

Launching the Newfoundland and Labrador Health Research Ethics Authority Act and Reflections on its Current Status

Penny Moody-Corbett et Sharon Buehler

Volume 5, numéro 1, 2022

URI : <https://id.erudit.org/iderudit/1087200ar>

DOI : <https://doi.org/10.7202/1087200ar>

[Aller au sommaire du numéro](#)

Éditeur(s)

Programmes de bioéthique, École de santé publique de l'Université de Montréal

ISSN

2561-4665 (numérique)

[Découvrir la revue](#)

Citer cet article

Moody-Corbett, P. & Buehler, S. (2022). Launching the Newfoundland and Labrador Health Research Ethics Authority Act and Reflections on its Current Status. *Canadian Journal of Bioethics / Revue canadienne de bioéthique*, 5(1), 16–32. <https://doi.org/10.7202/1087200ar>

Résumé de l'article

La Loi *Health Research Ethics Authority (HREA)* a été créée pour garantir que l'évaluation éthique de toutes les recherches sur la santé humaine dans la province de Terre-Neuve-et-Labrador est effectuée par un comité d'éthique de la recherche (CER) local, dans la province. La Loi HREA a été adoptée à la suite de plaintes déposées par des patients et des membres de leur famille participant à une étude de recherche clinique en génétique menée par une équipe de chercheurs de l'extérieur de la province qui n'ont pas assuré un suivi clinique approprié. Cet examen fournit un compte rendu des étapes de la rédaction de la loi et de la préparation de sa promulgation et comprend des informations sur les principaux intervenants impliqués dans le processus. Elle fournit également un bref commentaire sur la HREA et le nouveau Comité d'éthique de la recherche en santé, dans les années qui ont suivi la proclamation, et sur la façon dont la HREA s'aligne sur les intérêts nationaux d'harmonisation de l'évaluation éthique de la recherche dans plusieurs CER. Au départ, le processus a été envisagé comme un simple passage à un comité d'éthique de la recherche légiféré par la province ; cependant, la tâche réelle a consisté à établir une nouvelle entité pour superviser l'évaluation éthique de la recherche et à élargir ou améliorer le bureau nécessaire pour gérer cette supervision de l'évaluation éthique de la recherche. La tâche des comités de travail chargés d'établir la législation s'est avérée plus complexe que ne l'avaient envisagé les organisations partenaires, le gouvernement de Terre-Neuve-et-Labrador, l'Université Memorial de Terre-Neuve et l'Eastern Health Authority, et la charge de travail et le temps nécessaires pour établir et proclamer la législation ont été plus importants que prévu.



ARTICLE (ÉVALUÉ PAR LES PAIRS / PEER-REVIEWED)

Launching the Newfoundland and Labrador Health Research Ethics Authority Act and Reflections on its Current Status

Penny Moody-Corbett^a, Sharon Buehler^b

Résumé

La Loi *Health Research Ethics Authority (HREA)* a été créée pour garantir que l'évaluation éthique de toutes les recherches sur la santé humaine dans la province de Terre-Neuve-et-Labrador est effectuée par un comité d'éthique de la recherche (CER) local, dans la province. La Loi HREA a été adoptée à la suite de plaintes déposées par des patients et des membres de leur famille participant à une étude de recherche clinique en génétique menée par une équipe de chercheurs de l'extérieur de la province qui n'ont pas assuré un suivi clinique approprié. Cet examen fournit un compte rendu des étapes de la rédaction de la loi et de la préparation de sa promulgation et comprend des informations sur les principaux intervenants impliqués dans le processus. Elle fournit également un bref commentaire sur la HREA et le nouveau Comité d'éthique de la recherche en santé, dans les années qui ont suivi la proclamation, et sur la façon dont la HREA s'aligne sur les intérêts nationaux d'harmonisation de l'évaluation éthique de la recherche dans plusieurs CER. Au départ, le processus a été envisagé comme un simple passage à un comité d'éthique de la recherche légiféré par la province ; cependant, la tâche réelle a consisté à établir une nouvelle entité pour superviser l'évaluation éthique de la recherche et à élargir ou améliorer le bureau nécessaire pour gérer cette supervision de l'évaluation éthique de la recherche. La tâche des comités de travail chargés d'établir la législation s'est avérée plus complexe que ne l'avaient envisagé les organisations partenaires, le gouvernement de Terre-Neuve-et-Labrador, l'Université Memorial de Terre-Neuve et l'Eastern Health Authority, et la charge de travail et le temps nécessaires pour établir et proclamer la législation ont été plus importants que prévu.

Mots-clés

intégrité, responsabilité, législation provinciale, Comité d'éthique de la recherche, Autorité d'éthique de la recherche en santé

Abstract

The *Health Research Ethics Authority (HREA) Act* was established to ensure that research ethics review of all human health research in the province of Newfoundland and Labrador is conducted by a local, in-province, Research Ethics Board (REB). The HREA Act arose as a result of complaints by patients and family members enrolled in a clinical genetics research study being conducted by a team of researchers from outside the province who failed to provide appropriate clinical follow-up. This review provides a record of the steps taken to draft the legislation and prepare for proclamation and includes information on the key stakeholders involved in the process. The review also provides a brief commentary on the HREA, and the newly formed Health Research Ethics Board, in the years following proclamation and how the HREA aligns with national interests for harmonizing research ethics review across multiple REBs. At the outset, the process was envisioned as simply moving to a provincially legislated research ethics board; however, the actual task involved establishing a new entity to oversee research ethics review and expanding or enhancing the office required to manage this research ethics review oversight. The task for the working committees involved in establishing the legislation was more complex than envisioned by the partner organizations, the government of Newfoundland and Labrador, Memorial University of Newfoundland and the Eastern Health Authority, and the workload and time to establish and proclaim the legislation was more involved than anticipated.

Keywords

integrity, accountability, provincial legislation, Research Ethics Board, Health Research Ethics Authority

Affiliations

^a Northern Ontario School of Medicine, Thunder Bay, Ontario, Canada

^b Division of Community Health and Humanities, Faculty of Medicine, Memorial University of Newfoundland, St. John's, Newfoundland, Canada

Correspondance / Correspondence: Penny Moody-Corbett, pmoodycorbett@nosm.ca

INTRODUCTION

The province of Newfoundland and Labrador (NL), Canada, is considered a valuable source of genetic information as a consequence of limited European settlement and migration over the past 200 years (1). This has led to considerable genetic research on the population by researchers within the province and from elsewhere. While this has resulted in numerous positive outcomes for the people of NL, there have also been a number of instances in which researchers have arrived in the province, engaged in research and not appropriately followed up with participants. As a result of a particularly egregious case in the 1990s involving clinical and genetics researchers from out-of-province and a lack of clinical follow-up, the NL government began a process to review genetics research policies in the province and set the stage to establish provincial legislation to oversee the research ethics review of all human health research to be conducted in the province.

In Canada the *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans*, commonly referred to as TCPS (2)¹, established by the three major federal granting councils – the Canadian Institutes of Health Research (CIHR),

¹ There are three versions of TCPS cited in this document. The first is the original 1998 version (2). While working on the legislation and proclamation a second version became available with updates, TCPS2 (3). The current version of TCPS is TCPS2 2018 (20).

Natural Sciences and Engineering Research Council (NSERC) and the Social Sciences and Humanities Research Council (SSHRC) – sets the guidelines for conducting human health research based on the three hallmarks of research ethics: a) respect for persons, b) concern for welfare and c) justice. The ethics review process serves as a mechanism of checks and balances to ensure that research participants are not exposed to undue harm and that the research is conducted ethically. For clinical research, there is an added ethical consideration with regards to the dual role that clinician-researchers play; that is, duty to care and their interests in pursuing health research (2), and with respect to genetics research, there is a further consideration of how newly discovered genetic information will be managed and shared with participants and, where applicable, family members (3).

The work to develop legislation for local research ethics review in NL owes a great deal to participants who had been enrolled in a clinically-based genetics research study, and their families. They initially complained to the provincial and academic authorities about inappropriate research practices in a study in which they or their family members were asked to participate. Over the course of 11 years a small group with affiliations to government, Memorial University, the Eastern Health Authority, the pharmaceutical industry and the private sector worked together to help draft legislation and support its implementation.

THE HEALTH RESEARCH ETHICS AUTHORITY (HREA) ACT

On July 1, 2011, NL became the first province in Canada to require that all human health research (publicly and privately-sponsored) to be conducted in the province be reviewed by a local (within the province) Research Ethics Board (REB) approved by the legislated oversight body, the Health Research Ethics Authority (HREA) (4). The HREA Act (4), which received assent 12 December 2006 and came into force on 1 July 2011, proclaims that the HREA (the Authority) is to ensure human health research in NL is conducted in an ethical manner and to enhance public awareness of the ethical dimensions of research. The Authority is responsible to the Minister of Health and Community Services. The legislation includes the timeframe of research ethics review and imposes penalties for individuals who do not comply with the Act. Since the legislation was passed, there have been two changes: a regulation was added to specify that, despite any other REBs approved under the authority, all clinical trials and genetics research be reviewed by the Health Research Ethics Board (HREB) established under the Authority; and in 2011, Section 2.1 (4) was added, recognizing the relationship with the Labrador Inuit Land Claims Agreement Act (5).

