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Governance of research ethics involving human participants : is Canada a model?

Analysis of the Canadian governance of research ethics and its limitations from a European perspective

Anaïs LEGAND

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National Council on Ethics in Human Research, Ottawa, Canada

Professional advisor:
Dr Richard Carpentier
Executive director
National Council on Ethics in Human Research

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Acronyms

AAHRPP	Association for the Accreditation of Human Research Protection Programs (US)
CAREB	Canadian Association of Research Ethics Boards
CCAC	Canadian Council for Animal Care
CCQ	Civil Code of Quebec
CCRE	Central Committee on Research Ethics (Quebec)
CIHR	Canadian Institutes for Health Research
COI	Conflict of Interest
EMA	European Medicines Agency (previously EMEA: European Agency for the Evaluation of Medicinal Products)
EU	European Union
FDA	Food and Drug Agency (US)
FRSQ	Fonds de Recherche en Santé du Québec
GCP	Good Clinical Practice
ICH	International Conference on Harmonization
IRB	Institutional Review Boards (US)
NCEHR	National Council on Ethics in Human Research
NGO	Non-Gouvernemental Organization
NIH	National Institutes of Health (US)
NSERC	Natural Sciences and Engineering Research Council
OCREB	Ontario Cancer Research Ethics Boards
OHRP	Office for Human Research Protection (US)
PAM	Plan d'Action Ministériel en éthique de la recherche et en intégrité scientifique (Quebec)
PRE	interagency advisory Panel on Research Ethics
REB	Research Ethics Boards
SRE	Secretariat on Research Ethics
SSHRC	Social Sciences and Humanities Research Council
TCPS	Tri-Council Policy Statement
WMA	World Medical Association

Introduction

Context of the study - why focusing on research ethics?

- History of ethical concerns around researches on human

Research on human is a choice society has made. It has become necessary and helpful for the good of the whole society, for knowledge and science, and of course for individuals. But as we all know, experiments on humans can be particularly disastrous for participants, or for the community he or she is coming from. At the end of the World War II, the Code of Nuremberg was written in order to put some rules to protect human participants from abuses resulting from research. But unfortunately, the Code of Nuremberg was not sufficient enough to end these kinds of abuses. Twenty years later, an article revealed several research in the United States that were unethical[1] and this led (among other reasons) to the revision of the declaration of Helsinki in 1975, setting up more stringent principles to guide research when involving humans. Since the mid seventies, a strong ethical movement has tried to implement ethical mechanisms in order to avoid abuses. That was the birth of Review Ethics Boards[2] (REBs). This mechanism has been the one chosen and has become the model cornerstone. Each institution, each hospital has its REB and the REB in it-self is supposed to guarantee the ethics of research. But despite all the international guidelines, norms, regulations, and the proliferation of REBs, still some abuses have been observed and reported[3].

- Ethical tensions at stakes in research

In ethics of research, the issue at stakes is mainly to articulate three goods (generally recognized as “goods” by the society): science, society and individuals. These goods can have competing interests and can be difficult to manage. In the declaration of Helsinki and in all major guidelines, the good of individuals (research subjects[4]) is the one researchers must always protect and the one which should prevail on the other two in any case. Three main principles[5] frame research on human: the respect of people's dignity and their autonomy, the principle of bienfaisance and the justice principle. Used all together, these principles are powerful tools to prevent abuses. Nonetheless, with issues newly raised in research, the respect and the articulation of these principles can be difficult and sometimes end up in abuses.

Research ethics is not rigid and established once and for all. Ethics is in constant evolution, has to be adaptive and should even anticipate new challenges created by scientific techniques and/or global constraints. That is to say, ethics shouldn't be regarded as the “police” of research. Two main goals are usually attributed to research ethics: to protect the safety of all research participants and to promote potentially beneficial research. These two objectives can be met by building and maintaining a climate of trust around research. Participants have to be sure that their interests will be protected and will be the first concern of researchers. That is

why research ethics ought to promote cooperation between researchers, research participants and society. In this idea ethics is a way to improve social benefits of research, but it could also be considered a great competitive advantage as well for scientists and for industries.

- Governance of research ethics

Context of research has greatly evolved in the past 30 years[6]. Besides globalization of research, the number of actors involved in research has increased, creating a complex network of influences, practices and responsibilities that imply to re-think or re-question governance of research ethics. Processes by which ethics is promoted and implemented have to be studied in the light of the changes occurred in research. Developed countries have more or less implemented similar governance of research ethics. Ethical oversight of research relies on REBs and ethical principles are set up mainly by governmental or institutional bodies. Traditionally, oversight of research has focused on publicly funded research, research on which public bodies have the legitimacy to control. But with the development of privately funded research this system has been in depth restructured in some countries. That is particularly true in the case of clinical trials on drugs or medical devices that necessitate the approval of a given administration in order to be sold[7]. However, except the case of clinical trials, one can observe that for other kinds of research involving humans, a diversity of situations regarding ethical oversight. Thus governance of research aims at sheding light on the relationships between every actors in research (researchers, institutions, promoters, REBs, government, participants...) and at trying to improve the current situation.

