of blood samples that had been taken in the Boston area, let's say 25 or 30 years ago ... he was able to verify whether his theory held up because it had been possible to keep these samples for 25 years. In Quebec, it would be impossible to do this without obtaining, when taking the sample, consent to the use of the sample for that purpose. Now, you

can't give consent for a test that will come in 25 years and that hasn't yet been discovered. In this way there's a kind of problem with certain aspects of regulation of the use of samples and access to information in that context. (#10)

Once again, the basic dilemma of the members of ethics boards seems to be finding a balance between scientific progress, the protection of research subjects, and clinical benefits for the community as a whole. In effect,

In a way, I'd say that in itself is an ethical problem. As soon as a population, through its laws, is excluded from a major contribution to the development of knowledge for diseases that affect everyone, well, for me that's an ethical problem. (#10)

## V. CONCLUSION

The analysis of all the interviews conducted with a group of researchers directly involved in the protocol review process and in the development of research ethics guidelines gives us a better understanding of their views, their concrete experiences and the basic issues they see in these areas.

Most of the individuals interviewed mentioned the major changes that REBs have undergone in recent years. These changes seem to amount to an appreciable improvement, over past forms of regulation, in the mechanisms for controlling scientific research activities involving human subjects. The gains in terms of greater autonomy, more clearly defined mandates, greater openness to non-medical specialists and the public, even researchers' appreciation of them, were often mentioned in the interviews when describing the current functioning of REBs.

Concerning the basic objectives of the ethical review of protocols, there emerged a broad consensus among the respondents on the responsibility to ensure the protection of research subjects and to maintain an acceptable risk-benefit ratio. However, the search for a balance, in reviewing research projects, between the protection of subjects and the contribution to the advancement of science is an ongoing and fundamental dilemma for many of the interviewees. All those consulted who sit on various REBs seemed to agree on the main normative sources and guidelines designed to steer the protocol review process (Tri-Council Policy Statement, MSSS Action Plan, Good Clinical Practice, etc.). Also, several times during

the interviews, it was observed that adherence to these documents is a *sine qua non* condition of access to sources of funding of the main granting agencies.

While the respondents generally did not seem overly concerned about the abundance of guidelines, the overly broad room for interpretation the various intervenors have in the review process was of concern to several of the individuals interviewed. There was, however, no consensus on a possible unification of the normative sources in order to resolve the conflicts between contradictory guidelines, as the latitude local ethics boards enjoy at times seems essential for dealing with issues arising from the specificity of certain individual cases.

Most of the respondents expressed satisfaction with the effectiveness of the research ethics review process given the boards' lack of resources and their excessive workload. However, the criteria used to evaluate effectiveness were almost never mentioned during the interviews. Also, the topic of the non-existence of active follow-up seemed to be of great concern to those interviewees who sit on boards or are with institutions whose role it is, at least in part, to develop research ethics guidelines. There was, however, no consensus on how to implement realistic and effective follow-up mechanisms for research activities involving human subjects.

The perception that researchers have today of REBs seems much improved after a certain initial period of mutual taming, with its episodes of conflict. The gradual acceptance of the role of REBs in the protocol review process and the changes that seem to be taking place, according to the respondents, in ethical research practices seem to have helped fashion a new image of REBs. This does not, however, keep relations between REBs and researchers from becoming tense on occasion and some “implacable” «implacable» researchers still question the usefulness and relevance of REBs. Most of the interviewees also felt that, beyond the more or less resigned acceptance of research ethics requirements imposed by legislation or granting agencies, the interventions of REBs have a real impact on research practices in terms of educating researchers.

Multi-centre research projects, reviewed independently by each local REB, point up the existence of disparate review criteria and, occasionally, lead to conflicts between the various ethics boards involved. The context of multi-centre review also reveals the apparent lack of communication and limited exchanges between the various REBs. The current trend towards the international harmonization of research ethics standards and guidelines prompted a range of

responses from the respondents. Considered by some respondents to be an inevitable process nevertheless having very favourable aspects (simplification of the job of researchers, globalization of the mechanisms for protecting research subjects, etc.), the current trend towards harmonization is consistent, according to other respondents, with a logic of power and profit-seeking imposed by transnational companies and the West generally.

Relations with the pharmaceutical companies were perceived by a number of respondents as having favourable aspects (contribution to research funding, opportunity to draw on the expertise of company representatives, etc.). Other interviewees instead stressed the existence of two basic sore points between the members of REBs and the representatives of pharmaceutical companies: research involving human subjects for promotional purposes, and attempts to limit the legal liability of institutions, companies and researchers by including clauses in consent forms that violate the provisions of the Civil Code of Quebec.

The limits to the free and informed consent of research subjects raise many ethical issues that were discussed by several interviewees. For example, respondents cited a relationship of dependency of certain groups of people on care staff, apt to restrict the freeness of consent, and the complexity of some consent forms, making them difficult to understand for those who are supposed to be informed when signing them. Another problem raised in the context of the interviews, but not always immediately grasped by the interviewees, was that of the limits to individual consent when the research may negatively affect an entire collectivity that has not been consulted. Given the hegemony of North American bioethics discourse centred on respect for the individual subject, the interviewees occasionally expressed some concern that there are no guidelines for addressing cases of conflict between individual consent and collective consent. The consultation of ethnic, religious, social or political representatives or leaders was proposed as one possible response to the ethical dilemma posed by the diversity of values and interests of the parties affected, either closely or remotely, by the research being reviewed.

It is significant that the ethical dilemmas posed by cultural differences or by conflicts between individual consent and collective consent are almost systematically linked to genetics research projects or having to do with the handling and storage of human tissue. Genetics, described by several interviewees as an «evolving» field, seemed to raise the most complex ethical dilemmas for the persons consulted as part of this study. Many respondents admitted feeling some uncertainty or uneasiness about a field that is little-known and for which the

research ethics guidelines do not seem clear and specific. However, the more restrictive nature of Quebec legislation governing research ethics compared to other Canadian provinces and the United States was perceived alternately as a factor of protection for research subjects (and possibly their communities) or as a factor of frustration for Quebec geneticists, who see it as limiting their potential contribution to the advancement of science.

Finally, despite the fact that most interviewees operated within hospitals, institutes and organizations connected with the same university, there was a wide diversity of views on research ethics.



# APPENDIX ONE

## I. INTERVIEW GUIDE (G1) - RESEARCH ETHICS BOARD (REB)

1. Tell me about the structure of your REB, and its processes. What can you tell me about its history? (Probe: Why is it structured the way it is? Has it undergone any major changes?)
2. How do you think the members of the local research communities perceive your REB? (Probe: Are there differences of perception?)
3. To what extent do you think researchers “In the field”«in\_the\_field» are influenced by the ethics standards of your REB? (Probe: Other possible influences: local culture, professional guidelines, etc.)
4. How do you deal with a multi-centre trial brought to your REB that has already received ethics approval at other sites? (Probe: What pressures does that add?)
5. How effective to you think your review process is? Why do you think that? (Probe: What is your evidence? What do you actually measure?)
6. If you could change something to make your review process more effective, what would it be? (Probe: Discuss more than resource problems.)
7. In your opinion, what are the goals and objectives of research ethics review? What are the biggest challenges facing your REB in this regard?
8. Imagine that you are to review a case where a researcher proposes doing genetic screening of members of the local community (or of a local ethnic community) to pinpoint a rare mutation. In such a case, what would be your main ethical concern? (Help: If they have not mentioned the concerns of the community, or the problems this represents for the community: What risks and benefits do you see for the collectivity? How can these problems be approached?)
9. Some people have commented that it is particularly difficult to address the issue of benefits/risks to collectivities in a framework that centres around individual informed consent. What do you think? Are there effective ways to get at this issue?
10. How do you face the issue of cultural difference regarding informed consent? Is there an effective way to deal with informed consent in a cross-cultural context?

11. There seem to be a lot of “players”«players» involved right now in the arena of research ethics in biomedicine and health—federal and provincial legislation, Ministry of Health directives, international guidelines, national guidelines, industry standards, etc. How does this affect your work here at the local level? What impact do they have? (Probe: In the context of multiple guidelines, what do you see as authoritative?)
12. Do you see the abundance of research ethics guidelines as a help or a hindrance? Do you see remaining significant gaps in existing research ethics policies?
13. How is the Tri-Council Policy Statement affecting your REB at the local level? What are your concerns? The difficulties you foresee?
14. What impact do you see from globalization and the trend toward international harmonization of standards in research ethics?

## II. INTERVIEW GUIDE (G2) - NATIONAL ORGANIZATIONS

1. Tell me a bit about the structure of your REB and its processes. What can you tell me about its history? (Probe: Why did it get set up the way it is? Major changes over time?)
2. How do you see the relationship between your organization and other national organizations?
3. How do you see the relationship between your organization and local research ethics boards? Between you and industry? And government?
4. To what extent do you think researchers “In the field”«in\_the\_field» are influenced by the ethics standards of your organization? (Probe: Other possible influences: local culture, professional guidelines, local REB, accepted publishing standards, etc.)
5. What would you say are the goals or objectives of research ethics review? What would “effective” ethics review look like?
6. Some people have commented that it is particularly difficult to address the issue of benefits/risks to collectivities in a framework that centres around individual informed consent. What do you think? Are there effective ways to get at this issue?



7. How is the issue of cultural difference regarding informed consent being dealt with, in your view? Is there an effective way to deal with informed consent in a cross-cultural context?
8. There seem to be a lot of “players” «players» involved right now in the arena of research ethics in biomedicine and health—federal and provincial legislation, Ministry of Health directives, international guidelines, national guidelines, industry standards, etc. What kind of impact does this have on the work of your organization? What are the impacts? What advantages and disadvantages are there to the various ways of getting at ethical research?
9. How do you see the Tri-Council Policy Statement affecting local REBs? What are your concerns? The difficulties you foresee?
10. Do you see remaining significant gaps in research ethics guidelines? What directions do you see research ethics taking? Where would you like to see it go?
11. Do you see current ways of dealing with research ethics in Canada as effective, overall? Why do you think that?



## APPENDIX TWO

### I. INFORMATION ABOUT THE RESPONDENTS OBTAINED DURING THE INTERVIEWS

#### A. Network of Hospitals and Institutes Affiliated with the University of Montreal:

(#1) : a jurist who has chaired the REB of Hôpital du Sacré-Coeur for about 5 years;

(#2) : a physician, associate director of clinical research and member of the REC, at Hôpital du Sacré-Coeur for "a good many years";

(#3) : a jurist, chair of the REB of the CHUM, but who sits on and chairs the REB (sub-committee) of Hôpital Notre-Dame;

(#4) : a respirology researcher, member of the REB of Hôtel-Dieu and the CLERUM. The respondent said she has served as chair of the REB of Hôpital Notre-Dame;<sup>192</sup>

(#5) : an ethicist who has sat on the REB of the Institut universitaire de Gériatrie of Hôpital Côte-des-Neiges for about 6 years;

(#6) : a physician, chair of the REB of the Institut de cardiologie.<sup>193</sup>

#### B. University of Montreal:

(#7) : an ethicist, professor of theology, who sits on the CLERUM;<sup>194</sup>

(#8) : a professor of optometry, acting chair of the health sciences REB, who also participates in the activities of the CLERUM.<sup>195</sup>

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<sup>192</sup> This last information is taken from the interview.

<sup>193</sup> Interview inaudible.

<sup>194</sup> Training to be verified.

<sup>195</sup> Training to be verified.

### C. Government Agencies:

(#9) : an official of the MSSS (ministry of Health and Social Services), with training in philosophy. He plans to delegate management of the research ethics file soon;

(#10) : an epidemiologist, director of research at the FRQS, who sits on the REB of the board of directors of the FRQS and the Provincial Ethics Committee.

# SECTION F

## CONCLUSIONS AND RECOMMENDATIONS

Michael McDonald

Our focus in this study has been on the ethical governance of health research involving human subjects (HRIHS). Our interest in “ethical governance” has been two-fold. First, we have been concerned with whether or not current governance for HRIHS promotes the ethical treatment of research subjects as individuals and as a class, including non-participants who are affected by research. Second, we wanted to know whether or not current governance meets the ethical responsibilities of those organisations and groups that play key roles in health research involving human subjects, e.g., legal authorities, research sponsors, research institutions, and researchers (collectively as members of research communities and individually as investigators on particular projects).

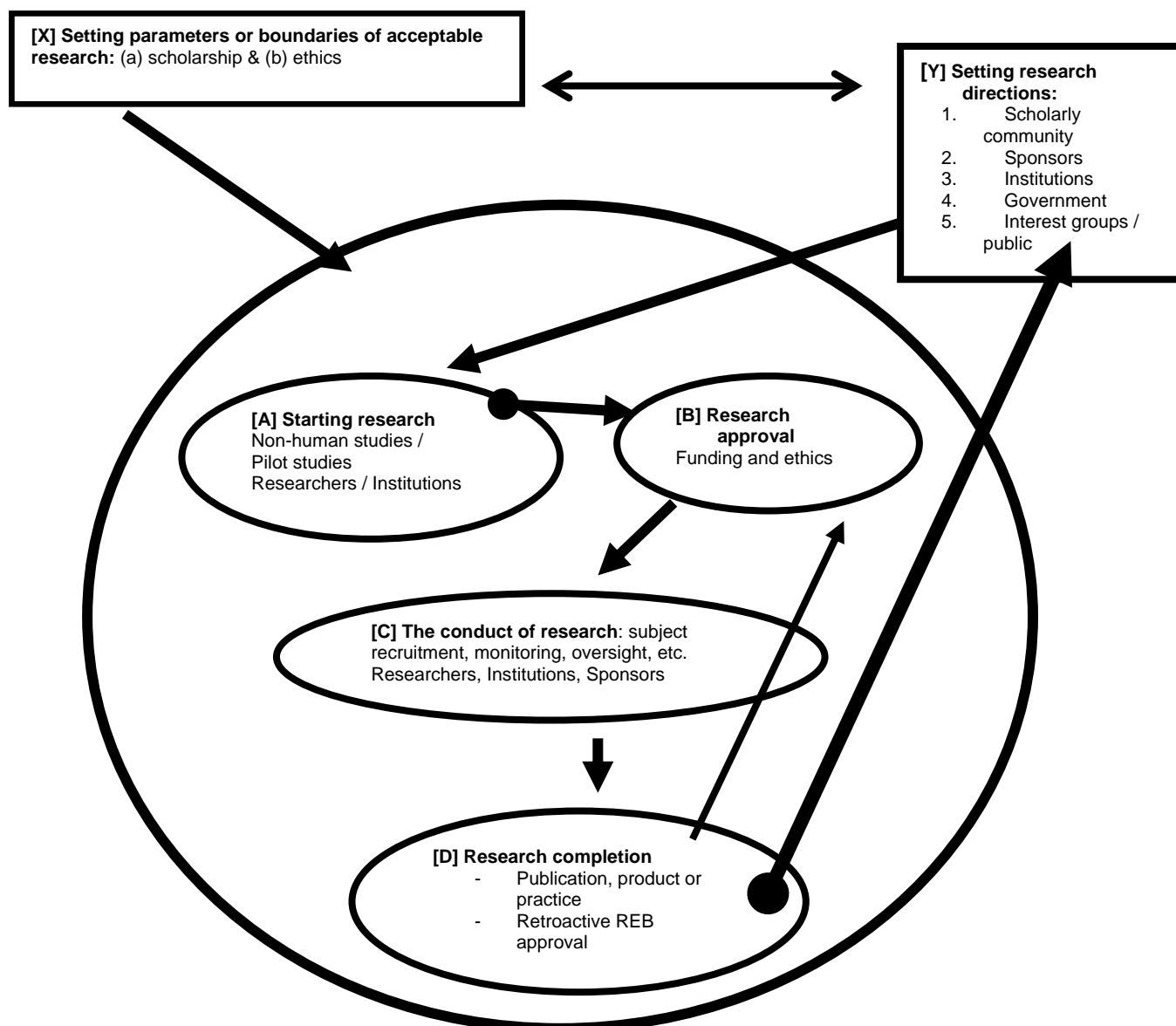
### I. THE COMPLEXITY OF CANADIAN GOVERNANCE ARRANGEMENTS FOR HRIHS POSES MAJOR ETHICAL CHALLENGES

Our first observation is an obvious but important one. Canada’s complex, decentralised, multi-sourced arrangements for governing HRIHS poses major ethical challenges in terms of consistency, transparency and accountability. Our study has identified three contributory factors: (1) the research process itself, (2) international factors, and (3) Canada-specific factors.

## A. The Complexity of the Health Research Process

We identified four stages in the research process: (A) research initiation, (B) research approval, (C) the conduct of research, and (D) the completion of research. But these stages took place within socially constructed parameters concerning: (X) shared understandings about scholarly and ethical parameters for HRIHS, and (Y) The research agenda or directions determined by multiple parties. We represent this complex picture with the following diagram.

### Complexity of HRIHS



## B. International Factors

This complex research process is very much affected by four pervasive international factors:

1. Rapid scientific and technological innovation and advances
2. Multiple disciplinary and interdisciplinary research modalities
3. Commercialization and privatization
4. Globalisation and harmonization

## C. Canada-Specific Factors

In addition, the conduct and governance of Canadian HRIHS is very much affected by factors specific to the Canadian context including, particularly (a) the debate and changes arising from the creation of the *Tri-Council Policy Statement* (TCPS), (b) the complex constitutional division of legal powers insofar as it affects the multiple modalities relevant to HRIHS (e.g., health, research, privacy, the registration and regulation of medical products, etc.) and (c) other factors now affecting Canadian research (e.g., federal regulations for clinical trials and both federal and provincial regulations for the management of health records).