The purpose of this article is to describe the path from public response to unethical research practices to legislated ethics review, implementation of the Act and its aftermath. The authors participated in this endeavour from its inception in 1999 to implementation of the Act in 2011. At the time of inception, PMC served as the Chair and SB a member of the two main committees, described below (the Provincial Health Research Ethics Board Working Group and the Transition Team) involved in helping to draft the legislation and in the implementation of the Act. PMC, as the Associate Dean, Research and Graduate Studies in Memorial University's Faculty of Medicine, the office responsible for the management of Memorial's Human Investigation Committee (HIC, the REB that reviewed the majority of health research in the province), had experience with the operational issues of the research ethics review process. SB was the co-chair of the HIC and provided considerable expertise in the running of a research ethics review committee, and ethical issues relevant to both clinical and qualitative human health research. Both PMC and SB had served for many years as members of the HIC and participated in national organizations concerned with research ethics review. This report is a subjective account – based on minutes and meeting notes, presentations, email exchanges and personal notes – to describe the sequence of events leading to implementation of the HREA Act. As there was no precedent for provincially legislated ethics review in Canada, the transition to legislation required consideration of a new approach to how to seek ethics approval. A list of the milestones leading up to the legislation is provided in Table 1.

Table 1. Milestones in the development of the HREA Act

Event	Date	Outcome
Formal stakeholders committee – Provincial Advisory Committee on Human Health Research	Jan 2000	Two committees were established: <ul style="list-style-type: none"> • Provincial Health Research Ethics Board (PHREB) Working Group • Genetics Standards Development Working Group
Skanes' White Paper presented to House of Assembly	May 2000	Discussion began on legislation for oversight of research ethics review for the province
National Council on Ethics in Human Research (NCEHR) Site Visit	1 Mar 2001	Review of the procedures and operations of the Human Investigations Committee (HIC)
Experts Panel	Jul 2001	Review of genetics research and the proposed legislation
1 st MOU signed by Minister of Health and the President of Memorial University	Apr 2002	Established the basis on which discussions would continue for province-wide research ethics review
Meeting with government Social Policy Committee	May 2003	Government gave support to proceed
Health Research Ethics Authority Act	12 Dec 2006	Assent

SETTING THE STAGE FOR LEGISLATION

In the 1990s a group of residents of central Newfoundland, who were participants in a genetics study conducted by an out-of-province American research team (from Baylor University, in Texas), complained to the provincial clinical genetics team and the local research community about lack of follow-up and clinical care associated with the research. At the time, researchers

affiliated with institutions from outside the province (out-of-province) interested in conducting research in NL were expected to have research ethics review from their home institutions; however, there was no requirement for contact with appropriate health care providers or local researchers within the province. These researchers would not necessarily have been known to the health professionals or researchers in the province. Following complaints from the research participants and family members, an investigation by both the out-of-province research team's university Institutional Review Board (IRB) and the U.S. Office of Health Research Protections of the National Institutes of Health, led the IRB to withdraw approval of the study and to suspend the research privileges of the three researchers associated with the study for a three-year period. This widely publicized situation (6-9) highlighted the vulnerability of participants in research studies where the researchers involved were not responsible to a local authority. As a result, the provincial Department of Health and Community Services (DHCS) commissioned Dr. Verna Skanes, a retired senior administrator of the Faculty of Medicine, Memorial University, to review how human genetics research was conducted in the province, in particular, with respect to patient participation, participant safety, research ethics review and commercialization of results. Dr. Skanes' White Paper concluded that the province needed "a clearly articulated policy, covering both academic and private studies, for research ethics review of all human research projects" and that the province should: "establish as soon as possible a provincial research ethics board" (10).

At the time, human health research conducted by researchers in NL received ethics review from several different REBs. Researchers affiliated with Memorial University of Newfoundland (the sole university in the province) or one of the regional health authorities were required to submit to a local (in-province) REB, following guidelines set by the TCPS (2), and Health Canada Guidelines for clinical trials. Several boards existed for this purpose throughout the province. The largest of these was the Human Investigations Committee (HIC), which served the largest group of health researchers from Memorial and the Health Care Corporation of St. John's (forerunner to the Eastern Health Authority). This was the largest teaching and tertiary care hospital system in the province. Clinical researchers in private clinics often acquired research ethics review through out-of-province, for-profit REBs. Researchers from out-of-province, who were interested in conducting research in NL, received ethics approval from their home institution. As described above, there was no requirement for these out-of-province researchers to contact appropriate health care providers, local researchers or REBs within the province.

In response to the Skanes' report, and following a meeting of provincial stakeholders (representatives from the regional health authorities, health boards, private and academic researchers, provincial government, and Memorial University), in May 2000 the Department of Health and Community Services (DHCS) established two working groups: the Provincial Health Research Ethics Board (PHREB) Working Group and the Genetics Standards Development Working Group². The PHREB Working Group was tasked with making recommendations on legislation for research ethics review of human health research conducted in the province. Topics identified and discussed by the PHREB Working Group became significant components of the HREA Act. Members of the Working Group had extensive experience in conducting research, REB review and administration, and included: the co-chairs of the Human Investigations Committee (HIC); the Associate Dean of Research and Graduate Studies, Faculty of Medicine, Memorial University; the Manager of the Patient Research Centre, Eastern Health; and representation from the Western Regional Health Authority, the DHCS, the NL Health Boards Association, private clinical practice, and the social sciences. With the assent of the legislation in December 2006, the Working Group was discontinued but its members, along with other members from relevant stakeholder communities, became the Transition Team responsible for the implementation of the legislation.

Background to drafting the HREA Act

At the time that the PHREB Working Group was created, the extent of the task ahead was not fully appreciated. The Skanes' report (10) provided a framework to begin consideration of a province-wide human health REB but the practical challenges (for example, the governance oversight of the REB, including financial and human resources) of how this would be accomplished needed to be addressed. Over the six years that the Working Group met, they engaged with members of the government, the university, the regional health authorities and existing REBs, and they invited input from recognized experts in the area of ethics review from outside the province. These meetings were important to understand the unique concerns of various jurisdictions, such as concerns related to the over-study of populations, and financial and human resource issues.

In working with government, it was clear that basic terminology sometimes created a challenge. For example, in Canada, the committees that provide ethics review of research are called Research Ethics Boards (REBs). However, the use of the term "board" does not imply that the REB is a business or corporate board reviewing and approving the operational activities or the strategic direction of an organization. Once this difference in the meaning of the term "board" was understood it became necessary to define a structure to oversee the management, human resources and financial operations, tasks which had been done by the University, for a province-wide REB. The task of the PHREB Working Group to "establish as soon as possible a provincial research ethics board" (10) was thus more complicated than originally anticipated and resulted in legislation that recognized the necessity of an overarching organizational entity, the HREA. The challenges of the Working Group centred around six topics.

Stand-alone versus amendment to existing legislation

Although Skanes had recommended legislation, it was not clear if this was best accomplished through existing legislation – such as the University Act (11), for example, which regulated the HIC, or the Health and Community Services Act (12) which

² The Genetics Standards Development Working Group, tasked with clarifying the policy implications of commercial genetic research, provided a final report to the DHCS (Jan 2003): *Policy Implications of Commercial Human Genetic Research in Newfoundland and Labrador*.

addressed the protection of the health of the public – or if new stand-alone legislation was required. The Working Group reviewed these options and following meetings with government and Memorial University’s legal counsel, it was determined that to satisfy the basic principles required for oversight of health research ethics review across the province, the most appropriate path was stand-alone legislation focused specifically on local (within the province) health research ethics review. Moreover, such legislation would need to apply to both institutional (all academic areas, including clinical) and community-based researchers. Stand-alone legislation would also provide a mechanism for an inventory of all human health research being conducted in the province. The proposal for stand-alone legislation for human health research ethics review was presented to and approved by the government’s Social Policy Committee (the committee responsible for reviewing Cabinet submissions on social policy, including health and community services) in May 2003, three years after we had begun the task.

Recommendation for the Health Research Ethics Authority (HREA)

At the time that the legislation was being developed, the existing REBs in the province were managed either through the hospitals or, in the case of the HIC, Eastern Health and the university shared management through an office of Memorial University. Once it was understood that the new provincial REB would not oversee human and budgetary resources, the PHREB Working Group proposed the establishment of the HREA (the Authority), with responsibility for oversight of the office responsible for the new HREB; educating current and potential researchers in research ethics and public awareness of ethics review of health research in the province (Section 5(2) of the HREA Act); providing government an annual report of all health research being conducted in the province (Section 22 of the HREA Act); and approving any other research ethics bodies that met the standard for research ethics review (Section 8 of the HREA Act). The recommendation was that the HREA be a small board with members from the three major stakeholders – DHCS, Eastern Health and Memorial University – and a representative at-large from the community; the Chair of the HREB would sit as an *ex officio* member of HREA (Section 3 of the HREA Act) (4).

Existing Research Ethics Boards

A major issue for the PHREB Working Group was to determine how the REBs that were currently in place should be considered with respect to the legislation. For example, should the REBs of Memorial University or of the regional health authorities continue to exist with the new legislation applying only to studies conducted by out-of-province researchers? Key to this discussion was what to do with HIC, the REB which reviewed the largest number of health research studies in the province. The HIC, established in 1969, was known to the health research community and was the REB used by the major health research institutions of the province (Memorial University and Eastern Health).

The outcome of meetings with members of the three University REBs – the HIC, the Interdisciplinary Committee on Ethics in Human Research (ICEHR), and the ethics board of Grenfell College – and the hospital ethics committees of the regional health authorities was that the legislation should apply to all health research in the province (Section 9 of the HREA Act) and that all of the currently existing boards would adhere to the new legislation. A regulation subsequent to the legislation required that the provincial Health Research Ethics Board (HREB, Section 7 of the HREA Act) would review all clinical trials and genetics research. Other REBs (which are referred to as research ethics bodies in the Act, Section 8 of the HREA Act) that met national standards for research ethics review – at the time of proclamation, the TCPS2 (3) – and were not-for-profit, would be eligible to be approved under the new legislation but they would not be eligible to review clinical trials or genetics studies. By the time the legislation was enacted, the REBs affiliated with Grenfell College and three of the regional health authorities (Central, Western and Labrador-Grenfell) had all declined to be approved under the Act. The Grenfell College REB would continue to review non-health research; the three regional health authorities would continue to review research for resource-appropriateness to their institution, but no longer include research ethics review.

