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The Status of Continuing Ethics Review and Continuing Ethics Review Practices by Canadian Research Ethics Boards

by

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Abstract

This thesis study examined Canadian Research Ethics Boards' (REB) practices with regard to continuing ethics review of approved studies. A mail-out questionnaire was used to elicit information from Canadians Research Ethics Board representatives about whether they engage in continuing ethics review and their current continuing ethics review methods.

This thesis study found that a majority of REBs conduct continuing ethics review (87.4%). The most commonly reported continuing ethics review method was a review of on-going research reports. REBs conduct continuing ethics review significantly more often for clinical trials research than for academic research. There was no significant difference between academic and other types of REBs with regards to their frequency in conducting continuing ethics review.

Implications from this study include the need to: (a) increase the REBs role in on-going research, (b) increase personnel and resources, and (c) reassess current REB continuing ethics review practices regarding low risk research.

Table of Contents

List of Tables

Chapter 1

Introduction

After human rights and ethical violations, such as those involving the Tuskegee syphilis or Nazi experiments, the research community and the general population has gained knowledge about protecting human subjects in research. However, research still has great potential to harm research subjects (Evans et al., 2002; Herrera, 2000; Shaul, 2002; Veatch, 1979). To protect human subjects and uphold ethical principles, Research Ethics Boards (REBs) were initiated in 1966 and have evolved since (Robertson, 1979; Rusnak, 1996). To date, their main role has been to perform a review of proposed research studies to determine their potential to harm research subjects (Rusnak, 1996). There is still the potential, however, that research subjects may be harmed after initial REB approval has been obtained (DeMarinis, 2002). This harm may be because of unintended research consequences or research misconduct (Chop & Silva, 1991; Hansen & Hansen, 1995; Hawley & Jeffers, 1992; Liddle & Brazelton, 1996; Riis, 1999). Changes in the research design and intentional or unintentional data falsification are the most common forms of research misconduct (Chop & Silva, 1991; Hansen & Hansen, 1995; Hawley & Jeffers, 1992; Liddle & Brazelton, 1996; Riis, 1999).

Although any type of research can harm subjects, qualitative research has recently been receiving attention for its potential to cause physical, emotional, and psychological harm (Banister, 2002; Goodwin et al., 2003; Grinyer, 2001; Holloway & Wheeler, 1995; Oberle, 2002; Pattullo, 1980; Peled & Leichtentritt, 2002; Sieber & Baluyot, 1992; Tigges, 2003). In contrast, clinical trials have

continually been in the spotlight for their potential to cause harm (ASCO, 2003; Mello et al., 2003). Authors and researchers have identified numerous forms of clinical trials research misconduct causing harm; including data laundering, data tampering, improper preparation and delivery of a study drug, neglecting approved protocol guidelines, non-disclosure of risks to subjects, enrolling inappropriate research subjects, failing to perform a proper systematic literature review, publishing only positive research results, and improperly signed consent forms (Cleaton-Jones, 2002; Kolata, 1980; Lynoe et al., 1999; Olgilvie, 2001; Rudy & Kerr, 2000; Savulescu, 2002; Smith, 1996). Other forms of quantitative research are susceptible to similar research issues.

The protection of research subject rights and physical safety is now considered the shared responsibility of the researcher, the researcher's institution, and the REB that reviews and approves the research (ASCO, 2003; Ashcraft, 2004). The protection of research subjects is the REB's primary focus and role (CIHR, NSERC & SSHRC, 2005; Thacker, 2002). REBs are also widely known as having the secondary function of providing educational and consultative services within the research community (CIHR, NSERC & SSHRC, 2005).

The Tri-Council Policy Statement is a guidance document available to all REBs. REBs that review agency-funded research, such as academic REBs and REBs that review studies being conducted under Health Canada regulations, such as sponsored clinical trials, are required to follow the Tri-Council Policy Statement. The Tri-Council Policy Statement was first drafted in 1998 (CIHR, NSERC & SSHRC, 2005). It was revised in 2003, when the genetic and

vulnerable populations chapters were expanded, and again in 2005 with the majority of these revisions being editorial changes, such as updated contact information and corrections for cited institutional names. All REBs that review research studies funded by federal agencies must follow the Tri-Council Policy Statement. The Tri-Council Policy Statement allows Canadian REBs to determine if a research study should be permitted to start and, where already approved, if research studies should be allowed to continue (CIHR, NSERC & SSHRC, 2005). REBs were also given the responsibility to ensure that researchers follow established research ethics guidelines and the procedural criteria of their approved proposals. The aim of these measures is to prevent harm to research subjects (CIHR, NSERC & SSHRC, 2005).

One method that REBs can use to ensure the protection of research subjects is by performing continuing ethics review (Meinert, 1998a), through either a passive or active process (CIHR, NSERC & SSHRC, 2005). A passive review encompasses only the review of a report completed by researchers who have detailed the study's status. An active review is more varied and can include: (a) a formal review of the informed-consent process, (b) monitoring by a safety-monitoring committee, (c) the periodic review of documents generated by the study, (d) a review of adverse events, (e) the review of patient charts, (f) a random audit of the informed-consent process, and (g) ongoing reviews of the contract and budget (Bevan, 2002; CIHR, NSERC & SSHRC, 2005; Lavery et al., 2004; Meinert, 1998a; Meinert, 1998b; Morse et al., 2001; O'Mathuna, 2004; Weijer, 2002).

REBs are obviously important to and instrumental in the protection of research subjects' safety, and therefore would understandably be the subject of research (Lind, 1992; Shaul, 2002). To date, the following aspects of REBs have been studied: Their composition, review or approval practices, types of and quantity of protocols reviewed, and informed-consent standards (Ankara, 2000; Berna, 2000; Bravo et al., 2004; Ceci et al., 1992; Dal-Re et al., 1999; Godfrey et al., 2001; Grondin et al., 1986; Hayes et al., 1995; McNeill et al., 1990; Olsen & Mahrenholz, 2000; NCBHR, 1995; Pich et al., 2003; Saito, 1992; Thompson et al., 1981). Only three studies of the continuing ethics review practices of REBs have been published; the first on Scottish REBs (Thompson et al., 1981), the next one on Australian REBs (McNeill et al., 1990), and the third on Canadian REBs (NCBHR, 1995).

1. Thompson et al.'s (1981) Scottish study, with findings from 34 returned surveys, found only 6 REBs had a formal procedure in place for the continuing ethics review of ongoing studies. An additional seven REBs requested final study status reports from the researcher. The data for this survey were collected in January 1980 (Thompson et al.).

2. The Australian study, which analyzed the findings from 89 returned surveys, revealed that less than half of the REBs reported conducting continuing ethics review of research projects in progress (McNeill et al., 1990). When a continuing ethics review was conducted, it was usually a review of the researcher's status reports. The data for this study were collected between August 1988 and February 1989 (McNeill et al.).

3. The Canadian study was undertaken in 1993, when the National Council on Bioethics in Human Research (NCBHR) surveyed Canadian REBs associated with medical schools regarding their continuing ethics review practices. The results of this survey were published in a 1995 NCBHR Communique. This study found 53% of the 68 Canadian REB representatives reported that their REB required an annual status report from researchers. In addition, 18.0% reported they performed continuing ethics reviews or audits of approved research, and 7.0% reported that periodic reviews of patient charts were reviewed to ensure compliance with the proposal and appropriate ethical treatment of research subjects (NCBHR, 1995).

As such, the first and only formal study of Canadian REBs and their practice of continuing ethics review of approved research took place over 10 years ago. No follow-up research studies have been conducted since in Canada. It is also notable that the two other studies of REB continuing ethics review were both older and addressed this issue outside of Canada. Given increasing concern regarding the protection of subjects' health information and privacy, and the importance of REBs for protecting subjects, further research is required on the current practice of continuing ethics review by Canadian REBs.

Purpose of the Study

The purpose of this exploratory-descriptive study was to explore and describe Canadian Research Ethics Boards' current involvement in and processes for continuing ethics review of approved research involving human subjects. The aim of this investigation was to both assess and raise awareness regarding the

current continuing ethics review policies and practices of REBs.

The specific research questions that this study sought to answer were:

1. What proportion of Canadian REBs perform continuing ethics reviews of previously approved research proposals?

2. What review processes or methods are used to conduct continuing ethics reviews of previously approved research proposals?

3. Do REBs perform continuing ethics review more often for clinical trials research then for other types of research?

4. Do REBs in academic institutions perform continuing ethics reviews more often than the REBs of other organizations?

Chapter 2

Literature Review

Seven key search engines (CINAHL, Pub Med, Medline, Bioethics, EMBASE, HealthStar, and PsycINFO) were used to identify literature relevant to a study of Canadian REBs' continuing ethics review practices of approved research studies. This search for literature was undertaken between May 2004 and October 2006. The following search terms were used: Research Ethics Boards, Institutional Review Boards, research ethics, research misconduct, ethical misconduct, continuing review, auditing, and policing. All search results were limited to the English language and the time period of 1966 to 2006. In addition, a hand search was conducted of the three most current years of three journals: *Nursing Ethics*, *Journal of Medical Ethics and Law*, *and Medicine and Ethics*. A hand search of all journals in the John Dosseter Health Ethics Library (at the University of Alberta) also took place. The Internet was also used to obtain information, using the following search terms: Research ethics history, research crimes against humanity, and research-conduct-guide documents. Historical research event articles were selected from Internet websites and included in the literature review. Internet articles may not be peer reviewed and therefore only articles stating historical facts were included in the literature review. The websites used to obtain historical research information are cited in the reference list. Prominent philosophers and researchers in health ethics were also consulted (i.e. Dr. Charles Weijer at Dalhousie University and Dr. Michael McDonald at the University of British Columbia) to obtain the most up-to-date literature on

research ethics continuing review.

All titles and abstracts obtained were reviewed, and relevant articles were retrieved for content analysis. A summary of the findings from this search is divided into the following 10 sections: (a) global historical research events, (b) Canadian historical research events, (c) research ethics principles, (d) research misconduct, (e) continuing ethics review- purpose and guidelines, (f) the roles and functioning of Research Ethics Boards, (g) Research Ethics Boards: Global continuing ethics review practices, (h) Research Ethics Boards: Canadian continuing ethics review practices, (i) continuing debate about continuing ethics review, and (j) research gaps.

Global Historical Research Events

A number of historical research crimes against humanity drove the development of policy documents to guide the conduct of research on humans (Gambrill, 2003; Historical Development of Ethical Considerations that led to the Creations of IRBs; Schiermeier, 2003). Subsequent documents include the Nuremberg Code (1946), the Declaration of Helsinki (1964), the United States National Research Act (1974), and the 1979 Belmont report (Gambrill, 2003; Schiermeier, 2003). Historical research crimes against humanity, four major research-guiding documents, and the development of REBs are discussed in the following paragraphs.

The Nuremberg Code (1946) was enacted in response to the Nazi war crimes committed during World War II (Gambrill, 2003; Historical Development of Ethical Considerations that led to the Creations of IRBs; Schiermeier, 2003).

These crimes included tropical-disease experiments in search of a malaria vaccine, in which 400 people died, and research regarding euthanasia, in which at least 9,000 people died (Schiermeier, 2003). The Nuremberg Code was the first guiding document for conducting research on humans. It focused on the need for: (a) voluntary informed consent, (b) research which would produce useful results, (c) in-depth literature search, (d) avoiding the infliction of physical and mental suffering, (e) preventing death or injury, (f) the weighing of risk versus benefits, (g) qualified scientists to conduct the research, (h) subjects' right to withdraw their consent and participation, and (i) researchers allowing research subjects to withdraw if doing so is in their own best interests (Gambrill, 2003; Historical Development of Ethical Considerations that led to the Creations of IRBs).

Eighteen years after the enactment of the Nuremberg Code, the World Medical Association created the Declaration of Helsinki in 1964 (Gambrill, 2003; Tadd, 2000). This document strengthened the rights of research subjects by declaring that their interests must be put first over the interests of researchers and that every subject should receive best-practice treatment (Historical Development of Ethical Considerations that led to the Creations of IRBs). Many revisions have been made since to this document, as new research techniques have been developed (Gambrill, 2003; Tadd, 2000). The current document outlines guidelines for various types of research (Gambrill, 2003). The guidelines in the Declaration of Helsinki apply to all researchers who are conducting, collaborating, or participating in research involving human subjects (Tadd, 2000). Unlike the Nuremberg Code, the Declaration of Helsinki allows for enrolling

certain research subjects in studies without consent (Gambrill, 2003). It also allows legal guardians to grant permission to enroll research subjects in research and recommends that researchers should obtain written consent from research subjects whenever possible (Gambrill, 2003). The 1975 revision requests independent REBs to review research (Tadd, 2000; Woodin & Schneider, 2003). In the most current version of 2004, changes include expanding the role of REBs to monitor the conduct of research studies and to ensure compliance with the proposed ethical standards (Tadd, 2000; Woodin & Schneider, 2003). The revisions also acknowledge the importance of other professions in the conduct of human research. It is notable that Tadd (2000) encouraged nurses to understand and get involved in the international consultation undertaken by the World Medical Association.

In 1966, following the 1964 Declaration of Helsinki, the first REBs in the United States were established to review research studies funded by Public Health Service grants. However, these REBs did little to protect research subjects. These REBs often approved research without requiring modification, accepted incomplete and sometimes unreadable consent forms, and did very little of the kind of monitoring, evaluation, and enforcement that is now considered essential to ensure that the researcher's conduct conforms to ethical norms (Robinson, 1979).

Despite the 1966 initiation of REBs in the United States, the Tuskegee syphilis study, a study conducted by the U.S. Public Health Service, which started in the late 1930s and did not end until the early 1970s, demonstrated the need for

further guidance for researchers and protection for research subjects (Brandt, 1978; Corbie-Smith, 1999; Thomas & Curran, 1999). This United States government-led study took advantage of a racial minority by studying the effect of untreated syphilis in a black male population (Brandt, 1978; Corbie-Smith, 1999; Thomas & Curran, 1999). In response to many issues in research misconduct, including the Tuskegee syphilis study, the National Research Act (1974) was passed in the United States. It is widely thought responsible for the modernization of REBs, as they were mandated to review all federally and privately funded research in the United States involving humans (Brandt, 1978; Corbie-Smith, 1999; Historical Development of Ethical Considerations that led to the Creations of IRBs; Informed Consent Overview; Thomas & Curran, 1999).