We have then (1) a complex system of research with multiple parties whose governance is affected by (2) international and (3) Canadian factors. However it is a very disjointed 'system' in several respects. There is, for example, no uniform set of standards that applies across the board to the protection of Canadian research subjects. Knoppers used the case of Quebec to show how provincial, Tri-Council and GCP standards can be in conflict. But the system is disjointed in many other ways. We do not have the sorts of unifying legal and regulatory authorities that countries like France and the U.S. have for most research involving humans. There are no uniformly accepted standards for accrediting REBs – a matter of considerable urgency given impending federal and (in some cases) provincial recognition of REBs in regulations and laws.<sup>196</sup> Such oversight as there is of REBs is piecemeal and haphazard at both

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<sup>196</sup> The need for credible accreditation is recognised in the "Regulatory Impact Analysis Statement" for the proposed (January 2000) changes in federal regulations of clinical trials (p. 239) Department of Health, "Regulations Amending the Food and Drug Regulations (1024 -- Clinical Trials)" Canada Gazette Part 1 (22 January 2000)

local and national levels. With respect to public health research and research conducted by independent physicians, Joly and Kinsella have respectively shown major gaps in oversight and accountability. Burgess and Brunger have pointed out the much debated but seriously under-researched issues with respect to research involving collectivities.

## II. THE “NARROWING” OF CONCERNS FOR ETHICS IN HRIHS

### A. The Broad Picture

The broad picture of Canadian governance for HRIHS is a multi-staged and progressive narrowing or funnelling of concerns for ethics. In Section A-1, we claimed that with respect to ethical conduct of HRIHS there were three central ethical objectives:

- a. The **promotion** of socially beneficial research
- b. The **protection** of research participants
- c. As an overarching aim, the maintenance of **trust** between the research community and society as a whole.<sup>197</sup>

These objectives enjoy broad social endorsement and are represented in the numerous international, national and professional codes and aimed at the conduct of ethical research involving humans. But when we compare these three objectives with what actually takes place in the name of ethical research, we find a narrowing of concerns that could aptly be described as **ethical tunnel vision**, in which the three ethical objectives are given the most minimal instantiation. In effect, our current governance processes for HRIHS reduce research ethics to a dangerously simplistic concern for REB approval that is often functionally an approval of consent forms. The result is that the REB approval process and informed consent bear far more moral weight than they can possibly sustain. We see the situation as follows:

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227, which refers inter alia to Auditor-General, *Report of the Auditor General of Canada* (Ottawa: Auditor General of Canada, 1999).

<sup>197</sup> In Section A-1, we suggested that the maintenance and / or the restoration of “warranted trust” is a crucial criterion for good governance in this area. By “warranted trust”, we mean the opposite of “unwarranted trust”.



1. REBs are unduly focussed on the review of consent forms as opposed to consent as a living process. The focus is understandable since the forms are tangible and immediate to the REB in the approval process. Moreover, this is what researchers, the research institution, and sponsors expect of REBs.
2. On the whole, REBs overemphasize consent and pay insufficient attention to potential benefits and harms for research subjects. In practice, there is considerable uncertainty and disagreement about what thresholds to set for unacceptable levels of risk to subjects. In part, this is due to time and resource pressures on REBs and also to failures in guidelines (in particular the TCPS) for offering plausible principles and guidance in applying those principles. More importantly, there is a paucity of independent, research-based evidence about the effects of research on subjects.
3. For researchers “ethics” has become in practice a matter of successfully navigating the ethics approval stage of research. In the minds of many researchers and often of REB members, the main business of the REB is to efficiently and rapidly process research protocols that may or may not bear much resemblance to the actual conduct and results of the research. However, the research approval stage is only one part of the research process. The research approved by sponsors and REBs may ultimately bear little resemblance to the actual conduct of research and its results. For this and a variety of other reasons, it is clearly imprudent to rely on a single-shot, front-end review of research protocols by REBs for ensuring the ethics of HRIHS particularly and research involving human subjects (RIHS) generally.
4. In terms of governance structures and the institutional resources devoted to them, research institutions also view “ethics” as a matter of efficiently processing applications for REB approval. REBs are supported to the extent that allows efficient and cost-effective processing of applications. Most REBs are generally pressed for time and have scant opportunities to reflect on larger issues and to both monitor and assess in meaningful ways the results of their work. Few institutions devote any resources to the education of REB members, let alone the ethical education of researchers generally.
5. Standard setters reinforce this funnelling. The operational agenda of domestic standard-setters has been mainly around REB performance particularly in the ethics approval stage. But none of those charged with responsibilities for governance – be they a standard-setter, research administrator or REB member – knows or really tries to find out whether REB ethics approval has anything much to do with whether subjects are treated well or badly in particular research projects.

For the research institutions, research sponsors, standard setters and the various communities of researchers, the scholarly quality of research has been the major preoccupation; by comparison the ethical quality of RIHS is given scant and unsystematic attention. This is reflected in both the formal and informal processes for research education and evaluation. While generally<sup>198</sup> there are in place very elaborate structures of peer review and regulatory mechanisms for assessing the quality of research and of researchers – all the way from the

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<sup>198</sup> As Kinsella has noted with respect to professional oversight, there are also gaps in current governance arrangements.

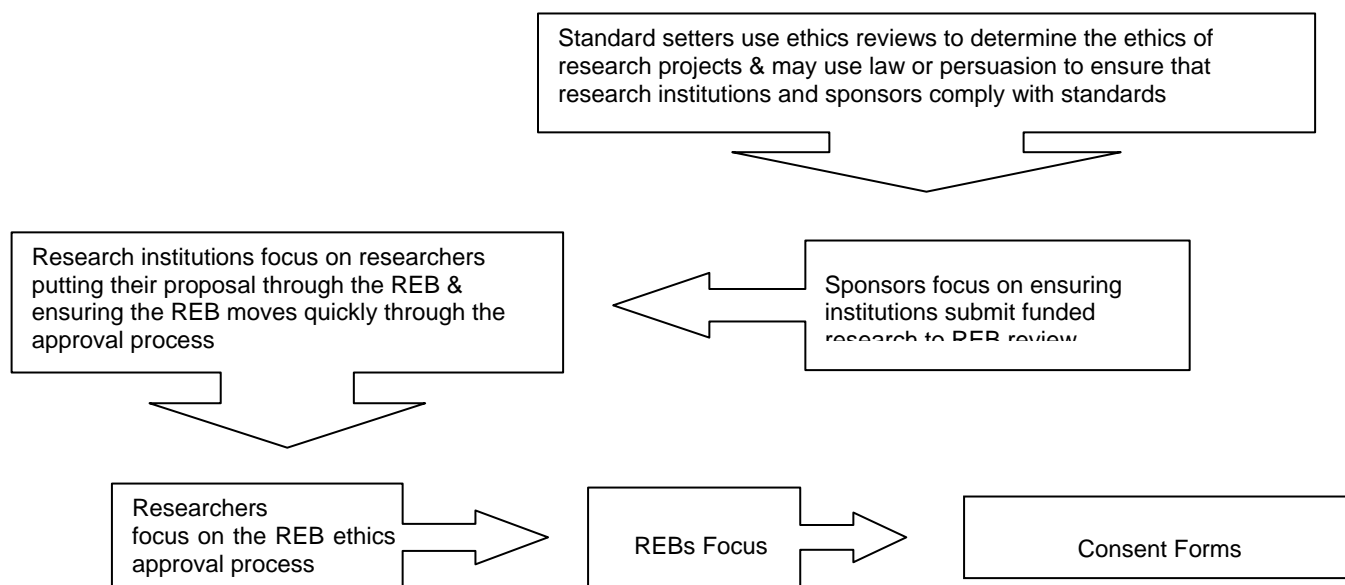
training and accreditation of researchers to grant reviews and the publication of results – there is little or no attention devoted to assessing the ethical preparedness of researchers. Almost nothing is done in the way of ethics education for researchers and REB members. Moreover, in important areas of human subjects research (e.g., research involving collectivities), little serious scholarly discussion has been devoted to the complex ethical issues such research raises. While research skills are carefully nurtured, honed, and monitored over the full life of research projects and of research careers, ethical skills receive far less attention. In short while scholarship, especially leading edge research scholarship, is seen to require a substantial and continuing investment by all parties concerned, ethics is not seen as requiring a similar investment of time, energy, insight, and resources. Operationally then, all the major parties seem to be operating on the assumption that researchers are ethical by nature rather than by nurture or training.

**Results.** The underlying moral equations seem to be:

- (a) [The ethics of RIHS = REB approval];
- (b) [REB approval = Processing research applications]; and
- (c) [Processing research applications = Modifying and approving consent forms].

This tunnelling and funnelling can be represented graphically in the following diagram:

### Narrowing of concerns – ethical tunnel vision



In short, ethics is funnelled into a bureaucratic process, and the process itself is reduced to a bare minimum. That bare minimum consists of the tangible parts – consent forms and other items, like adverse incident reports. Harms are reduced to simple measures of pain, morbidity and mortality. An important general result of this funnelling and narrowing down of ethical concerns is that important issues are missed at all levels and at all stages. For example, the focus on consent forms tends to distract attention from the realities of consent – that for example, many subjects neither heed nor even read consent forms. It ignores the extent to which subjects make their decisions on the basis of trust.<sup>199</sup> More generally in terms of governance processes and structures designed to promote ethical RIHS, the REB is seen as the focal institutional tool and in turn its role is defined in terms of front-end research protocol approval. This ignores other possible tools or structures for promoting ethical research. It also ties too much of ethics in research to a particular stage – a very preliminary one at that – taken in isolation from the rest of the research process. The big picture is missed – concerning the larger cultural environment of research.

To generalise, what is missing in current governance arrangements are the following:

#### **What is Missing**

1. Consent forms and even consent are not enough.
2. There is more to ethical governance than the REB and the ethics approval process.
3. A major result is inattention to quality assurance and quality improvement.
4. An 'ethics culture' requires cultivation.

## **B. Corrective Tendencies**

However, this is a big picture painted with a broad brush. There is some evidence of contrary indications. The concern for monitoring expressed in the TCPS and the proposed new regulations for clinical trials represents an important corrective tendency.<sup>200</sup> The recognition given to REBs in proposed federal regulatory changes for clinical trials is likely to lead to a

<sup>199</sup> See Part III of OIG Office of the Inspector-General, *Institutional Review Boards: A Time for Reform* (Department of Health and Human Services (U.S.), June 1998), and N.E. Kass *et al.*, "Trust: The Fragile Foundation of Contemporary Biomedical Research" (1996) 26/5 *Hastings Center Report* 25.

<sup>200</sup> See Department of Health, *supra* note 196.

process of REB accreditation, which should cover both regular and private sector REBs. Depending on how monitoring is done, these regulatory changes increase the chances for more transparent processes and more effective REBs.<sup>201</sup> As indicated in Beagan's interviews, two institutions have experimented with monitoring including random audits. At least some institutions have conducted research ethics workshops or, even more impressively, have integrated research ethics into the academic curriculum for new researchers. At the national level, NCEHR is working on gathering resources and conducting workshops for ethics education for REB members. We are also very much impressed with the calibre of scholarly, ethics and legal expertise represented on many REBs. And at a general level, Canadian scholars are prominent internationally in research regarding legal and ethical aspects of human subjects research.

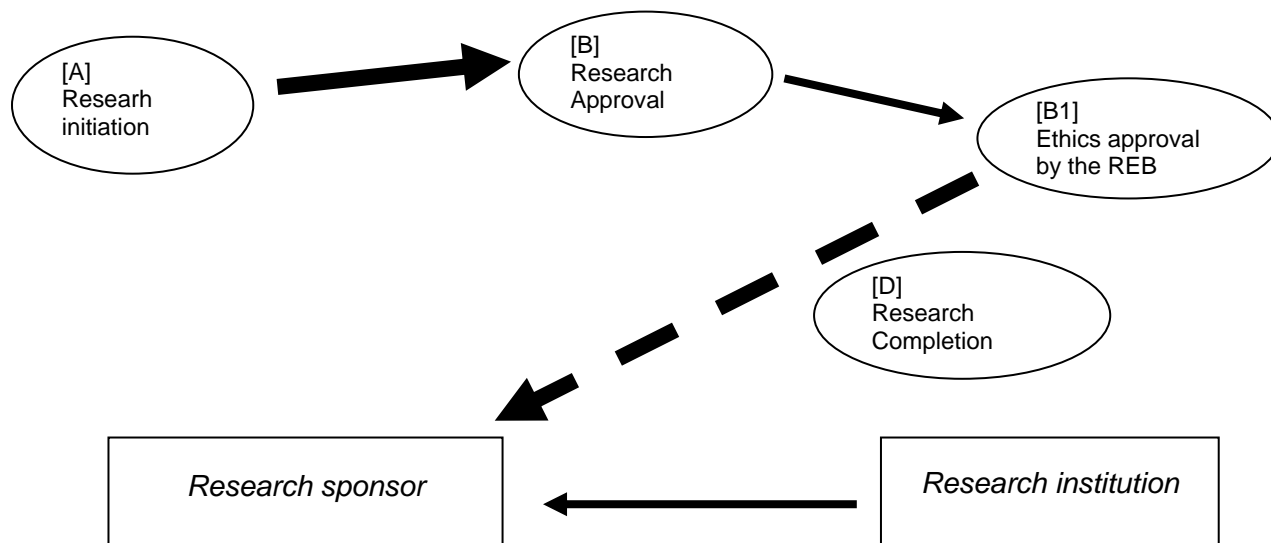
### III. MISSING LINKS: EVIDENCE, EFFECTIVENESS AND LEARNING

In B-2, we said that there are four stages in the research process. When we consider governance of HRIHS with respect to the ethical treatment of human subjects, we ask how the stages are connected in terms of information flow and accountability.

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<sup>201</sup> With respect to the new clinical trials regulations, there are important questions still to be answered: "Who monitors what for whom?" "How is the monitoring done?" and "How are monitors accredited?"

## Ethics information / accountability flow



What is interesting in the diagram is how few and anaemic are the reporting relationships. In other words, what is important in the diagram is what is not there. Missing are linkages that are essential to good governance. The linkages we mean are those that allow organisations to learn from their successes and failures and over time improve their performance.<sup>202</sup> What is needed are “**virtuous learning loops**”— that is learning loops that lead to improved ethical performance. Or in more familiar terms, what is missing are the information gathering, learning and accountability processes necessary for quality assurance (QA) and quality improvement (QI).

Currently, REBs have little knowledge of what actually happens in research after protocols have been approved.<sup>203</sup> Institutions and sponsors have a far better idea of what happens to research funds than what happens to research subjects. Almost without exception, research offices are reactive rather than proactive with regard to the concerns and interests of

<sup>202</sup> Of course, having such linkages is meaningless without also having standards of performance against which one gauges actual performance, which in turn allows organisations to adjust, refine and revise not just performance but the standards of performance. As we point out below, developing appropriate standards of performance requires research.

<sup>203</sup> The US OIG Report *A Time for Reform* recommends several changes in reporting relations to better inform IRBs about “feedback on developments concerning multi-site trials”, reports of actions taken by the FDA against investigators, and to “require sponsors and investigators to notify IRBs of prior reviews”. See recommendation 2. Office of the Inspector-General, *supra* note 199.

research subjects.<sup>204</sup> Many sponsors require reports about publications, patents and other products of research but do little to find out what happens to subjects beyond demanding assurance that research is REB approved. But it is fair to ask sponsors (and research institutions) how they know if (i) REBs are doing their jobs well and beyond that if (ii) researchers and other agents in the research process are playing their appropriate parts?

For both quality assurance and quality improvement, an important baseline of information is missing because of the lack of high quality research on the multiple ways in which subjects are affected for good or ill by research.<sup>205</sup> Good qualitative studies of how subjects are affected in different types of research could help fill this gap. Such research could lead to the development of reliable indicators of effectiveness and also help to identify many of the multiple variables that determine whether a subject's experience with research is good, bad or indifferent.<sup>206</sup> But such research won't be done unless sponsors are interested enough in the well being of the subjects whose participation is essential for research progress in health and other types of research.<sup>207</sup>

## A. Who Needs the Information for QA and QI?

To start with, REBs could use reliable information to improve their own performance over time. For example in evaluating a research protocol, an REB will explicitly or implicitly make an assessment of the project's risks and benefits. It then seems reasonable to ask if the REB's prediction was on target or not. Research institutions should be in a position to determine how good its REBs are at forecasting risks and requiring effective mitigating strategies. In turn, research sponsors should be concerned about how well the research institutions they support deal with issues of risk to research subjects. Here, a basic question would be to ask whether the institution has the virtuous learning loops necessary to improve its performance. A research

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<sup>204</sup> Whether offices of research are the appropriate place to take such proactive steps is a matter we discuss below.

<sup>205</sup> Important exceptions to this are the studies done for the Presidential Commission on Human Radiation Experiments on contemporary research practices, particularly the subject interview study in Part III of President's Advisory Committee on Human Radiation Experiments, *The Human Radiation Experiments: Final Report of the President's Advisory Committee* (New York: Oxford University Press, 1996).

