

Challenges to Ethics Review in Health Research

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“Whereas Parliament believes that health research should ... take into consideration ethical issues”¹

The legislation creating the Canadian Institutes of Health Research (CIHR) in 2000 specifically mentioned ethics in the preamble (as noted above). This historic legislation first led to the inclusion of an ethics member in boards across the Institutes and the creation of an Ethics Office within CIHR. Prior to the creation of the CIHR, the Medical Research Council of Canada (MRC) had mandated ethics review and provided guidelines to researchers since 1978.² Indeed, it was the MRC that provided the initial leadership in the creation of a Tri-Council committee to prepare the 1998 *Policy Statement on Ethical Conduct for Research Involving Humans*.³ This *Statement* is unique in that all ethics review of research involving human beings, whether in the social sciences, the humanities, engineering or the pure sciences, were regrouped together. While well-intended, logical and unifying, this approach has had unintended consequences in the social sciences and the humanities.⁴ The National Council on Ethics in Human Research created in 1989 has as its mandate “to provide leadership in advancing the knowledge and practice of the ethical conduct of research involving humans through advice, guidance and education to stakeholders.”⁵ Yet, in spite of all this guidance in health research ethics, there are problems concerning the need to share and access data as exemplified by the report of the CIHR’s task force on privacy.⁶ The other federal initiative that came to fruition after a decade of discussion and a Royal Commission is the law on assisted human reproduction and related research.⁷ Again, the principles underscoring this legislation mention Parliament’s “ethical concerns”

as justifying certain prohibitions.⁸ This legislation has far-reaching potential, well-beyond the prohibited criminal activities. Indeed, the federal regulatory powers extend to the Agency created by the *Act*, which has amongst its objectives to identify ethical issues (s. 18(1)) and to foster the application of ethical principles (s. 22).⁹

It is against this background, and that of further provincial legislative and ethical overlay for biomedical research, that Canada’s health research community attempts to fulfill its desire to advance research and yet protect participants through ethics review. Moreover, increasingly international norms also come into play as the Canadian research community becomes part of consortia that cross borders and share data and research tools. This latter and very recent phenomenon is not without influence on the nature and impact of ethics in health research. Indeed, it may well be time to examine the role of ethics review in Canada as research becomes increasingly international and collaborative in terms of the research teams themselves and the data and tissue samples they seek to share. Furthermore, as we will see, the ethical principles underlying international projects particularly in population genomics research (while not denying the importance of autonomy and privacy), center on the values of solidarity and equity¹⁰ and consider international databases as “global public goods.”¹¹

This paper will focus first on a discussion of the literature on the nature and role of ethics review generally and in Canada (i) and second, on the confounding factor of the international nature of modern health research on the underlying ethical principles that have governed review until now (ii).



(i) Nature & Role of Ethics Review

Since the revision of the *Declaration of Helsinki*¹² in 2004, increasing attention has surrounded the discussion on the role of commercialization, the use of placebos, the return of research (as opposed to clinical research) results and on the biobanking of tissues and DNA, especially at the level of populations. The latter topic in particular, where confined to sampling in defined and identifiable populations such as aboriginal peoples, has resulted in the CIHR adopting guidelines specific to this population.¹³

Ethics review in Canada has also been influenced by the adoption in 2000 of the *Personal Information Protection and Electronic Documents Act* (PIPEDA),¹⁴ as well as the adoption of provincial legislation specific to personal information in the health care sector.¹⁵ As already mentioned, the CIHR itself undertook a study of *Best Practices for Protecting Privacy in Health Research*.¹⁶ An ongoing evaluation of the contents of the *Tri-Council Policy Statement* by the Interagency Advisory Panel on Research Ethics¹⁷ as well as a move towards the consideration of multi-centered ethics review¹⁸ are influencing the role and nature of ethics review.

In the decade following the adoption in 1998 of the *Tri-Council Policy Statement*, there has been an integration of multidisciplinary ethics review in both publicly and privately funded research.¹⁹ Not only have professional societies adopted increasingly specific codes of conduct,²⁰ but funding bodies (e.g. Genome Canada) themselves have insisted on the integration of ethics in applications for funding.²¹ The same trend is appearing in the requirements for attestations of ethics review prior to publication in certain journals.²² Publication requirements include providing proof in the case of clinical trials that: informed consent was obtained, the trial was registered, the privacy of participants is respected, REB approval was obtained and that the *Declaration of Helsinki* was followed.²³ Universities have added internal Codes on conflicts of interest²⁴ to this multi-layered, complex panache of obligations and “guidance.”

There are signs however of a reaction against what has been called ethics review “mission creep.”²⁵ Indeed, mission creep in ethics review is endangering the system “by excessive paperwork and expanding obligations to oversee work that poses little risks to subjects.... [t]he result is that we have simultaneous overregulation

and underprotection.”²⁶ Focussing on procedures and documentation, “many protocols receive exaggerated review”²⁷ Most importantly, “[s]ociety loses as potentially productive research is discouraged or self-censored.”²⁸ Worse no centralized clearing house of decisions and supporting arguments from the letters sent by ethics review committees exists to guide future applicants, to demonstrate transparency or to foster natural justice through a public “jurisprudence” of decisions rendered.²⁹ “All this has generated a trend in which researchers increasingly think of IRBs as the ethics police.”³⁰ The result is decreasing trust and respect, to say nothing of unknown personal, social and economic costs. The “dysregulation” of human subjects research with inflexible requirements for adherence to narrow interpretations of every word in regulations

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and “guidance” policies has created a stranglehold and a loss of respect for ethics by scientists.³¹ The spectre of possible institutional liability has led to “reactive hyperprotectionism.”³² Nowhere is this more evident than in the area of protection of personal privacy and the transfer of data between and within institutions and provinces to say nothing of international collaboration.³³