The 1979 Belmont Report was also established in response to the Tuskegee syphilis study and other issues in research misconduct. The Commission which developed the Belmont Report also developed other research guidance reports on research in prisons, and on women and children. However, the Belmont Report is the most widely known research guidance document developed by this Commission. This report outlined key ethical principles in research, notably "respect for persons," "beneficence" (doing good and causing no harm), and "justice" (Department of Health, Education and Welfare, 1979). The first principle, respect for persons, is demonstrated through an informed-consent process, safeguards for vulnerable populations, and the maintenance of privacy and confidentiality (Brandt, 1978; Corbie-Smith, 1999; Department of Health, Education, and Welfare, 1979; Thomas & Curran, 1999). Beneficence is

demonstrated through good research designs, competent investigators, and a favorable risk/benefit ratio (Brandt, 1978; Corbie-Smith, 1999; Thomas & Curran, 1999). Justice includes ensuring appropriate inclusion and exclusion criteria, and a fair system of subject recruitment and randomization (Brandt, 1978; Corbie-Smith, 1999; Thomas & Curran, 1999).

Despite the creation of the four major research guidance documents mentioned above and the formation of REBs, major abuses of human research subjects continued to occur. For example, a live hepatitis virus was administered to children at the Willobrook Institution for the mentally handicapped (1963-1966), and live cancer cells were administered in 1963 to patients of the Brooklyn Jewish Chronic Disease Hospital (Moreno, 2001). Continuing research misconduct led the U.S. Department of Health, Education, and Welfare in 1974 to request REBs to review all research involving human subjects, even if a study was not federally funded; to focus on protecting the welfare of research subjects; to ensure the obtaining of adequate informed consent; and to determine the risks and benefits of research projects (Moreno, 2001; Robertson, 1979).

In summary, from 1946 to 1979, four major research-guiding documents were enacted, and REBs were established largely in response to research crimes against humanity. The Nuremberg Code (1946) and the Declaration of Helsinki (1964) were attempts by global institutions to establish ethical guidelines for research. In the United States, after its first REBs failed to prevent research misconduct, the National Research Act (1974) required REBs to review all federally and privately funded United States research involving humans. When

major abuses of human research subjects continued to occur, the United States Department of Health, Education, and Welfare implemented stricter guidelines for REBs in 1974.

Canadian Historical Research Events

In concert with global historical research events, the Canadian government also realized the importance of protecting research subjects (Rocher, 1999). During the 1960s and 1970s, Councils to promote research were established, including the Canada Council for the Arts, the Social Sciences and Humanities Research Council, and the Medical Research Council. In addition to promoting and funding research, these Councils ensured the protection of research subjects by stipulating that all researchers awarded grants must follow their individual research-conduct guidelines. In 1982, the National Council on Bioethics in Human Research (NCBHR) was established (Rocher, 1999). Contrary to the above-mentioned funding councils, the NCBHR's main focus was the protection of research subjects. Each of these Councils developed its own set of research-conduct guidelines, guidelines that were often based on United States research-conduct documents (Rocher, 1999).

The Medical Research Council (MRC) developed its own research-conduct guidelines in 1978, which were later updated in 1987 by the Working Group on Research involving Human Subjects and the Standing Committee on Ethics in Experimentation. According to Dinsdale (1998), this 1987 document by the Medical Research Council indicated that guidelines, rather than laws, allowed for the flexibility required by the ever-changing face of research.

In 1994, representatives of the Medical Research Council of Canada (now the Canadian Institute of Health Research), Social Sciences and Humanities Research Council of Canada, and the Natural Sciences and Engineering Research Council of Canada started to develop a single set of research-conduct guidelines (Rocher, 1999). The need for a single set of guidelines resulted from the growing number of social science researchers who were involved in health research projects, the difficulty for REBs to evaluate research projects using three different guidelines, and the desire among academics for strong guidelines for research involving humans (Rocher, 1999).

This three-party document evolved in three directions: (a) initially driven by philosophical reflection, it became more pragmatic, (b) legal wording was eliminated as much as possible, and (c) a single document with diverse applications was formulated (Dinsdale, 1998; Rocher, 1999). The final version was completed in 1998 and was entitled the *Tri-Council Policy Statement: Ethical Conduct for the Research Involving Humans* (Rocher, 1999). This statement deals with research ethics principles, the process for ethical review within REBs, free and informed consent, privacy and confidentially, conflict of interest, inclusion in research, research involving aboriginal peoples, clinical trials, human genetic research, and research involving human gametes, embryos, fetuses, or human tissue (Dinsdale, 1998; Rocher, 1999).

According to Dinsdale (1998), the Natural Sciences and Engineering Research Council, the Social Sciences and Humanities Research Council, and the Medical Research Council all endorsed and then followed the 1998 Tri-Council

Policy Statement. Research projects submitted for ethical review in Canada began to be evaluated by REBs, with most REBs guided by the Tri-Council Policy Statement; consequently, all researchers needed to become familiar with its' details (Dinsdale, 1998).

While the Tri-Council Policy statement was being developed, the Deschamps Report was developed and then published in 1995 (Deschamps, 1999). This report focused on control mechanisms for clinical research in Quebec (Deschamps). In 1998, a follow-up action plan to the Deschamps Report was also developed (Deschamps). This action plan stipulated that during a proposal review, a REB and a researcher must agree on a follow-up mechanism for ongoing continuing ethics review (Deschamps). This mechanism would vary depending on the risk to subjects through the project. Mechanisms could include regular reports by the researcher, consent form review, or any other mechanisms believed to be appropriate for the project (Deschamps).

The Law Commission of Canada addressed the issue of guidelines versus legal influence on research involving humans by producing the *Governance of Health Research Involving Human Subjects (HRIHS),* a document compiling the results of a study of Canadian governance for health research involving human subjects (McDonald, 2000). This document's main objectives were to promote socially beneficial research, and respect for the dignity and rights of research subjects, and to maintain trust between the research community and society (McDonald). This document also provided a brief overview of Canadian REB continuing ethics review practices (McDonald). Included were continuing ethics

review practices consisting mainly of annual reports, notification of the completion or end of the study, adverse-incident reports to the sponsor and REBs, protocol revision notifications, and a mandated interim report for higher-risk research (McDonald). As well, this document also stated that some, but not all, REBs required annual reports and adverse-events reports from researchers who had been granted ethical approval to initiate projects.

Research Ethics Principles

Basic ethical principles are a major foundation for the Nuremberg Code, the Declaration of Helsinki, the U.S. National Research Act, the Belmont Report, and the Tri-Council Policy Statement (Dinsdale, 1998; Gambrill, 2003; Rocher, 1999; Schiermeier, 2003). Research (both qualitative and quantitative) in all disciplines, including nursing, is steadily increasing (Rogero-Anaya et al., 1994). Therefore, nurse researchers and nurses who have a role in research must understand the ethical implications of their research and have a thorough knowledge of the most current research-guiding documents (Rogero-Anaya et al., 1994).

The main ethical principles that are discussed in the literature to date are respect for autonomy, nonmaleficence (causing no harm), beneficence (promoting good), and justice (Holloway & Wheeler, 1995; Weijer et al., 1997). These principles generally emphasize the rights of the research subject, the responsibility to obtain free and informed consent, voluntary participation, the confidentiality and anonymity of subject information, and the right to be treated with dignity and respect (Holloway & Wheeler, 1995; Weijer et al., 1997).

Rogero-Anaya et al. (1994) described how these ethical principles specifically relate to research subjects, society, and the profession of nursing; listing seven "rights" of the research subject: (a) self-determination for choosing to participate in a study, (b) the right to have access to relevant research information, (c) the option to withdraw from an experiment without retribution, (d) privacy, (e) dignity and confidentiality, (f) protection from harm or potential harm, and (g) protection for vulnerable populations.

When undertaking a research study, the researcher must first evaluate the study's impact on society, focusing particularly on the social impact (Rogero-Anaya et al., 1994). The researcher should evaluate the existing publications on the research subject to assess the proposed study's suitability and to orientate the study to the research population's needs, thus ensuring that the values of the research subject and the community will be addressed (Rogero-Anaya et al., 1994). Moreover, one of the researcher's final obligations is to ensure that the findings of research studies are published in the public domain (Rogero-Anaya et al, 1994).

The nursing profession and society are enriched by research, so nurse researchers must have strong ethical principles in research (Ghazi & Cook, 1993; Rogero-Anaya et al., 1994). To ensure the development of nursing is based on solid research, the nurse researcher must ensure that a research project is conducted with maximum rigour, that the research results (including both positive or negative results) are discussed, that the scientific idea is adapted to the public interest, and that the communication of the results is clear with no possibility of

inferred conclusions (Rogero-Anaya et al., 1994).

Grinyer (2001) detailed 10 ethical guidelines a nurse researcher should follow to develop a framework for the initiation and conduct of research:

1. Determine how the research would be understood and viewed from the research subject's point of view.

2. Understand the meaning and impact of the research question on the research subject.

3. Establish trust with the research subject based on a mutually acceptable agreement about who will have access to the results, and in what form.

4. Address what obligations the researcher has to other bodies within or outside the research facility.

5. Establish at an early stage with manager, employer, institution, or other powerful bodies what their rights are to access confidential data and who has ultimate ownership of this data.

6. Communicate to the research subject his or her right to withdraw from the research project without retribution.

7. Define what constitutes "legitimate data." For instance, can legitimate data be collected by other ways other than with the explicit consent of the research subject?

8. Anticipate that some research subjects may experience anxiety or distress and be prepared to counsel them or direct them to someone else for appropriate support.

9. Clarify in advance who owns the data and how an institution may

access and use data that reflects both positively and negatively on the research subjects.

10. Anticipate potential ways to solve problems that the research may expose.

Given the importance of ethical principles in research, nurse researchers need to understand the guidelines in the most current research-guiding documents. In particular, nurses must understand the four main ethical principles of respect for autonomy, nonmaleficence, beneficence, and justice; and their relationships to the rights of research subjects. As well, a researcher must evaluate a proposed research study's social impact and ensure that the study addresses the research subjects' and the community's values. Finally, Grinyer's (2001) 10 ethical guidelines for nurse researchers remind them to focus on the perceptions and interests of the research subjects, and to clarify the researchers' relationships with bodies within and outside the research facility.

Research Misconduct

Research guidelines, regulations, and ethical principle applications in human research have undergone progressive change since the inception of the Nuremberg Code in 1946 (Moreno, 2001). This ongoing change has occurred to decrease research misconduct and increase the protection of research subjects (Moreno). Moreno divided the history of subject protection since the inception of the Nuremberg Code into three eras. The first era was the period of what he defined as "weak protectionism" from 1947 to 1981. This era granted flexibility and independence to researchers, and was followed by what Moreno termed the

era of "moderate protectionism," which allowed for investigator discretion with modest external oversight. Moreno explained that the moderate protectionism era lasted for about 20 years, from 1981 to 2001, and he argued that moderate protectionism was a good compromise between investigator independence and bureaucracy. Moreno further explained that the era of moderate protectionism possibly would have lasted longer if the research environment had not changed so drastically. Research budgets increased, private research funding began and expanded, and the number of complex studies increased drastically. Since 2001, a strong protectionism era has emerged, which includes third–party monitoring of consent forms and study procedures (Moreno). This era also requires researchers to disclose their financial arrangements or other potential conflicts of interest, and to receive training in research ethics and research regulations (Moreno).

Despite the development and use of research guidelines and ethical principles, research misconduct continues to occur (O'Mathuna, 2004). Evans et al. (2002) illustrated this issue through a study of the impact of a mail-out questionnaire on women's breast-cancer awareness and management. The questionnaire elicited numerous emotional responses from the surveyed women, including psychological distress and anger. Some women required medication management for these emotional responses. The research proposal had failed to list the steps to be taken for support to any subjects whom the survey might distress. During this research, the researcher also failed to change the design to ensure that the distressed subjects received help. If the REB had conducted adequate continuing ethics review, the REB would have been able to periodically

assess the adequacy of protection for the research subjects.

Even in qualitative research, upholding the rights of research subjects may be difficult. Ethnography, for instance, which includes observation for the purpose of research, has potential risks (Banister, 2002; Goodwin et al., 2003; Herrera, 2000; Oberle, 2002). For instance, the researcher who observes illegal activity while in the field must decide if he/she will intervene by reporting the action to the authorities (Herrera). Doing so could put the research subject at risk of being incarcerated; incarceration may be thought of as causing potential harm to the research subject, both physical and psychological (Herrera).

Moreover, Liddle and Brazelton (1996) found that some researchers who participated in a study regarding compliance with REB procedures in psychological research reported putting their research subjects at risk for other reasons. Liddle and Brazelton found 14% of the researchers who were seeking REB approval for their proposal had collected data before REB approval was obtained. Also, 13% of the researchers did not submit a proposal for REB approval for one or more of their studies; 8% included one or more research subjects who had neglected to sign, date, or supply their consent forms; and 3% of the researchers who had received REB approval for their proposals used different research procedures from those approved by the REB. The most common reasons given for lack of REB compliance were: (a) hurried researchers who could not wait for REB approval, (b) lack of knowledge of when to seek REB approval, and (c) frustration with the amount of work and time involved in the ethics review process. However, Liddle and Brazelton defended REBs, pointing out that in both

social and behavioral research, they have to deal with various issues such as discrepancies in consent-form information, protocols treated as bureaucratic red tape rather than planning tools, inappropriate protocols for alternative consent methods, unclear protocols, haphazard protocols, and failure to explain possible risks in consent statements.

Examples of research misconduct are found not only in qualitative research but also in quantitative research, including clinical trials. Five examples follow of misconduct identified in clinical trials during the 1990s and 2000.

1. Olgilvie (2001) found a research subject died from the improper preparation and delivery of a study drug; protocol guidelines were also neglected. Furthermore, the consent process was not fully explained to the research subject, and the researcher did not explain that the drug had not been approved in the form in which it was provided to subjects.