The Working Group determined that under the new system, researchers would be required to notify the HREA of their submission for ethics review and to name the REB (that is, HREB, ICEHR or another approved research ethics body) to which the protocol was submitted. In transitioning to the new system, it was also recognized that it would be essential to establish a “board of record” process for research that had been initially approved by a REB that ceased to exist.

Ethics review of health research in the social sciences and humanities

Considerations of the broad spectrum of research to be included under the rubric of “health” helped formulate the legislation. These discussions also confirmed the need to include, in the guiding “principles” of the PHREB Working Group and, subsequently in the legislation, a broad definition of health research that included the social determinants of health. It was this definition that was written into the HREA Act (4). A particular concern was raised with respect to health-related social sciences and humanities research. The first iteration of the TCPS (2) was based on the Medical Research Council’s “*Guidelines on Research Involving Humans*” and “*Guidelines for Research on Somatic Cell Gene Therapy in Humans*” and replaced the SSHRC document “*Ethics Guidelines for Research with Human Subjects*”. Social sciences and humanities researchers, particularly those using qualitative methods, were concerned that new legislation would further impose a medical model of research ethics review. In order to appropriately consider these issues, the membership of the Working Group and Transition Team always included one or more social scientist researchers.

Timing of research ethics reviews

The length of the review process was a significant issue for the PHREB Working Group and Transition Team. Time to approval was frequently criticized by researchers despite data indicating that delays were often due to delayed responses from the

researchers to REB queries (personal communication, Chairs of HIC). Community physicians were particularly apprehensive and repeatedly noted that delays in approval for clinical trials could mean losing the opportunity to participate in national and international studies. This issue was of sufficient concern to prompt several community physicians to meet with the Minister of Health. The Working Group met with clinicians within the greater St. John's area individually and in group dinner-meetings to discuss the timing of the review process, and how to improve efficiency and to encourage the involvement of private physicians as members of the HREB. As a result, the legislation specifically incorporated clauses to require a timely ethics review of all health research (Sections 9(3) and 9(4) of HREA Act).

Financial and human resources

Early on in its deliberations, the PHREB Working Group established a basic budget and work-plan for the operation of a provincial REB. The initial estimates of expenses for province-wide research ethics review modeled the operation of the HIC. At that time (1999-2000) the cost of running the HIC was borne by the two partner institutions, the Faculty of Medicine of Memorial University and the Health Care Corporation of St. John's (forerunner of the Eastern Health Authority). Expenses included hosting bi-weekly REB meetings, a single secretarial position, an honorarium for the chair of the HIC, a small travel budget to attend national meetings, funding for distribution of the review packages and office expenses for communicating with members of the HIC review board, particularly those outside the hospital and university. Expenses such as office and meeting space, insurance, phone and internet, were in-kind contributions provided primarily through the Faculty of Medicine. The earliest budgets, submitted to the DHCS, reflected the need for a senior level person, an Ethics Officer, to manage the office and additional secretarial support, and that expenses would also be required to fund monitoring, additional office space and start-up costs including upgrades to computer facilities. Budgetary information also included revenue derived from fees for review of industry-sponsored clinical trials. In May 2003 the government's Social Policy Committee, in a meeting with the Working Group, continued to acknowledge their commitment to the province-wide research ethics review. It was recognized that the DHCS, Memorial University and Eastern Health would be the primary parties involved in offsetting expenses for the HREA. However, from the outset it was acknowledged that the new HREA would be a unique entity not directly administered by any one of the participating organizations. Where possible, efficiencies would be achieved to reduce overall expenses, including in-kind contributions that would allow for savings in such areas as space and IT support. As with most organizations, budgetary considerations and human resources continued to be major points of discussion for the Transition Team, and as expected, remain as complex issues for the HREA.

Memorandum of Understanding

During the course of discussions by the PHREB Working Group, Memorial University and the DHCS signed a Memorandum of Understanding (MOU) to acknowledge their on-going commitment to province-wide research ethics review and to establish the basis on which the discussions would continue. Included in the MOU was a commitment by both organizations to protect and safeguard research participants by ensuring a comprehensive ethics review of all human health research, to promote the education of health researchers and the community and to provide recommendations on health research ethics policy. The MOU acknowledged financial support from Memorial University in partnership with the Health Care Corporation of St. John's (forerunner of the Eastern Health Authority) and the role of DHCS to provide funds to cover any additional costs associated with the operation. The MOU was signed by the Minister of Health and the President of the University in April 2002 and was used as a basis for further discussions leading up to the proclamation of the legislation.

External consultations and information sessions

As noted previously, leading up to the legislation being passed, consultations were held with research ethics experts from outside the province. These included consultations that were purposely requested to obtain feedback from national experts in the field, including an Experts Panel³ and members of the Federal Panel on Research Ethics (PRE), which was responsible for the TCPS; consultations that took advantage of other meetings being held in the province, (e.g., National Council on Ethics in Human Research (NCEHR) site visit in 2001); and informal interactions with ethics scholars at meetings in other parts of the country, in particular, the annual meetings of the newly formed Canadian Association of Research Ethics Boards (CAREB). The consultations were useful in confirming the value of establishing a provincial REB. They were especially helpful in focusing attention on aspects of the legislation that would need to be considered if the provincial REB was to provide timely review: addressing issues around publicly and privately funded research, triaging clinical versus social science and humanities health research, and addressing the need for monitoring approved studies and their review process. These early consultations often focused on the issues related to the REB and less on the management of the research ethics office.

Members of the PHREB Working Group had several meetings to consult with the research community and research ethics or resource committees across the province to consider the legislation and how it would change the way in which research ethics would be reviewed and by whom. These sessions were meant to provide information to the community on the development of the new law as well as to gain feedback to be considered in the final legislation and how it would be administered across the breadth of the province. Not least important was softening the loss of autonomy of the smaller REBs being subsumed under the HREA. These sessions continued through the transition period and consisted of face-to-face meetings as well as teleconferences and phone conversations with departments, REBs, individual researchers and clinicians.

³ The Experts Panel consisted of three internationally recognized experts in the field: Timothy Caulfield (Research Director of the Health Law Institute, University of Alberta), Michael McDonald (Maurice Young Chair in Applied Ethics and Director of W. Maurice Young Centre, University of British Columbia) and Douglas Kinsella (Professor of Medicine (Rheumatology), Director of Medical Bioethics and Assistant Dean of Research and Bioethics, University of Calgary).

TRANSITION TO THE HREA

Following assent of the HREA Act in December 2006, the PHREB Working Group was discontinued and the Transition Team⁴ appointed. Several members of the Working Group continued as part of this Team, including the past and current chairs of the HIC, the Associate Dean Research and Graduate Studies (Faculty of Medicine, Memorial University), the Manager of the Patient Research Centre (Eastern Health) and a member from the NL Health Boards Association. In addition, the Transition Team added a representative from the DHCS, an additional member from Eastern Health (Vice President Quality, Patient Safety and Planning), the Chair of the ICEHR, and representatives from private clinical practice and Rx&D (Canada's Research-Based Pharmaceutical Companies). When appointed in 2007, the Ethics Officer for HIC also became a member of the Transition Team. As with the Working Group, the members of the Transition Team had extensive experience with research and research ethics review. Although there were slight changes in the work titles and job positions of members of the committee, over the next five years (2006-2011), only one member – who had retired – resigned from the Transition Team. Three members of the Team had been present from the outset (since 1999) and they continued to provide the historical context in which this legislation was developed. Several members of the Transition Team participated in national organizations and committees that related to the establishment of province-wide research ethics review for NL. One member of the Transition Team sat on Health Canada's REB; three members participated in CIHR committees (to provide recommendations for the National Strategy for Patient-Oriented Research, privacy best practices, and research involving Indigenous Peoples); one had been a board member of the NCEHR; one had been a board member of CAREB; and two members of the Team sat on the Canadian General Standards Board (CGSB) developing standards for REBs overseeing biomedical clinical trials. Four members regularly attended CAREB meetings.

The Transition Team developed Terms of Reference which focused on the four primary activities described in detail below: 1) communication and information sharing, 2) planning for implementation of the HREA Act, 3) implementation of concurrent legislation, i.e., the Personal Health Information (PHI) Act, and 4) developing the policy manual. The Team regularly informed its three partners – DHCS, Eastern Health and Memorial University – of activities and progress, either directly through their representatives on the Team or by formal correspondence from the chair of the Transition Team to the Minister, CEO and President of those organizations. In addition, the Rx&D received feedback through their representative member on the Team.

The development of the policy manual was done by the Policy Advisory Group (PAG), which had evolved from the Policy Advisory Committee of the HIC established in 1996. The PAG included four members of the Transition Team in addition to a representative from the School of Nursing at Memorial University and the community, all with the same breadth of ethics review experience as the Transition Team. The considerable overlap in membership between the two committees ensured that development of recommendations on policies informed discussion for the Transition Team and that, as the policy manual was drafted, it was aligned with the recommendations of the Transition Team. This was particularly important in operationalizing the activities of the HREA office and the HREB and, at proclamation, facilitated a more seamless transition. Initially, the Transition Team and PAG met on alternate weeks but moved to more frequent meetings in the year leading up to proclamation.