<sup>206</sup> A weakness in the recommendation of the US OIG Report *A Time for Reform's* proposal that IRBs conduct be evaluated on the basis of outcomes including those that reflect the "perspective of and experiences of [subjects of] research as well as researchers" is that subjective measures of participant satisfaction are not sufficient measures of the performance of REBs/IRBs without the development of clear baselines through validated research. Office of the Inspector-General, *supra* note 199 at 12.

<sup>207</sup> See section V below on innovative research.

institution should be concerned with how its researchers deal with human subjects.<sup>208</sup> Beyond this, researchers individually and collectively should be interested in the effects of their research on research subjects and on the population of which the subjects are a “sample”. Individually, a given researcher should want reliable comparative information on how her treatment of research subjects compares to other researchers working in similar areas. Collectively, communities of scholars should discuss general issues of risk in their areas of research, share mitigating strategies, and develop common norms around standards for good human subjects research in their areas that can be used for education and quality improvement. Social barriers to recruitment and representativeness of research samples might be addressed by ethical discussions, thereby improving the quality of research and its “public” relevance.

Standard setters, be they in industry or the public sector – or provincial, national, or international – ought to be intensely concerned about the effects of the research they sponsor on research subjects and in particular for ensuring that appropriate and effective standards are in place. In a broad sense, such information is vital to the public legitimacy of the conduct they regulate. To ask for this information and to act upon it would seem a basic and essential part of governance for standard setters. A standard setter ought also to try to discover if the standards and processes they adopt are appropriate, realistic, and effective.

To sum up, we list some of the key missing links:

### **Missing Links**

1. Good governance requires virtuous learning loops so all the actors can learn from their successes and failures.
2. Virtuous learning loops should be based on evidence-based standards.
3. Thus, there is an urgent need for research on what happens to human subjects in research.
4. Such research requires resources from sponsors and research institutions; it also requires a commitment to use the research results in improving governance.
5. Failure to establish evidence-based learning loops represents a serious failure in governance for which research institutions, sponsors and standard setters should be held accountable.

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<sup>208</sup> In The US OIG Report *A Time for Reform*, the FDA asks a number of pertinent questions, e.g., “How do we know if protocols that should be submitted for review are not submitted? Or if approved protocols stray in ways that are not identified in paperwork submitted to the IRB?” *Ibid.* at 23.

## IV. MISSING SUBJECTS

We have argued that our current governance processes funnel ethics into the REB approval process and that the approval process is all too focussed on consent forms. In the research process, the only active role played by human subjects is as signatories on consent forms and potentially as complainants. Typically research subjects have no role in the governance of HRIHS. Others, usually research sponsors in concert with the research community and research institutions, design the policies that govern RIHS. While there are supposed to be “lay” or “community” representatives on many REBs, there is no requirement that lay representatives be knowledgeable about research subjects, let alone have been involved in research as subjects or as parts of groups that are often studied.<sup>209</sup>

We have already noted many gaps in accountability **for** the use of human subjects in research. What is less obvious are the many gaps in accountability **to** research subjects. We see major differences in principle and practice between a system in which the stress is on accountability **for** the treatment of certain people and one that adds a significant degree of accountability **to** those people. We argue in favour of a system of governance for HRIHS that has much greater accountability **to** research subjects on several grounds:

1. As a matter of moral respect
2. As a potential source of wisdom
3. As a basis for public trust
4. As a means for achieving greater balance in the system of governance.<sup>210</sup>

We see two missing “accountabilities **to**” subjects. First, our current system for dealing with actual and potential concerns of subjects is entirely too passive and reactive. Simply listing on a consent form the name of a contact person in the research office does not demonstrate appropriate zeal for the welfare of research subjects. It assumes that subjects will complain if they feel they have problems. But that may be a mistaken assumption. Politeness, timidity,

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<sup>209</sup> We depart here from U.S. recommendations that contemplate the use of outside academics, e.g., scientists from outside areas being reviewed by the REB, as lay members (cf. *Ibid* at 18).

<sup>210</sup> Cf. *Ibid* at 17. Recommendation 4a. “Individuals not associated with the institution or with the research enterprise can provide a valuable counterbalance to pressures that threaten IRB independence. But to do so, it is important that they be well-trained, but also that there be enough of them on a board so that their voices are more likely to be heard and their sense of belonging more likely to be enhanced.” It is noteworthy that this recommendation is described as meeting a 1997 commitment made by the U.S. President regarding the infamous Tuskegee syphilis experiments.



ignorance of the rules, cultural traditions, fear of authority figures, simply misplacing a copy of the consent form, or even fear of retaliation or withdrawal of regular health services are only some of the reasons why subjects may not take the initiative. Given this, would it not, for example, be appropriate to have skilled interviewers occasionally ask sample research subjects about their research experiences and then use that information to deal with specific problems and to improve performance generally? It is essential then that research institutions, REBs, NCEHR, research sponsors and researchers seek the opinions of human subjects and where appropriate act upon them.

The second missing “accountability **to**” subjects is in terms of representative participation in governance. At the moment we have a system of governance that is, so to speak, almost completely producer-driven. A more consumer-driven model has much to recommend it. It would be a smarter and more robust system in terms of maintaining and enhancing public trust. Moreover, encouraging representative research subjects to participate in the administration and design of standards and processes for governing research involving humans would (if properly managed and sincerely conducted) be a win-win situation for both the research community and research subjects.<sup>211</sup>

## V. INVOLVEMENT, INDEPENDENCE AND INNOVATION

To address many of the issues of accountability and effectiveness of governance, we see the need for “three I’s” -- a mixture of (1) greater **involvement** on the part of major actors; (2) more **independence** in specific areas for ethical oversight, monitoring and standard-setting; and (3) much more **innovation** in terms of careful experimentation with alternative forms of governance and more research on the effects of research on human subjects.

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<sup>211</sup> We recognise that the selection of ‘representative’ community members for participation in any form of governance is likely to raise a number of generic issues that are not specific to HRIHS. For example, there could be capture of a public process by special interest groups or manipulation and co-option by those with the power to appoint.

## A. Greater Involvement

The first “I” is involvement. Our governance system for HRIHS needs much more involvement on the part of major actors, e.g., research subjects who are now largely treated as passive participants in the research and its governance. We have also said sponsors, institutions and researchers should take greater ownership of the larger responsibilities for ethical research. The ethics of research involving humans is much more than REB approval and signed consent forms. But whose involvement is needed where? We would suggest attention to the following areas.

### 1. REBs

REBs must have adequate resources to do their jobs – before, during and after the ethics approval stage. This includes support for:

- Secretarial and other office services
- Time-release or other in-kind compensation for researchers, ethicists, lawyers who serve on public sector REBs
- Reimbursement of the expenses of community members and where necessary reasonable remuneration, e.g., to allow economically disadvantaged individuals to serve as community members
- Regular educational events for REB members, e.g., attendance at research ethics conferences, annual retreats, visiting speakers, orientation for new members
- Resources to allow REBs to conduct workshops for researchers on research ethics
- Support for one or more bioethicists as part of a professional support staff for high-volume REBs, especially those that deal with higher risk research.

Adequate support for REBs involves providing back-up and support services at appropriate levels. In a report on Quebec REBs, Parizeau offers a number of useful suggestions about support staff.<sup>212</sup> Parizeau also suggests remuneration as well as covering the costs of community members. Institutions should provide appropriate time-release from other responsibilities or other types of in-kind compensation for academics and health professionals who serve on REBs as well as appropriate career recognition for such service to the research

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<sup>212</sup> See M.-H. Parizeau, *Rapport d'enquête concernant des comités "éthique cliniques et comités de la recherche au Québec* (Québec: Ministère de la Santé et des Services sociaux, September 1998).

community. We think that a strong case can be made that high volume REBs be supported by a professional staff with one or more full-time bioethicists on it. This is especially important given the moral complexities posed by new forms of health research – e.g., genetics and new reproductive technologies – and the significant regulatory changes taking place with respect to clinical trials. For these complex and controversial areas, it may be advisable to consider shared resources in the form of professional support and specialised REBs that could act on a regional or national basis.

How should this be paid for? In some cases, this should be seen as a recoverable cost of research, e.g., for privately sponsored clinical trials. But here efforts must be made to protect REBs from becoming dependent on revenue from reviews. In other cases, research institutions need to reach an understanding with various research sponsors about the costs and support of REBs. In return research sponsors should expect that protocol approvals and monitoring issues will be addressed fairly and efficiently by an appropriately trained, duly accredited REB, supported by a suitably trained and professionally accredited staff where the volume and value of research warrants.

## 2. Virtuous Learning Loops

We have pointed out that there is a lack of the virtuous learning loops that would ground quality assurance and quality improvement for ethical RIHS. Virtuous learning loops are needed at two levels. The first is **within** particular institutions that are involved in health research and its governance, especially for research institutions and research sponsors. For example, research institutions like universities and health centres should carefully assess their own research activities for areas in which there are significant gaps in knowledge about what happens to research subjects. The education and training of researchers on relevant issues in research ethics should be a high priority. We would stress however the importance of making such an educational effort intellectually credible. This is something that researchers demand in their own work; no less should be expected for providing research ethics education with a sound basis in research ethics scholarship.

The second level is **amongst** the many institutions that interact in the research process. We see the need for better communication between, for example, research institutions and sponsors about appropriate accountabilities in HRIHS. Accountabilities go well beyond the REB ethics approval process and should include monitoring, quality assurance and quality improvement. Thus, boards of not-for-profit health research sponsors should be determining

how they could best reassure their stakeholders (donors, public supporters, professional staff, etc.) that the research they sponsor is being conducted ethically. But this requires dialogue with researchers and research institutions about the kinds of accountability that would be appropriate for this task – illuminating, effective and not overly bureaucratic. To initiate second level, inter-institutional initiatives, a number of bodies need to work together. For example, in the case of health research involving humans, this would include organizations such as CIHR, private sector research sponsors, NCEHR, health charities, Deans of Medicine and other health related faculties, and related academic groups like the Canadian Bioethics Society to name but a few. A series of stakeholder meetings would also be an effective means of creating an inclusive dialogue.

### 3. Involving Research Subjects

There has been little involvement of research subjects in the processes and policies for the governance of HRIHS. This contrasts markedly with the significant and beneficial role that animal welfare advocates play in the governance of research involving animals.<sup>213</sup> We realise of course that there is not a human equivalent of the animal welfare movement in Canada. But we do think that people who have had experience as research subjects, especially in higher risk areas of health research (e.g., cancer therapy trials) would likely bring important new perspectives to the governance of this area, e.g., as members of REBs, NCEHR, ethics secretariats for research sponsors, ethics advisory groups for directors of research. Representatives should be sought from groups whose members are frequently studied in health research involving humans, e.g., from the communities of those living with AIDS, cancer survivors, ethnocultural groups, and disability groups.

### 4. Creating a Research Ethics Culture

This is one of the most important of our recommendations but one of the hardest to implement. It is an area that readily invites window-dressing in the form of superficial efforts and

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<sup>213</sup> In a recent study (released in March 2000) of the governance role of NCEHR, the authors argue that CCAC enjoys the “credibility and trust” of “the broad research community”. Centre on Governance, University of Ottawa, *Governance of the Ethical Process for Research Involving Humans* (Ottawa: Centre on Governance, University of Ottawa, March 15, 2000) at 36. This is contrasted with the lack of support in the social sciences and humanities research community for the TCPS (*Ibid.*). The authors however do not comment on whether the research subject communities (animal and human subjects) and their advocates find the policies and processes credible and trustworthy. Our suggestion is that the prominent role played by representatives of the humane movement on CCAC contributes not only to CCAC’s credibility with animal welfare advocates, but also with the research community generally. This is in part because animal welfare and animal rights advocates have motivated the animal research community to seek effective policies.

ineffective delegation in the form of asking others to take the first steps. Yet we think that it is only through continuous and concerted activities of research communities, research institutions, research sponsors, and regulators that research ethics will become a central part of the culture of research. We think research sponsors – particularly public sector sponsors of research and the pharmaceutical industry – should be encouraging innovative teaching and research on significant current ethical issues in health research involving human subjects. Academic leaders should play a major role in putting ethics on their particular research community's agenda. Centres for bioethics and health law are important resources that could be utilised to much greater advantage by research institutions.

Ethics education and mentorship should be central parts of the process by which new researchers are educated and socialised. Ethics should be as central to the educational curriculum as research methodologies.<sup>214</sup> Indeed, it is by critically reflecting on methodologies and their uses in practice that offers some of the best insights into major ethical challenges in research. However, this is not something that can be imposed on researchers. Rather it is a matter of encouraging and supporting credible researchers who are willing to take the initiative in their own disciplines. Here again we think that what will be needed is support for partnerships between, for example, bioethicists and anaesthesiologists, in designing appropriate educational materials.

## B. Independence and Trust

The second “I” is independence. Counter-balancing our recommendation for greater involvement in HRIHS by all parties is our recommendation for greater *independence* in key areas where it is essential to avoid conflict of interest or its appearance. We have pointed out that those with vested interests in its outcomes – researchers, research institutions, and research sponsors – dominate the research process. While there is nothing illegitimate about these interests *per se* (in fact a strong interest in generating valuable knowledge through research is a laudable interest), current governance arrangements are such that the process appears or may actually be biased in favour of research interests. It is not, we think, enough for researchers, research institutions and research sponsors to ask research subjects and the general public to trust blindly that all is well.

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<sup>214</sup> CCAC is currently developing a model curriculum that can be used in whole or part by research institutions for the education of those conducting research involving animals.

## 1. The Case for a “Trust but Verify” Approach

In this respect, we agree with the U.S. OIG recommendation for “insulating IRBs from conflicts that can compromise their mission in protecting human subjects”.<sup>215</sup> The U.S. Report states:

Two long-time analysts of IRBs have described IRB regulations as “a permeable shield with no strong framework to ensure that the subjects’ interests take precedence over institutional ones.” They added that in balancing risks and benefits, an IRB “that consistently makes the calculus in favour of research will hardly ever be identified.” While many Federal and IRB officials are likely to object to this assessment, the minimal information they have on the effectiveness of IRBs makes it difficult for them to rebut it. Even more troubling, in an environment where IRBs are expected to be responsive to the financial pressures facing their parent institutions and/or sponsors, some IRBs are finding it difficult to maintain sufficient focus on their core mission ... (p. 17)<sup>216</sup>

The authors of the U.S. report just cited go on to say that:

We suggest that an IRB with sufficient independence is one that is not under any institutional or ownership pressure whatsoever to approve protocols or related documents; bases its reviews on the merits of a proposal and attendant risk/benefit ratio, without regard for business concerns; does not report directly to the part of the institution responsible for bringing in research funds; is not compensated based on the outcome of a review; and has recourse should it be subject to any pressure.<sup>217</sup>

In short, the American recommendation is for a “‘trust but verify’ thrust”.<sup>218</sup>

To be frank, we see the pressures on Canadian REBs as potentially much greater in Canada than the U.S. In Canada we lack the strong counterbalance provided in the U.S. by independent federal governance of research ethics approval and by the significant level of research support provided by NIH and other U.S. agencies. Moreover, American institutions of higher learning – especially the most highly productive research institutions – enjoy much greater public and private support than do their Canadian counterparts.<sup>219</sup> This makes Canadian institutions much more vulnerable to the need to compete for scarce research funding.

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<sup>215</sup> Office of the Inspector-General, *supra* note 199 at 17.

<sup>216</sup> *Ibid.*

<sup>217</sup> *Op cit*, 287.

<sup>218</sup> *Op cit*. at 290. By contrast, the Commission reviewing Australian ethics committees reached the opposite conclusion: “The Review Committee has no persuasive evidence of unsatisfactory or poor conduct in the current operation of IECs to justify the introduction of more stringent inspection (for example, external independent audits) of IECs.” Review of the Role and Functioning of Institutional Ethics Committees IECs, *Report of the Review of the Role and Functioning of Institutional Ethics Committees* (Canberra, Australia: Australian government, March 1996). We comment below that governance including inspection is a positive responsibility and not simply a negative one.

<sup>219</sup> Even so, Americans are concerned about the independence of their universities from corporate interests. Cf. A. Press & J. Washburn, “The Kept University” *The Atlantic Monthly* (March 2000) 39.

## 2. Independent REBs

If we are right in thinking the risks for compromising the independence of ethics review and monitoring are substantially higher in Canada than in the U.S., Canadian research institutions, sponsors, federal and provincial governments, and researchers need to take greater steps than their U.S. counterparts to insulate REBs and parallel bodies (e.g., data safety monitoring boards) from pressures that would compromise their independence. It is crucial we think – both for substantive reasons and for the sake of appearances – that REBs not report to or be appointed by offices of research. In commenting about the U.S. model of ethics review by local IRBs, Edgar and Rothman ask, “Does it make sense to give the leadership of an institution, which by its very nature cannot survive without funds and fame brought in by clinical research, the responsibility of appointing the membership of a monitoring committee?”<sup>220</sup>

This is not to say that REBs should work independently of research offices. Clearly REBs in universities and hospitals should work cooperatively with offices of research in regard to the registration of research protocols, the management of records, and the like. Research offices may well be better suited to handle monitoring functions than REBs. But the current widespread reporting relationship of REBs to university and hospital offices of research sends the wrong message to research subjects and the research community and enhances the possibility of significant conflicts of interest, especially when the institution has a major stake in research being approved by the REB (e.g., when the institution has an equity position in a company’s whose research is being reviewed or with joint employment responsibilities).