2. Savulescu (2002) similarly reported the deaths of research subjects due to the improper administration of a drug (i.e. haxamethonium). Failure to perform a systematic literature review and publication bias were the two main reasons cited for these deaths. The researcher of the study with the above-mentioned subject deaths failed to perform a complete systematic review, as literature was available documenting the pulmonary toxicity of hexamethonium. Researchers from previous studies of hexamethonium were biased as they failed to report adverse events in publications. Savulescu also reported the death of an inappropriate research subject; one who should not have been used as he had a mild genetic disorder.

3 and 4. Both Rudy and Kerr (2000), and Smith (1996) found major problems with improperly signed consent forms, including researchers who had forged signatures on consent forms.

5. Cleaton-Jones (2002) found misrepresentation of data from the control arm of a study and determined that this study had been started before ethical approval had been granted.

In summary, since the inception of the Nuremberg Code in 1946, the ethical guidelines for the protection of research subjects have become increasingly stronger through three eras of protectionism. Nevertheless, research misconduct has continued to occur. It would appear that researchers do not always strictly follow REB procedures, and REBs do not always adequately perform their roles.

Continuing Ethics Review - Purpose and Guidelines

The following paragraphs describe the purpose of continuing research ethics review and continuing research ethics review guidelines in what Moreno (2001) defined as the current era of strong protectionism. The purpose of continuing ethics review is widely understood as seeking to ensure that human subjects' rights and well-being are protected (CIHR, NSERC & SSHRC, 2005). Continuing ethics review is also thought necessary for attempting to ensure that the reported research project data are accurate, complete, and verifiable from source documents (CIHR, NSERC & SSHRC). As well, continuing ethics review in Canada should be undertaken to investigate whether the conduct of the study complies with the REB-approved proposal and also the Tri-Council Policy Guidelines (CIHR, NSERC & SSHRC).

The Medical Research Council (1987), the International Conference on Harmonization-Good Clinical Practices (1997), the action plan for the Deschamps Report (1998), The Declaration of Helsinki (2004), and the Tri-Council Policy Statement (2005) all contain guidelines for REB continuing ethics review practices. These guidelines are discussed in the following paragraphs, in chronological order.

The 1987 Medical Research Council Guidelines on Research involving human subjects require REBs, as part of its initial ethics review process, to determine whether active or passive continuing ethics review is required (Medical Research Council of Canada, 1987). If so, the type of continuing ethics review practices should be set by the REBs as one of the conditions of ethics approval (Medical Research Council of Canada, 1987). Review of the informed consent process, including interviewing the subject, are some suggestions of types of continuing ethics review practices. The Medical Research Council Guidelines further explain that if no active or passive continuing ethics review is required, the reason should be given (Medical Research Council of Canada, 1987). The Medical Research Council Guidelines state, at a minimum, researcher should be required to provide an annual update on the status of any approved study (Medical Research Council of Canada, 1987).

The International Conference on Harmonization-Good Clinical Practices, were adopted in 1997. This document recommends that REBs conduct continuing ethics reviews of ongoing trials at intervals appropriate to the degree of risk to human subjects, but at least once per year (Minister of Public Works and

Government Services Canada, 1997).

The *Action Plan on Research Ethics and Scientific Integrity* was issued by the Quebec Minister of Health in 1998, in a follow-up to the 1995 Deschamps Report. Deschamps (1999) explained that the 1998 Action Plan included the stipulation that, at the time of REB approval, the REB and researcher must agree on an appropriate continuing ethics review (follow-up) mechanism. The continuing ethic review practice may vary according to the study and can include a regular report by the researcher, verification of the consent form, and/or any other mechanism for continuing ethics review the board deems relevant (Deschamps).

The World Medical Association's Declaration of Helsinki, in 2004, states that REBs can actively monitor ongoing trials. At a minimum, researchers must provide updates to their REB, especially about any serious adverse events (World Medical Association, 2004).

Similarly, the Tri-Council Policy Statement, in 2005, also stated that REBs can actively monitor ongoing trials. At a minimum, researchers must provide updates to their REB, especially about any serious adverse events (CIHR, NSERC & SSHRC). A serious adverse event is defined as: (a) any untoward medical occurrence that results in death, (b) an event that is life threatening, (c) an event that requires inpatient hospitalization or the prolongation of an existing hospital stay, (d) an event that results in persistent or significant disability/incapacity, or (e) an event that results in a congenital anomaly/birth defect (Minister of Public Works and Government Services Canada, 1997).

The 1996 National Council on Bioethics in Human Research (NCBHR) workshop focused on the topic of REBs and continuing ethics review. In this workshop, the Medical Research Council's (1987) guidelines were discussed in relation to continuing ethics review, which, according to these guidelines, is a duty of REBs. In contrast, the Tri-Council Policy Statement is less strict regarding the REB's role in continuing ethics review. Members of the NCBHR made an important point at this workshop; the members stated that the REBs must protect the research subject, and that this responsibility does not end when a proposal is approved (NCBHR, 1996).

All of the guidelines discussed in the above paragraphs are complimentary to each other. They differ in that REBs can conduct continuing ethics review during various aspects of a study. The following paragraphs describe three examples of situations in which a REB should implement continuing ethics review.

1. Gordon et al. (1998) examined the interaction of data-safety-monitoring boards (DSMB) and REBs in randomized clinical trials to ensure a comprehensive approach to the protection of research subjects. Gordon et al. highlighted the regulations for the data-safety-monitoring committees. The FDA regulations require a DSMB for studies conducted in emergency settings, and for large and high-risk clinical trials. Gordon et al. advocated for an enhanced working relationship between DSMBs and REBs, which would better meet their mandated obligations for continuing review, subject safety, and data quality. Gordon et al. also described the process of the continuing ethics review of a study

proposal from submission to the study's end. Gordon et al. mentioned that a REB first reviews a research proposal before a study begins and then continues to review it throughout the course of the study, particularly for any adverse reaction. Gordon et al. also stressed that guiding documents do not specify how this ongoing review should be conducted, and, as a result, REBs carry out continuing ethics reviews in many different ways.

2. Prentice and Gordon (1997) discussed the REB's role in regards to continuing ethics review of adverse events in investigational drug studies. In the United States, REBs are required to establish a procedure for prompt reporting of adverse events by the investigator. However, the exact procedure is not outlined, and therefore, many REBs are unsure of their responsibilities and vary their reporting of adverse events (Prentice & Gordon). Prentice and Gordon argued that adverse events are the responsibility of the REBs, as they are charged with the continuing review of ongoing research. According to Prentice and Gordon, continuing ethics review of adverse events allows a REB to make a more informed and valid decision about a study's continuation or termination.

3. Sherwin and Fromell (2002) examined the issue of continuing ethics review of clinical trials. They listed the following most common continuing review findings: (a) subject and study files incomplete, inaccurate, and not appropriate for safety tracking, (b) informed consent inadequacies, (c) ill-equipped research staff, (d) poorly written data collection tools, and (e) failure to appreciate ethical mandates in the conduct of human research. Sherwin and Fromell recommended that REBs perform continuing ethics reviews of both

qualitative and quantitative research on humans.

In summary, continuing ethics review is intended to ensure that human subject rights and well-being are protected. Despite guidelines for the continuing ethics review process that were developed during the era of moderate research subject protection, the three examples discussed in this section suggest continuing ethics review may be required in a variety of situations.

The Roles and Functioning of Research Ethics Boards

The main role of REBs is widely understood as consisting of reviewing all research proposals that involve living human subjects and human cadavers, tissues, biological fluids, embryos or fetuses; with the overall goal of ensuring that researchers adhere to ethical principles (CIHR, NSERC & SSHRC, 2005; Minister of Public Works and Government Services Canada, 1997; World Medical Association, 2004). REBs have the authority to approve, reject, propose changes to, or to terminate any proposed research involving human subjects, of which research institutions have no power to overturn. This authority extends to ongoing research involving human subject or human materials (CIHR, NSERC & SSHRC; Minister of Public Works and Government Services Canada; World Medical Association).

REBs must consist of a least five members including both men and women (CIHR, NSERC & SSHRC). At least two of these members must have a broad expertise in the methods or areas of research that are covered by the REB (CIHR, NSERC & SSHRC). At least one member must be knowledgeable about ethics and biomedical research, at least one member must be knowledgeable about

the relevant law, and at least one member must be a non-institutional-affiliated citizen of the community (CIHR, NSERC & SSHRC, 2005). REBs should meet regularly in face-to-face meetings to assess each study's balance, and distribution of harms and benefits. Other issues requiring assessment are respect for human dignity, respect for free and informed consent, respect for vulnerable persons, respect for privacy and confidentiality, respect for justice and inclusiveness, balancing harms and benefits, minimizing harm, and maximizing benefit (CIHR, NSERC & SSHRC). All of these REB's decisions should be documented, to clearly identify the ethics review process and the documents reviewed (CIHR, NSERC & SSHRC; Minister of Public Works and Government Services Canada, 1997; World Medical Association, 2004).

The roles and functioning of REBs in continuing research ethics review is further highlighted by nine authors who have addressed various aspects of this emerging role and functioning. This information is presented in chronological order of publication date.

1. Hilgartner (1990) discussed how and when REBs should become involved in issues of research misconduct, stressing that the main function of REBs is to protect the rights and interests of research subjects. Furthermore, Hilgartner said that a secondary function is to assure research projects are conducted ethically.

2. The NCBHR's working group on REB continuing ethics review practices advocated a standardized continuing ethics review for annual reviews. This working group further recommended that specific guidelines be produced to

clearly outline REB responsibilities with regards to continuing ethics review, including the scope and source of funding (NCBHR, 1996).

3. Fortin and Leroux (1997) produced a working document in which they discussed the need for REBs to be audited or monitored to ensure they are following review guidelines. The working document called for REB continuing ethics review practices to be the main criteria used to evaluate REBs and for auditing reports to be prepared annually. This practice would provide a general picture of continuing ethics review practices in Canada (Fortin & Leroux).

4. and 5. Weijer et al. (1995) and Berry (1997) both stated that REBs should have a role in the active monitoring of four areas of research: Annual reviews of continuing research, informed consent forms, adherence to approved protocols, and integrity of the data. Berry also believed that REB monitoring should focus on the ethical recruitment of research subjects and the process of obtaining consent forms from research subjects to ensure that they are informed about all aspects of the research study.

6. To help ensure REBs are conducting continuing ethics reviews regularly, Smith and Moore (1997) suggested that REBs perform on-site continuing ethics review of at least 10% of approved research studies each year, with all other approved research monitored by questionnaire. They believed that continuing ethics review by REBs promotes and preserves ethical standards, protects subjects and researchers, and discourages research misconduct.

7. Lynch (1999) focused on the operational issues of REBs, stating that their two main responsibilities, other than those for reviewing and approving

research, are for: (a) the continuing ethical review of ongoing research and (b) education. Lynch also discussed the challenges of continuing ethical review, including limited financial and administrative assistance. She stressed that REBs must be adequately staffed to properly perform continuing ethics review. Lynch also mentioned that during the continuing ethics review process, a REB must maintain a good relationship with the researcher.

8. Jamrozik (2000) called for REBs to focus on detecting researchers who are not complying with their research guidelines. Jamrozik stated that REBs must not only actively monitor research but also educate researchers in ethical research in order to prevent poorly conducted research. He also mentioned that very little is known about how many REBs are currently conducting active monitoring.

9. Hanna (2002) reported that REBs are already overburdened and, therefore, need to decide what particular types of research might need more attention than others. Hanna recommended that continual on-site review should be conducted for more-than-minimal-risk studies to ensure that emerging information has not altered the original risk-benefit ratio. Hanna also argued that REBs should actively monitor to ensure all data collected are valid and collected according to applicable standards; and that subject safety, privacy, and confidentiality are maintained throughout a study. To achieve this, Hanna suggested monitoring certain documents; such as informed consents and subject charts, and results.

In summary, the main role of REBs is to ensure that researchers adhere to ethical principles when carrying research involving human subjects or human

tissues and materials. In Canada, clear guidelines stipulate the membership of REBs and the initial ethics approval process. A number of research ethicists have emphasized that REBs must carry out continuing research ethics reviews. However, how this would be done is not standard across REBs. One research ethicist has suggested that REBs should focus only on more-than-minimal risk studies (Hanna, 2002), and at least two have emphasized that REBs should educate researchers in ethical research (Jamrozik, 2000; Lynch, 1999).

Research Ethics Boards: Global Continuing Ethics Review Practices

The following section outlines what has been reported about REB continuing ethics review practices around the world. REB continuing ethics review practice literature is available for Eastern Europe, South Africa, Latin America, Britain, United States, Australia, and Scotland. Three of these are research studies that were aimed at identifying continuing ethics review practices. Canadian continuing ethics review practices are discussed in the next section.

Eastern European REBs have been reported as having varying degrees of ongoing active monitoring of approved research (Coker & Mckee, 2001). Continuing ethics review of research results by REBs in Albania, Bulgaria, Croatia, Estonia, and Hungary have been identified (Coker & Mckee). In South Africa, a national health research ethics council has been established for the inspecting, surveillance, and active monitoring of health research (Cleaton-Jones, 2002). In a review of REBs in Latin America, 68% of REBs did not require progress reports during the course of an ongoing study, and 59% did not have an established continuing ethics review procedure in place (Rivera & Ezcurra, 2001).

British REBs have no formal active monitoring program but rely on the researcher to submit an annual report to notify the REB of any changes to the protocol, and of adverse events or unforeseen events (Pickworth, 2000). In a review of REB annual reports for London and the surrounding area, Gilbert Foster et al. (1995) found only 23 percent of these reports referred to any form of continuing ethics review. Bergkamp (1989) reviewed the structure and operations of REBs in the United Kingdom, West Germany, France, Switzerland, and Sweden; and found continuing ethics review practices were a problem because of different REB working methods. These different working methods were thought to be due to REB ill-defined authorities and powers, and the varying workloads among REBs. The United States relies on passive monitoring, requesting researchers to submit an annual report which includes information about serious adverse events, unexpected adverse events, and any changes to the protocol during the course of their study (Amdur & Bankert, 1997; Weijer, 2001).