Communication and Information Sharing

Informing the local communities

The purpose of the Transition Team's communication strategy was to ensure that there was continuing and consistent messaging to the community, expanding the communications that had begun under the PHREB Working Group in 1999. Several tools were used, including development of a website and newsletters and presentations and messaging notes for specific groups, as well as articles in the *University Gazette* and letters to a variety of stakeholder groups. In addition, the Transition Team met, either face-to-face or by conference call, with groups from across the province to describe the transition to the new province-wide research ethics review process and discuss how the new legislation would affect their work.

In order to assist with consistency the Transition Team used a common slide template, in every presentation, which included the names of the members of the Transition Team and their affiliations; a statement from the Act indicating that all health research in the province would need to be approved by the HREB or an approved research ethics body; membership and role of the Authority; the organizational chart; distinction between the HREB and other research ethics bodies; distinction of research ethics review from resource allocation reviews; and the website and contact information for the HREA Transition Team. As necessary, additional slides were included that provided unique information for a particular audience. For example, in presentations to the clinical community, information was provided on timelines of the review process and review fees for clinical trials. In contrast, presentations to the ICEHR community focused on how existing boards, such as ICEHR, would relate to the HREA and how qualitative research studies would be reviewed. A second measure, which helped with consistency and also gathered feedback from the stakeholder communities, was to have at least two members from the Transition Team present at the information sessions, one to lead discussion and the other to take notes. The issues raised from these sessions were helpful in discussions at the regular meetings of the entire Transition Team.

⁴ The Transition Team included: F Brunger, S Buehler, R Coates, L Felt, B Fisher, J Harnett, J House, M Khraishi, W Miller, P Moody-Corbett, R Neuman and L Purchase.

Sessions were conducted with a number of groups to reach as many researchers, REB members and the public as possible to describe the role of the transition team and the new legislation in relation to their work and research ethics review. Often, sessions were repeated in order to provide updates and progress. This was done, for example, with the physicians and administrators in the three regional health authorities not represented on the Transition Team (Central, Western and Labrador-Grenfell), Indigenous groups, physicians and nurses in the community, and the university community at large. In addition, upon request, sessions were held with specific groups such as the Cancer Care Program, the Health Research and Primary Healthcare Research Units, the Privacy Commissioners Office and the Newfoundland and Labrador Centre for Health Information. The information sessions were well attended and feedback from the participants was useful in aiding the Transition Team to address details necessary for proclamation, e.g., timing of review, storage of data.

Participation in national organizations and committees

Through associations with national organizations and committees, members of the Transition Team were aware of, and participated in, strategies being used in other provinces and nationally to streamline and harmonize the research ethics review process. The connections provided an opportunity to solicit information on best practices and proved useful in directing the Transition Team on common procedures. These interactions were also an opportunity to inform the community outside NL of the changes that would be occurring in research ethics review in the province. In addition, contacts with two national offices, PRE and NCEHR, were particularly important during the transition period. During these five years from assent of the HREA Act to proclamation, PRE was undertaking an update of the TCPS (2). One face-to-face meeting and correspondence with the Executive Director, responsible for the TCPS, was important to ensure conformity of the HREA Act with the 2nd edition (TCPS2 (3)) as well as to provide input to the Executive Director on points of the legislation relevant for consideration in TCPS, such as implied consent and protecting vulnerable participants. The President of NCEHR also provided advice and support for the HREA Transition Team. It was hoped that NCEHR, as an independent body, would provide the required appraisal of the HREB and any other research ethics bodies approved under the HREA Act. However, financial support for NCEHR from the national granting councils was discontinued prior to the proclamation of the HREA Act. Consequently, the Transition Team recommended that this critical assessment be provided by experienced former members of the NCEHR site visit team living outside the province.

Communicating the date of proclamation

A frequent question asked by community members, researchers and others during the many information sessions was the date when the HREA Act would come in to affect. However, throughout the time leading up to implementation of the Act, the government was unclear on the date of proclamation. Initially, the timeline for proclamation had been set for early in 2008; that date was cancelled. The DHCS was unable to commit to a suitable timeline and by 2009 the date of proclamation was indefinite. The HREA Act was eventually proclaimed in 2011, four years after the Transition Team had received their first notification to be ready. This resulted in ongoing information sessions over an extended period of time, with concern raised by both local and national groups on whether the province would be capable of implementing the Act.

Planning for implementation of the HREA Act

As described in this section the Transition Team focused on five major themes that needed to be in place in order to implement the Act.

HREA Board

The Act established the Authority as the oversight body to ensure human health research was conducted in an ethical manner and to enhance public awareness. One of the first roles of the Transition Team was to make recommendations to the Minister, DHCS, the President of Memorial University and the CEO of Eastern Health on the appointment of members to the Authority. The initial members of the HREA Board were named in December 2007 and although this group met informally by conference call and for one face-to-face meeting, the HREA Board of Directors would not be a formal entity until the time of proclamation on July 1, 2011. By this time there had been a number of changes to the status of the originally named board members, and new appointments were made close to the date of proclamation. While the HREA was still an unofficial entity, the Transition Team was given responsibility for providing the plan and procedures to implement the Act and to keep the HREA Board of Directors and the partner organizations apprised of progress in this regard.

Ethics Officer and human resources

Although the HREA was to be a stand-alone entity it was also recognized that it initially would not have the resources or expertise to hire permanent staff. A major challenge in implementing the legislation was to provide a continuation of services for research ethics review through the transition period. For instance, an application submitted to the HIC would have a response from the newly established HREB, within the legislated time period. In order to assist the Transition Team in making recommendations, the staff undertook a review of similar offices in other health research institutions (both university and academic healthcare organizations) in Canada. The review was valuable but clearly demonstrated considerable variation in both human resources and workload among institutions. Given the importance of retaining experienced staff immediately before and after proclamation, it was recommended that the HREA continue the arrangement with the partner organizations, Memorial University and Eastern Health, regarding staff assignments. However, as described below, in anticipation of the new HREB, which would replace the HIC, there were necessary changes in the office arrangement and staffing.

On recommendation of the PHREB Working Group a senior level position had been created, the Ethics Officer, financed by an arrangement between Memorial University and Eastern Health. The Ethics Officer became a member of the HIC office, the Transition Team and the PAG and worked with the HIC co-chairs to manage the application process and oversee the daily office management. In reviewing human resource needs for the HREA office and considering the projected workload it was recommended that the office have, in addition to the Ethics Officer, two ethics coordinators, one for each sub-committee and also a general secretarial position; as described in the next section, the HREB would operate with two subcommittees, one responsible for clinical trials and genetics research and the other a general health research review committee. The Transition Team also suggested that from time-to-time additional staff might be required, e.g., during vacation periods or times of particularly heavy workload.

HREB review committees

Through the transition period the HIC continued to operate as a REB for the Faculty of Medicine and Eastern Health and was used as the basis for establishing the HREB. However, it was not clear how the HREB would be structured in order to efficiently review an expanded clinical workload. Under the legislation, all health research – including research by community physicians or researchers from outside of the province not currently reviewed by the HIC – would be reviewed by the HREB. While it was not possible to get an exact account of the number of community physicians engaged in clinical research, it was clear (through meetings with physicians in the greater St. John's region and individual discussions with physicians) that, despite the overlap in trials being conducted through both institutions and private practices, there could be a substantial increase in the number of applications to the HREB. The legislation had indicated clear timelines for review of applications; in order to accommodate an expected increase in numbers, particularly of clinical trials, the breadth of research to be reviewed, and legislated timelines, the Transition Team recommended that the HREB have two research ethics review subcommittees: the Clinical Trials Committee (HREB-CT) responsible for reviewing clinical trials of drugs, devices, and genetics research, and the Non-Clinical Trials Committee (HREB-NCT) responsible for reviewing all other human health research.

In anticipation of the earlier proclamation date communicated by government (i.e., 2008), an advertisement for Expressions of Interest to serve on the HREB had been publicized in local newspapers, as well as in the Memorial *University Gazette*. A list of potential members for the HREB was established based on fulfilling the membership requirements described in the legislation (Section 7 of HREA Act), the TCPS2 guidelines for membership to REBs (3), and recommendations being made by the CGSB (Canadian General Standards Board) committee for REBs reviewing clinical trials (13). Fortunately, a number of the HIC members were interested in continuing to serve as members of the new HREB and would provide experience and continuity. From the pool of eligible applicants, HREB members were assigned to each of the two subcommittees, allowing for staggered terms of appointment from one to three years. Through the work of the PAG (Policy Advisory Group), it was proposed that the HREB have a Chair and Vice-Chair, each of whom would serve as chair of one of the subcommittees. In addition, the Chair would sit on the HREA as an *ex-officio* member. To ensure a smooth transition period, the selection of the initial Chair and Vice-Chair was from those research members of the HIC who had considerable experience in the ethics review process.

Approval of HREB and Research Ethics Bodies

The purpose of the HREA Act is to ensure that all human health research conducted in the province is approved by the HREB or a local HREA approved research ethics body (Section 9(1) HREA Act). This required the Transition Team to develop a procedure for approval of the research ethics bodies as well as putting in place a mechanism to record all the human health research being conducted in the province. The Transition Team identified NCEHR as the national body that was most suited to provide an assessment of the HREB and other research ethics bodies in the province, based on their experience in assessing Canadian REBs. However, as noted earlier, national funding for NCEHR was cancelled in 2010 prior to the proclamation of the HREA Act and the NCEHR assessment process was discontinued. As a result, the Transition Team recommended that assessment of the HREB and any other research ethics bodies applying for approval be provided by experienced members of the former NCEHR site visit team who lived outside the province.