REB independence would be strengthened by clearer rules for membership on REBs. Edgar and Rothman make the following useful suggestion:

IRBs processing a substantial number of protocols should, however, include experts drawn from scientific groups outside the institution. Moreover, there should be more focus on the appointment and renewal process. We should also seek to quasi-professionalise the role of outside members, linking them to groups that could come together to study common issues, so that there might be greater uniformity given to concepts like minimal risk.<sup>221</sup>

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<sup>220</sup> H. Edgar & D.J. Rothman, “The Institutional Review Board and Beyond: Future Challenges to the Ethics of Human Experimentation” (1995) 73/4 *The Milbank Quarterly* 489 at 490.

<sup>221</sup> *Ibid.* at 504.

### 3. Independent National Oversight

At the national level, we would make a parallel recommendation. NCEHR should enjoy the same status and a proportionately equivalent degree of support as CCAC. The current situation in which national oversight of research involving animals is far more effective and independent than that for research involving humans would we believe be profoundly upsetting to the Canadian people. The Tri-Council does not do itself, other research sponsors, research institutions, or the research community any favours in maintaining the current close and controlling relationship to NCEHR and the TCPS in regard to policy setting, interpretation and enforcement. To maintain and deserve public trust, it is essential that there be an appropriate distance between the arms of government that promote research and those that protect human subjects. Moreover, the arm that protects human subjects must be in a position to verify the effectiveness of its efforts.

If, however, NCEHR, is to be a credible and knowledgeable national oversight body for REBs, then it will need a membership that is representative of its stakeholders' interests: sponsors, research institutions, researchers, and, most crucially, research subjects. The membership must be knowledgeable – including experienced members of REBs; experts in ethics, health law, and research; those with experience in research ethics standard setting; etc. Like CCAC, it should not try to do everything internally, rather it should reach out to commission expert opinion and enlist support from its many stakeholders. There may be a role here for supplementary expert specialist panels on specific research areas, e.g., xenotransplantation, genetic testing, new reproductive technologies, collectivities.<sup>222</sup> NCEHR needs a firm base of funding for an experienced and enhanced professional and support staff. Ideally it should enjoy a broad base of financial support from both public and private research sponsors. There also should be a clear and effective mechanism for periodic review of NCEHR's effectiveness and direction. Like CCAC, NCEHR faces the challenge of working as a standard setter with limited powers of enforcement due in large part to the complex constitutional division of powers in Canada. So it will have to lead by persuasion, public advocacy, and reputation.<sup>223</sup>

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<sup>222</sup> Edgar and Rothman have an interesting suggestion for such committees *Ibid.* at 503.

<sup>223</sup> An interesting recent development at CCAC is for the legal registration of its "Good Animal Practice" certificate. This provides a way for CCAC to gain greater public recognition and to provide a publicly recognisable standard for the humane treatment of animals involved in research.



#### 4. Why Arm's Length?

For both REBs and NCEHR, we would draw a parallel to external auditing. External auditors are valued because they provide independent expert verification of the financial (or in the case of federal and provincial auditors general, the functional) status of private and public sector organisations. While it is reasonable for such organisations to have internal auditors and other means of internal control, these cannot replace expert external verification.<sup>224</sup> But to have credible external verification, those doing the verifying must be trained and accredited. This in turn involves independent oversight by an arm's length body, e.g., by an independent professional association. Such oversight includes education as well as the granting and, if appropriate, withdrawal of accreditation.

There are then two stages of verification with external auditing. First, there is the verification of the books of a company by an external auditor. Second, there is the verification of the verifiers by an independent accrediting body – associations of professional accountants. At both stages, the process is open to public scrutiny. Something similar has to happen with ethics review and monitoring. Steps have to be taken at the first stage to ensure the visible independence of REBs from research institutions. We have already suggested closer attention to membership rules and the addition of outside experts would help here. Below we also suggest strengthening the role of community members. At the second stage, there is a need to have independent assessments of the effectiveness of REBs. NCEHR could play an important role here. However, more may be needed. If, for example, one wants to ensure that there are properly qualified bioethicists on REBs – which should be a minimal requirement for health research REBs – then it would be natural to ask for credentialing for such bioethicists.<sup>225</sup>

Finally in our comparison with external auditing, we would note that the external auditing function has value not only for affected third parties (e.g., financial investors) but also for the companies whose books are audited. That is, those audited recognise the clear value **to them** of having arm's length verification because their reputation and credibility depend on such verification. For what is at stake is "reputational capital". In this regard, Canadian management

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<sup>224</sup> See W.E. Chadwick, "Tough Questions, Tougher Answers" *Internal Auditor* (December 1995) 63 on typical issues faced by internal auditors.

<sup>225</sup> Professionalising bioethics has been controversial in Canada. See F. Baylis *et al.*, "Women and Health Research: From Theory, to Practice, to Policy" in A. Donchin & L. Purdy, eds., *Embodying Bioethics: Recent Feminist Advances* (Lanham: Rowman & Littlefield, 1999) 253. Our concern here is for professional accreditation for a certain role – membership on REBs as a bioethicist – and not for professionalisation generally although we suppose a similar argument could be made for bioethicists on clinical ethics committees.

professor and business ethicist Leonard Brooks says that we have moved “from the ‘trust me’ world, to the ‘tell me’ and finally the ‘show me’ world of public and multi-stakeholder opinion”.<sup>226</sup> We need a parallel move in Canada to the “show me” stage for research involving humans.

## 5. The Ottawa Governance Study

Our position here on NCEHR and in general on REBs is quite different than the position taken in the University of Ottawa’s Centre on Governance recent study of the management of the TCPS, especially in regard to NCEHR’s role.<sup>227</sup> The authors raise the concern that “since the objective of funding university research falls on the three Councils (MRC, NSERC, and SSHRC) that they are in a conflict of interest position regarding the protection human research.” The response of the authors of the Ottawa report is instructive:

We reject that argument. The previous chapter outlined 25 years of efforts to ensure ethical research. There is no indication that suggests that the three Councils have no regard for protection of human subjects in research. The development of a common policy and structure suggests otherwise.

Some have suggested that there is an inherent adversarial relationship where one group of stakeholders promotes research of whatever ethical stripe while another exists to protect human subjects from their efforts. We reject that dichotomy. Our view is that all the primary groups involved in this process, the three Councils, the universities, and the researchers desire to promote ethical research and to see a system put in place that is both effective and fair.<sup>228</sup>

We think this response to the conflict of interest problem is quite unconvincing. For one thing, it would have been quite remarkable if Canada had not developed some sort of policy for the protection of research subjects given the world-wide push to this end. So the existence of policy is not on its own convincing evidence of sincere commitment. Even if “**all** the primary groups ... desire to promote ethical research,” the central question is whether there is actually in place a system that is “both effective and fair.”

The primary question as we see it is not that of “good will” or “good intentions”. It is rather that of creating an effective system that balances the promotion of research and the protection of research subjects. In other words, we see the governance issues here as less about the stated intentions of institutional actors and much more about the design of those

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<sup>226</sup> L.J. Brooks, “Reputational Capital and Business Ethics” *The Corporate Ethics Monitor* (September-October 1999) 65.

<sup>227</sup> Centre on Governance, *supra* note 213.

<sup>228</sup> *Ibid.* at 16.

institutions and their performance. We take the problem of agency-risk seriously; professed good will – no matter how sincerely intended – is not enough.<sup>229</sup> The institutions in question have been designed to promote research. REBs and ethics policies were put in place to counter-balance research promotion. Institutional commitment to ethical research is shown in large part by how much the institutional actors are willing to place effective constraints on the pursuit of primary objectives in order to protect innocent third parties.<sup>230</sup>

## 6. Accrediting and Monitoring Private REBs

We also see the need for the registration and accreditation of private (for-profit) REBs. If private REBs are going to play a credible role in the research process, there has to be a publicly accessible and independent way of verifying their independence, expertise, good judgement, and capacity. Competent private REBs should welcome such a move as a way of ensuring their 'reputational capital'. Given that there are U.S.-based private REBs active in Canada, it is essential for accreditation to ensure that all REBs overseeing Canadian research be knowledgeable about Canadian laws, regulations, and moral sensitivities. There are important differences between the U.S. and Canada that must be acknowledged especially in health research. For example, there are very serious issues about the off-loading of research costs on to the Canadian public health care system in the form of sponsors expecting provincial health care systems to pay the costs of adverse health effects resulting from research.

## 7. Effectiveness in Protecting Research Subjects

REB certification and accreditation must encompass more than the research ethics approval stage. REBs must also demonstrate the capacity for monitoring or continuing review.<sup>231</sup> We very much like the two-pronged suggestion of the U.S. OIG to recast requirements to "grant IRBs greater flexibility and hold them more accountable for results."<sup>232</sup> This involves (a) eliminating or lessening procedural requirements "to enable IRBs to be more strategic in how they use their limited time and resources and ... concentrate their attention on

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<sup>229</sup> See the discussion in Section A-1 of Buchanan's ethical theory for bureaucratic organizations. A. Buchanan, "Toward a Theory of the Ethics of Bureaucratic Organizations" (1996) 6/4 Business Ethics Quarterly 419.

<sup>230</sup> McDonald has described this as "hands-tying manoeuvre". M. McDonald, "Hands: Clean and Tied, Dirty and Bloody" in P. Rynard & D.P. Shugarman, eds., *Cruelty and Deception: The Controversy over Dirty Hands in Politics* (Peterborough: Broadview, 2000) 1987.

<sup>231</sup> Office of the Inspector-General, *Institutional Review Boards: Their Role in Continuing Review* (Boston: Department of Health and Human Services, Office of the Inspector General, June 1998) and Office of the Inspector-General *supra* note 199.

<sup>232</sup> Office of the Inspector-General, *supra* note 199 at 11.

those research practices posing the greatest risks to human subjects” and emphasising “performance-focussed evaluations.”<sup>233</sup> For the latter, they say,

Among the basic questions ... that we believe warrant particular attention are the following: “1) Are IRBs successfully representing the interests of human subjects in research and not merely those of the sponsoring institution?” and “2) Do IRBs generally fulfil their goals?”<sup>234</sup>

We also like the idea of performance-focussed review being conducted by “independent, outside parties”. But to have adequate review of performance, we see the need for both innovation and research (see below). We note that the context of clinical research has shifted considerably in recent years. Rather than seeing participation in research as a burden and “a dangerous activity,”<sup>235</sup> many potential subjects now see such participation as a benefit involving, for example, increased attention and access to care, state-of-the-art treatments and trust that their physician, the researcher or the institution would not offer research with substantial risk. In this situation, it is quite possible that subjects will not be sufficiently self-protective or evaluate the potential benefits of research participation and so, for example, ignoring the warning about risks on consent forms. If this is so – and there is reason to think that it is so – then there is an even greater burden on REBs to accurately assess risks and benefits. This again strengthens the case for performance-focussed reviews of REBs.

## 8. Conflict of Interest Provisions

The current context of funding for significant areas of health research, including among other things the drive to produce marketable products and commercial applications, makes it imperative to ensure adequate conflict of interest provisions. *Mutatis mutandis*, there are analogous pressures on many health researchers in less commercialisable areas of health research, e.g., to maintain research funding for the sake of reputation, tenure and promotion, or simply to ensure continued employment for those on soft (i.e., research grant) money. For research with significant commercial potential, we think that it would be wise preferably to “preclude investigators from recruiting patients and conducting clinical evaluations where the product being tested is one in which they hold a commercial stake”<sup>236</sup> (or more minimally to add a significant level of independent third party oversight). Random inspection and audit

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<sup>233</sup> *Ibid.*

<sup>234</sup> *Ibid.* at 12.

<sup>235</sup> Edgar and Rothman p. 499.

<sup>236</sup> *Ibid.* at 504.

procedures commissioned by REBs or NCEHR would likely be a worthwhile endeavour especially for higher risk areas of research.

## C. Innovation and Research

The third of the “three I’s” is innovation. Under the heading of innovation, we include two thrusts (p) experimentation and (q) research. We see (p) and (q) as intimately linked. They arise for the same reasons – gaps in knowledge particularly of appropriate standards (e.g., for performance-focussed review) and the need for evidence-based governance processes. We are particularly lacking in empirically grounded work on the effects of research on human subjects as well as on the effectiveness of governance procedures. There is another important linkage between (p) and (q), namely that there is little point in experimentation (e.g., in different forms of monitoring) without careful research-based assessments of processes and results. Vice-versa, research in the governance of HRIHS without experimentation is unlikely to provide a sufficiently wide range of plausible policy options – especially given the general trend towards devolution in regulation.

### 1. Monitoring

An area ripe for experimentation and research is that of monitoring or continuing review. As Fortin and Leroux point out in their 1997 article on monitoring, there are a number of policy options and models with respect to monitoring.<sup>237</sup> They look at four different models ranging in strictness from informal visits through site visits within a formal agreement or framework to formalised accreditation on the model of CCAC to a legislatively based “investigative” model. In the Canadian constitutional context they see a number of tradeoffs.

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<sup>237</sup> L.-N. Fortin & T. Leroux, “Reflections on Monitoring Ethics Review of Research with Human Subjects in Canada” (1997) 8/1 Communiqué 11.

<b>Models</b>	<b>Strengths</b>	<b>Weaknesses</b>
<b>Informal Visits</b>	<ul style="list-style-type: none"> <li>• Education</li> <li>• training</li> </ul>	<ul style="list-style-type: none"> <li>• no guarantee of universality</li> </ul>
<b>Visits within formal framework</b>	<ul style="list-style-type: none"> <li>• more consistent monitoring</li> <li>• atmosphere conducive to information exchange</li> </ul>	<ul style="list-style-type: none"> <li>• no guarantee of universality</li> </ul>
<b>Accreditation or certification</b>	<ul style="list-style-type: none"> <li>• status is clear</li> </ul>	<ul style="list-style-type: none"> <li>• Repercussions of non-compliance uncertain</li> </ul>
<b>Investigation</b>	<ul style="list-style-type: none"> <li>• compellability</li> <li>• universality</li> </ul>	<ul style="list-style-type: none"> <li>• complex structure</li> <li>• rigorous formalism</li> </ul>

We see the first two models as inadequate. We would like to see a hybrid model that combines the merits of the accreditation and investigation models but is reasonably simple and avoids needless formalism. We see the need for a more experimental approach to monitoring (for example) whereby NCEHR would encourage research institutions to try different modes of monitoring and assist these institutions in assessing the merits and demerits of various modes for various contexts – type of research, institutional resources, degree of risk, etc. Thus, we would expect that some types of monitoring would work better for the more controlled and regulated contexts of clinical trials than for other areas of health research. Similarly, some modes of monitoring that work well in large health research institutions will not be readily adaptable to smaller institutions.

A major question for monitoring is who should do the monitoring. Should it be REBs, the professional staff of the research institution or sponsor, NCEHR, or other outside agencies (e.g., TPP inspectors as suggested in the proposed regulations for clinical trials of new pharmaceuticals)? There are governance issues with respect to appropriate accountability and reassurance. There are also efficacy issues with respect to how well human subjects are protected and the achievement of the social benefits of research. One cannot adequately address governance in a vacuum without looking at efficacy, but efficacy requires a context of responsibility – an answer to the question of “Efficacy for what purposes and to whose satisfaction?”

## 2. Context-sensitivity vs. Uniformity

Another crucial area where judicious experimentation and research would be useful is in terms of the inherent tension between governance processes that address specific contexts and those that serve the ends of uniformity and universality. Is the right model of the ethics approval process for the REB to function as a wise case-sensitive assessor of specific research proposals, to be assessed in terms of the research context and the likely subjects of research, or is the model one of an administrative tribunal striving to achieve universality and consistency in its judgements?<sup>238</sup> Posed this way, the choice looks stark and uninviting since we want to have it both ways; so realistic choices will be between hybrid models. Yet depending on the more favoured model of the two extremes, there will be different emphases in each hybrid. For example, in recruiting REB membership, we called for a substantial component of REB membership being genuinely representative of the non-research community and particularly of those who are part of the research subject population. But this may turn out to be in tension with the desire to run an REB that can meet the requirements of natural justice, e.g., to provide clear and consistent decisions backed by generalisable reasons under previously promulgated rules.<sup>239</sup> Here, we suggest that there is room for both experimentation and research with different combinations of the two models.

## 3. Concern for Subjects or Researchers?

Similarly, we have to see what are the tensions between having standards of performance, monitoring, accreditation, and processes that are sensitive to the needs, concerns and rights of research subjects and those that stimulate and facilitate research. As a society, it is not a question of “either / or”: Canadians want **both** the benefits of research **and** the

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<sup>238</sup> In jurisprudential writing, a familiar image for the first model is that of “palm tree justice”. The English political philosopher J.R. Lucas contrasts four types of judges: (1) “Judex I decides individual cases, but does not record decisions or give reasons”; (2) “Judex II decides individual cases, treating like cases alike, and records his decision but does not give reasons”; (3) “Judex III decides individual cases, treating like cases alike, records decisions, and gives reasons; and (4) “Judex IV subsumes individual cases under general, antecedently promulgated laws, but ideally, has not authority to interpret the law or make any innovation in it.” J.R. Lucas, *The Principles of Politics* (Oxford: Clarendon Press, 1966) at 368. Judex I represents ideal palm tree justice. Lucas says: “Judex I is the ideal customary law judge. He is a good man who lives in his tent and judges Israel righteously. Every morning he goes to the gates of the city, and there hears all the disputes the children of Israel bring him; and after hearing what either side has to say, gives his decision, for the one party or the other, as the Lord saith unto him. And then goes on to the next case.” Judex II is “the original common law judge”. Judex III is “the judge of law reports”; while Judex IV is “the ideal legal code or statute law judge” J.R. Lucas, *The Principles of Politics* (Oxford: Clarendon Press, 1966) at 135. Lon Fuller in his classic story of “eight ways to fail to make law” takes a much less sanguine view of palm tree justice, L.L. Fuller, *The Morality of Law*, Revised Edition ed. (New Haven: Yale University Press, 1969) at 33.