The first study that sought to explore continuing ethics review was undertaken in Australia. McNeill et al. (1990) surveyed 101 Australian REBs. Of the 89 REB representatives that returned surveys, 26% reported that their REB always undertook a review of research in progress, 18% reported that their REB usually reviewed research in progress, 16% reported that their REB sometimes did this, 21% reported that they rarely did this, and 16% reported that they never reviewed a study in progress. Of the REBs that did some form of continuing ethics review, 99% of respondents reported that their REB used passive monitoring as they requested and reviewed a report from the researcher. Twenty-

three percent of the REB representatives responded, however, that their REB had at some time performed an on-site visit to a study in progress.

Although McNeill et al.'s (1990) Australian study also surveyed REB composition, types of protocols reviewed, frequency of meetings, and difficult ethical issues; the study's main focus was on the continuing ethics review of research in progress. REBs were asked about the frequency of unethical research practices and disciplinary actions for problematic researchers with studies in progress. Fifteen percent of the REBs reported receiving formal or informal reports of research misconduct, and 14% had to warn or discipline researchers about the misconduct.

A similar study of REBs in Scotland was completed in 1981. Thompson et al. (1981) surveyed 41 REBs regarding their composition, ethical problems encountered, and mode of operation - including continuing ethics review practices. Six out of the 34 respondents reported they had formal procedures in place for continuing ethics review. Three reported that they requested progress reports regularly, one requested them infrequently, and 15 never requested them. Seven reported that they requested a final report. Moreover, 14 did not know whether the studies they had approved were actually started. It is also notable that in 1997, Smith and Moore (1997) still found Scotland had no formal active continuing ethics review practices in place, although Scottish REBs were working on implementing such a program.

In summary, the reviewed literature on global REBs continuing research ethics review practices suggests that these practices needed to be improved on, or

at least standardized within or across countries. Standardizing continuing ethics review practices may assist in coordinating this role for research such as multi-national clinical trials. For example, a study of REBs in Latin America revealed 59% of participating REBs had no established continuing ethics review practices in place (Rivera & Ezcurra, 2001). Even in a developed country like Australia, only 26% of REBs always undertook a review of research in progress (McNeill et al., 1990). Moreover, as recently as 1997, REBs in Scotland were working on developing a continuing ethics review program (Smith & Moore, 1997). It would appear that Great Britain and the United States have such a program in place, but both rely on passive monitoring of research in progress.

Research Ethics Boards: Canadian Continuing Ethics Review Practices

The previous global perspective of REB continuing ethics review practices demonstrates diverse interpretations of research regulations. Even within Canadian REBs, continuing ethics reviews is considered as being performed in a variety of ways, as demonstrated in the major Canadian report regarding REBs and continuing ethics review (NCBHR, 1995). In 1990, the National Council on Bioethics in Human Research began a three-year project to study the function of REBs within Canadian University Medical Faculties. The results of this project were made public in 1995. This three-year project used a pre-site questionnaire and a site visit to gather data.

Overall, the results obtained from the NCBHR (1995) pre-site questionnaire indicated that most participating Canadian medical faculty REBs were not carrying out continuing ethics review procedures. Fifty-three percent of

the representatives for these REBs reported that they required an annual report from each investigator who had an ongoing study, but only 36% reported that they required an end-of-protocol report. Moreover, only 18.0% of the REB representatives reported that they carried out ongoing reviews or audits of research in progress, and only 12.0 % reported that they dealt with issues of scientific integrity. Perhaps the most important response was to the question "If you are not monitoring ongoing research, why are you not doing so?" Most answers to this question indicated they did not consider monitoring was part of their mandate, nor did they feel they had the time and resources to do so.

After obtaining these results and additional onsite data, the NCBHR (1995) working group was concerned about a lack of communication between researchers and REBs after the initial study approval. The NCBHR recommended further investigation of this area, particularly to define "continued ethical review" and to determine its proper process (NCBHR).

A much smaller study by Lemmens and Thompson (2001) of REB continuing ethics review practices took place in Canada and the United States. This study reviewed for-profit REBs only. This type of REB is independent, as they are not located within an institution, and they offer their services to researchers who are not required to use or do not have access to a hospital REB or an academic REB. Data collection took place between May 1997 and June 1999. Thirteen United States and 3 Canadian REBs were surveyed for REB activities such as member composition, procedural research review aspects, and general continuing research ethics review practices. The researchers combined the results

in order to conceal the identities of the two responding Canadian REBs. The response rate was 81.25%, as only two American and one Canadian REB did not respond. All the respondents reported that they monitored or followed up research that had been approved. However, their continuing ethics review practices varied; included quarterly reports, annual reviews, adverse-event reports, control of consent forms, spontaneous audits, site visits, and reports on completion of the research protocol. Unfortunately, the researchers did not provide detailed information on their findings.

Three more studies examined the effectiveness of Canadian REB continuing ethics review practices (Bortolussi & Nicholson, 2002; McCusker et al., 2001; Skrutkowski et al., 1998). These studies all noted the importance of active continuing ethics review, as discrepancies in research would not have been detected by relying only on annual summary reports from investigators. Each of these studies is described below in chronological order by publication date.

1. Skrutkowski et al. (1998) focused on continuing ethics review of informed consent. Skrutkowski et al. described the findings of the McGill University REB in their performing continuing ethics review of informed consents and the informed consent process in an ethics-approved oncology study in which the risk to research subjects was high. This REB decided that active continuing ethics review of the consent process was required to ensure that research subjects were informed and that their decision to participate was voluntary. The REB used a semi-structured interview, with pre-determined questions to assess if the research subjects were informed. One example of the

interview questions they used was: Do you think you have a fair understanding of your disease? After conducting the semi-structured interview with the first 10 research subjects enrolled in the study, the REB gave immediate approval for nine subjects to enter the study, but one research subject expressed considerable uncertainty and wanted further time to think. This subject was given one week to consider, and then he or she agreed to participate in this study. Overall, the consenting process was thought to have been performed very well, with the research subjects considered to be well informed about their disease and the requirements for their participation in this study.

2. McCusker et al. (2001) stated that active monitoring is important for REBs. At St. Mary's Hospital (in Montreal), their REB developed a pilot program, which was the first of its kind in Canada. This three-year pilot program was carried out to determine the effectiveness and functionality of active monitoring for the REB. Researchers conducted active continuing ethics review of recruitment logs and consent forms, and conducted interviews with research subjects. McCusker et al. discussed how the pilot project monitored recruitment logs and found that the same research subjects were participating in more than one research study, but that the researchers had concluded that the studies did not overlap otherwise and were not unethical or burdensome for the research subjects. McCusker et al.'s study focused on the auditing of informed consent forms and it found that 3.8% of the reviewed forms were different from the approved ones and that 2.5% of the subjects had been enrolled in a study based on verbal consent only, before the date of the ethics approval of the protocol. Also, in 7% of the

consent forms reviewed, discrepancies were found between the date of the research subject's signature and the recruitment logs or cover sheet. When interviewing research subjects, McCusker et al. found 19% had little understanding of experimental treatments or possible risks and benefits.

3. Bortolussi and Nicholson (2002) also focused on research audits. Bortolussi and Nicholson argued that research audits are valuable for identifying deficiencies and improving research ethics performance, but require considerable resources. Bortolussi and Nicholson conducted an eight-year study using random and selective methods to monitor good record keeping, data monitoring, adherence to protocol, consent forms, and recording of adverse events during a study. They identified consent, medication, and poor documentation as major problems. Bortolussi and Nicholson also found some researchers failed to file the original ethics approval (7%) or ethics renewal documentation (9%). They also found one instance of improper storage of medication, several uses of outdated informed consent forms, 4% of enrolled subjects' signatures were not clear, and 2% of forms had other consent discrepancies.

In summary, the most detailed report (NCBHR, 1995) about Canadian continuing research ethics review practices found most medical faculty REBs were not carrying out such practices and did not consider the monitoring of ongoing research to be a part of their mandates. Additional Canadian studies have indicated that continuing ethics reviews by REBs are important. McCusker et al. (2001), and Bortolussi and Nicholson (2002) reported that such audits uncover problems with consent forms. Skrutkowski et al. (1998) found that the consenting

process at McGill University had been performed well. Overall, the reviewed literature emphasized the diversity in continuing research ethics review procedures across Canada.

Ongoing Debate About Continuing Ethics Review

Even though it would appear that continuing ethics review is an expected function of REBs, the involvement of REBs in continuing ethics review is still being debated in the research ethics community (Noah, 2004; Weijer, 2002). It would appear that REBs in different countries and even within Canada conduct varying degrees of continuing ethics review today.

An illustration of this debate is provided by Bankert and Amdur (2000), who stated that REBs should not act as data and safety monitoring committees. These authors argued instead that REBs should ensure that an appropriate plan for data and safety monitoring is in place at the time of the initial review. The authors explained that REBs are already over-burdened by having to review protocols and proposals, and they do not have the time or expertise to actively monitor studies. Pickworth (2000) similarly argued that increasing the monitoring role of REBs in the present climate would be inappropriate; mainly because of their workloads, voluntary nature, and the change to the relationship that a monitoring role might cause between a researcher and a REB (Pickworth).

In contrast, McNeill et al. (1992) argued that REBs should take an active role in the continuing ethics review of research in progress. More than half the researchers surveyed by McNeill et al. agreed that continuing ethics review would ensure the ethical conduct of research. Maloney (2000a) also argued that an

overall improvement in subject protection could be obtained through continuing ethics review. Maloney (1998, 2000b) also concluded that REBs were not placing enough attention on active research projects and were not sufficiently monitoring the recruitment of human subjects.

Maloney (1998) summarized the key findings of a report by the United States Office of the Inspector General of the Department of Health and Human Services, entitled *Institutional Review Boards: Their Role in Reviewing Approved Research*. This report's findings included: (a) the REBs' current continuing ethics review practices were of limited scope and effectiveness, (b) REBs were limited to using paperwork to carry out their responsibilities and needed to perform more active, on-site continuing ethics review, (c) due to their workloads, financial constraints, and limited knowledge and expertise, REBs were prevented from doing a better job of continuing ethics review, and (d) maintaining trust with researchers is difficult when a continuing ethics review is being viewed as "policing" and not "assisting." Maloney (2000b) subsequently encouraged REBs to further develop their continuing ethics review practices to include active monitoring of the informed consent process and the researcher's recruitment practices. Pich et al. (2003) also later called for REBs to get involved in continuing ethics review and went as far as to argue that REB continuing ethics review practices should include the monitoring of the dissemination of the results from clinical trials. Lavery et al. (2004) stated that even though continuing ethics review in clinical research has long been recognized as an essential feature of sound research ethics they are seldom exercised in ways that fulfill their

motivating goals.

In short, the literature to date on the topic of continuing ethics review practices by REBs reveals disparity in the practices of continuing ethics review by REBs and ongoing debate about the need for or value of continuing ethics review by REBs.

Research Gaps

As disparity still exists on both the need for and practices of continuing ethic review by REBs, it was important to take a critical look at current REB continuing ethics review involvement and practices. The last survey of Canadian REB continuing ethics review practices was completed in 1993, more than 10 years ago. Another survey is needed to document current practices. The methods of continuing ethics review used by REBs was an important topic then and it is still an important topic. Research is also required on their perceived effectiveness for actually protecting research subjects.

Literature Review Summary

The literature for this chapter was discussed in ten sections. The first section focused on the main historical events, including the development of four main research-guiding documents: (a) the Nuremberg Code (1946), (b) the Declaration of Helsinki (1964), (c) the United States National Research Act (1974), and (d) the Belmont Report (1979). Another major historical event was the development of Research Ethics Boards in 1966.

The second section described the development of Canada's main research guiding document, the 1998 Tri-Council Policy Statement, which was then

amended in 2003 and 2005. This document was originally developed by Canada's three main research councils. It guides both Canadian researchers and Research Ethics Boards.

The third section focused on research ethics principles. The above-mentioned five research guiding documents and the formation of Research Ethics Boards demonstrate the importance of the main research ethical principles of respect for autonomy, non-maleficence, beneficence, and justice.

The fourth section focused on research misconduct. As a result of the development of numerous research guidance documents, and the formation and evolution of REBs, current research is being performed within an era of strong protectionism. Despite the current era of strong protectionism, research misconduct continues to occur, with some research misconduct resulting in research subject deaths.

The fifth section described the main documents guiding the conduct of continuing ethics review. In the hopes that REBs may help to reduce research misconduct through continuing ethic review, the Medical Research Council (1987), the International Conference on Harmonization-Good Clinical Practices (1997), the action plan for the Deschamps Report (1998), the Declaration of Helsinki (2004), and the Tri-Council Policy Statement (2005) all were published to provide guidelines regarding REB continuing ethics review practices.

The sixth section outlined REB roles. The main role of a REB is to protect research subjects. The REB carries out this role through various functions; including reviewing and approving research prior to the start of research,

performing continuing ethics review and educating researchers, research subjects, and the general public regarding ethically conducted research.

The seventh section described REB continuing ethics review practice research that has taken place globally. Two non-Canadian studies have been published regarding REB continuing ethics review practices, one in Scotland (Thompson et al., 1981) and one in Australia (McNeill et al., 1990). Both studies showed that very few REBs perform active continuing ethics review and that the main form of continuing ethics review consists of asking for and reading a report submitted by the investigator.

The eighth section described REB continuing ethics review practice research that has taken place in Canada. Only one study has taken place on Canadian REBs continuing ethics reviews practices (NCBHR, 1995). This study had similar results as the Scottish and Australian studies.

The ninth section focused on the continuing debate about continuing ethic review. Even though it would appear that continuing ethics review is an expected function of REBs, the implementation of continuing ethics review practices by REBs is still being debated in the research ethics community (Noah, 2004; Weijer, 2002).

The tenth section outlined research gaps. REB current continuing ethics review practices and the effectiveness of these practices is not clear, particularly as the last Canadian study of continuing ethics review was conducted in 1993 (NCHBR, 1995).

All 10 sections provide a foundation for this thesis study. This thesis study

was aimed at assessing and raising awareness regarding REBs' current continuing ethics review policies and practices.