In order to document human health research being conducted in the province the Transition Team recommended that a notification form be submitted along with the application to the HREA. The proposed notification form was a simple document that, in addition to identifying the name and contact information for the researcher and affiliated institution(s) or organization(s), identified the position of the principal investigator, the type of research being conducted, where the research was to be conducted and from which REB or research ethics body the researchers were seeking approval. This process would provide an inventory and a single point of information regarding all health research being conducted in the province. With this notification, it would be possible to provide accurate information on the number of human health research studies submitted for review, approved and being conducted in the province of NL, information that would be unique in Canada.

Financial considerations

Once legislation was in place, a major responsibility for the Transition Team was estimating the budgetary requirements of the HREA, including potential sources of revenue. As described earlier, the initial budget for the provincial HREB was proposed to DHCS in 2000 and was based on the expenses of operating the HIC in the late 1990s. At that time, the expenses were shared between the Faculty of Medicine of Memorial University and Eastern Health; in addition, the Faculty provided a number of in-kind contributions. However, by the time the legislation was drafted there had been a number of changes that made it clear that the new HREA would require more resources than those originally anticipated. For example, it became clear that in addition to a provincial health research ethics board (the HREB) to replace the HIC, the HREA would be responsible for approving additional research ethics bodies, documenting all human health research in the province, managing the operations

of the HREA office and providing public education regarding health research ethics review. As well, the legislation included a requirement for reviews to adhere to strict timelines; with the anticipated increase in the number of protocols to be reviewed, it was expected this would translate to increased workload, and thus expenses, despite increased income from industry trials. As noted earlier, the recommendation that the HREB have two subcommittees (HREB-CT and HREB-NCT) to manage the workload required additional staff. Furthermore, with the stand-alone nature of the HREA came new expenses related to meeting and office costs, insurance, and audit. It was also clear that the national and international procedures for research ethics review were changing, and it would be important for the HREA to ensure representation at national and international meetings to maintain up-to-date information. As a result, the estimates were outdated by a decade and the financial needs were considerably higher than originally envisioned. Any additional or new activities, such as an appropriate system to monitor on-going research for adherence to ethics approvals, would result in further expenses.

There were four sources of revenue for operating the HREA and HREB: the government, Memorial University, Eastern Health and review fees for industry-sponsored clinical trials. During the lead-up to proclamation there was no way to know how many community trials might need to be reviewed by the HREB and so the fourth source of revenue, review fees, was an unknown. The final budget, prepared by the Transition Team for the partner organizations (DHCS, Memorial University and Eastern Health), included estimates of revenues considering varying numbers of research protocols to be reviewed, in-kind contributions and continuation of revenue from Memorial University and Eastern Health. However, full agreement on the budget, from all parties, was never completely resolved prior to proclamation. Particularly worrying was how a shortfall would be handled, which relied upon the MOU signed in 2002 and verbal commitments through joint meetings of the parties. Despite this risk, plans for proclamation proceeded.

Concurrent legislation: Personal Health Information (PHI) Act

Two years after the HREA Act was passed, the government of NL passed legislation (June 4, 2008) for handling personal health information (PHI Act (14)). The PHI Act, which applies to both public and private data custodians, establishes rules related to the collection, use and disclosure of personal health information as well as an individual's right of access to and correction of their own health information. Because of the significance of the use and disclosure of personal health information in research, and to assist in coordinating proclamation of both HREA and PHI Acts, the Chair of the HREA Transition Team was also a member of the PHI Act Implementation Steering Committee. The Steering Committee established seven Working Groups. The HREA Transition Team Chair was the Chair of the Working Group focused on health research, the role of which was to provide advice and recommendations to the Steering Committee on the implications of the PHI Act for the health research sector.

The relationship between the HREA Act (4) with the PHI Act is found in Section 44 of the PHI Act (14). This section provides that disclosure of personal health information for research purposes can only occur if the research has been approved by a REB or research ethics body approved by the HREA. As outlined in the HREA Act, the HREB or ethics review body must be assured that the researcher will take sufficient measures to safeguard personal health information, including confidentiality, privacy and security of the information. The REB approving the research study is required to monitor the researcher's recordkeeping, adherence to the approved protocol, conduct of the study and privacy safeguards (Section 11, HREA Act); it has the authority to suspend research that it believes is not being conducted properly (Section 11(5), HREA Act).

Policy Manual for the HREB

Over the many years that the HIC provided ethics review it had established policies to facilitate consistent review and practices, and in 1996 a policy review committee was formally created to look after policies. Once the HREA legislation was passed in 2006 this committee was renamed the Policy Advisory Group (PAG) to serve a role similar to the HIC policy review committee in providing advice to the HREB and taking responsibility for developing and maintaining a Policy Manual for the new HREB. The PAG prepared a Policy Manual to document for the Transition Team the policies to guide the new HREA and HREB. The Manual continues to be available as a resource document (HREB Policy Manual) at the HREA website (www.hrea.ca). The manual includes a brief introductory section to provide the context for the HREA Act and the establishment of the HREB as well as a brief description of the historical context and the principles of research ethics review. It addresses a number of specific policy topics, including: the membership, function, operation and documentation of the HREB; the management of the ethics office, including staffing and staff responsibilities; the review process, monitoring, appeals, consent-assent, and required signatures; policies related to handling special populations including Indigenous communities, children and youth, and those with cognitive impairments; and policies protecting privacy the membership and personal health information.

REFLECTIONS ON THE PROCESS

The establishment and implementation of the HREA was a long process and along the way there were challenges and opportunities for the committees. In this section, we provide a description of five major issues that demonstrate the strengths and weaknesses of the process. The information may be useful for those involved in developing similar legislation or for those research ethics review organizations that are undergoing change. Before considering these issues, however, it is important to recall why the legislation came to exist. In the late 1990s and early 2000s members of the public had made a complaint to the NL government and provincial clinical genetics team regarding clinical genetics research being conducted by out-of-province researchers; the lack of follow-up was at the crux of the issue for families and participants in these studies. Given that the

TCPS identifies duty to care and to “act in the best interests of patients” as crucial considerations for clinical researchers conducting health research (TCPS2 Chapter 11.A (3)), it was unclear how or why the lack of clinical follow-up had occurred. The government of NL needed to understand what could be done to avoid similar circumstances from happening in the future. The Skanes’ report (10), in 2000, was the starting point for developing provincial legislation that would require local research ethics review of research involving Newfoundlanders and Labradorians. As the process to establish legislation proceeded over the years, the fundamental issue at the heart of the legislation – protection of research participants – was often lost from sight as key players from the partner organizations came and went.

Working committees and resources

There were three primary committees involved in the process of drafting legislation, shepherding the transition to proclamation and implementation: the PHREB Working Group, the Transition Team and PAG. Minimal resources were provided to these committees, and no specific secretarial staff was available for this task. The PHREB Working Group initially met monthly then biweekly, a pattern that was continued by the Transition Team; PAG and the Transition Team met on alternate weeks. In the year leading up to proclamation more frequent meetings were held. In addition, as described above, members of these committees participated in communication meetings with researchers, community members and the partners as well as national meetings dealing with research ethics review and meetings associated with the concurrent PHI legislation (14). These activities required an unanticipated major time and workload commitment over the 11 years from the initial government sponsored meeting in 2000 to proclamation in 2011.

Although the membership of the three committees varied slightly over the years there were three members who participated continuously over this time and five who were members of the PHREB Working Group and, subsequently, the Transition Team until proclamation. It is unlikely that the transition to HREA would have succeeded without the considerable commitment of these key persons to meeting attendance and participation in tasks assigned outside the formal meetings, such as community visits. The partners owe much to this group for their continued commitment to the provincial research ethics review concept. It is possible that appropriate resources from the outset, including secretarial support, may have facilitated the process and reduced the length of time required to develop and implement the legislation; but, as described below, the many changes in the senior administrations of the HREA partners, particularly government, also contributed to the delay.

Changes in senior governance – Government, Memorial University and Eastern Health

At the outset, the move to implement province-wide legislation to govern the ethics review of human health research was established by the senior levels of the government, the University and Eastern Health. However, as the years went by the commitment from government waned and similarly, there was a reduced engagement by the senior administration of the University and Eastern Health. This was likely the result of two main factors. First, the initial problem of unethical research being conducted by researchers from out-of-province, with inappropriate follow-up with patients and families in the province, was no longer an on-going, political issue. With the large amount of publicity, the subsequent withdrawal of the approval for the study and the suspension of the privileges of the investigators involved in the initial incident, the original problem was eventually resolved. As a result, the government was no longer receiving complaints from community members and therefore, no longer actively involved in the issue. For the members of the PHREB Working Group and the Transition Team, many of whom continued to be involved in research ethics review on the HIC, the very real problem of access for out-of-province researchers to Newfoundlanders and Labradorians, continued to be a concern.

Also contributing to decreased attention by the partner organizations were the changes in senior administrative positions. Because of the length of time from the initial request for legislation to implementation (over ten years) there was continuing change in the senior levels of all three organizations. This was particularly problematic in the government, where, in addition to changes in the party in power and its leadership, there were numerous changes in Ministers, Deputy Ministers and Assistant Deputy Ministers in the DHCS. The government saw five changes in premiers, ten Ministers of Health and eight changes in Deputy and Assistant Deputy Ministers. Therefore, there was a continuous challenge with corporate memory at the senior levels of government and the DHCS regarding the HREA legislation.

The healthcare delivery system was also re-structured in 2005, shifting from fourteen regional boards to four regional health authorities (Regional Integrated Health Authorities Order (15)); and the Health Care Corporation of St. John’s (one of the original partners in the legislation) became part of the Eastern Regional Health Authority. In addition, Eastern Health had four changes in the senior executive positions. The University also underwent changes, including four Presidents and two Deans of Medicine. This situation was in contrast to the stable membership on the PHREB Working Group, Transition Team and PAG. There is no question that the changes in the senior administrations of the partner organizations had an impact on the ability of the PHREB Working Group and Transition Team to engage with the people who were ultimately responsible to sign off on the legislation and the necessary budgetary and human resource arrangements for the HREA.