<sup>239</sup> See previous footnote (re Judex I through Judex II).

protection of research subjects. Insofar as there are tensions between these objectives, then these need to be identified, studied, and acted upon. There are numerous debates here that cannot be settled *a priori* or simply by resort to anecdotal evidence. For example in the debates around appropriate TriCouncil policy for RIHS, there were allegations that provisions in the proposed 1997 Code for research involving collectivities and for research involving deception or partial disclosure would undermine various types of research. But this was asserted rather than evidenced. It would be far more productive to debate such issues in ways that are informed by the sort of careful research that distinguishes cases and is sensitive to different contexts.

#### 4. Support for Experimentation and Research

If there is to be experimentation and research then two preconditions need to be met. First for experimentation to be useful, key institutional stakeholders – research institutions, sponsors, researchers and research subjects – have to be open to the various kinds of social experimentation, e.g., with different processes of monitoring, performance-focussed standards of assessment, etc. Moreover, they will have to be open to the sorts of open and honest research that can accurately gauge results. Secondly, research and experimentation will have costs – both financial and other – if they are to be done well. Unless research sponsors provide the support and commission the research and unless well-qualified researchers also take up the challenge, we will face increasing knowledge gaps with respect to RIHS generally and HRIHS specifically. The new CIHR with its strong emphasis on ethics in its mandate as well as its integrative and transformative vision of health research (from bench to application to results) is in an ideal position to play a leadership role here. The same is true of SSHRC, which has also staked out an important role in supporting health research. Indeed, one of the primary modalities for such research is qualitative research joined to solid bioethical/health law research.

In larger terms, we see this as an opportunity for Canadian researchers and research sponsors to play an important role in forwarding international research in the area of HRIHS. To take one important example, research in developing countries is a matter of considerable concern both from social justice and cross-cultural ethical perspectives.<sup>240</sup> Canada has important and multiple interests in this area that are linked to trade, international relations, and

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<sup>240</sup> WHO and NIH convened an international conference on this topic in Bethesda, Maryland in November 1999 with a view to future conferences on the same area. A significant undercurrent issue at the conference was whether the NIH was trying to impose U.S. federal standards for research ethics review on developing countries.



human rights. Through research, we can also learn from the experience of other nations on governance issues with respect to RIHS.

## VI. GENERAL CONCLUSIONS: REFLECTIONS ON NORMATIVITY AND GOVERNANCE

From talking to many people about this project, we know that all too often “research ethics” is read in a negative, prohibitive way. “Why,” we have been asked, “are you so negative about researchers, research institutions and sponsors? Is it because you see lots ‘going wrong’?” This, we think, is the wrong take on research ethics and related governance issues. Rather we would emphasize the need to have things “go right” and especially to “go visibly right.” This should move the discussion a considerable step beyond the negative and reactive view of the ethics of research as essentially “responding to wrongdoing.” An adequate system of governance should be more than ‘putting out brush fires’ and managing paper flows. It should be pro-active, transparent and accountable to its stakeholders. We recognize that institutional inertia makes it difficult to gather support for a pro-active approach; however, maintaining the status quo in the face of significant concerns has, we believe, much greater costs. One would do well to think here of the Krever enquiry into the management of Canada’s blood supply.<sup>241</sup>

Although we made recommendations on specific aspects of the governance of health research involving humans, our main concern is with the broader picture. Unlike other studies<sup>242</sup>, this report has not been centred on ethics committees and the ethics approval process. Indeed, one of our primary concerns has been with the limitations of an REB-centred perspective (as important as we take REBs to be in the total research process). Ultimately, our concerns have been directed at the culture of research and the larger social, political and economic climate in which research is supported and regulated. It is only with this larger picture – marked with globalisation and commercialisation as well as rapid scientific advances and changing social sensibilities – that one can accurately gauge the challenges that must be met for the ethical governance of research involving humans in Canada.

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<sup>241</sup> H. Krever, Ontario Commission of Inquiry into the Confidentiality of Health Information. *Report of the Commission of Inquiry into the Confidentiality of Health Information* (Toronto: J. C. Thatcher, Queen's Printer for Ontario, [1980 or 1981]).

<sup>242</sup> See for example, for the United States (Office of the Inspector-General, *supra* note 199), Quebec (*supra* note 212), and Australia (Review of the Role and Functioning of Institutional Ethics Committees IECS, *supra* note 218).

From this larger picture, we return in the end to the fundamental concerns that motivate health research involving human subjects – the desire for socially beneficial research and the concern for the protection of human subjects. It is our conviction that this cannot be posed as an “either-or” choice. It is a “both-and” choice. We need both socially beneficial research and the protection of human subjects. Without these two together, there is the serious risk of undermining the fundamental trust relations that underwrite health research – the public’s trust in researchers, research institutions and sponsors and more specifically the trust of research subjects whose continuing participation in research is so essential not only to health research but also to health care. Governance is about maintaining, enhancing and, where necessary, restoring trust in transparent, accountable and effective ways. It is around this goal of trust that this study has been oriented.

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# SECTION G-1

## BIOMEDICAL RESEARCH ETHICS: CONVERGENCE AND DIVERGENCE OF NATIONAL AND INTERNATIONAL STANDARDS

(Section G-1 is a translation of the original French version)

Delphine Roigt

### I. INTRODUCTION

Given the multiplicity of ethical standards that increasingly govern biomedical research, it is worthwhile attempting to determine whether these standards tend to converge towards harmonization, if not standardization, or to diverge in such a way as to create inconsistencies that undermine their effectiveness.

This document will take a very brief look at some international standards as well as standards from a specific selection of countries for comparison with each other. This comparison will be in two stages: In the first stage, we will look at the main international standards in order to identify their requirements for consent, capacity and confidentiality with respect to the participation of human subjects in research, requirements that prove to be the real cornerstone of research ethics. We will then identify, in these same standards, the specific requirements governing the participation of incapable persons (children and incapable adults), participation in an emergency situation, and the possibility of bypassing the duty of confidentiality in respect of a patient who is a research subject. In the second stage, we will look at the national standards of Canada, the United Kingdom, France, the United States and Australia in relation to each other, in view of the same general and specific themes.

We will begin, in the first two parts, by presenting a summary of these standards, without comment, in order to clearly bring out the essentials of the rules of ethics. In the third part, we will provide a brief analysis of the possible convergences and divergences observed.

## II. REVIEW OF INTERNATIONAL STANDARDS

The international standards we will look at are the following:

- *Declaration of Helsinki*, World Medical Association (WMA) (1964-1996).
- *International Ethical Guidelines for Biomedical Research Involving Human Subjects*, Council for International Organizations of Medical Sciences (CIOMS) (1982-1993).
- *Good Clinical Practice: Consolidated Guideline*, ICH Harmonized Tripartite Guideline, International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use, (1997).
- *Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine*, Council of Europe (1997).

We have deliberately confined ourselves to these primary sources in order to get an overview of the trends in the regulation of biomedical research according to the standards generally accepted in most countries.

Although the rules of international law decree that in order for an instrument issuing from an international organization to have any import, the State must have enacted national legislation adopting it, these four normative instruments are part of what might be referred to as the "*common law of ethics*," in the sense that they constitute the formal ethical framework within which most biomedical research is carried out.

### A. *Declaration of Helsinki*, World Medical Association (WMA) (1996)

This document is aimed at physicians in the field of biomedical research involving human subjects. It was first adopted in 1964, then amended several times until its final version in 1996, the one used here.

It states, in the introduction, that "[t]he purpose of biomedical research involving human subjects must be to improve diagnostic, therapeutic and prophylactic procedures and the understanding of aetiology and pathogenesis of disease."

It distinguishes between research combined with care (Section II) and that for essentially scientific ends (Section III).

The five basic principles are: scientific character, beneficence, autonomy, collective evaluation, and confidentiality. It also broaches the rule of proportionality, the notion of free and informed consent, and substituted consent for minors and incapable adults.

Nevertheless, it specifies that it is the physician's duty to "remain the protector of the life and health of the person on whom biomedical research is being carried out " (art. 1, Section III), and that "the interests of science and society should never take precedence over considerations related to the wellbeing of the subject" (art. 4, Section III).

## 1. General Standards

With respect to consent, it states that the subject must be adequately informed of the research and that his informed consent must be obtained, preferably in writing (art. 9, Section I).

It is possible, in the case of clinical medical research and in certain conditions, not to obtain the subject's informed consent if the physician considers this essential (art. 5, Section II). The *Declaration* does not say what these conditions are, but states that the researcher who wants to proceed in this fashion must mention in the protocol the specific reasons why he believes the person's consent should not be required, which protocol will be reviewed by an independent committee (see art. 2, Section I). As for capacity, when a subject is legally incapable, informed consent should be obtained from the legal guardian in accordance with the country's national legislation (art. 11, Section I).

There is no specific mention of patient-physician privilege, but it might be possible to invoke the right to respect for privacy (art. 6, Section I).

## 2. Specific Standards

In the case of physical or mental incapacity making it impossible to obtain the subject's consent, or when the subject is a minor, permission of the responsible relative should be obtained, in accordance with the legislation in force. If the child is in fact able to give consent, it must be obtained in addition to that of the legal guardian (art. 11, Section I).

The *Helsinki Declaration*, however, has no specific standard governing research in an emergency situation or exceptions to the general duty of confidentiality.

## B. *International Ethical Guidelines for Biomedical Research Involving Human Subjects*, Council for International Organizations of Medical Sciences (CIOMS) (1993)

The *World Health Organization* (WHO) and the *Council for International Organizations of Medical Sciences* (CIOMS) have worked together on the subject of research ethics, and in 1982, CIOMS published the *Proposed International Guidelines for Biomedical Research Involving Human Subjects*, with a revision in 1993. These guidelines were intended to make public, and guide research in accordance with the basic ethical principles set out in the *Helsinki Declaration*, which came into effect in 1964.

These guidelines have been widely distributed to many countries and commented on in order to bring about the necessary changes as biotechnological and scientific advances are made. They have also been revised, retaining their primary objective of protecting the rights and well-being of human subjects in the context of biomedical research. The revised version of 1993 is the one now used.

The general ethical principles are: respect for the individual (autonomy), beneficence, and justice. One can see here strong influences of the Belmont Report and the *Helsinki Declaration*.

In the preamble, research is defined as being "clinical," which entails the verification of a hypothesis and is not systematically aimed at the subject's well-being, as is "therapeutic research." It is designed to be diagnostic, prophylactic or therapeutic.

The main headings are: *Informed Consent of Subject*, *Selection of Research Subjects*, *Confidentiality of Data*, *Compensation of Research Subjects for Accidental Injury*, *Review Procedures* and *Externally Sponsored Research*.

### 1. General Standards

The subject's informed consent is necessary for him to participate in the research. In the case of an incapable person, the consent of an authorized representative is required (*Guideline*



1). Moreover, they clearly state what the information must include and the researchers' obligations regarding informed consent (*Guideline 2*). The enrolment of participants and the incentives or forms of compensation that may be used are also discussed (*Guideline 3*).

Concerning patient-physician privilege, the researcher must put in place mechanisms for ensuring the confidentiality of data obtained in the research context and subjects should be informed of the limitations of these mechanisms and of the foreseeable consequences of a breach of confidentiality (*Guideline 12*).

## 2. Specific Standards

Research involving children is permitted, but on certain conditions: it must be necessary, it must address the needs of the children, the consent of the parent or legal guardian is required, the child's consent must have been obtained to the extent that the child is able to give it, and the child's refusal must be respected unless there is no other therapeutic alternative. The risk of the intervention, if the intervention does not directly benefit the child, must be low and proportional to the importance of the knowledge expected to be gained. Finally, there must be an expectation that the therapeutic interventions will be at least as beneficial to the child as any other available alternative (*Guideline 5*).

Research involving individuals with mental or behavioural disorders is permitted on certain conditions: it must be necessary, it must address the specific needs of these individuals, the consent of each subject must have been obtained to the extent that the person is able to give it, and the refusal to participate in "non-clinical" research must always be respected. In the case of incapable persons, consent is obtained from the legal guardian or any other authorized person. The degree of risk of interventions not aimed at benefitting the subject himself must be low and proportional to the importance of the knowledge expected to be gained. Finally, there must be an expectation that the therapeutic interventions will be at least as beneficial to the subject as any other alternative (*Guideline 6*).

The *C/OMS* guidelines do not, however, contain any specific standard governing research in an emergency situation or the possibility of breaching the duty of confidentiality towards the patient.

C. *Good Clinical Practice: Consolidated Guideline, ICH Harmonized Tripartite Guideline*, International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (1997).

These guidelines were drafted in accordance with the *Helsinki Declaration*. They apply primarily to the European Union, Japan, and the United States, but were ratified by Canada's Department of Health in 1997, giving them legal effect. These rules apply to clinical trials.

### 1. General Standards

Consent must be free and informed, and have been obtained from subjects before participation in the trial (guidelines 2.9 and 4.8.1).

The investigator must respect "the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with GCP and the applicable regulatory requirement(s)" (guideline 2.1). The ethics board must have approved the consent form and the written information to be provided to subjects (guidelines 3.1.1-3.1.2 and 4.8.2).

If the subject or his legal representative is unable to read, a witness should be present to ensure that they are given all the information, to attest that they have understood it, and to date and sign for them if they are incapable of doing so (guideline 4.8.9).

Regarding the duty of confidentiality and respect for patient-physician privilege, guideline 2.11 states as a general rule that "[t]he confidentiality of records that could identify subjects should be protected, respecting privacy and confidentiality rules in accordance with the applicable regulatory requirements."

### 2. Specific Standards

In the case of "minors, [or] patients with severe dementia," the consent of the legal representative is required, but these subjects, if capable, should also date and sign the written informed consent (guideline 4.8.12). Specific measures are also called for in the case of non-therapeutic trials, including the fact that the risks to the patient must be low and, unless an exception is justified, that the trials are conducted in patients having a disease or condition that may be treated by such trials (guideline 4.8.14).

Article 4.8.15 provides specifically for research in emergency situations. The consent of the legal representative is required, if present; otherwise, enrolment of the subject "should require measures described in the protocol and/or elsewhere, with documented approval/favourable opinion of the IRB/IEC [institutional review board/independent ethics committee], to protect the rights, safety and well-being of the subject and to ensure compliance with applicable regulatory requirements."

As for the possibility for the researcher to breach his duty of confidentiality, *Good Clinical Practice* (GCP) does not broach this subject specifically. Guideline 2.11 does, however, leave it to the various government or other authorities to put in place measures to ensure confidentiality, which implies that these authorities could provide exceptions to the physician's or researcher's duty of confidentiality towards the patient involved in the trial.

D. *Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine, Council of Europe (1997)*

We reproduce here elements from the summary of the Convention, as presented by the Council of Europe:

- a. first international legal constraining instrument concerning the protection of the dignity, rights and freedoms of human beings from any improper application of biological and medical advances.
- b. the interests of the human being must prevail over the interest of science or society.
- c. principles and interdictions covering genetics, medical research, the consent of the person concerned, the right to respect for private life and the right to information, organ transplantation, the organization of public debate of these issues, etc.
- d. prohibition of any form of discrimination against a person on grounds of his genetic heritage.
- e. authorization of tests which are predictive of genetic diseases only for health purposes.

- f. interventions on the human genome only for preventive, diagnostic or therapeutic purposes and only if their aim is not to introduce any modification in the genome of any descendants.
- g. use of techniques of medically assisted procreation not allowed for the purpose of choosing a future child's sex, except where serious hereditary sex-related disease is to be avoided.
- h. rules governing the conduct of medical research; detailed and specific modalities, notably for persons not able to consent to research.
- i. interdiction of the creation of human embryos for research purposes, and, in countries where the law allows research on embryos in vitro, the law must ensure adequate protection of the embryo.
- j. principle of intervention in the health field only after the person concerned has given informed consent, except in an emergency situation.
- k. withdrawal of consent at any time.
- l. intervention on a person who does not have the capacity to consent (child or incapable person of full age) only for his direct benefit.
- m. every patient entitled to know any information collected about his health, notably, the results of tests which are predictive of genetic diseases.
- n. wish of an individual not to be so informed must be respected.
- o. interdiction of the removal of organs or non-regenerative tissue from a person who does not have the capacity to consent (except, in certain instances, when the recipient of the regenerative tissue is a brother or sister.)
- p. recognition of the importance of public debate and consultation on these issues (except, in certain instances, when public health and safety are threatened, or for the prevention of crime, or when the rights and freedoms of third parties are seriously compromised.)
- q. additional protocols, aimed at clarifying, reinforcing and developing the general provisions of the Convention.