Chapter 3

Study Design

Methods

A mail survey was used in this thesis study to gather information from Canadian REBs about their continuing ethics review practices. This exploratory - descriptive survey targeted all known REBs across Canada (N=187). For external validity purposes, all 187 REBs were sent a questionnaire. As there is no official central REB register in Canada, this list of 187 REBs was obtained through an Internet search and from information sources which included: (a) the Canadian Association of Research Ethics Boards (CAREB), (b) the National Council on Ethics in Human Research (NCEHR), (c) searching the Internet using Canadian Research Ethics Boards as a search term, and (d) contacting hospitals and academic institutions across Canada.

A devised questionnaire (Appendix A) was sent, by postal mail, addressed to the "Chair" of each REB. Accompanying this questionnaire was an introduction letter (Appendix B), which stated the purpose of the research study and contained instructions for completion. One instruction was that the questionnaire be completed by the Chair or delegate. As REBs rotate Chairs and members of the board periodically, these introduction letters were not addressed to a specifically named person. The questionnaire was to be returned in an enclosed pre-addressed stamped envelope. By July, 2006, 35 questionnaires were returned. A follow-up reminder post card (Appendix C) and another copy of the questionnaire, along with the introduction letter, were sent to 152 REBs in the

month of July, 2006 as they had not responded as requested within three weeks following the initial mail out. Both an English and French version of all of the above-mentioned materials were sent to all REBs, both initially and later in the reminder mail-out.

A mail survey was chosen for data collection as it was: (a) inexpensive for the researcher, (b) relatively convenient for respondents to complete and return, and (c) it did not require the respondents to use a computer or the Internet.

The data received was primarily quantitative in nature. All quantitative data was entered into an SPSS spreadsheet, with data entry accuracy checked by the researcher's supervisor. The SPSS computer data analysis program (version 14) was then used to summarize or tabulate the responses to each question. Most data was grouped and analyzed using descriptive frequencies. The chi-square test was used to compare academic REBs and non-academic REBs, and to compare academic research and other types of research to determine if these groups were similar or different. This test is appropriate for comparing the responses from two nominal groups. All data analyses were rechecked by the researcher's supervisor.

Qualitative data was reviewed and coded into categories. SPSS was used to determine the frequency of each category. General comments retrieved from the questionnaire were reviewed and a narrative summary is included in the findings section of this thesis study. As indicated, all data analysis, both qualitative and quantitative, were completed by the thesis student and then checked by the thesis supervisor.

Population Size and Sampling

The population targeted by this study consisted of all academic and non-academic Research Ethics Boards across Canada. These REBs may be affiliated with a hospital, an academic institution, or a for-profit independent ethics board. All of these REBs review and approve research (both quantitative and qualitative) undertaken in such fields as medicine, pharmaceuticals, nursing, physiotherapy, occupational therapy, psychology, sociology, nutrition, physical education, social work, engineering, dentistry, and general arts and science. For inclusion criteria, only those questionnaires returned with a positive response to the question: "Does your REB use the Tri-Council Policy Statement Guidelines?" were included in the data analysis. This question in all returned questionnaires was answered positively.

The response rate for past studies of REBs ranged from 75% to 100% (Hayes et al., 1995; Lemmens & Thompson, 2001; McNeill et al., 1990; NCBHR, 1995; Rivera & Ezcurra, 2001; Sieber & Baluyot, 1992; Thompson et al., 1981). Based on a power of 0.8 for the expected effect size and a significance level of 0.05, the sample size required to detect a medium effect within a population of 187 was 50 (Brink & Wood, 1998). The response rate of 55.1% yielded 103 respondents in this thesis study; this is well above the medium effect size.

Instrument

A questionnaire (Appendix B) was developed largely from questions asked in a similar research study conducted by the National Council on Bioethics in Human Research (1995). The questions were adapted for all types of REBs, not

just medical ones. Although these questions were used by the NCBHR, the researcher and the researcher's three University of Alberta thesis committee members reviewed them for readability and appropriateness. The researcher's thesis committee suggested revisions to the questionnaire and the questionnaire was updated. A total of 14 questions were the result, each of which was designed to seek information on REB continuing ethics review. The questionnaire was then translated from English to French by an experienced translator.

All of the persons on the thesis committee had experience in research ethics and in developing questionnaires. It was anticipated that this questionnaire would take approximately 20 minutes to complete. The reading level was at a Microsoft word reading level of 3.6, a level appropriate to the target respondents.

Timeline

After successfully passing the thesis committee proposal defense in February 2006 and receiving ethics approval from the University of Alberta Research Ethics Board (Panel B) in June 2006, this study commenced at the end of June 2006. The initial mail-out of the questionnaire took place during the month of June with data collected over the following six weeks. The analysis of study results and thesis study report were completed by the beginning of November, 2006.

Budget

The researcher primarily funded this study. The translations costs were covered by a grant from one of the researcher's thesis committee members. The cost of this study was as follows:

1. 187 stamps at $1.05 each (to mail surveys) = $196.35

2. 187 return envelopes at $0.51 each = $95.37

3. 152 stamps at 1.05 each (for reminder mail-outs) = $159.60

4. 152 for return envelopes at $0.51 each = $77.52

3. Printing/photocopying= $303.00

4. Three box of envelopes = $24.00

5. Translation of documents from English to French = $90.83 (at $0.10 per word)

Total Cost = $946.67 + $66.27 = $1,012.94

Ethical Consideration

As this exploratory-descriptive study was conducted through the University of Alberta in Edmonton; research ethics approval was obtained from Panel B of the University of Alberta Health Research Ethics Board. During this thesis study, Dr. Glenn G. Griener, PhD was co-chairperson of this ethics board, and he was a member of this researcher's thesis committee, Dr. Griener was not involved in the ethics review of this thesis study. Expedited research ethics approval for this study was received in June 2006, largely due to the voluntary participation in this survey study, with respondent consent implied with the return of their completed questionnaire. Respondents were not remunerated for completing the questionnaire.

The information gained from the results of this thesis study is expected to be beneficial to Canadian REBs and other groups or individuals primarily as it will contribute to raising awareness of REB current continuing ethics review policies and practices. No risks to the subjects participating in this thesis study

were expected nor encountered, and all REB identifying information was kept confidential during the conduct of this thesis study and will forever remain confidential. To maintain confidentiality of the REBs and anonymity of the data, the questionnaires were coded with a unique number identifier. Only the researcher's thesis supervisor and the researcher had access to the master-decoding list. The master-decoding list was kept locked in a filing cabinet. The unique number identifier protected the anonymity of REBs both during and after this thesis study through the publishing of results. No respondent or REB will be named or otherwise identified in any written or verbal report.

During the conduct of this thesis study, the REB list and completed questionnaires were stored in the researcher's locked filing cabinet. During the conduct of this thesis study, only the researcher's thesis supervisor and the researcher had access to the computer data base. No agencies or individuals had access to any confidential or research data during the conduct of this study nor will they in the future. After analysis was completed, the master-decoding list was destroyed under the supervision of the researcher's thesis supervisor. The data will be destroyed in seven years; as per University of Alberta policy, until then, the data will be safely archived with the thesis supervisor. The researcher is not anticipating any secondary analysis of the data. If secondary data analysis is planned in the future, additional research ethics approval will be sought and obtained prior to any further analysis.

Chapter 4

Findings

The purpose of the mail survey was to explore and describe Canadian Research Ethics Board current practices and processes for continuing ethics review of approved research involving human subjects. As indicated in Chapter 3, during the month of June, 187 questionnaires were mailed out to REBs across Canada. Reminder post-cards with another copy of the questionnaire and invitation information letter followed three weeks later. A total of 103 completed questionnaires were returned by the end of August, 2006; a 55.1% response rate.

The survey tool collected information regarding the following: (a) REB participation in continuing ethics review, (b) the methods of continuing ethics review conducted, (c) the type of REB, (d) the types of research studies each REB reviewed, (e) REB participation in continuing ethics review conducted for detecting issues in scientific integrity, and (f) methods for detecting issues in scientific integrity. Information regarding the following REB characteristics was also collected: (a) Tri-Council Policy Statement Guidelines adherence, (b) profit or non-profit status, (c) continuing ethics review policy status, (d) consequences of non-compliance with the researcher's approved proposal, (e) consequences of scientific integrity issues, (f) perceived adequacy of continuing ethics review practices to protect the safety and ethical rights of a research subject, and (g) additional comments on continuing ethics review practice.

The data received from the returned questionnaires was primarily quantitative in nature. All quantitative data was entered into an SPSS spreadsheet.

The SPSS computer program (version 14) was used to summarize or tabulate the responses to each question. Most data was grouped and analyzed by SPSS using descriptive frequencies. The chi-square test was used to compare academic REBs and non-academic REBs, and academic research and other types of research to determine if the groups were alike. Qualitative data was reviewed for common categories. The questionnaire comments were then assigned to the most appropriate category. Data entry and data analysis was completed by September 2, 2006.

This chapter presents the findings of this thesis study. The findings to the four research questions are presented below. Additional findings are then presented.

Question 1. What proportion of Canadian Research Ethics Boards perform continuing ethics reviews of previously approved research proposals?

Information regarding REB participation in continuing ethics review was obtained through the question: Does your REB conduct continuing ethics review of approved research approvals? Of all 103 respondents, 90 or 87.4% answered yes, while 12 or 11.7% answered no. Only 1 or 1.0% answered "not sure" to this question. As demonstrated in Table 1, a majority of the respondents indicated that their REB conducts some sort of continuing ethics review.

Question 2. What review processes or methods are used to conduct continuing ethics reviews of previously approved research proposals?

To gather information on the methods of continuing ethics review used by REBs, responses to the following seven continuing ethics review method

questions was collected and analyzed: (a) review of informed consent and informed consent process, (b) review of study documents, (c) review of adverse events and incidents, (d) review of on-going research reports, (e) review of end-of-study research reports, (f) data-safety-monitoring board activities, and (g) other types of continuing ethics review. Among these, the most common method of continuing ethics review was found to be the routine review of on-going research reports. Of the 90 respondents who reported their REB conducted some sort of continuing ethics review, 76 or 84.4% reported they review on-going research reports completed by the researcher. The second most common continuing ethics review method was the review of adverse events and incidents. Of the 90 respondents who reported their REB conducted continuing ethics review, 73 or 81.1% reported they review adverse events and incidents reported by the researcher or other persons. Review of end-of study research reports was the third most commonly reported continuing ethics review method. Of the 90 respondents who reported their REB conducted continuing ethics review, 68 or 75.6% reported they review end-of-study research reports completed by the researcher. The fourth most common method of continuing ethics review was the review of informed consents and the informed consent process. Of the 90 respondents who reported their REB conducted continuing ethics review, 45 or 50.0% reported they review informed consents and the informed consent process.

Less common methods of continuing ethics review were also found. The fifth most common method of continuing ethics review was a review of study documents generated by the study. Of the 90 respondents who reported their REB

conducted continuing ethics review, 42 or 46.7% reported they review study documents generated by the study. The sixth most common method of continuing ethics review was the formation of a data-safety-monitoring-board or participation in data-safety-monitoring board activities. Of the 90 respondents who reported their REB conducted continuing ethics review, 14 or 15.6% reported the formation of or participation in data-safety-monitoring board activities. In addition, of the 90 respondents who reported their REB conducted continuing ethics review, 6 or 6.7% reported their REB conducts "other" methods of continuing ethics review. All "other" cited methods of continuing ethics review were reviewed and categorized into two themes: (a) verbal or written communication with researchers and (b) required annual re-approvals of research studies. Table 2 summarizes all findings on REB methods of continuing ethics review.

In most cases, each REB performed more than one method of continuing ethics review. Of the 90 respondents who reported their REB conducted continuing ethics review, 23 or 25.6% of the REBs conduct 5 of all 7 reported methods of continuing ethics review. Table 3 shows REBs and their conduct with regard to number of methods of continuing ethics review.

Continuing ethics review could also be used to detect various types of unethical research conduct, including issues in scientific integrity. Some REBs had already implemented continuing ethics review to detect issues in scientific integrity. The number of respondents who reported their REB conducts continuing ethics review to detect issues in scientific integrity was 22 or 21.4% of

the 90 respondents (see Table 4).

Of the 22 who responded yes, their REB conducts continuing ethics review to detect issues in scientific integrity, 11 or 50% do this through conducting a review of study data; while 9 or 40.9% conduct "other" methods of continuing ethics review, 7 or 31.8% conduct a review of the data analysis, and 7 or 31.8% conduct a review of the published literature arising from the approved study (see Table 5). All "other" reported methods of continuing ethics review to detect issues in scientific integrity were reviewed and categorized into three themes. These "other" reported methods of continuing ethics review are: (a) scientific literature review as part of standard practice, (b) the review of study documents for internal consistency and accuracy, and (c) the implementation of any process necessary to follow-up suspected or alleged issues.

Of the 22 who responded "yes" to the question if they conduct continuing ethics review to detect issues in scientific integrity, 13 respondents or 59.1% reported their REB conducts one method of continuing ethics review, 5 respondents or 22.7% reported their REB conducts 2 methods of continuing ethics review, 2 respondents or 9.1% reported their REB conducts 4 methods of continuing ethics review, 1 respondent or 4.5% reported their REB conducts 3 methods of continuing ethics review, and 1 respondent or 4.5% did not specify the number of methods of continuing ethics review (see Table 6).

Question 3. Do REBs perform continuing ethics review more often for clinical trials research then for other types of research?

Of the 33 REBs that reported reviewing only academic research, 24 or

72.7% conduct continuing ethics review. Of the 5 REBs that reported reviewing only clinical trials, all 5 or 100 % conduct continuing ethics review. Of the 65 REBs that were reported reviewing both academic research and clinical trials, 61 or 93.8% conduct continuing ethics review. In contrast, continuing ethics review is conducted 72.7% of the time for academic research alone and 100% of the time for clinical trials alone. According to the results of a chi square analysis, continuing ethics review is obviously conducted significantly more often for clinical trials than for other types of research (see Table 7).

Question 4. Do REBs in academic institutions perform continuing ethics reviews more often than the REBs of other organizations?