Relationship with PHI Act

The PHI Act (14) received assent July 2008 (14), two years after the HREA legislation was passed and although there was a section in the PHI Act that referenced the HREA, the Transition Team was not invited to discussions regarding this new legislation until after it had passed. There was a lack of understanding by the PHI Act Implementation Steering Committee of the roles of the HREA, researchers and data custodians which resulted in two issues that needed to be resolved prior to

implementation of both Acts. One issue that arose was the lack of understanding of the role of REBs in safeguarding personal health information. In adhering to TCPS, the HREA Act (4) states that research ethics approval requires researchers to specify how they propose to safeguard the privacy and confidentiality of research information (including personal health information, data collection, storage and destruction). All REBs in the province, moreover, had been applying this policy in their reviews for over 15 years. This was not well understood by the PHI Implementation Steering Committee and considerable time was spent discussing how the HREA approved REBs would handle this responsibility. An additional issue that raised concern for the HREA Transition Team was the possibility that the PHI Act would be proclaimed in the absence of the HREA Act, which could jeopardize some health research. Specifically, the wording of Section 44 (PHI Act), in which, secondary use of personal health information for research purposes was disallowed without approval of an HREA approved REB. In the end, the PHI Act was proclaimed April 1, 2011 and the HREA Act on July 1, 2011; consequently, under the law no secondary use of personal health information would have been allowed from April to July 2011.

Proclamation Date

As described above the date of proclamation was changed repeatedly. In December of 2007 the Transition Team was asked to have implementation details in place for proclamation of HREA in March of 2008. This necessitated notifying the research community; recruiting and assigning members to the HREB; appointing the HREA board; confirming human resources and budget; and having the approval process for research ethics bodies, a notification strategy, and appropriate review procedures in place. However, the lack of agreement on financial issues resulted in these dates being changed and eventually no firm date being considered for several more years. This situation not only created concern from the local research community, but it also brought into question the entire credibility of the move to a province-wide research ethics review system for researchers and industry outside the province. This concern was further heightened by the introduction of the PHI Act, which appeared to be set for proclamation without having the accompanying HREA Act proclaimed.

It had been anticipated that there would be a six-month lead-in period for proclamation; this was not the case. The date of proclamation, July 1 2011, was announced to the Transition Team approximately one month prior to its occurrence. By then, one proposed member of the new HREA Board was transitioning to a new position out of province and had resigned, as too had the Ethics Officer. Both positions were essential for the implementation of the HREA and the new HREB; thus immediate action was required to fill the HREA Board position and an expedited search for a new Ethics Officer to be in place in time for proclamation. Also, government's notification of the proclamation date occurred at a time when most of the members of the Transition Team were out of town and many service offices, such as support for information technology, were working with reduced staff. Ensuring a seamless rapid transition from the HIC to the HREB supported by the required forms and policies, a new website, two new committees and adherence to legislated timeline was a significant challenge for the few Transition Team members on site and reachable and required a number of very long days.

Budgetary issues and human resources

There was much anxiety about proclaiming the HREA without a written statement clearly outlining the financial support and human resources available from the three partners at the outset, or at least early in the process of establishing the province-wide ethics review process. Among the budgetary challenges was the change from establishing a single provincial REB, as recommended by the Skanes' report (10), to developing the HREA which would oversee all approved REBs in the province and including the HREB which would be reviewing all the clinical trials previously submitted to private REBs. The final budget, recommended by the Transition Team to the partners was considerably higher than that originally envisioned, which had been based on the cost of operating the HIC in 1999. By the time of proclamation, the estimate of expenses was nearly three times that which had been originally proposed by the PHREB Working Group ten years earlier. In addition to inflation, the expenses for the new HREA included increased staffing and expenses associated with the increased workload for the HREB. Although the revenues included the fees for the review of industry-sponsored clinical trials, it was not possible to estimate the number of additional protocols for review or confirm what might be the actual revenues. As the date of proclamation approached, there was significant concern on the part of the Transition Team as to how the expenses would be covered, particularly if the situation arose that these exceeded the revenues. The three partners – Memorial University, Eastern Health and DHCS – also recognized this concern and, although a formal written commitment from the partners was not obtained before proclamation, the original MOU (2002) signed by Memorial University and the DHCS fortunately included a clause to address any potential shortfall. Further complicating this situation was the lack of clarity on human resources. For example, the staff in the HIC office was employed by Memorial University and the Ethics Officer was an employee with Eastern Health. Establishing the HREA as a stand-alone entity was undertaken with the assumption that, at least in the short term, the arrangement with the partner organizations for human resources would be maintained. However, the lack of a formal arrangement or a MOU to address the responsibilities of each of the partners regarding human resources was a concern.

The budgetary issues and human resource concerns created considerable angst among the Transition Team members and serious apprehension regarding potential consequences if the HREA failed to meet its commitments. It was felt by the Transition Team that much of this uneasiness during the lead up to proclamation could have been relieved with appropriate consideration of the budget at the outset and a firm written commitment from the partners for financial security for the HREA.

FOLLOWING PROCLAMATION

The White Paper prepared by Dr. Skanes highlighting the issues of human genetics research (10) was presented to the NL government 20 years ago and the HREA Act was proclaimed 10 years ago. The focus of this paper was to describe the process of developing and implementing the legislation, not to provide a review of the outcome of the legislation on health research in the province. Before reflecting on five areas that have stood out since proclamation, described below, it is worth noting that the legislation has created an opportunity for positive changes that improve the ability to review and assess human health research in the province. For instance, establishing three ethics committees to focus on distinct research areas, offers more focus to the review of human health research. In particular, given the number of research studies in the area of genetics and genomics, a specific review committee dedicated to this area has the potential to strengthen the review process. In addition, the provincial legislation provides a unique opportunity for a simple tracking system to monitor the number and type of human health research studies being conducted in the province. Once the Constituency Committee is established, as outlined in the legislation, this will provide direct access to feedback from the community on the effectiveness of the HREA and the province will be in a position to ask more specific questions regarding participant protection.

Memorandum of Understanding 2012

An important milestone that occurred after the HREA Act was proclaimed, in September 2012, was the signing of a second MOU by all four parties: Eastern Health, HREA, Memorial University, and DHCS (on behalf of the Government). The MOU addressed two major issues that had been raised by the PHREB Working Group and the Transition Team and which had created challenges prior to proclamation, i.e., human resources and budget, including overbudget backup. The 2012 MOU clarified the responsibilities of each party to the financial and human resource requirements of the HREA. In addition, the MOU described the necessary transition of the HREB to serve as the Board of Record for studies which had been approved under the HIC.

Communications

Communication of the research ethics review process to the NL public is a key element of the legislation (Section 5(2), HREA Act) and as such, an important focus of the HREA. A major component of a good communication strategy is maintaining a publicly accessible website. The first HREA website was developed prior to proclamation and although there were updates and modifications it was only in 2016-2017 that the website underwent a major refresh. Procedures for submission, guidelines, forms and resource materials, including a helpful video on “The Ethics Review Process”, are now more accessible and the website itself appears more user-friendly. Some information was not retained from the original website, for example, the early HREA Annual Reports, which allowed for a retrospective of the activities over the years are no longer available. However, the update now posted is a welcome change. As such, it would be useful to survey the users and determine the ease of accessibility and to incorporate a system to receive on-going feedback on the website.

Other aspects of communication are the on-going orientation and educational sessions for members of the HREBs, ICEHR, researchers, students, and staff. The sessions include national and regional activities on streamlining and facilitating research ethics review of studies that affect specialized groups (such as oncology, pediatrics, Indigenous groups). These have been useful to ensure that in-coming REB members and the research community are familiar with the legislation, and the related offices and procedures, as well as national policies. However, the HREA has yet to identify the Constituency Committee required in legislation (Section 19, HREA Act). This Committee is necessary to bring together researchers and the public to raise awareness of research involving human participants in health research in NL and the research ethics review process. This committee is required to meet with the HREA and approved REBs, at least once a year, to discuss responsibilities in research ethics related matters.

HREA and HREB and Office Workload

HREA

As expected, since it was initiated the HREA has seen changes in membership as individuals in the partner organizations come and go in their respective home positions. There have been three Chairs of the Authority. However, there has been continuity in the membership over the years, including at least two members of the HREA who participated in the transition to the provincial legislation, therefore retaining its corporate history.

HREB and Office Workload

The work on a REB is demanding and requires a considerable commitment of time before meetings and during meetings, to complete thorough ethics reviews of research protocols, which are often detailed and highly complex. Although the membership is voluntary the review committee must include members knowledgeable in human health research, research ethics, and law, and includes representation from the general public. It has been particularly difficult to maintain an adequate roster of eligible members for the HREB, and their subcommittees. As a result, the HREB chair and co-chairs and the Ethics Office engaged in a rigorous recruitment initiative in 2018 and were able to report the membership was in good standing in the 2018-2019 Annual Report (16). This area will continue to be a challenge for the HREA and one might expect that improved communication, in particular with the establishment of the Constituency Committee, will improve their ability to seek volunteers for the HREB.