## 1. General Standards

Consent must be free and informed, that is, the person must have been given adequate information (Art. 5).

Under the general provisions governing consent, an intervention on a person who does not have the capacity to consent can only be carried out if it is for his direct benefit (Art. 6, para.

1). The exceptions to this principle are set out in articles 17 and 20, which will be discussed later.

The right to patient-physician privilege is not specifically broached, but the *Convention* discusses respect for the person's private life "in relation to information about his or her health" (Art. 10, para. 1). Thus, everyone is entitled to know any information collected about his health, and his wish not to be so informed must be respected (para. 2).

## 2. Specific Standards

With respect to the participation of a minor in research, the authorization of a third party, be it his representative or an authority or a person or body provided for by law, is required. The opinion of the minor will also be taken into consideration in proportion to his age and degree of maturity (Art. 6, para. 2).

In the case of an incapable person of legal age, the same criteria apply as for minors (Art. 6, para. 3). Whether the person is of legal age or not, the principle is to the effect that the research must yield a direct benefit for the individual, subject to the exceptions stipulated in Articles 17 and 20.

Also discussed are persons who have "a mental disorder of a serious nature," who may be subjected, without their consent, to an intervention if it is aimed at treating their disorder where, without such treatment, serious harm would likely result to their health (Art. 7).

Chapter V sets out the specific conditions for the protection of persons in the case of scientific research, as well as exceptions to the general principles of Article 6. Thus, in the case of persons without the capacity to consent to research, the persons authorized to consent for them must have given their consent in writing, and the person concerned must not object (Art. 17, para. 1). Also, where the trials are of no direct benefit to the incapable person, further conditions are stipulated concerning future benefit to the person concerned or to other persons in the same category, and in accordance with the notion of minimal risk (Art. 17, para. 2). This constitutes an exception to the general principle that research must not be carried out on incapable persons unless it is of direct benefit to them.

Article 8 of the *Convention on Human Rights and Biomedicine* provides specifically for research in an emergency situation. An intervention may be carried out in an emergency situation when consent cannot be obtained. The intervention must be medically necessary and

be for the benefit of the individual concerned. This seems to apply to a decision involving essentially a medical diagnosis, when there is no specific recourse for obtaining the opinion of a research ethics board or the consent of an authorized third party.

Finally, it states that a person has the right to know any information about his health, and that his wish not to be so informed must be respected (Article 10, para. 1 and 2). It also states that, in exceptional cases, the law may place restrictions on the exercise of the rights contained in paragraph 2 in the interests of the patient (Art. 10, para. 3). Thus, no specific provision is made for the possibility for the physician or researcher to breach his duty of confidentiality.

### III. REVIEW OF NATIONAL STANDARDS

In this section, we will look basically at three specific themes: the notion of emergency, the notion of consent of incapable persons, and the possibility of breaching the duty of confidentiality. The countries of reference are Canada, the United Kingdom, the United States, Australia and France.

But before tackling the three specific themes, we will attempt to provide an overview of the system into which these notions and rules fit legislatively and normatively.

#### A. Canada

The documents that "guide" biomedical research in Canada are few in number and, for the most part, have no formal legal character and therefore cannot be considered laws, as is the case in France or the United States, for example.

The coming into effect in September 1998 of the *Tri-Council Policy Statement on the Ethical Conduct of Research Involving Human Subjects* gave Canada an internal document that establishes the procedures and ethical limits for research. Several headings set out the different rules designed to help researchers steer ethics towards respect for persons and ethics. While it is not a legislative instrument, its import is considerable as any research subsidized by one of its three councils (*Medical Research Council of Canada, Natural Sciences and Engineering Research Council of Canada and Social Sciences and Humanities Research Council of*

*Canada*) must, as a minimum, observe the principles and rules it sets out. The Councils hope, moreover, that this document will serve as a general reference for all research in Canada for achieving some standardization of the rules of ethics.

Incidentally, in June 1998, the *Ministère de la santé et des services sociaux du Québec* (MSSS) published its ministerial action plan on research ethics and scientific integrity (*Plan d'action ministériel: Éthique de la recherche et en intégrité scientifique*), which establishes a scientific framework within which all research activities are to be carried out in the health and social services system, that is, in the institutions governed by the MSSS. The *Plan* clearly stipulates that the standards to be met must be in accordance "with the broad normative frameworks in effect at the international level with respect to research ethics and scientific integrity, frameworks adhered to by the *three main granting agencies of reference in Canada*" [translation] (authors' italics). This *Plan* thus enshrines in a legislative document the standards of the *Statement*, thereby giving them quasi-legislative import in the context of research done within Quebec's health system. The *Plan* also refers to the following international rules: the Nuremberg Code (1947), the different versions of the Declaration of Helsinki (1964-1975), and the CIOMS guidelines (1993). It also provides for a specific regulatory framework for research involving incapable persons, in view of the application of Article 21 of the Civil Code of Quebec.

In this study, we have confined ourselves to a review of the *Statement*, the *Plan*, and the Civil Code of Quebec.

## 1. General Standards

In Canada, as in Quebec, consent is a fundamental notion linked to respect for the autonomy and integrity of the person. As a rule, the individual's consent is always required, whether it be to provide him with care or for his participation in a research project. The Civil Code of Quebec (C.C.Q.) stipulates specific rules in Articles 11 *et seq.* governing consent to care and research on persons of full age, minors and incompetent persons of full age.

In the *Statement*, the notion of free and informed consent is covered in a special section (Section 2). It states generally that consent must be obtained in writing (Article 2.1), that it must be voluntarily given (Article 2.2), and that full and frank information must be disclosed to the subject (Article 2.4), in order to satisfy the criteria of free and informed consent.

In Quebec, the principle of patient-physician privilege is enshrined in Quebec's *Charter of Human Rights and Freedoms* (R.S.Q., c. C-12), in the *Medical Act* (R.S.Q., c. M-9) and in the *Code of Ethics of Physicians* (R.R.Q., 1981, c. M-9, r. 4), this last being a regulation enacted in accordance with the *Professional Code* (R.S.Q., c. C-26, s. 87) and the *Medical Act*.

Similar principles exist in the rest of Canada<sup>243</sup> and are enshrined in the Code of Ethics of the *Canadian Medical Association*, which, unlike the Quebec Code of Ethics of Physicians, has no legal effect, but is adhered to by its members.

In Canada and Quebec, a distinction is usually made between the right to privacy and the right to confidentiality, the second being defined as the right to authorize or refuse the disclosure of confidential medical information.

The principle of the respect for privacy is set out in Article 35 C.C.Q. Article 37 C.C.Q. applies to files established on persons, which includes files established in the context of research involving human subjects. The information they contain is confidential, and must have been obtained and can only be communicated with the person's consent. In particular instances, however, information can be obtained without the person's consent, for example pursuant to law or a court order.

The *Statement* has a separate section on the privacy and confidentiality of medical information (Section 3). The basic principles are the protection of personal information, which applies to information obtained "directly from subjects or from other researchers or organizations that have a legal obligation to maintain personal records confidential" (p. 3.1 of the *Statement*).

## 2. Specific Standards

In Canada, as in Quebec, the competence or capacity to give consent, whether to receive care or to participate in research, are governed according to the notion of informed consent. Since in civil law, as well as in common law, capacity is presumed (Art. 4 C.C.Q.), every person should thus be able to give consent to submit to an experiment, provided the risk is proportional to the benefit that can reasonably be anticipated (Art. 20 C.C.Q.). However, the notion of "substituted consent" makes it possible for a person deemed incapable, because of age, or physical or mental condition, to submit to an experiment provided the experiment does

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<sup>243</sup> G.B. Robertson and E.I. Picard, *Legal Liability of Doctors and Hospitals*, 3<sup>rd</sup> Ed., (Toronto: Carswell, 1996).



not involve serious risk to his health, and the person, if he understands the consequences, does not object, and the experiment has the potential to produce benefit to the person's health or to other persons in the same category (Art. 21 C.C.Q.).

Thus, in the case of incapable persons, consent to submit to an experiment is given by the person having parental authority or the tutor, and in the case of incapable persons of full age, by the mandatary, tutor or curator. Similar principles are stated in articles 2.5-2.6 and 2.7 of the *Statement*, although they refer instead to "authorized third parties" and state that subjects should not be exposed to more than minimal risks if the research has little potential for direct benefits for them (Article 2.5 (b) and (c)). Moreover, the refusal of the legally incapable individual who understands the nature and consequences of the research should be respected (Article 2.7). The *Statement* also states the principle that incapable persons should not be automatically excluded from research which is potentially beneficial to them as individuals or to the group that they represent (Article 5.3).

Article 21 of the C.C.Q. makes special provision for obtaining consent to an experiment in an emergency situation, where a person of full age suddenly becomes incapable of consent: if there is no time to designate a legal representative, consent is obtained from the person authorized to consent to care, that is, the spouse or, if there is no spouse or the spouse is prevented from giving consent, by a close relative or a person who shows special interest in the person of full age (Art. 15 C.C.Q.). A competent ethics board will have to determine, when reviewing the research project, whether the experiment meets that condition. Obviously, this review can only be done *a posteriori*, unless an *ad hoc* board or special meeting gives approval to proceed.

The *Statement* also proposes specific measures to Article 2.8: research in emergency health situations must address the emergency needs of the persons involved, and be in accordance with criteria established by research ethics boards (REBs), and these boards may allow such research to be carried out without the free and informed consent of subjects or their authorized third parties on certain strict conditions. These conditions are:

- a) a serious threat to the prospective subject requires immediate intervention;
- b) either no standard efficacious care exists or the research offers a real possibility of direct benefit to the subject in comparison with standard care;

- c) either the risk of harm is not greater than that involved in standard efficacious care, or it is clearly justified by the direct benefits to the subject;
- d) the prospective subject is unconscious or lacks capacity to understand the risks, methods and purposes of the research;
- e) third-party authorization cannot be secured in sufficient time, despite diligent and documented efforts to do so;
- f) no relevant prior directive by the subject is known to exist.

Consent must then be obtained promptly, either when the subject regains capacity, or from an authorized third party when one is found.

In neither common law nor civil law does the physician have a formal and legal obligation to disclose or warn third parties of the possibility of their contracting a disease owing to a disorder diagnosed in one of his patients. The physician may, at his discretion, decide to warn one or more persons close to the patient when the patient refuses to do so and he believes this may cause serious harm, and in this regard Quebec's Code of Ethics of Physicians allows this exception (art. 3.04 and art. 3.05). In this case, however, he is discharging a *moral* obligation and risks being sued by his patient for breach of patient-physician privilege.

The *Statement* stipulates that the results of genetic testing and genetic counselling records are protected from access by third parties, unless free and informed consent is given by the subject (Article 8.2).

## B. United Kingdom

According to the information we were able to obtain, while the rules of common law are the foundation of the system for the countries of the United Kingdom, medical research is governed by guidelines published by the Royal College of Physicians of London,<sup>244</sup> by the Medical Research Council of 1992,<sup>245</sup> and specifically by documents published by the Department of Health.<sup>246</sup>

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<sup>244</sup> Royal College of Physicians of London. *Research involving patients* (1990).

<sup>245</sup> Medical Research Council. *Responsibility in Investigations on Human Participants and Material and on Personal Information* (1992).

<sup>246</sup> Department of Health. *Local Research Ethics Committees*, HSG (1991).

## 1. General Standards

An individual's participation in an ethical research program is based on his free and autonomous participation, which depends on informed consent. The extension of informed consent *to treatment* is not part of English law. The subject's consent is necessary and sufficient in most cases.

Research or experimentation is permitted on adults in both England and Wales. In Scotland, however, persons under 16 years of age may also consent to certain surgical, medical or dental procedures or treatments, on certain conditions. Under the guidelines published by the Royal College of Physicians, an analysis of the risks and benefits must be done in each case, in addition to obtaining the patient's fully informed consent.<sup>247</sup>

The obligation of confidentiality is recognized in common law in the *Medical Act*, as confirmed by the authors of the volume *Medical Law: Text with Materials*.<sup>248</sup> There seem, however, to be exceptions when this is in the patient's interest.<sup>249</sup> For example, a physician who might believe his patient incapable of driving a vehicle could, after encouraging the patient to disclose this information to the motor vehicle registry, send a confidential memorandum to the physician at the registry office. Other statutory exceptions are also mentioned under the laws on abortion and public health.<sup>250</sup>

## 2. Specific Standards

In the case of an unconscious, and therefore incapable, patient, the main justification for intervening without his consent is the criterion of medical necessity, but only in cases of standard treatment. Otherwise, treatment of an incapable person must always be based on the criterion of the best interests of the person. This same criterion applies to minors.

Research involving children must be in their best interests, for their well-being. In the case of children under 16 years of age, the parents' consent is needed. Ethics boards must assess the risk-benefit ratio for the child.

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<sup>247</sup> D. Morgan and E. Hitchings, *Regulating Artificial Reproductive Technology & Genetics. National Report: United Kingdom*, (presented at the International Conference on Biomedicine, The Family and Human Rights, August 1999) a 3.

<sup>248</sup> I. Kennedy and A. Grubb, *Medical Law: Text with Materials*, 2<sup>nd</sup> Ed. (London: Butterworths, 1994) a 639.

<sup>249</sup> General Medical Council, *Duties of a Doctor: Confidentiality (1995)* para. 10

<sup>250</sup> *Id.*, at 644 et seq. and *Id.* note 243, at 7.

Emergencies and certain public health grounds are exceptions where the subject's consent is not required. The principle of "medical necessity" then seems to apply, involving basically a medical decision.

For the participation of incapable persons in research, it is necessary to refer, in the case of children, to the *Guidelines for the Ethical Conduct of Medical Research Involving Children*, British Paediatric Association, 1992. The notion of risk is essential here, as is that of whether the research is therapeutic or not.

In the case of incapable adults, the need to use them must also be justified, that is, the knowledge the researcher wants to obtain cannot be obtainable from capable adults. There is, moreover, a document that provides a number of guidelines in this regard, namely *The Ethical Conduct of Research on the Mentally Incapacitated* (MRC), 1991.

There is no legal obligation to inform in the absence of a particular relationship. The physician's duty of confidentiality exists under common law. The duty to warn is subject to the *Bolam* principle, which states that a physician is not negligent if he acts in accordance with a practice currently accepted by an entity responsible for giving a medical opinion. According to the *Nuffield Council on Bioethics*, genetic information could, in some circumstances, be disclosed to family members without the patient's consent. The individual should then have been warned in advance that the results could be useful to members of his family and have been encouraged to disclose the information himself before the physician does so. This view differs from the position of the *Select Committee on Science and Technology*, which believes that the individual's decision has priority. This, however, is a discretion granted to the physician, rather than a legal obligation to warn.<sup>251</sup>

## C. United States

The information we present to you here is only a very general look at the basic criteria governing biomedical research in the United States. We referred essentially to the opinions issued by the *National Bioethics Advisory Commission*, to the rules of the *Code of Federal Regulations* and to those of the *National Institutes of Health*. We will therefore present no information on the rules governing the various states.

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<sup>251</sup> Id. note 243, at 20.

## 1. General Standards

Medical law in the United States rests essentially on three fundamental principles: the autonomy of the patient, the public interest, and professional competence. The doctrine of informed consent applies to obtaining the patient's consent to treatment, except in an emergency setting, in which case the patient waives his right to be informed and consents in advance to any action the physician deems appropriate and in accordance with the doctrine of "therapeutic privilege."<sup>252</sup> With regard to this doctrine, however, we have to say that it is more of a possibility for the physician to "breach" his obligation to inform, than an exception to the rule of informed consent.

Informed consent is a mandatory component of the ethical use of persons as subjects of research or medical experiments. It is largely accepted and explicit in the federal regulations that informed consent must be obtained from prospective subjects before enrolling them in any research protocol (Sec. 46.116 CFR and Sec. 50.25 CFR).

Thus, the *Federal Policy for the Protection of Human Subjects (45 CFR 46)*,<sup>253</sup> known as the "Common Rule," sets out a series of rules adopted independently by seventeen federal agencies that conduct, support or otherwise govern research involving human subjects. The *Food and Drug Administration* has also adopted certain provisions of the "Common Rule." The *National Institutes of Health*, for its part, ensures, within the federal government, that the protection of human subjects is consistent from one government agency to another.

In the context of federal regulation, research is defined as "a systematic investigation designed to develop or contribute to generalizable knowledge" (45 CFR 46.102(d)), which encompasses both clinical trials and genetic research.

## 2. Specific Standards

Minors can participate in research presenting minimal risk with the written consent of parents or legal guardians, and with the child's consent if he is capable of giving it (Sec. 46.404 and Sec. 46.408. CFR). Aside from minimal risk, the research must provide a direct benefit to

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<sup>252</sup> C.E. Schneider and L.D. Wardle, *Biomedicine, The Family and Human Rights: National Report on Genetics, Artificial Reproduction and the Law in the United States of America* (presented at the International Conference on Biomedicine, The Family and Human Rights, Oxford, August (1999) at 5.

<sup>253</sup> United States Department of Health and Human Services (DHHS), National Institutes of Health (NIH), Office For Protection From Research Risks (OPPR), *Protection of Human Subjects*, Part 46, Subpart A *Federal Policy for the Protection of Human Subjects (Basic DHHS Policy for Protection of Human Research Subjects)*, 1991.

the child or develop generalizable knowledge about the child's disease or condition (46.405 and 46.406 CFR). In the case of incapable persons, it is the legal representative who must provide the consent (Sec. 56.111 (4) CFR).