Of all 103 respondents, 49 out of 60 (81.7%) Academic/University REBs conducted continuing ethics review; while all 36 or 100% hospital-based REBs conducted continuing ethics review and 5 out of 7 (71.4%) Independent REBs conducted continuing ethics review. According to the results of a chi square analysis, there is no significant difference between the frequency of continuing ethics review and the type of REB (see Table 8).

Other Findings

Supplementary questions in the questionnaire sought more information regarding REB continuing ethics review policies and practices. These supplementary questions cover the following topics: (a) Tri-Council Policy Statement Guidelines adherence, (b) profit status or non-profit status, (c) continuing ethics review policy status, (d) consequences of non-compliance by the researcher with the researcher's approved proposal, (e) consequences of

detected issues in scientific integrity, (f) adequacy of continuing ethics review practices to protect the safety and ethical rights of research subjects, and (g) additional comments on continuing ethics review practices.

The following paragraphs describe the findings from these supplemental questions. All 103 (100%) respondents reported their REB uses the Tri-Council Policy Statement Guidelines. Of the 103 respondents, 98 or 95.1% reported their REB was not-for-profit and 3 or 2.9% reported their REB was for-profit (see Table 9). A majority of the respondents, or 89 (86.4%) stated their REB has a policy on continuing ethics review. Of the 103 respondents, 13 or 12.6% stated their REB does not have a policy on continuing ethics review and 1 or 1.0% of the respondents was not sure if their REB has a policy on continuing ethics review (see Table 9). Of the 13 respondents who reported their REB does not have a continuing ethics review policy; 5 or 38.5% plan to develop a policy in the near future, 4 or 30.8% do not plan to develop a policy in the near future, and 4 or 30.8% did not respond to this question (see Table 9).

Of all 103 respondents, 91 or 88.3% provided comments regarding their REB's consequences if a researcher is not in compliance with his/her approved research proposal. These comments were grouped into 16 categories. The results are depicted in Table 10. The most common two consequences, provided by more than one quarter of the REBs representatives, were: (a) REB approval is withdrawn and (b) the study is halted.

Of all 103 respondents, 28 or 27.2% provided comments regarding their REB's consequences if issues in scientific integrity were detected. These

comments were grouped into nine categories. The results are shown in Table 11. The two most common consequences provided by one quarter of the REB representatives were: (a) the study is halted and (b) the researcher's name and scientific integrity issue are reported to the appropriate authorities.

To gather information on the effectiveness of REB continuing ethics review practices for the protection of subject safety and ethical protection for the research subject, the following two questions were asked: (a) Do you believe your REB's continuing ethics review practices are adequate to address the safety needs of the research subjects? and (b) Do you believe your REB's continuing ethics review practices are adequate to ensure research is conducted in an ethical manner? A total of 70 or 68.0% of the 103 respondents believe their continuing ethics review practices are adequate for protecting subject safety, 13 or 12.6% did not believe they were adequate, 17 or 16.5% were not sure, and 3 or 2.9% did not answer the question (see Table 12). In addition, a total of 72 or 69.9% of the 103 respondents believe their continuing ethics review practices are adequate to ensure the research is conducted in an ethical manner, 14 or 13.6% did not believe they were adequate, 15 or 14.6% were not sure, and 2 or 1.9% did not answer the question (see Table 12).

Some respondents provided additional information in response to the following questions: (a) Do you believe your REB's continuing ethics review practices are adequate to address the safety needs of the research subjects? and (b) Do you believe your REB's continuing ethics review practices are adequate to ensure research is conducted in an ethical manner? The respondents' explanations

regarding the adequacy of their continuing ethics review practices for protecting subject safety were grouped into 10 categories. The most common explanation, from 14 or 34.1% of the respondents, was that most of the research the REB reviews is minimal or low risk to subject safety and therefore their continuing ethics practices were adequate to protect the subject's safety (see Table 13). One respondent stated that "most projects are low risk from a safety perspective." Respondent explanations regarding the adequacy of their continuing ethics review practice for ensuring the ethical conduct of research were also grouped into 10 categories. The most common explanation, from 15 or 38.5% of respondents, was that their REB needs to begin, improve on, or has just started a formal continuing ethics review program (see Table 14). One respondent stated that "we are just starting a process of reviewing research sites." Another respondent stated "we are in process of planning an auditing program."

Summary of Questionnaire Comments

The questionnaire also provided an opportunity to collect additional information regarding REBs' continuing ethics review practices in response to the statement, "please proved any additional comments about your REB's continuing ethics review practices." Of all 103 respondents, 39 or 37.9% provided additional comments. These comments are summarized in narrative form in the paragraphs below.

Respondents commented on the issue of lack of financial resources and personnel to do more than the basic review of reports submitted by researchers, stating "no resources to perform greater ongoing monitoring." Small REBs and

REBs that review low-risk research did not generally find continuing ethics review difficult to implement, but they added that if the amount of research being reviewed increased, then proper continuing ethics review may be a concern due to a lack of financial resources and personnel. REB respondents are already finding it difficult to keep up with the demanding work-load, as they receive many research proposals and other study documents to review each year. This heavy workload was said to be making it difficult to implement an effective continuing ethics review practice. Respondents commented that because their REB's time is limited, their REB's main focus should be on how the subjects will be treated during the course of the study. One respondent commented that REBs need to know "best practices" to conduct continuing ethics review with limited resources.

One respondent said that REBs face challenges in the fast-paced research environment today: (a) ensuring compliance with privacy legislation, (b) ensuring the safety of subject enrolment in more than one research study at the same time, and (c) including minority ethnic populations (such as First Nations persons) in research. Respondents mentioned the need to involve the researchers and study staff in educational programs on the ethical conduct of research. The respondents also mentioned the importance of getting the researchers to "buy in" to the continuing ethics review activities, thus ensuring the relationship is a more cooperative one between the researcher and their REB. Respondents provided comments that voiced their frustration with the reporting structure of their REB, as it gives them little authority to take action when issues arise. One respondent reported revoking approval of a study when new risks effected subject safety were

identified. Some respondents reported the recent implementation of an active continuing ethics review program that includes: (a) a review of informed consent, (b) a chart review, (c) meeting with subjects, and (d) a review of safety reports after the first few subjects were enrolled. One respondent reported their REB currently conducts a fully active continuing ethics review program.

Some respondents also commented that the final responsibility of conducting ethical research rests with the researcher. Some respondents also commented that "we feel we are doing everything possible to protect human subjects." One respondent commented they rely on the experience and "good judgment" of their REB to ensure that research is conducted ethically.

In conclusion, a majority of REB representatives who responded to this questionnaire reported their REB conducts continuing ethics review (87.4%). Of the REBs that conduct continuing ethics review, the most common continuing ethics review method was said to be a review of on-going research reports. REBs conduct continuing ethics review significantly more often for clinical trials research than for academic research. There was no significant difference between academic and other REBs with regards to their frequency in conducting continuing ethics review. Many other findings illustrate that REBs take continuing ethics review seriously.

Chapter 5

Discussion of Findings

This study was designed to explore and describe Canadian Research Ethics Boards current involvement in and process for continuing ethics review of approved research involving human subjects. The findings to the following four research questions were presented in the previous chapter:

1. What proportion of Canadian Research Ethics Board perform continuing ethics review of previously approved research proposals?
2. What review processes or methods are used to conduct continuing ethics reviews of previously approved research proposals?
3. Do REBs perform continuing ethics review more often for clinical trials research then for other types of research?
4. Do REBs in academic institutions perform continuing ethics review more often than the REBs of other organizations?

The following chapter discusses the findings for these four research questions in relation to previous research and other relevant information.

Question 1. What proportion of Canadian Research Ethics Board perform continuing ethics review of previously approved research proposals?

A total of 103 REB chairpersons or delegates completed and returned a questionnaire. As such, this thesis study had a return rate of 55.1%. It is apparent from their responses that a considerable majority (87.4%) of responding REBs conduct some form of continuing ethics review. This majority finding is considerably different from the two other studies conducted on this topic by

McNeill et al. (1990) and Thompson et al. (1981). The Australian study by McNeill et al. found only 26% of 89 respondents reported their REB always undertook a review of research in progress. The Scottish study by Thompson et al. (1981) found 47% of the 34 respondents reported their REBs conducted continuing ethics review in one form or another. It has been 16 years since the McNeill et al. study findings were published and 26 years since the Thompson et al. study findings were published. This considerable passage of time could be one reason why this thesis study found a much higher proportion of REBs were now conducting continuing ethics review. It would be reasonable to expect that over a 16-26 year span, REBs would implement changes, such as starting to conduct continuing ethics review.

It has been almost 10 years since the implementation of the Tri-Council Policy Statement in 1998. The Tri-Council Policy Statement of 1998, and the updates in 2003 and 2005, state that REBs can actively monitor ongoing research studies. At a minimum, researchers must provide research updates to their REB, especially about any serious adverse events (CIHR, NSERC & SSHRC, 2005). The implementation by Canadian REBs of this continuing ethics review criteria could be a reason for a high proportion of Canadian REBs currently conducting continuing ethics review. REBs have had 10 years to either start or improve upon their continuing ethics review program since the first Tri-Council Policy Statement became available.

It is also notable that this thesis study found 12 or 11.7% of the respondents reported their REB does not conduct continuing ethics review. In the

study conducted by the National Council on Bioethics in Human Research (1995), the most common response regarding why their REB was not conducting continuing ethics review was they did not consider it their mandate, and they did not have the time and resources to do so. Only 2.4% of the respondents in this thesis study reported that conducting continuing ethics review for the protection of subject safety was not their REB's role. Furthermore, only 7.7% of the respondents in this thesis study reported that conducting continuing ethics review to ensure the ethical conduct of research was not their REB's role. As such, only a minority of reporting Canadian REBs do not conduct continuing ethics review, and the vast majority see that it is part of their mandate.

In contrast, Bankert and Amdur (2000) argued that conducting continuing ethics review, in particular acting as a Data and Safety Monitoring Board for reviewing adverse events, is not a function of the REB. These authors asserted that such work overburdens an already busy REB, thus distracting the REB from its main function which is the review of research proposals to protect research subjects. These authors suggested that continuing ethics review is a role for the governing institution, not the REB.

In this thesis study, among the 12 respondents who said their REB does not conduct continuing ethics review, 5 or 41.7% plan to develop a continuing ethics review program in the near future, thus meeting the continuing ethics review criteria in the Tri-Council Policy Statement. Other than the requirement that researchers must provide updates to their REB, especially about any serious adverse events, the methods of continuing ethics review are not stated in the Tri-

Council Policy Statement. A discussion regarding the methods of continuing ethics review is presented in the next section.

Question 2. What review processes or methods are used to conduct continuing ethics reviews of previously approved research proposals?

This thesis study revealed that the methods of continuing ethics review vary considerably among REBs across Canada. However, a majority of the responding REBs conduct a review of on-going research reports that have been submitted by researchers (84.4%). In contrast, 53% of Canadian respondents in the 10-year-old study conducted by the National Council on Bioethics in Human Research (NCBHR, 1995) reported requiring an annual report from the researcher. That same study revealed that only 36% of the respondents said their REBs required an end-of-study report from the researcher. This thesis study found 75.5% of the respondents reported their REB reviews end-of-study reports submitted by the researcher. Furthermore, this thesis study revealed 46.7% of the respondents reported their REB reviews study documents, a drastic increase from the NCBHR (1995) study that found only 18.0% of the respondents reporting their REB conducted audits of research in progress. The NCBHR study also found only 7.0% of the respondents reporting their REB reviews patient charts to determine whether researchers are in compliance with REB recommendations.

The Tri-Council Policy Statement (1998, 2003, 2005) does not cite the methods of continuing ethics review that REBs must use. The variety of methods reported in this thesis study may be due then to a lack of direction in the Tri-Council Policy Statement, but this variety could also be related to the many types

of research that REBs review. Just over one quarter of the REBs (25.6%) were said to conduct five different methods of continuing ethics review. Most respondents felt their REB's continuing ethics review methods were adequate to protect the safety of research subjects, particularly as the types of research they review were considered to be low risk for subjects.

Continuing ethics review may be used to detect issues in scientific integrity. In the 1995 study by the NCBHR, only 12.0% of the respondents reported their REB dealt with issues in scientific integrity. In contrast, 21.4% of the respondents in this thesis study said their REB conducts continuing ethics review to detect issues in scientific integrity. The most commonly reported type of continuing ethics review method to detect issues in scientific integrity in this thesis study was the review of study data. The two most common consequences of detected issues in scientific integrity reported in this thesis study were: (a) the study being halted and (b) the reporting of a researcher's name and the scientific integrity issue to appropriate authorities. A comparison of these two studies reveals there has been a modest increase, over the past 10 years, in REBs conducting continuing ethics review to detect issues in scientific integrity. This modest increase could illustrate the reluctance of REBs to accept this as their role. Debate in the ethics community regarding the roles of REBs in dealing with issues of scientific integrity is therefore likely to continue.

In addition to gathering information regarding continuing ethics review for detecting issues of scientific integrity, general themes about REB continuing ethics review methods emerged through comments provided by REB respondents.

One theme that emerged was the lack of personnel and resources to conduct a fully active continuing ethics review program. In 2001, Weijer advocated that institutions should support their REBs through sufficient financial resources and personnel so as to ensure an adequate continuing ethics review program. In situations where REBs are not associated with an academic institution, Weijer thought such REBs could pay for continuing ethics review by charging researchers.

Question 3. Do REBs perform continuing ethics review more often for clinical trials research then for other types of research?

No previous research investigations that studied the relationship of REB continuing ethics review and the type of research being reviewed by the REB were located. The results from this thesis study reveal that continuing ethics review is conducted significantly more often for clinical trials than for other types of research. This difference may be due to the higher risk to research subjects who participate in clinical trials than those participating in other types of research. However, other types of research, such as social science and educational research, have recently been in the spotlight over concerns about adequate human subject protection, including issues related to the principles of "respect for persons," "beneficence," and "justice" (Morahan et al., 2006). REBs, regardless of the type of research they review, still have responsibilities which include, but are not limited to: (a) ensuring all subjects are properly consented and (b) research subject information remains confidential (Green et al., 2006).