While not lamenting “mission creep,” the Canadian research community has been active in decrying the quality of REB review and indeed, the governance of research generally.³⁴ Whether calling for a central independent review agency³⁵ or a legal statute,³⁶ the aim is to ensure greater accountability, uniformity of approach and effective oversight. More effective may well be an administrative law approach since REBs are in fact acting as quasi-judicial tribunals.³⁷ Indeed, this may be a welcome approach in the absence of any of the above sought after reforms as, at a minimum, there



would be transparency in decision-making, procedural protections for members and an available “case law” (jurisprudence) for guidance. As early as 2000, there was a call by the Law Commission of Canada for a national database of REB decisions.³⁸

Close to a decade later, there is finally a “Sponsors Table”³⁹ and an expert committee⁴⁰ to look at the protection of human research participants as well as the accreditation or an alternative system of ethics review committees, and governance structures. Nevertheless, the bioethics debate and hence, the appraisal of clinical research (and so this recent initiative) may well continue to be coloured by the “Nuremberg” legacy⁴¹ and the presumed social dangers of medical research.⁴² This situation has its parallel in the field of social sciences and humanities research which has also found itself (often inappropriately) subsumed within the biomedical model of research review. Many forms of such research involve observation and can be compromised by the rigid biomedical model with its over-emphasis on individual autonomy of informed consent irrespective of context or discipline.⁴³ Similarly, retrospective studies involving the records or samples of deceased persons are stymied by consent requirements and paternalistic ethics committees.⁴⁴ In short, the process, the forms,⁴⁵ and the review have become legalistic without the transparent protections and procedures offered by law. If REBs are acting as quasi-administrative tribunals, it’s time for regulatory reform.⁴⁶ Most importantly, current Canadian lethargy and REB over-protectionism are also being challenged by the fact that research is increasingly international.

(ii) International Research

Limiting ourselves to the biomedical arena, there is no doubt that the Human Genome Project exemplified the beginning of truly international research initiatives. Founded in 1990 and culminating in 2001 with the first version of the map of the genetic sequences making up the human genome,⁴⁷ it also represented a private-public endeavour to establish a map of what has been termed pre-competitive information. Through the SNP Consortium, companies, foundations, academic institutions and national funding bodies participated in this effort. Three percent of funds were officially dedicated to the study of the ethical, social and legal issues.⁴⁸

Since the SNP Consortium, other international initiatives such as the HapMap Project⁴⁹ and more recently the International Cancer Genome Consortium,⁵⁰ have followed this model of creating formal, international research infrastructures as resources for scientists around the world to use in their search for candidate genes and biomarkers. What distinguishes this research from traditional academic collaboration is the involvement of both the private sector and national funding bodies *per se* as well as, the largely open-source nature of the databases, and their commitment to a common set of ethics policies and guidelines.

In spite of these common principles and practices, their implementation at the national level has not been straightforward. Biomedical research ethics being largely founded on individualistic ethics, that is, respect for autonomy and privacy. REBs are uncomfortable with the “common good(s)” and public health nature of such international collaboration population research infrastructures. The result is that the creation of these international, collaborative resources are subject to reviews unsuitable to their nature often based on hypothetical, futuristic concerns about possible privacy invasions.⁵¹

Canadian researchers involved in international clinical trials are well-served by the *Guideline for Good Clinical Practice* of the International Conference on Harmonization (ICH).⁵² But it is of note that the *TCPS* is lacking in guidance for longitudinal, epidemiological biobanking endeavours requiring as they do broad consent to future research access by third party researchers for as yet unspecified projects. Yet, in June 2008, the Canadian Partnership Against Cancer announced a project involving the creation and collaboration of cohorts across Canada with a view to involving 300,000 participants in a longitudinal analysis of chronic diseases.⁵³ Among them, one cohort, CARTaGENE in Quebec is gathering genomic, sociodemographic and health data on 20,000 randomly selected individuals (and 30,000 more in a future Phase) over a period of fifty years.⁵⁴ The application and interpretation of the *TCPS*, which contains no specific guidance on such research, is particularly cumbersome and ill-suited to this project. Finally, the Public Population Project in Genomics (P³G) is creating the tools for the international harmonization of 25 major population genomic biobanks around the world.⁵⁵



While the OECD is attempting to provide preliminary guidance for countries involved in such efforts,⁵⁶ Canadian REBs are less prepared for the implications of the ethics of solidarity and reciprocity underlying the building of these research tools where international access and use are the norm. Likewise, retrospective access to leftover specimens from medical care or to pathological samples are stymied by paternalistic, hypothetical concerns over individual privacy and consent.⁵⁷ In short, it may well be time to examine the guiding principles and procedures influencing Canadian REBs since research itself is increasingly international and collaborative in terms of data and samples. The nature of interventionist clinical trials with their attending personal physical and health dangers may not be present in population research and thus, REBs require a different framework and mindset in order to handle the implications of this type of research. The same holds for the review of the international, open source approach to fundamental data. In these publicly available datasets, the samples and data are anonymized so as to enable online access.

Conclusion

The Interagency Advisory Panel on Research Ethics ("PRE") has assembled a number of studies on the need for revisions to the TCPS.⁵⁸ Building on this report, the independent Experts Committee of the Sponsors Table,⁵⁹ identified four priorities in 2008: policy, education, accreditation and proportionate review. These are laudable and urgent goals. While waiting for the first three priorities to be formalized "together into one organisation", and having rejected the call for federal legislation, would it be possible for REBs in Canada to begin considering a more proportionate approach to ethics review in health research?⁶⁰ In all likelihood, revamping the current system in order to meet international demands could result in a better domestic system as well.

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