Research may be conducted in an emergency setting and constitutes an exception to obtaining the subject's consent (Sec. 50.23-50.24 CFR). Obviously, the protocol must have been reviewed by an ethics board, and the subject must be in a life-threatening situation where standard treatment is ineffective, making it necessary to test a new procedure or treatment. Also, it is not necessary for the research to be of direct benefit to the subject, but the risks must be reasonable and proportional (50.24 (a) (1), (2), (3) CFR).

Confidentiality is a right protected by American law, and in the context of medical information the right to privacy is rendered by the protection of personal information, confidentiality, and freedom of choice.

In medicine, the American tradition provides for the duty to protect and preserve life, a more worthy duty than confidentiality. Thus, two government bodies (the *President's Commission for the Study of Ethical Problems in Medicine and Bioethical and Behavioral Research (1983)* and the *Committee on Genetic Risks of the Institute of Medicine (1994)*) established conditions that allow a physician to "ethically" breach the duty of confidentiality and inform families of risks arising from the identification of a genetic disease in a patient.

Thus, families might be informed if (1) all attempts to have the patient disclose the information have failed; (2) the likelihood is great that irreversible or mortal harm will be caused to family members as a result of non-disclosure; (3) disclosure of the information will prevent harm being caused; (4) disclosure is limited to the information necessary for the diagnosis and/or treatment of the family member.

However, unlike the other countries studied in the context of this project, the United States prides itself on an ethical, but formal, obligation to warn third parties or disclose to them confidential information in certain conditions: (1) there must be a particular relationship between the physician and either the person who could cause the harm, or the potential victim; (2) the potential victim or the person at risk is identifiable; and (3) the harm caused is foreseeable and

severe.<sup>254</sup> In these instances, a physician who is sued for breach of confidentiality would have a defence to present and could be exonerated.

## D. Australia

Medical research is governed primarily by the *Statement on Human Experimentation 1992* of the National Health and Medical Research Council. This document has been revised and is now replaced by the *National Statement on Ethical Conduct in Research Involving Humans*, except for supplementary notes 5 and 7, which remain in effect from their date of publication, i.e., October 1983 and November 1992, respectively (hereafter called the *Statement*). This new document came into force in June 1999, and this is the version used.

### 1. General Standards

The subject's consent is nearly always required, except in emergency situations and cases of epidemiological research.

As in the United Kingdom, and before the coming into force of the new *Statement* of 1999, at least with respect to research involving humans, the American doctrine of "informed consent" was not part of Australian law. It seems, then, that a patient's consent was legal if it was based on a broad understanding of what was proposed, even if the patient had not been fully informed.<sup>255</sup> In contrast, the rule of informed consent now prevails in the case of research. The test used by a physician to determine the degree of information is as follows: more information should be provided in the case of non-therapeutic research than in the case of therapeutic research, because it is expected that the average person will weigh less foreseeable risks more heavily if the research does not benefit him in any way.

The age of majority in Australia is 18, but the districts of New South Wales and South Australia have special legislation governing a child's consent to medical procedures, at age 14 and 16, respectively. Until the child reaches legal age, either parent may consent for him. But

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<sup>254</sup> The American Society of Human Genetics Social Issues Subcommittee on Familial Disclosure, ASHG Statement, "Professional Disclosure of Familial Genetic Information" (1998) 62 Am. J. Hum. Genet 474.

<sup>255</sup> *Rogers v. Whitaker* (1992) 175 CLR 479 (HCA).

"mature minors" can independently consent to treatment under the application of the "*Gillick*" test.<sup>256</sup>

The main justification for research or the disclosure of confidential information without the patient's or subject's consent is the utility criterion: the project's benefit to society is more significant than minimal invasion of the patient's physical integrity or privacy. Chapter 18 of the *Statement* concerns the confidentiality of data in the context of research involving human subjects.

There are many exceptions to the general duty of confidentiality, the essential one having to do with the public interest (for example, the disclosure of confidential information to the partners of HIV patients). Physicians must often disclose information about patients to various government departments: reportable diseases, child abuse, distribution of certain drugs, diseases affecting the ability to drive, and so on.

The medical duty of confidentiality is a duty under common law, but also under legislation (*Privacy Act 1988*).

## 2. Specific Standards

Non-therapeutic research may be conducted on incapable adults who have been fully informed and have given their consent (Art. 1.7 *Statement*).

Such consent obtained from an adult constitutes authority ensuring sufficient legal import. Consent for a child is given by the parents, who can only consent to procedures that are in the child's best interests (Art. 4.1 *et seq. Statement*). Consent will also be obtained from the child when he is sufficiently able to make this decision. The consent of incapable persons is required to the extent possible, and consent must be obtained from the person's guardian or an authority or other organization or person having that responsibility at law (Art. 5.1 *et seq. Statement*). The "best interests" criterion prevails. Thus, the range of non-therapeutic research is reduced in the case of children and other vulnerable persons. The invasion must be minimal and the potential benefits significant.

In the case of incapable adults, some Australian jurisdictions have legislation governing the appointment of a guardian. However, even in the absence of such legislation, informal

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<sup>256</sup> *Gillick v. West Norfolk AHA* [1986] AC 112 (HL)



consent is given by family members or persons caring for the patient, in the case of procedures that are recommended by a physician and in the patient's best interest. With the coming into force of the new *Statement*, consent must now be obtained from persons authorized to give it (guardian or other legal authority) and their refusal must be respected (Chapter 5).

In the case of non-therapeutic research, the risk for the child should be so minimal as to be similar to the risks incurred in everyday life. Consent should be obtained from the child and from the parent if the child does not have the maturity and intellectual capacity to exercise such consent (Supplementary Note 2 of the old *Statement*). As for the new *Statement*, any research involving children and young people must meet specific criteria concerning their best interests, and their refusal must be respected (Chapter 4).

There is now a specific standard in the new *Statement* (Chapter 6). For emergency care research, consent has to be obtained rapidly (6.1). The general rule that applies when it is not possible to obtain consent, in emergency cases, from the person or from his legal representative, is that a human research ethics committee must approve the project if it is in the patient's best interests, and the research must be in the person's best interests and involve minimal risk.

The research must be scientifically valid and the patient or his legal representative must be informed as soon as possible of the patient's inclusion in the research, and of his option to withdraw from it (6.9).

Australian law governing genetic research and reproductive technology, for example, varies depending on the state or territory. The following territories have no specific legislation: the Australian Capital Territory, New South Wales, Northern Territory, Queensland, Tasmania, and New Zealand.

It is interesting to note that in the chapter on human genetic research, provision is made to allow the human research ethics committee, in certain conditions, to suspend the researcher's obligation to obtain consent (16.12 *et seq.* of the *Statement*). The ethics committee must take into account the nature of any existing consent relating to the collection and storage of the genetic material and genetic information, the justification presented for seeking waiver of consent, the proposed arrangements to protect privacy and confidentiality, the risks related to a breach of confidentiality, the possibility of commercialization, and relevant laws and regulations.

No duty to warn is recognized in Australia, as it is in the United States. In the Commonwealth, the collection, storage, use and disclosure of personal information by Commonwealth agencies are regulated by the *Privacy Act 1988*. An excerpt from this legislation is provided in Appendix 2 of the *Statement* and stipulates certain cases where the disclosure of personal information is permitted, thus constituting exceptions to the duty of confidentiality (Principle 11). These are essentially cases where the person has been made aware that information might be disclosed (such as the standard endorsement on research consent forms), or the person has consented to the disclosure, or the record-keeper has legitimate reasons for believing that the disclosure is necessary to prevent more serious harm to the individual concerned or another person, or the disclosure is required or authorized by law or, finally, the disclosure is necessary for the enforcement of the criminal law or to protect the public (Principle 11 para. 1).

## E. France

Of all the countries we have looked at so far, France has the most detailed regulations. Every aspect of biomedical research seems regulated and sanctioned by legislation, as opposed to being covered by guidelines, as in the case, for example, of Canada and Australia.

While the conditions in which biomedical research is carried out are regulated by statute, some authors maintain that "one cannot conceive of respect for laws as simply the enforcement of substantive provisions, but as respect for the spirit of the texts, especially when it is a question of information, consent, the protection of persons" [translation] (comments of the *Comité Consultatif National d'éthique* on the *Code de déontologie médicale*).

The *Lois bioéthiques* govern and enshrine the practice of biomedical research involving humans. They include, notably, the following: *Loi du 20 décembre 1988 modifiée (Loi Huriot-Sérusclat) et son instruction de procédures; Décret no 90-872 du 27 sept. 1990 modifié; Loi relative au respect du corps humain: loi 94-653 du 29 juillet 1994* (governing respect of the human body); *Extraits de la loi relative au don et à l'utilisation des éléments et produits du corps humain, à l'assistance médicale à la procréation et au diagnostic prénatal: loi 94-654 du 29 juillet 1994* (governing the donation and use of components and products of the human body,

medical assistance for procreation and prenatal diagnosis); *Décret relatif à l'importation et l'exportation d'organes, de tissus et de cellules du corps humain, à l'exception des gamètes* (governing the import and export of human organs, tissue and cells, other than gametes). These *Lois bioéthiques* are supplemented by certain legislative texts governing identifying information in the field of health.

In France, biomedical research is divided into two areas: research of direct benefit to the individual, and research of no direct benefit to the individual. Thus, specific rules apply depending on whether or not a direct benefit is anticipated for the person consenting to the research. Also, specific penal sanctions are incorporated into the *Loi Huriet-Sérusclat* in the event these rules are breached (Titre V, art. L. 209-19 et ss.).

## 1. General Standards

In France, consent is a basic principle, "both a legal and a deontological pillar" [translation] of the practice of biomedical research involving humans. In this regard, France echoes the principles set out in various international documents such as the *Helsinki Declaration* and the *Convention on Human Rights and Biomedicine*.

Biomedical research requires the person's free, informed and express consent, after the investigator or a physician who represents him has explained the research to him (art. L. 209-09). In exceptional cases, and when it is in the patient's best interests, the investigator may withhold certain information about his diagnosis, and the protocol must mention this possibility (art. 209-09). This is the doctrine of "therapeutic benefit," which is also enshrined in the *Code de déontologie médicale* (article 35).

The *Loi Huriet-Sérusclat* makes no special provision respecting patient-physician privilege. However, pursuant to articles 226-14 and 226-14 [sic] of the French Penal Code, the disclosure of privileged information by someone entrusted with it, by reason of either status or profession, other than as required or authorized by law, is liable to punishment. Health professionals are therefore bound by the duty of confidentiality, but are also obliged to disclose or declare certain information to legal, medical or administrative authorities when required by law to do so.

## 2. Specific Standards

The principle of "direct benefit" applies to research involving minors and protected persons of full age (art. L. 209-6). Research of no direct benefit may, however, be conducted if the following three conditions are met: (1) the research presents no serious risk to their health; (2) it must be helpful for persons of the same age, disease or disability; and (3) it cannot otherwise be conducted. Consent is subject to the general rules of art. L. 209-9 and must be given by the person having parental authority, the legal representative, the guardian authorized by the family council, or the guardianship judge, according to whether the person is a non-emancipated minor, a minor or a protected person of full age. In addition, the consent of the minor or of the protected person of full age will be sought when he is capable of expressing his wish. The research cannot be conducted if the minor or protected person of full age refuses (art. 209-10).

The notion of emergency is dealt with specifically. Article L. 209-5 of the *Loi Huriet-Sérusclat* stipulates that research in emergency situations is permissible without the consent of the persons concerned, if "there is the prospect of a direct and significant benefit to their health" [translation]. The consent will then be obtained from members of the subject's family, if they are present, and the consent of the person concerned will be required as soon as possible for any continuation of the research (art. L. 209-09). It seems that physicians, according to the interpretation given the text of the law, are also authorized to conduct research without a person's consent, provided the advisory committee for the protection of persons involved in biomedical research has given its favourable opinion.

Finally, the obligation or duty to warn that exists in American law has no equivalent in French law.

## IV. ANALYSIS AND COMMENTS

The regulations governing biomedical research are becoming increasingly refined with the many and rapid technological and scientific developments. Some countries, like Canada and Australia, prefer to set guidelines, while others, like France and the United States, prefer to proceed by means of formal, legislative means. The United Kingdom seems to be standing back

somewhat, preferring to refer to the special opinions emanating from various boards and *ad hoc* commissions.

We nevertheless believe that the growing trend is aimed at presenting and bringing into force documents that will serve as primary sources for the "sound management" of biomedical research in various countries, whether by means of legislation or otherwise.

Various international documents have often served as a reference for the drafting of national documents; which implies a convergence of standards, rather than a divergence, in these instances. The *Helsinki Declaration*, the *Belmont Report* and the *CIOMS* guidelines are all documents that have inspired the national documents we have touched on here. We can even see an obvious similarity between Canada's *Statement* and that of Australia, prompting one to think that the various national entities look at what has been done elsewhere, rather than reinvent the wheel.

We believe the number of similarities is growing because research is tending more and more towards a kind of standardization, owing to forces such as the multiplicity of multi-centre studies, which, although subject to a separate ethics review in each institution, oblige these institutions to publish or comply with standards that are often uniform. We cannot help but note that as far as our personal experience in Quebec is concerned, when establishing REBs at an institution, the rules are nearly always identical from board to board. Each board may have its own requirements, but basically, the sources of reflection remain the same.

The divergence is at various levels. First of all, the more recent national documents are more exhaustive than the initial international regulatory documents. This is not a real divergence, but rather a vision enriched by the contribution of the scientific discoveries of the last thirty years. Incidentally, there have been a number of major scientific breakthroughs since the *Nuremberg Code* was drafted, and it was therefore not possible at that time to speak directly of genetic research, for example. Also, while the international documents seem less detailed, this may be the result of an attempt to harmonize the views of different countries, the desire to achieve some consensus.

Secondly, some areas of divergence are attributable to the inherent social values of each country. Standards are something of a vehicle for conveying the values of a society. These values have changed greatly over the last thirty years. Thus, the coming into force of various human rights charters and the drafting of different legislative or other texts on the rights of

patients, the rights of the disabled, the rights of children, are so much evidence of changing social values.

Finally, there are also fundamental areas of divergence, such as the duty to warn, as well as more subtle areas of divergence, such as research in an emergency situation.

Let us take another look, for example, at *Good Clinical Practice* (4.8.15) and compare with the *Statement* (Article 2.8): we can see that the former speaks of seeking the consent of the legal representative and, if none is available, states that "the enrollment of the subject should require measures described in the protocol and/or elsewhere, with documented approval/favourable opinion by the IRB/IEC, to protect the rights, safety and well-being of the subject and to ensure compliance with applicable regulatory requirements." In contrast, the *Statement* stipulates that it is possible for research in emergency health situations, subject to all applicable legislative and regulatory requirements, to be conducted without the free and informed consent of the subject or of his authorized third party if all of the conditions set out under Article 2.8 apply. The notions of "*legal representative*" and "*authorized third party*" do not have the same import, which in this particular case might lead one to think that since the appointment of a legal representative is a fairly complex undertaking, the rule of obtaining consent under the *GCP* could be easily bypassed, and the experiment could easily be conducted without anyone's consent. Also, since the rules of the *Statement* do not have the imperative and mandatory nature ascribed to the *GCP*, a strict interpretation could render them inoperative in the eyes of some.

The *Civil Code* (Art. 21) seems to have provided for this situation in stating that if a legal representative cannot be designated in time, "consent may be given by the person authorized to consent to any care the person requires," that is, the spouse, or, if there is no spouse, a close relative or someone who shows a special interest. In this case, it would be up to the competent ethics board to determine, when reviewing the protocol, whether the experiment satisfies this condition. However, the ethical essence of the conditions set out in the *Statement* is found in neither the *Civil Code* nor the *GCP*. This could therefore lead to conflicting interpretations of the standards, which would not necessarily be to the subject's benefit.

There are also differences with respect to the participation of incapable persons. Some organizations require, allowing for exceptions, a direct benefit for the subject (*Convention on Biomedicine*), while others make no distinction between the direct or indirect benefit of research

involving incapable persons (*Helsinki*). *Good Clinical Practice* requires that, unless an exception is justified, non-therapeutic trials should be conducted in patients having a disease or condition which may be treated by the trial (guideline 4.8.14). This, in itself, is a paradox, since it seems to require a direct benefit, although it concerns trials entailing no such benefit. Most of the documents studied converge with respect to the requirement of "minimal risk" attached to the participation of incapable persons in research (*CIOMS*, *GCPs*, *Convention on Human Rights and Biomedicine*, and the relevant documents of the five countries analyzed).

It can also be seen, for example, that Australia makes no provision for a legal obligation to warn, leaving the door open to the possibility of legislative intervention if necessary, as is done in the United States. This position differs from that of Quebec, for example, which also makes no provision for a legal obligation, but which leaves the disclosure of confidential information to the discretion of the physician, which discretion is incorporated into a document having legal effect (*Code of Ethics of Physicians*).

There is also a difference between France and the other countries with respect to the notion of "therapeutic benefit" in the context of research. This notion does not seem to have force in the other countries.

Without insisting that every country have its own legislation on biomedical research ethics, it would be worthwhile for guidelines such as Canada's *Statement*, that of Australia, and the different opinions of national ethics organizations, to come to be considered rightly as elements of the "*common law of ethics*." Otherwise, a "pure," strictly legalistic interpretation would relegate these sources to the ranks of reference documents.