Question 4. Do REBs in academic institutions perform continuing ethics

review more often than the REBs of other organizations?

No previous research reports were located on the topic of continuing ethics review and the relationship of this topic to the type of REB. The results from this thesis study show there is no significant difference between the types of REBs, such as academic or hospital-based and the frequency of continuing ethics review being conducted by REBs. Again, this may be due to the successful implementation over the last 10 years of the Tri-Council Policy Statement's criteria to conduct continuing ethics review.

The findings to the above four research questions reveal most REBs conduct continuing ethics review in some form or another, in keeping with the expectations of the Tri-Council Policy Statement. Most Canadian REBs conduct a review of reports submitted by researchers. However, these REBs also perform numerous methods of continuing ethics review, with this number depending in some measure on the type of research and the understood risk to research subjects. Most of the respondents felt their REB's continuing ethics review methods are adequate to protect the safety of research subjects. However, the respondents mentioned that there was also room for improvement in their continuing ethics review methods to ensure research is being conducted ethically. Such improvements in continuing ethics review methods could still be delayed by limited resources and lack of personnel.

As such, the findings of this thesis study indicate that most Canadian REBs are fulfilling a continuing ethics review role. However, REB methods of continuing ethics review remain passive for the most part, which could be

considered efficient given limited resources, including a lack of personnel. Determining the effectiveness of passive continuing ethics review methods in detecting research misconduct remains a concern.

In conclusion, the proportion of REBs who are conducting some form of continuing ethics review has increased considerably over the past 10 years in Canada. Continuing ethics review continues to be mainly passive, however, consisting most often of researcher-submitted reports. REBs also conduct continuing ethics review significantly more often for clinical trials research than for academic research. No significant difference between academic and other REBs in regards to the frequency of conducting continuing ethics review were found, indicating that all REBs appear to have an awareness of the need for continuing ethics review.

Chapter 6

Conclusion

This concluding chapter summarizes this thesis study and provides implications of its findings for the research ethics community and other communities, such as research and academic institutions administrations. As well, limitations of this thesis study are presented. Finally, topics in continuing ethics review for additional research are outlined.

Summary of Thesis Study

As planned, during the month of June 2006, a devised questionnaire was mailed to 187 REBs across Canada with the aim of exploring and describing their current continuing ethics review practices. A total of 103 completed questionnaires were returned in July or August, 2006. All 103 questionnaires were included in this thesis study as they met all inclusion criteria, none were excluded. During the month of August 2006, all questionnaire data were entered into an SPSS spreadsheet, with data entry checked by the researcher's supervisor. Data analysis was completed in the month of September 2006. To ensure accuracy of the findings, all data analyses were conducted twice. Frequencies for descriptive data were performed, with the chi-square test used to analyze differences between variables with nominal data.

Returned questionnaires revealed four key findings. The first is that the majority of REBs conduct continuing ethics review; this illustrates a considerable increase compared to over 10 years ago. The second key finding is that the type of continuing ethics review that is conducted continues to be passive, consisting

mainly of reviewing researcher-submitted reports. The third finding is that REBs conduct continuing ethics review significantly more often for clinical trials research than for other types of research. The fourth finding is that there was no significant difference between academic and other REBs with regard to their frequency of conducting continuing ethics review.

Implications

The information obtained regarding Canadian REBs continuing ethics review practices has implications for the research ethics community and other communities such as researcher and academic or non-academic institutions. These implications include the need to: (a) increase the REB roles in research that is on-going, (b) increase personnel and resources, and (c) reassess current REB continuing ethics review practices regarding low risk qualitative research or non-clinical trial research.

The findings of this thesis study indicate that most REBs currently conduct passive continuing ethics review in the form of reviewing researcher-submitted reports. Respondents indicated that their REB needs to begin, improve upon, or had just started a formal continuing ethics review program. These findings suggest, REBs may conduct more active forms of continuing ethics review of on-going research as they further develop their continuing ethics review program.

Limited personnel and resources for continuing ethics review were presented as an issue in past studies on REBs and continuing ethics review. This issue continues to be a concern as identified in this thesis study. REBs may need

to request additional personnel and/or resources in order to conduct more active forms of continuing ethics review or may need to advocate for administrative scrutiny of scientific integrity.

Many respondents felt their REB's continuing ethics review practices were adequate for the low risk research they oversaw. However, with the increased attention that qualitative research is now getting for its potential to cause harm, REBs may want to reassess their current continuing ethics review practices to ensure they are adequate for the protection of subjects and thus to ensure the ethical conduct of research in all types of research, including qualitative research.

Limitations of Thesis Study

All research has limitations. The three limitations identified for this thesis study are in the areas of: (a) a lower than expected response rate, (b) questionnaire design, and (c) identifying REBs in Canada. The following paragraphs describe these three limitations.

1. The response rate for this thesis study was not as high as anticipated. The response rate for this thesis study was expected to be 75% or higher and the actual response rate was 55.1%. This low rate may be an outcome of the questionnaire being mailed out during the summer months when REB representatives were likely to be on summer vacation. However, this response rate is similar or higher than the response rates for other studies. Thabane et al. (2005), who surveyed Canadian REBs regarding the participation of a statistician on their REB, had a response rate of 55%. A summary of chiropractic survey response

rates by Russel et al. (2004), found return rates ranged from 7.0% to 91.4%, with an average 52.7% response rate. Russel et al. also indicated that response rates have been declining over time. This decline in response rates may be one reason why the previous surveys of REBs had a higher response rate than this thesis study.

2. The questionnaire developed for this thesis study was effective for eliciting the desired information, but improvements could have been made to it before it was used. These changes could have reduced the free text that respondents provided, thus allowing for easier analysis of data. Another change would be to reformat the questionnaire to make the different sections more distinct. Clearer instructions could also have been given to respondents, such as to more specifically tell them what questions to complete as they progressed through the questionnaire.

3. Although considerable effort was expended to identify all REBs in Canada, it is not certain that all were included in the mail out. No official central listing of REBs currently exists in Canada. The response rate of 55.1% may illustrate it was representative of the entire REB population. According to Spooner (2003), a response rate above 50% is usually characteristic of the population studied. REBs from all provinces, English and French-speaking REBs, and academic and non-academic REBs were included in this thesis study. As such, it is anticipated that the findings of this thesis study are fairly representative of REBs across Canada.

Future Research Topics

Despite this thesis study, further research on the topic of continuing ethics review is needed. More research needs to be conducted on the effectiveness of continuing ethics review methods or programs for detecting and preventing research misconduct or improperly conducted research. If continuing ethics review is proven to be effective for detecting or preventing research misconduct and improperly conducted research, more resources may be allocated to REBs for this role. Another important topic requiring further research is: For REBs that conduct continuing ethics review, what are the results of this active continuing ethics review?

In conclusion, this thesis study showed considerable growth in continuing ethics review among Canadian REBs. Regardless, continuing ethics review needs further research. The effectiveness of current continuing ethics methods for detecting and preventing research misconduct, and improperly conducted research is a key area for ongoing research. Despite the limitations of this thesis study, the results shed light on the current involvement in and processes for continuing ethics review of approved research involving human subjects by Canadian REBs. The aim of this thesis was to assess and raise awareness regarding continuing ethics review policies and practices by Canadian REBs. The dissemination and subsequent discussion of the results of this thesis study should fulfill this aim.

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Appendix A

The Status of Continuing Ethics Review and Continuing Ethics Review Practices by Canadian Research Ethics Boards

Questionnaire
Instructions: Please complete the following 14 questions about your Research Ethics Board (REB) and return the completed questionnaire in the envelope provided.

General REB Information
1. Does your REB use the Tri-Council Policy Statement Guidelines? (Check one category) ☐ Yes ☐ No ☐ Not Sure **Note:** If you answered **No** to this question your questionnaire responses will **not** be included in the data analysis.
2. Please describe your REB (Check one category): ☐ Academic/University ☐ Hospital-based ☐ Independent
3. Please describe your REB (Check one category): ☐ For Profit ☐ Not for Profit

4. What types of research does your REB review? (Check all that apply)

☐ Academic research (e.g. Professor-derived research)
☐ Sponsored or industry funded (e.g. Clinical trials)
Other (Please specify):

Please answer the following questions on continuing ethics review.

Continuing ethics review is defined as the ongoing review by a REB of approved research proposals. This may include: (a) a review of informed-consent practices, (b) a review of reported adverse events or incidences, (c) the periodic review of documents generated by the study to ensure research proposal compliance and subject safety, (d) reviewing research reports completed by researchers, and (e) the formation of or participation in data safety-monitoring board activities.

5. Does your REB have a policy on continuing ethics review of approved research proposals?

☐ Yes
☐ No
☐ Not Sure
If no, please describe any current or future plans to develop a policy:

6. Does your REB conduct continuing ethics review of approved research proposals?

☐ Yes
☐ No
☐ Not Sure

If you answered yes to question 6

6 a. Please indicate how continuing ethics review is carried out (Please check all that apply):

☐ Review of informed consents and the informed consent process
☐ Review of documents generated by the study to ensure research proposal compliance and subject safety
☐ Review of adverse events/incidents reported by researchers or other persons
☐ Review of on-going research reports (continuing updates) completed by researchers during the course of the study
☐ Review of end-of-study research reports completed by researchers
☐ Formation of or participation in data-safety-monitoring boards activities
Other (Please describe):

6 b. Please describe the consequences if a researcher is not in compliance with his/her approved research proposal:

Please answer the following questions on issues in Scientific Integrity.

Issues in Scientific Integrity is defined as any fabrication, falsification, plagiarism, or any other practices that seriously deviate from those that are commonly accepted within the scientific community for proposing, conducting, or reporting research.

7. Does your REB perform continuing ethics review to detect issues of scientific integrity?

☐ Yes
☐ No
☐ Not Sure

If you answered yes to question 7

7 a. Please indicate how continuing ethics review for issues of scientific integrity is performed by your REB:

☐ Review of study data to detect any fabricated data
☐ Review of data analysis to detect incorrect findings
☐ Review of published literature to ensure accurately reported study results
Other (Please describe):

7 b. Please describe any consequences of detected issues of scientific integrity:

8. Do you believe your REB's continuing ethics review practices are adequate to address the safety needs of research subjects?

☐ Yes
☐ No
☐ Not Sure
Please Explain:

9. Do you believe your REB's continuing ethics review practices are adequate to ensure research is conducted in an ethical manner?

☐ Yes
☐ No
☐ Not Sure
Please explain:

10. Please provide any additional comments about your REB's continuing ethics review practices here:

Thank-you!
Karleen Norton
Address deleted

If you wish to have a copy of the study results mailed to you, please provide your name and mailing address.

Name:

Mailing Address:

City:

Province:

Postal Code:

Le statut des évaluations continues d'éthique et pratiques d'évaluation continues d'éthique par les conseils d'éthique de recherche

Questionnaire
Instructions: Veuillez répondre aux 14 questions suivantes sur votre Conseil d'Éthique de Recherche (CER) et retourner le questionnaire complété dans l'enveloppe fournie.

Informations générales sur votre CER
1. Votre CER adhère t-il aux balises de la déclaration de politique générale des trois Conseils ? (Choisissez une catégorie) ☐ Oui ☐ Non ☐ Incertain **Note**: Si vous répondez **non** à cette question, les réponses de votre questionnaire **ne seront pas incluses** dans l'analyse des données.
2. Veuillez décrire votre CER (Choisissez une catégorie): ☐ Académique/Université ☐ Hôpital ☐ Indépendant
3. Veuillez décrire votre CER (Choisissez une catégorie): ☐ À but lucratif ☐ À but non-lucratif

4. Quel genre de recherche votre CER évalue t-il ? (Cochez tout ceux qui s'appliquent)

☐ Recherche académique (e.g. Recherche provenant de professeurs)
☐ Recherche parrainée ou financé par l'industrie (e.g. essai clinique)
Autre (veuillez spécifier):

Veuillez répondre aux questions suivantes sur l'évaluation d'éthique continue.

L'évaluation d'éthique continuel est défini comme l'évaluation continuelle par un CER de projets de recherche proposés. Incluant: (a) examen des pratiques de consentement éclairé, (b) examen d'événement indésirables rapportés, (c) l'examen périodique de documents associés par l'étude afin d'assurer la conformité du projet de recherche et la sécurité des participants, (d) examen des rapports de recherche complétés par les chercheurs, et (e) la formation de ou participation à des activités d'évaluation de sécurité des données.

5. Votre CER a-t-il une politique sur l'évaluation d'éthique continue de propositions de projets de recherche approuvées ?

☐ Oui
☐ Non
☐ Incertain

Si votre réponse est non, veuillez décrire les plans en cours ou futurs pour développer une politique:

6. Votre CER effectue t-il des évaluations d'éthique continus de propositions de recherche approuvés ?

☐ Oui
☐ Non
☐ Incertain

Si vous avez répondu oui à la question 6

6 a. Veuillez indiquer comment l'évaluation continue d'éthique est effectuée (Cochez tout ceux qui s'appliquent):

☐ Examen des pratiques de consentement éclairé et processus de consentement éclairé
☐ Examen des documents associés à l'étude afin d'assurer la conformité du projet de recherche et la sécurité des participants.
☐ Évaluation d'événement indésirables rapportés par les chercheurs ou autres personnes
☐ Évaluation de rapports de recherche en cours (mise à jour continue) complété par les chercheurs au cours de l'étude
☐ Évaluation de rapports de recherche de fin d'étude complété par les chercheurs
☐ Formation ou participation à des activités d'évaluation de sécurité de données par le conseil
Autre (Veuillez spécifier):

6 b. Veuillez décrire les conséquences si un/une chercheur (euse) ne conforme pas a son projet de recherche approuvé :

Veuillez répondre aux questions suivantes sur l'intégrité scientifique.

Les problématiques associées à un manque d'intégrité scientifique sont définies comme toute fabrication, falsification, plagiat ou toute autre pratique qui dévie sérieusement des pratiques communément acceptées par la communauté scientifique pour proposer, réaliser, ou rapporter les résultats de recherche scientifique.