When legislation was proclaimed the HREB included two subcommittees: HREB-CT dedicated to clinical trial research and HREB-NCT dedicated to non-clinical trial research. In 2018-2019 a new HREB subcommittee was established specifically responsible for genetics and genomics research (HREB-GG). This committee began meeting in the fall of 2019 and its impact has yet to be considered in the HREB Annual Report to the HREA. In 2018 the HREA also commissioned a review of the HREB by Clinical Trials Ontario (CTO) (17). The CTO Review Team focused on the clinical trials subcommittee, HREB-CT, and compared the HREB-CT review process with that used by CTO eligible REBs and a small number of REBs from elsewhere in Canada. The report noted that the frequency of meetings for the HREB was higher than that for the other REBs: HREB-CT and HREB-NCT each meet every two weeks compared with the more typical monthly review cycle for REBs elsewhere in Canada. This means that every week the Ethics Office staff are preparing and distributing meeting materials, screening for incomplete or unclear applications, drafting minutes, and communicating committee decisions. The CTO Review Team reported that this probably places a large burden of work on the Ethics Office staff, that is not directly related to ethics review and, as a result, hinders more efficient timelines. The CTO Review Team also noted that the ethics office staff at REBs elsewhere in Canada tend to be in higher level managerial positions compared with HREB staff who work at a more administrative level. Since the CTO report was completed the HREA Ethics Office has changed the office positions to include an Ethics Director overseeing two Ethics Officers, an Administrator and a Receptionist. The meeting frequency has not been modified but it will be important to assess whether these changes in staffing improve the efficiencies of the ethics review process.

The Submission Process

At the time of proclamation, the procedure for submission of study protocols to the HREB was by paper, however, over the years the HREA Office has worked with Memorial University to now submit applications electronically through the university on-line administrative services system, ROMEO. Among the many advantages to electronic submission (reduced workload, ease of access, reduction in paper use, and ease of tracking of all research protocols) is that the ROMEO system is used by a number of REBs across Canada. One might hope that in the future this system could provide an opportunity for a more harmonized or streamlined research ethics review across the country, especially of clinical trials being conducted at multiple sites.

Research Review Turn-around Time

In establishing the HREA and the HREB, concern was raised by local clinical researchers that the turn-around time for research ethics review would be slower and create a reluctance of industry to support clinical trials research in the province. As a result, Section 9(4) of the HREA Act specifically speaks to the timeline of the review process. However, the review process and specifically, turn-around times by the HREB-CT have become a major challenge for this committee and for the HREA. Initially, it appeared that the HREB was succeeding in supporting the increased workload following proclamation. In a report presented at the annual CAREB meeting in 2013, the HREB Chair and Ethics Officer tracked the review process and timeline to approval (18). In contrast to the concerns raised by local clinician researchers prior to legislation, they found that the number of clinical trials had steadily increased, rising from 45 applications in the year prior to the legislation, to 62 in 2011 and 74 in 2012. The average turn-around time for clinical trials applications (from submission to final full approval) was 36.8 days, with an average of 14.8 days spent with the ethics review committee, HREB-CT and 22 days with the research team. They also reported that, in collaboration with the province's Indigenous communities, an innovative iterative process had been created for navigating between the initial Indigenous community approvals, health board resource reviews, and HREB review. It would appear that all was well with the research ethics review process and on a positive path moving forward.

However, in the spring of 2018 the CBC published an article reporting that a local biotech company, Sequence Bioinformatics Inc. (Sequence Bio), had filed a court order with the NL Supreme Court against the HREA and HREB (19). Sequence Bio had been waiting more than six months for the HREB-CT to make a final decision on a pilot study. They challenged that the HREB was required by law "to decide on a research application within 30 days of receiving it, as set out in provincial legislation." The Supreme Court found in favour of the biotech company that the wording of the legislation (Section 9(4) HREA Act) be interpreted such that "within 30 days of receipt of an application, the Board must approve the application, reject the application or approve the application subject to conditions" (20). This case draws attention to the importance of research ethics review timing. It is interesting to note that although the PHREB working group contributed to the legislation they were not allowed to see the final wording of the Act prior to enactment and therefore they were not aware of the flawed wording of this clause. It was at this time, that the HREA commissioned CTO to conduct a review of the HREB, in particular to review the timing of ethics reviews done by HREB-CT compared with REBs elsewhere in Canada (17). The CTO review team identified a small number of clinical trials (six) that could be compared with a small number of study sites (one to four) in other parts of Canada. The results indicated that the HREB-CT review from time of first submission to approval was longer than at most of the other study sites (four of the six studies). However, the results also showed that in NL the research studies spent much more time in revision with the research study teams than with the HREB-CT, a feature which was only seen in one of the other comparator REBs. The data also showed that HREB-CT and the other REB offices spend considerable time pre-screening applications to ensure they are complete and clear before the study is presented to the REB for ethics review. Unfortunately, the data are based on small numbers, but what is apparent from the CTO 2018 report (17) is the considerable degree of variability in the time taken to review clinical trial studies. The results raise the concern that there is little standardization to the research ethics review process, a complaint that has been voiced by many researchers across Canada over many years and discussed below.

NATIONAL CONSIDERATIONS

In the late 1990s, at the time that the NL government initiated the working groups to address concerns with clinical and genetics research in the province, clinical researchers across the country and several national organizations were reporting the challenges in conducting multicentre clinical trials in Canada. A major complaint was the time taken to receive final ethics approval to conduct any large, multi-site study. It was felt that the review process, requiring each participating institution to provide research ethics approval, unnecessarily duplicated the review process, occasionally resulting in delayed study starts and did not address, as intended, the concern of identifying local ethical issues. With no national standards and no REB accreditation system in place each board bases its decision on its own set of procedures, albeit following the national TCPS Guidelines (21) and, for clinical trials, the international *ICH - Good Clinical Practice* guidelines (22). Given the national interest in streamlining the research ethics review process, the move in NL to legislation that would result in a single oversight body, the HREA, and cover all human health research, was watched closely by research ethics organizations from across the country.

For decades, Canada has talked about implementing an oversight system for human health research ethics review, in particular clinical trials, and numerous recommendations have been made by taskforces, national committees and organizations to introduce an accreditation system or required standards for research ethics review. There have been a number of significant attempts.

1. In 1988 the Canadian Medical Research Council, Health and Welfare Canada (Health Canada) and the Royal College of Physicians and Surgeons jointly established the *National Council on Bioethics in Human Research* (NCBHR). As reviewed by Verdun-Jones and Weisstub in 1997 (23), NCBHR advised and consulted with REBs across Canada to enhance knowledge of research ethics issues through educational seminars and workshops, and through the regular *NCBHR Communiqué*. During NCBHR's nine years they arranged site visits of REBs and produced the *Review of the Function of Research Ethics Boards in Canadian Faculties of Medicine* (23). Many of the same issues were of concern then as now: challenges in providing educational standards for REB members; issues of financial and administrative resources; ethics review of clinical trials conducted at multiple sites. In the mid-1990s NCBHR broadened its mandate to include the two other granting councils, NSERC and SSHRC, and became established as the *National Council on the Ethics of Human Research* (NCEHR) (24). Although both NCBHR and NCEHR recognized the importance of oversight for REBs, in Canada (for example, NCEHR had recommended in 2003 a *Taskforce for the Development of an Accreditation System for Human Research Protection Programs* (25)) there was no follow-up by the government on these recommendations and in 2010 funding was discontinued for NCEHR.
2. In 2000 McDonald (24) published a comprehensive review of the *Governance of Health Research Involving Human Subjects*. The review looked at the role played by REBs in the governance of research ethics review, noting that there is "no uniform set of standards that applies across the board to the protection of Canadian research subjects" and that "such oversight as there is of REBs is piecemeal and haphazard at both local and national levels" (24). By comparison, the oversight of research involving animals is "far more effective and independent than that for research involving humans". McDonald suggested that NCEHR might play a similar role to the Canadian Council on Animal Care in the oversight of REBs in Canada.
3. The 2004 report from the Standing Committee on Health, *Opening the Medicine Cabinet: First Report on Health Aspects of Prescription Drugs* (26), noted "there is no single national body mandated to provide oversight for the ethical conduct of human research in either the public or private sector." One of the recommendations of this committee was to establish an accreditation system with oversight for REBs that review clinical trials.
4. From 2005 to 2008, the Sponsors Table Experts Committee met (with representation from the Royal College of Physicians and Surgeons, Association of Universities and Colleges, Health Canada, Association of Faculties of Medicine of Canada, CIHR, NSERC, SSHRC, Rx&D, and others), producing the document *Moving Ahead Final Report of the Experts Committee for Human Research Participant Protection in Canada* (27). Their fundamental recommendation was a Council that "would bring the three elements of education, policy and accreditation together in a single standalone entity".
5. In 2007, Health Canada and the CIHR tasked the *Canadian General Standards Board* (CGSB) to establish "unambiguous Research Ethics Board policies and procedures that adhere to Canadian and international norms" for clinical trials. The committee, which included representatives from REBs and user organizations (including university and healthcare organizations) from across Canada, produced the CGSB Standard, *Research Ethics Oversight of Biomedical Clinical Trials*, which was posted in 2013 as a voluntary standard. However, by 2018 it was withdrawn due to limited use (13).
6. In 2011 the CIHR, Rx&D and the Association of Canadian Academic Health Care Organizations co-hosted the Clinical Trials Summit in Ottawa (28); one of the main areas of focus was the challenges in research ethics review. Following this, the Senate Standing Committee on Social Affairs, Science and Technology published *Canada's Clinical Trial Infrastructure 2012* highlighting the "need for standardization of research ethics review process and the accreditation of research ethics review boards" (29).