Our analysis is therefore more an observation, since we could extend our thinking much further, for example, by attempting to identify the philosophical, historical or legal origins of the choices of each country and each entity to develop one type of standards rather than another. We might also have identified more legislative sources for each country, since common law sources use essentially case law to establish precedents that have force of law, and we have cited very few. Also, as each country is divided into regions, provinces or states, we might have identified the differences between federal jurisdictions and regional jurisdictions with respect to biomedical research. But since this document is intended merely as a general reference tool, we leave that opportunity to other authors.





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## SECTION G-2

### LIST OF COMMON ABBREVIATIONS

<b>Abbreviation</b>	<b>Explanation</b>
CA	Conseil d'administration
CCAC	Canadian Council on Animal Care
CEP	Comité d'éthique provincial
CER	Comité d'éthique de la recherche
CES	Comité d'évaluation scientifique
CHUM	Centre hospitalier de l'Université de Montréal
CIHR	Canadian Institutes for Health Research
CIOMS	Council for International Organizations of Medical Sciences
CLERUM	Comité de liaison en éthique de la recherche de l'Université de Montréal
CMA	Canadian Medical Association
CMDP	Conseil des médecins, dentistes et pharmaciens du Québec
CAN	Canadian Nurses Association
CPA	Canadian Psychological Association
CQRS	Conseil québécois de la recherche sociale
CRM	Conseil de recherches médicales du Canada
CUE	Comité universitaire d'éthique
FRSQ	Fonds de la recherche en santé du Québec
G1	Guide d'entrevue - comité d'éthique de la recherche
G2	Guide d'entrevue – organismes nationaux

GCP	Good Clinical Practice
GCPG	Good Clinical Practice Guidelines
HPB	Health Protection Branch
HRIHS	Health Research Involving Human Subjects
ICH	International Conference on Harmonization
IRB	Institutional Review/Research Boards
MRC	Medical Research Council
MSSS	ministère de la Santé et des Services Sociaux
NCBHR	National Council on the Bioethics of Human Research
NCEHR	National Council on Ethics in Human Research
NHRDP	National Health Research and Development Program
NIH	National Institutes of Health
PA	Plan d'action ministériel en éthique de la recherche et en intégrité scientifique
QA	Quality Assurance
QI	Quality Improvement
REB	Research Ethics Boards
RFP	Request for Proposals
RIHS	Research Involving Human Subjects
TCPS	Tri-Council Policy Statement
TPP	Therapeutic Products Programme
UdM	Université de Montréal

## SECTION G-3

# STUDY PANEL ON BIOMEDICAL RESEARCH INVOLVING HUMAN SUBJECTS

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Executive Director  
Heart and Stroke Foundation of Canada

**Susan Zimmerman**

Director of Research  
Law Commission of Canada

**Dr. Mary Vachon**

Consultant in Psycho-Social Oncology and  
Palliative Care  
Toronto Sunnybrook Regional Cancer  
Centre



# SECTION G-4

## BIOGRAPHICAL STATEMENTS

**Dr. Michael M. Burgess** is the first occupant of the Chair in Biomedical Ethics at the University of British Columbia's Centre for Applied Ethics, and the Department of Medical Genetics, beginning in January 1996. Burgess also has a clinical appointment to the B.C. Children's Hospital.

Burgess has an M.A. and Ph.D. in philosophy with a concentration in health care ethics from the University of Tennessee. In 1984 he joined the Department of Philosophy and the Faculty of Medicine at the University of Calgary. At the University of Calgary, Burgess worked with Dr. T.D. Kinsella in the Office of Biomedical Ethics, with teaching in the undergraduate and graduate programs of the Faculty of Medicine, conducting ethical reviews of research and serving as an ethicist on the Conjoint Medical Ethics Research Committee. Burgess also chaired the University of Calgary's General Faculty Council Standing Committee on the Ethics of Human Studies from 1990-1994. Burgess prepared and presented a special report on decentralization of ethics review of human subject research to the Children's and Women's Health Care Facility.

Burgess' recent work is focused on issues of consent, cross-cultural ethics, the use of qualitative methods in ethical analysis, administrative ethics, and genetic testing. Burgess' current research projects emphasize understanding an everyday life perspective on ethical issues and the effects on social issues of genetic understanding, technology and commercialization. The research team includes faculty in anthropology, genetics and oncology, graduate students in interdisciplinary studies and post-doctoral fellows in the social sciences. The Canadian Huntington Society, the Canadian Breast Cancer Foundation, the Earl and Jennie Lohn Foundation, the Canadian Kidney Foundation, and the Centre for Applied Ethics fund current research projects and personnel.

**Dr. T. Douglas Kinsella**, CM, MD, FRCPC is the Director of Medical Bioethics and Professor of Medicine, University of Calgary, where his academic appointments have included

Director, Division of Rheumatology, Assistant Dean (Medical Bioethics), and Chairman, Conjoint Health Research Ethics Board. Amongst other appointments, he has been President, Canadian Rheumatism Association; Chairman, Canadian Arthritis Society Medical and Scientific Committee; Member, Royal College Biomedical Ethics Committee; Member, Clinical Investigation Committee, and Standing Committee on Ethics in Experimentation, Medical Research Council of Canada; Visiting Scholar, Centre for Medical Ethics, University of Chicago; President, National Council on Bioethics in Human Research; Member, Editorial Committee and Tri-Council Working Group for the Canadian Code of Ethical Conduct for Research Involving Humans; and President, Canadian Bioethics Society.

Kinsella's clinical and research interests encompass rheumatology and immunology, medical education, and ethical issues inherent in human experimentation and euthanasia. He has recently completed several research studies of physicians' opinions about ethical, legal and medical issues involved in assisted suicide, involuntary euthanasia, and genetics research.

Kinsella received his MD degree from McGill University in 1957, and completed his training in internal medicine and rheumatology at McGill and the University of Texas (Dallas). In 1988-89 he was awarded a scholarship in medical ethics at the University of Chicago. He is a Fellow of the Royal College of Physicians and Surgeons of Canada, and the American College of Physicians. Dr. Kinsella was awarded the Queen Elizabeth II Silver Jubilee Medal in 1977 for his contributions to Canadian Rheumatology, and the Order of Canada in 1995 in recognition of his contributions to education and research in biomedical ethics.

**Dr. Thérèse Leroux** is a professor of law and a researcher at the Centre de recherche en droit public of the University of Montreal Faculty of Law. She received her B.Sc. in biology at the University of Sherbrooke in 1973 and her Ph.D. in medical biochemistry from Laval University in 1981, before obtaining her law degree from the University of Sherbrooke in 1984. Professor Leroux has been a Fellow of the Order of Chemists since 1981, and a member of the Quebec Bar since 1986.

Professor Leroux serves on both clinical ethics and research ethics committees in the hospital, university, provincial and national institutional settings. Among others, she is member of the Montreal General Hospital-Research Ethics Board, Centre hospitalier Universitaire de Montréal, Campus Hôtel-Dieu - Research Ethic Board, the Comité d'éthique universitaire of the University of Montreal and the Comité aviseur d'éthique et d'intégrité scientifique of the Fonds



de la recherche en santé du Québec. She is vice-president of the Quebec's provincial research ethics committee. She also sits on the National Council on Ethics in Human Research. She is the president of the Canadian Bioethics Society.

Her current research projects include a focus on legal and ethical aspects of human experimentation, allotransplantation and xenotransplantation, biotechnology and biodiversity. Last year, her research team received a grant from the Social Sciences and Humanities Research Council of Canada to examine legal and ethical issues relating to xenotransplantation.

**Dr. Michael McDonald** is the first occupant of the Maurice Young Chair of Applied Ethics and the founder and Director of the Centre for Applied Ethics. The Centre is a research unit in the Faculty of Graduate Studies at the University of British Columbia. McDonald is also a Professor in the Department of Philosophy. McDonald came to the University of BC in 1990 to establish the Centre for Applied after a twenty-one year career in the Department of Philosophy at the University of Waterloo.

McDonald received an Honours BA in Philosophy from the University of Toronto and an MA and PhD in Philosophy from the University of Pittsburgh. His research has been in ethical, political and legal theory as well as in applied ethics. He has written on such topics as collective rights, particularly linguistic and religious rights, aboriginal rights, business ethics, and cross-cultural issues in health care ethics, professional ethics, and the ethics of research involving humans. SSHRC and the Ford Foundation have supported McDonald's scholarly work. McDonald's 1988 report to SSHRC, *Towards a Canadian Research Strategy for Applied Ethics*, led to the establishment of the highly successful SSHRC Strategic Theme in Applied Ethics.

McDonald served as a member and Co-Chair of the Tri-Council Working Group on Ethics. The Working Group prepared the *Code of Ethical Conduct for Research Involving Humans*, which was submitted in July 1997 to the President of the MRC, NSERC, and SSHRC for adoption. He has also served as President of the Canadian Philosophical Association, English-Language Editor of the Canadian philosophical journal *Dialogue*, and President of the Canadian Section of the International Association for Philosophy of Law and Social Philosophy. He has also served as ethics consultant to a variety of groups including the Certified General Accountants of Canada and the Aboriginal Research Coalition of Ontario. McDonald serves on several ethics committees in British Columbia and is the Canadian Bioethics Society

representative to the Canadian Council on Animal Care. As well, he was member the Royal Society of Canada's Expert Panel on the future of Health Canada's Non-Human Primate Centre.

**Dr. Barbara C. McGillivray**, MD, FRCPC (Paediatrics, Medical Genetics), FCCMG is Professor of Medical Genetics at the University of BC. She chairs the UBC Clinical Research Ethics Board and is a member of both the BC Children's Hospital and BC Women's Hospital Ethics committees. She is a member of the MRC Standing Committee on Ethics, and was a member of the TriCouncil Working Group writing the Code of Ethical Conduct for Research involving Humans. She is currently a member of the National Council on the Ethics of Human Research. She practices clinical genetics at BC Children's Hospital and the BC Cancer Agency. Her research interests include gender anomalies, prenatal diagnosis and inherited cancers.

**Dr. Michael Asch** is a Professor Emeritus at the University of Alberta, is a Visiting Professor in Anthropology at the University of Victoria and an Associate of the Centre for Applied Ethics at University of British Columbia. He has served as the Director of the Dene/Metis Mapping Project for the Dene Nation and as Senior Research Associate for Anthropology with the Royal Commission on Aboriginal Peoples. Dr. Asch's research focus is on relations between Aboriginal people and Canada. Among his publications are *Home and Native Land: Aboriginal Rights and the Constitution* first published in 1984, *Kinship and the Drum Dance in a Northern Dene Community* (1988) and an edited volume: *Aboriginal and Treaty Rights in Canada: Essays on Law, Equality and Respect for Difference* (1997). He has a particular interest in ethical issues respecting collectivities especially in cross-cultural situations.

**Dr. Brenda Beagan** is a sociologist who specializes in medical sociology, social inequality, sociology of health and illness, professional socialization and qualitative research methods. After completing her PhD at the University of British Columbia in 1999 she has been conducting SSHRC-funded postdoctoral research there through the Office of the Health Sciences Coordinator, Division of Educational Support and Development. This research investigates the impact of gender, race, class and sexual orientation on student experiences of medical school. In September 2000 she will begin a tenure track position as a sociologist in the School of Occupational Therapy at Dalhousie University in Halifax. Dr. Beagan has also been involved in research on such topics as women's beliefs about diet and breast cancer; the economic integration of women with disabilities; the social impact of care giving for elderly

family members; the reproductive health care needs of ethno-cultural minority women. She was research associate for The Canadian Task Force on the Periodic Health Examination for 18 months and for the Nova Scotia Advisory Council on the Status of Women for 8 months.

**Dr. Fern Brunger** is a post-doctoral fellow at the Centre for Applied Ethics and the Centre for Health Services and Policy Research. Fern's perspective is that of cultural anthropology. Her research focuses on culture, ethnicity and research ethics in relation to genetic testing. She relates genetic testing and research ethics to wider social and political contexts, to examine how the normative assumptions of each are mutually defining and transforming. Fern obtained her PhD in Anthropology, from McGill (1994), and was a SSHRC postdoctoral fellow in the Department of Social Studies of Medicine, McGill, from 1994 to 1996.

**Dr. Bernard Dickens** graduated with a law degree (LL.B.) at King's College, University of London, in 1961. After being called to the English Bar by the Inner Temple in 1963, he undertook graduate studies (LL.M. 1965) and doctoral studies in law (Ph.D. 1971) at the University of London, and earned a higher doctorate (LL.D.) in 1978 for research and publication in the area of Medical Jurisprudence. He taught at the Law Society's school, The College of Law, in London, England until 1974 when, as Principal Lecturer, he left to join the Faculty of Law at the University of Toronto. He was Research Professor there until 1980, cross-appointed to the Faculty of Medicine, and was called to the Ontario Bar in 1977.

In 1980, he became a Professor at the University of Toronto in the Faculty of Law, Faculty of Medicine, Centre of Criminology and Institute of Medical Sciences, specializing in medical law. He was a founding member of the University's Joint Centre for Bioethics, and continues to teach at the University's law school, medical school and bioethics centre. He was an elected board member of the American Society of Law, Medicine and Ethics for the maximum of two consecutive three-year periods, and was the first Canadian President of the Association, in 1990-91. He is currently a member of the board of governors, and a Vice-President, of the World Association for Medical Law. He has been consultant on several projects for the World Health Organization and Council for International Organizations of Medical Sciences (W.H.O. – U.N.E.S.C.O.), particularly concerning medical research, and for the Commonwealth Secretariat, Commonwealth Medical Association, Canadian Medical Association and similar organizations. He chaired the Medical Research Council of Canada Committee of Ethics' Working Group to develop the MRC's 1987 Research Ethics Guidelines,

and was a member of the Tri-Council Working Group developing the 1998 Tri-Council Policy Statement in research ethics. He was also a founding member and, from 1995 to 1999, Chair of the Research Ethics Board of the National Research Council of Canada. He is a Fellow of the Royal Society of Medicine (London) and, since 1998, a Fellow of the Royal Society of Canada.

**Dr. Jean Joly** is a medical specialist in infectious diseases with a strong interest in their epidemiology and prevention. He was trained at the Université de Montréal and at the University of Washington (Seattle) and has pursued a research career at Université Laval in Quebec City. His interest in research ethics stems from his past participation in the Tri-Council Working Group on Ethics. He is currently working at the Institut National de Santé Publique du Québec in Quebec City.

**Dr. Bartha Maria Knoppers**, Ph.D. (Sorbonne, Paris I) is Professor at the Faculté de droit, Université de Montréal, Senior Researcher (C.R.D.P.) and Counsel to the firm of McMaster Gervais. She is a graduate of McMaster University, (B.A.), University of Alberta (M.A.), McGill University (LL.B., B.C.L.) and Cambridge University, U.K., (D.L.S.), and was admitted to the Bar of Quebec in 1985. Her current research and teaching concentrates on genetics, law and ethics, pharmacogenomic research and consent and DNA/tissue banking.

Professor Knoppers has served as an expert of the committee of the World Health Organization (WHO) (Geneva), and is a Forum Fellow of the World Economic Forum (Davos). She is Past-Commissioner of the Royal Commission on New Reproductive Technologies (1991-94) and Past-Chair. She was named Visiting Heritage Scientist by the Alberta Medical Research Heritage Fund (1993-95).

Past-President of the Canadian Bioethics Society and Past Vice-President of the National Council on Bioethics in Human Research, she co-chaired the Quebec Bar Committee on the Representation of Children (1993-1995). From 1995 to 1999, she was a member of the Management Committee of the Canadian Breast Cancer Research Initiative (CBCRI), the Canadian Pediatric Tumor Bank (Health Canada), the National Expert Advisory Committee on Xenotransplants (Health Canada) and became Chair of the Social Issues Committee of the American Society of Human Genetics (1995-98).

Currently, Chair of the International Ethics Committee of the Human Genome Project (HUGO), she was a member of the International Bioethics Committee of the United Nations, Educational, Scientific and Cultural Organization (UNESCO) which drafted the Universal Declaration on the Human Genome and Human Rights (1993-98). She is also a member of the Interim Board of the Canadian Institutes of Health Research, a consultant to the Ministry of Industry (Ottawa), and is also Co-Director of the Institute for Population Studies (IREP) and of the Quebec Network of Applied Genetic Medicine (RMGA). In 1998, she became a member of the Standing Committee on Ethics of the Medical Research Council of Canada (MRC), as well as of the Task Force for Genome Canada.

In September 1996, she chaired the Organizing Committee of the First International Conference on *DNA Sampling Human Genetic Research: Ethical, Legal and Policy Aspects*, held in Montreal. In 1997 she was named "Scientist of the Year" by Radio-Canada and by the newspaper *La Presse* and received the Medal of the Quebec Bar.

**Dr. Marcelo Otero** earned a degree in social history at the Faculty of Philosophy of the University of Buenos Aires (1992), a Master's degree in sociology at the Université de Montréal (1994-1995) and a doctorate at the same university (1999). His areas of expertise are sociological theory, the sociology of interventions in mental health and the sociology of deviance. He has been a sessional lecturer in a number of sociology courses and is currently a research officer with the Centre international de criminologie comparée at the Université de Montréal.