7. Votre CER effectue t-il des évaluations d'éthique continues afin de détecter des problématique reliés à l'intégrité scientifique ?

☐ Oui
☐ Non
☐ Incertain

Si vous avez répondu oui à la question 7

7 a. Veuillez indiquer comment l'évaluation d 'éthique continue pour des problématique d'intégrité scientifique sont effectués par votre CER :

☐ Évaluation des donnés de recherche afin de détecter toute donnée fabriquée
☐ Évaluation de l'analyse des données afin de détecter des résultats erronées
☐ Évaluation de littérature déjà publiée afin d'assurer des résultats d'étude rapportés correctement
Autre (Veuillez spécifier):

7 b. Veuillez décrire les conséquences de problématiques d'intégrité scientifique détectés:

8. Croyez vous que les pratiques d 'évaluation d'éthique de recherche effectués par votre CER sont adéquates pour répondre aux besoins de sécurité des personnes qui participent à de la recherche scientifique ?

☐ Oui
☐ Non
☐ Incertain
Veuillez expliquer:

9. Croyez vous que les pratiques d'évaluation d'éthique continue de votre CER sont adéquates pour assurer que la recherche est réalisée de manière éthique ?

☐ Oui
☐ Non
☐ Incertain
Veuillez expliquer :

10. Veuillez fournir toute remarque supplémentaire sur les pratiques d'évaluation d'éthique continues de votre CER ici :

Merci ! Karleen Norton Address Deleted
Si vous désirez recevoir une copie des résultats par la poste, veuillez fournir votre nom et adresse postale.
Nom:
Adresse:
Ville:
Province:
Code Postal :

Appendix B

24 June 2006

Dear Research Ethics Board Chairperson:

My name is Karleen Norton and I am a Master's in Nursing student at the University of Alberta. I am inviting you to participate in my thesis project "The Status of Continuing Ethics Review and Continuing Ethics Review Practices by Canadian Research Ethics Boards." In the past 10 years there has been an increasing focus on the continuing ethics review of approved research. This study intends to look at current continuing ethics review practices by Research Ethics Boards (REBs) across Canada.

All 187 REBs across Canada are asked to participate in this study. Participation is completely confidential and there is no risk to you or your REB for participating in this study. Your name and your REB's name will not be published. All study documentation, including completed questionnaires, will be kept in a secure and confidential manner for seven years. The master code will be destroyed upon the analysis of the data so that individual questionnaires cannot be traced back to you or your REB. The benefit of your participation may be the contribution to assessing and raising awareness of REBs current continuing ethics review policies and practices.

If you choose to participate in this study, please complete the questionnaire within the next 3 weeks and return it in the envelope provided. This questionnaire will take approximately 20 minutes of your time.

Participation is completely voluntary. Your consent to participate in this study is implied with the return of the completed questionnaire. This study has been approved by the University of Alberta REB (Panel B). If you have any issues or concerns regarding this study you may contact my supervisor, Dr. Donna Wilson at (780) 492-5574. If you have any ethical concerns or issues you may contact the University of Alberta Health Research Ethics Board at (780) 492-0302. If you have any questions regarding the study you may contact me at (780) 463-6535.

If you would like a copy of the study results mailed to you, please indicate this wish in the space provided on the detachable sheet, last page of the questionnaire, and provide your name and mailing address. There is no charge for this report.

Thank you for considering this request.

Sincerely,
Karleen Norton, RN, BScN, MN (student)
Address deleted

Le 24 Juin 2006

M./Mme. Président/Présidente de Conseil D'Éthique de Recherche

Je me m'appelle Karleen Norton et je complète présentement une maîtrise à l'Université d'Alberta. Je vous invite à participer à mon projet de thèse intitulé:

«Le statut et pratiques d'évaluation d'éthique continue par les conseils d'éthique de recherche ».

Au cours des 10 dernières années il y a eu une emphase accrue sur le contrôle continuel d'éthique des projets de recherche approuvés. Cette étude entend examiner les pratiques courantes d'évaluation continues d'éthique par les Conseils d'Éthique de Recherche (CER) à travers le Canada.

Chacun des 187 CER à travers le Canada sera sollicité pour participer à l'étude. La participation à cette étude est confidentielle et ne comporte aucun risque à vous ou votre conseil. Votre nom et celui de votre CER ne sera pas publié. Toute documentation reliée à l'étude, incluant les questionnaires complétés, sera conservé de façon sécurisé et confidentielle pour une période de sept (7) ans. Le code principal sera détruit suite à l'analyse des données afin que les questionnaires individuels ne soient jamais retracés à vous ou votre CER. Votre participation contribuera peut-être à mieux évaluer les pratiques courantes et conscientiser le public au sujet des politiques d'évaluation d 'éthique des CER.

Si vous choisissez de participer à cette étude, veuillez compléter le questionnaire dans un délai de trois semaines et le retourner dans l'enveloppe fournie. Ce questionnaire prendra 20 minutes à remplir.

La participation est complètement volontaire. Le retour d'un questionnaire rempli implique que vous consentez à participer à cette étude. L'étude à été approuvée par le REB de l'Université d'Alberta (comité B). Si vous avez des questions ou des préoccupations relatives à cette étude,vous pouvez contacter ma superviseure, Dr, Donna Wilson au (780) 492-5574. Si vous avez des préoccupations ou questions de nature éthique, vous pouvez contacter le Conseil d'Éthique de Recherche en Santé de l 'Université d'Alberta au (780) 492-0302. Si vous avez des questions sur l'étude vous pouvez me contacter directement au (780) 463-6535.

Si vous voulez recevoir une copie des résultats de l'étude par la poste, veuillez s.v.p l'indiquer dans l'espace approprié sur la feuille détachable, dernière page du questionnaire en plus de fournir votre nom et adresse postale. Il n'y a pas de frais associés à ce rapport.

Je vous remercie de considérer ma demande.

Sincèrement,

Karleen Norton, RN, BScN, MN (étudiante)
Address deleted

Appendix C

Reminder Notice Post Card

The Status of Continuing Ethics Review and Continuing Ethics Review Practices by Canadian Research Ethics Boards

Hello. It has been 3 weeks since a questionnaire for the above titled thesis project was mailed to you.

I have enclosed another copy of the questionnaire, along with the invitation letter originally mailed to you. If you wish to participate in this study, please complete the questionnaire as soon as possible and mail it in the envelope provided. Please note this is the first and only reminder notice you will receive.

If you would like a copy of the study results mailed to you, please indicate this wish in the space provided on the detachable sheet, last page of the questionnaire, and provide your name and mailing address.

Thank-you for your time and contribution to this thesis project.

Sincerely,

Karleen Norton, RN, BScN, MN (student)
Address deleted

Carte Postale de Rappel

« Le statut et pratiques d'évaluation d'éthique continue par les conseils d'éthique de recherche »

Bonjour;

Il y a trois semaines vous avez reçu par la poste un questionnaire pour la projet de thèse mentionné ci-haut.

Vous trouverez ci-joint une autre copie du questionnaire, ainsi qu'une copie de la lettre explicative qui vous a été envoyé initialement. Si vous désirez encore participer à cette étude, veuillez compléter le questionnaire le plus tôt possible et le retourner dans l'enveloppe fournie. Veuillez noter que ce rappel sera le premier et le dernier que vous recevrez.

Si vous voulez recevoir une copie des résultats de l'étude par la poste, veuillez s.v.p l'indiquer dans l'espace approprié sur la feuille détachable, dernière page du questionnaire en plus de fournir votre nom et adresse postale.

Merci à l'avance de prendre le temps de contribuer à ce projet de thèse.

Sincèrement,

Karleen Norton, RN, BScN, MN (étudiante)
Address deleted

Table 1. REB Conducts Continuing Ethics Review

Response	N	Response (%)
Yes	90	87.4
No	12	11.7
Not Sure	1	1.0
Total	103	100

Table 2. Methods of Continuing Ethics Review

Method of Continuing Ethics Review	N	Response (%)
Review of On-going Research Reports	76	84.4
Review of AEs and Incidents	73	81.1
Review of End-of-Study Research Reports	68	75.6
Review Informed Consent & Informed Consent Process	45	50.0
Review of Study Documents	42	46.7
Data-Safety-Monitoring Board Activities	14	15.6
Other	6	6.7

Table 3. Number of Continuing Ethic Review Methods per REB

Response	N	Response (%)
1	11	12.2
2	13	14.4
3	18	20.0
4	17	18.9
5	23	25.6
6	8	8.9
7	0	0.0
Total	90	100.0

Table 4. REB Conducts Continuing Ethics Review to Detect Issues in Scientific Integrity

Response	N	Response (%)
Yes	22	21.4
No	78	75.7
Not Sure	3	2.9
Total	103	100.0

Table 5. Continuing Ethics Review Methods for Detecting Issues in Scientific Integrity

Method of Continuing Ethics Review	N	Response (%)
Review of Study Data	11	50.0
Other	9	40.9
Review of Data Analysis	7	31.8
Review of Published Literature	7	31.8

Table 6. Number of Continuing Ethic Review Methods to Detect Issues in Scientific Integrity per REB

Response	N	Response (%)
0	1	4.5
1	13	59.1
2	5	22.7
3	1	4.5
4	2	9.1
Total	22	100.0

Table 7. Continuing Ethics Review by Type of Research

	Conducts Continuing Ethics Review						Total
	Yes	% Responses	No	% Responses	Not Sure	% Responses	
Academic Research	24	72.7	8	24.2	1	3.0	33
Clinical Trials only	5	100.0	0	0.0	0	0.0	5
Both Academic and Clinical Trial	61	93.8	4	6.2	0	0.0	65
Total	90		12		1		103
X^2=0.039, df=4, α = 0.05							

Table 8. Continuing Ethics Review by Type of REB

	Conducts Continuing Ethics Review						Total
	Yes	%	No	%	Not Sure	%	
Academic/University	49	81.7	10	16.7	1	1.7	60
Hospital-Based	36	100.0	0	0.0	0	0.0	36
Independent	5	71.4	2	28.6	0	0.0	7
Total	90		12		1		103
X^2=0.061, *df = 4, α = 0.05							

Table 9. Profit Status and Policy Practice Characteristics of REBs

Demographic	N (Yes)	(%)	N (No)	(%)	N (Other)	(%)	Total
Profit Status	98	95.1	3	2.9	2 (Missing)	1.9	103
Continuing Ethics Review Policy	89	86.4	13	12.6	1(Not Sure)	1.0	103
Plans to Develop Continuing Ethics Review Policy	5	38.5	4	30.8	4 (Missing)	30.8	103

Table 10. Consequences of Non-Compliance

Protocol Non-Compliance Consequence Themes	N	Response (%)
REB approval is withdrawn	31	34.1
Study is halted	24	26.4
Report researcher and non-compliance issues to appropriate authorities	21	23.1
Notify researcher of issues	16	17.6
Funding is withheld	14	15.4
Study halted – until issue is corrected	13	14.3
Disciplinary action and/or academic consequences for the researcher	11	12.1
Researcher is requested to explain the situation	10	11.0
Non-compliance issues have not arisen or been detected	8	8.8
Request for re-approval to changed proposal is sent to the researcher	6	6.6
Study halted – until a review is conducted	5	5.5
Support and guide researcher in addressing the issues	5	5.5
Re-educate researcher	4	4.4
Level of corrective action is proportionate to the seriousness of deficiencies	4	4.4
Request researcher to revise research documents	3	3.3
No action is taken	2	2.2

Table 11. Consequences of Detected Issues in Scientific Integrity

Consequences	N	Response (%)
Study halted	7	25.0
Report researcher and scientific integrity issues to appropriate authorities	7	25.0
Academic consequences for the researcher	6	21.4
Communicate with researcher regarding the issue	6	21.4
Refusal of REB approval of initial proposal	3	10.7
Detecting issues in scientific integrity is not an REB's role	3	10.7
Disciplinary action	3	10.7
Funding is withheld	2	7.1
Issues have not arisen or been detected	1	3.6

Table 12. Continuing Ethics Review Practice Adequacy for Safe and Ethical Research

	Yes	(%)	No	(%)	Not Sure	(%)	Blank	(%)	Total
Subject Safety	70	68.0	13	12.6	17	16.5	3	2.9	103
Ethical Conduct	72	69.9	14	13.6	15	14.6	2	1.9	103

***Response %**

Table 13. Explanations of Continuing Ethics Review Practice Adequacy for Conduct of Safe Research

Categories	N	Response (%)
Most research is minimal/low risk to subject safety	14	34.1
Need to begin, improve on, or just started a formal continuing ethics review program	10	24.4
In-dept continuing ethics review is limited by lack of personnel and resources	9	22.0
Trust researcher is ensuring subject safety during the study/ensuring subject rests with the researcher during the study	6	14.6
Concerns regarding safety rests with the subject to report and/or there has been no complaints from research subject	5	12.2
Continuing ethics review of AEs and other CER practices are conducted	4	9.8
In some cases, more in-depth continuing ethics review is/should be conducted	2	4.9
Continuing ethics review needs to be combined with education programs in research	2	4.9
REB does not view continuing ethics review (policing) as a REB role, rather as an institutions role	1	2.4
Small REB, with small number of on-going studies allowing for adequate continuing ethics review	1	2.4

Table 14. Explanations of Continuing Ethics Review Practice Adequacy for Ethical Research

Categories	N	Response (%)
Need to begin, improve on, or just started a formal continuing ethics review program	15	38.5
In-depth continuing ethics review is limited by lack of personnel and resources	11	28.2
Trust researcher is conducting ethical research during the study or responsibility of conducting ethics research rests with the researcher	7	17.9
Mechanisms are in place to conduct continuing ethics review (including annual reports, informed consents and other study documentation	6	15.4
Most research is minimal or low risk to subject safety	5	12.8
Review of research is important but "policing" of research is not an REB's role	3	7.7
In some cases, more in-depth continuing ethics review is/should be conducted	2	5.1
Continuing ethics review needs to be combined with education programs in research	1	2.6
Support and guide researchers to resolve ethical dilemmas	1	2.6
REB at time of initial review of proposal reviews for ethical, scientific integrity and safety issues	1	2.6