7. In 2013 CIHR’s Strategy on Patient Oriented Research, commissioned yet another group to produce a report on *Streamlining of Health Research Ethics Review (SHRER)*. The report listed 13 recommendations focused on harmonization and standardization of REBs (30). The recommendations highlighted the value of streamlining the review process through standard operating procedures, common forms, and a training curriculum, supported through a system of evaluation, qualification of REB members and chairs and using common benchmarks and metrics to assist REBs in their work based on developing a widely available database of Canadian REBs and a repository of resources that would be widely distributed.
8. An outcome of the Clinical Trials Summit (point 6 above) was the establishment of the *Canadian Clinical Trials Coordinating Centre (CCTCC)*, which in 2015 commissioned yet another group to “identify strategies to improve efficiencies of ethics reviews and advance strategic issues like accreditation in regards to clinical trials”. The CCTCC REB Accreditation Working Group relied heavily on the work of the SHRER group and in 2017 in their *Final Recommendations* report (31), listed as the first recommendation: “Distribute the SHRER Report committee recommendations widely and take action on the applicable recommendations.”
9. Recently, Nicholls et al., 2018 (32), have provided a summary of the work in this area over the past several years and propose a similar national approach: “that the best solution for Canada would be to develop a national leadership body to work with provincial initiatives and develop national cooperation and support, facilitating acceptance of reviews between provinces.”

Despite these numerous efforts to address accreditation of REBs and harmonization and standardization of the research ethics review process, especially clinical trials, a national system does not yet exist in Canada. It would be of interest to determine to what extent this is an issue in other countries and how it has been resolved. For example, the UK has undergone a change to coordinate research ethics committees and standardize protocols through their Research Ethics Authority (33). In exploring this topic, it would be important to consider successes and challenges to other approaches. In Canada, it appears that the two major stumbling blocks for establishing such a system appear to be 1) governance – who would be the oversight body, and 2) funding – who would pay, aside from the seemingly trivial but substantial problem of agreement on forms. These were the same challenges faced by NL in moving to a provincially legislated research ethics review process. Given the countless dollars that have been spent for committees, reports, workshops and taskforces, not to mention lost trials or research that never proceeded, it is long past overdue for Canada to move forward and provide the necessary resources and meaningful dialogue with all stakeholders (research participants, researchers, administrators, funders, and the public) to address this issue.

CONCLUSION

Two elements of the HREA Act have yet to be fully realized: the ability to document all health research involving humans being conducted in the province and the engagement of a constituency community to serve as a representative body for members of the population. A third element that continues to be a challenge for REBs across Canada is how to monitor on-going research. These three aspects of the research ethics review process are interconnected. The first step in monitoring is a clear and accurate listing of on-going and completed human health research in the province. At a minimum this would include information on where and by whom the work is being conducted. This information would provide the focus for annual meetings of the constituent committee, the HREA, the HREB, including each of its subcommittees, and approved research ethics body (ies) to discuss the issues arising in the review of human health research in the province of NL.

Reçu/Received: 11/03/2021

Remerciements

Les auteurs souhaitent reconnaître et remercier le travail des membres du CRSP, de l’équipe de transition et du GCP. En particulier, les auteurs souhaitent reconnaître et remercier le Dr Lawrence Felt, professeur au département de sociologie de l’Université Memorial de Terre-Neuve, qui a travaillé sur les premières versions de ce manuscrit et qui est décédé en avril 2016. Les auteurs souhaitent également reconnaître et remercier le Dr. Verna Skanes pour sa disponibilité et ses observations sur le travail du PHREB, de l’équipe de transition et du PAG.

Conflits d’intérêts

Aucun à déclarer

Publié/Published: 01/03/2022

Acknowledgements

The authors wish to acknowledge and thank the work of the members of the PHREB, Transition Team and PAG. In particular, the authors wish to acknowledge and thank Dr. Lawrence Felt, Professor, Department Sociology, Memorial University of Newfoundland, who worked on the early drafts of this manuscript and passed away in April 2016. The authors would also like to acknowledge and thank Dr. Verna Skanes for being available and providing insight on the work of the PHREB, Transition Team and PAG.

Conflicts of Interest

None to declare

Édition/Editors: Patrick Gogognon & Aliya Affdal

Les éditeurs suivent les recommandations et les procédures décrites dans le [Code of Conduct and Best Practice Guidelines for Journal Editors](#) de COPE. Plus précisément, ils travaillent pour s'assurer des plus hautes normes éthiques de la publication, y compris l'identification et la gestion des conflits d'intérêts (pour les éditeurs et pour les auteurs), la juste évaluation des manuscrits et la publication de manuscrits qui répondent aux normes d'excellence de la revue.

The editors follow the recommendations and procedures outlined in the COPE [Code of Conduct and Best Practice Guidelines for Journal Editors](#). Specifically, the editors will work to ensure the highest ethical standards of publication, including: the identification and management of conflicts of interest (for editors and for authors), the fair evaluation of manuscripts, and the publication of manuscripts that meet the journal's standards of excellence.

Évaluation/Peer-Review: Leslie Gelling & Karine Morin

Les recommandations des évaluateurs externes sont prises en considération de façon sérieuse par les éditeurs et les auteurs dans la préparation des manuscrits pour publication. Toutefois, être nommé comme évaluateurs n'indique pas nécessairement l'approbation de ce manuscrit. Les éditeurs de la [Revue canadienne de bioéthique](#) assument la responsabilité entière de l'acceptation finale et de la publication d'un article.

Reviewer evaluations are given serious consideration by the editors and authors in the preparation of manuscripts for publication. Nonetheless, being named as a reviewer does not necessarily denote approval of a manuscript; the editors of [Revue Canadian Journal of Bioethics](#) take full responsibility for final acceptance and publication of an article.

REFERENCES

1. Rahman P, Jones A, Curtis J, et al. [The Newfoundland population: a unique resource for genetic investigation of complex diseases](#). *Human Molecular Genetics*. 2003;12(2):R167-172.
2. Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council, Social Sciences and Humanities Research Council of Canada [Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans](#) (TCPS). Ottawa; 1998.
3. Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council, Social Sciences and Humanities Research Council of Canada, [Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans](#) (TCPS2). Ottawa; 2014.
4. [Health Research Ethics Authority Act](#). St. John's: Government of Newfoundland and Labrador. 2006.
5. [Labrador Inuit Land Claims Agreement Act](#). St. John's: Government of Newfoundland and Labrador. 2005.
6. Abraham C. A world gene hunt targets Canada. *The Globe and Mail*. Nov 28 1998.
7. Gillis C. Doomed Newfoundlanders opt to eat, drink and be merry. *National Post*. Apr 12 1999.
8. Staples S. Bio-piracy or bio-cure. *Ottawa Citizen*. Jul 4 2002.
9. Baird M. Group wants DNA returned. *The Telegram*. March 22 2001.
10. Skanes V. Issues arising from commercialization of human genetics research: A preliminary report and some recommendations. St. John's: Government of Newfoundland and Labrador. 2000.
11. [Memorial University Act](#). St. John's: Government of Newfoundland and Labrador. 1949.
12. [Health and Community Services Act](#). St. John's: Government of Newfoundland and Labrador. 2006.
13. Canadian standard for research ethics oversight of biomedical clinical trials. Ottawa: Canadian General Standards Board; May 2013.
14. [Personal Health Information Act](#). St. John's: Government of Newfoundland and Labrador. 2008.
15. [Regional Integrated Health Authorities Order](#). St. John's: Government of Newfoundland and Labrador. 2005.
16. [HREA Annual Report](#). St. John's: Health Research Ethics Authority. 2019.
17. [Clinical Trials Ontario: External Review of the Newfoundland & Labrador Health Research Ethics Authority's \(HREA\) Health Research Ethics Board \(HREB\)](#). St. John's: Health Research Ethics Authority. 2018.
18. Reid S, Brunger F. The Newfoundland and Labrador Health Research Authority: Twenty months later. CAREB; Calgary, Alberta, Canada; 2013.
19. Antle R. [St. John's company wants court to speed up application process for genome project](#). St. John's: CBC; March 16, 2018.
20. [Sequence Bioinformatics Inc. v. Health Research Ethics Authority for Newfoundland and Labrador](#) 2018 NLSC 129.
21. Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council, Social Sciences and Humanities Research Council of Canada, [Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans](#) (TCPS2). Ottawa; 2018.
22. [International Council for Harmonisation of Technical Requirements of Pharmaceuticals for Human Use \(ICH\) Guidance](#). Geneva: International Council for Harmonization. 2016
23. Verdun-Jones S, Weisstub DN. [The Regulation of biomedical research experimentation in Canada: Developing an effective apparatus for the implementation of ethical principles in a scientific milieu](#). *Ottawa Law Review*. 1997;28:297-339.
24. McDonald, M. [The Governance of Health Research Involving Human Subjects \(HRIHS\)](#). Ottawa: Law Commission of Canada; May 2000.
25. [National Council on Ethics in Human Research \(NCEHR\)](#). Ottawa; 2003.
26. [Opening the medicine cabinet: First report on health aspects of prescribing drugs](#). Ottawa: Standing Committee on Health; 2004.
27. The Experts Committee for Human Research Participant Protection in Canada. [Moving Ahead, Final Report of the Experts Committee for Human Research Participant Protection in Canada](#). Ottawa; June 15, 2008.

28. [An Action Plan to help attract more clinical trials to Canada](#). Ottawa; March 30, 2012.
29. Senate Canada. [Canada's clinical trial infrastructure: A prescription for improved access to new medicines](#). Ottawa; November 2012.
30. [Strategy for Patient-Oriented Health: Streamlining of health research ethics review external advisory committee](#). Ottawa: Canadian Institutes of Health Research; February 22, 2013.
31. Canadian Clinical Trials Coordinating Centre (CCTCC) Research Ethics Board (REB) Accreditation Working Group (WG) [Final Recommendations](#) (FRs). Ottawa; August 21, 2016.
32. Nicholls SG, Morin K, Evans L, Longstaff H. [Call for pan-Canadian approach to ethics review in Canada](#). Canadian Medical Association Journal. 2018;190:E553-55.
33. [Health Research Authority](#). Department of Health, United Kingdom; January 1 2015.