Developed countries are facing serious issues in terms of research ethics governance. Research ethics is governed by various actors whose interests may be greatly different even competing. Building a culture of ethics while having huge budget constraints is problematic. Setting up an efficient model has to take into account the role and the power of each actor in this field, actors who definitely don't have the same weight in terms of decision making and implementation of decisions. The current governance of ethics is the result of a gradual implementation of norms and practices that have been developed over few decades not necessarily with a coherent planning. Governance of ethics is made up of various strata which may challenge in some cases participants safety. Finding a way to improve governance of ethics has become a great deal for almost every developed countries. The United States have implemented an accreditation system of REBs, with more or less success, in order to harmonize and to give credibility to the ethical oversight of research. European Union, very fragmented, has passed two directives[8] in order to harmonize clinical trials in every state members. Concerns in Canada towards restructuring ethics of research have increased over the past few decades. It's in this context that this study will try to analyze challenges at stakes in Canada and will question whether or not some lessons can be learned from it through a European[9] perspective. Indeed, some characteristics such as political organization, structure

of research, and comparable social values attributed to research may allow comparison between these two political entities. If one should definitely be cautious with comparison, it seems nonetheless appropriate to analyze other models when similar processes are in place as long as comparison is questioned ant put in perspective.

Current state of knowledge on the subject

Research ethics is by definition a field in constant evolution. The state of knowledge in ethics is rarely evidence-based and cautions should always been taken with what one can consider taken as granted. However, some facts or observations can be regarded as (more or less) consensual and have reached a general agreement in Canada. As described by Brody, *"a clear cut consensus"* on a minimal form and the substance framing research ethics has emerged. *"Procedurally, such research needs to be approved in advance by a committee that is independent of the researchers. Substantively, informed voluntary consent of the subject must be obtained, the research must minimize risks and involve a favorable risk-benefit ratio, there should be an equitable non-exploitative selection of subjects, and the privacy of the subjects and the confidentiality on data must be protected. These substantive standards are rooted in fundamental moral commitments to respect for persons, to beneficience, and to justice"*[10].

- Ethics as a way to regulate research

The recognition of the fact that "good" science can also put participants at risk seems nowadays to be widely shared. Research ethics is regarded as a good way to solve some difficult dilemmas when dealing with participants' protection on one side and the potential benefits of research on the other side. Even if some abuses are punished by the law or by legal norms, protection of participants remains the area of ethics. Many on-going debates try to shape ethical principles and many issues still remain unresolved[11]. But what seems to be taken for granted is the way research should be regulated: through ethical regulation[12]. It is worth noticing that in Canada, ethical review of research is not limited to biomedical field. Indeed, a lot of efforts have been made to reach (not without difficulties) research involving human in social sciences as well.

There is, an emerging consensus on what research ethics should promote. The recurrent objectives given to research ethics are to respect the dignity, the rights and the autonomy of research participants, to protect participants safety, to promote fair, beneficial and effective research, to distribute fairly and socially harms and benefits and at the end, to create and reinforce a climate of trust between research community and participants.

- REB process and its limitations

In Canada, the role of REBs and the process of ethical review is well documented. REBs in Canada are the primary oversight mechanisms in place to protect participants. There seems to

be an agreement over REB composition[13], REB ethics review process[14] and REBs role in ethical process. According to the role given to REBs, it's unsurprisingly that REBs have been one of the central subjects of studies in the field of research ethics. Limitations of REBs are thus well-known as well. Independence, budget constraints, bureaucratic drifts, among other things, have been heavily criticized and commented[15].

To sum up the main ideas, REBs play a key role in research ethics. *"As gatekeepers of research with humans"[16],* they are recognized, almost by all actors involved in research as the legitimate body to approve or refuse a research protocol. However, too often, time, budget and implementation constraints are seen as potentially threatening both research process and participants' protection. There is a consensus on the fact that a balance has to be reached between too much control (that could delay or prevent research) and not enough oversight (that could threaten participants safety).

- Complexity of Canadian governance and definition of indicators

It goes without saying that Canadian governance of research ethics has been commented widely. Identification of actors involved is quite well known and so as the complexity of Canadian frame of research ethics. The system is often described as "decentralized"[17] which implies a "soft" regulation not mainly based on the law but on some various authorities having a legitimate action on a defined area[18]. Analysis of this system has often been made in terms of governance. "Good" governance is often thought as based on a precise definition of roles and responsibilities of actors involved and on "good" processes or standards. Thus, indicators to evaluate a "good" governance seem to reach a general consensus. Efficiency, accountability and responsibility, comprehensiveness, transparency, clear definition of role and mission of actors are the most quoted[19]. A good and well-governed system has thus to be efficient in its two given goals (participants have to be protected and research shouldn't be unnecessarily delayed), cost-effective, coherent and educational.

- Something needs to be done but what?

At last, a well-shared knowledge in Canada is that something needs to be done, but no agreement or consensus has been reached yet. In a few words, "*despite the broad recognition that the governance of research in Canada must evolve, proposals for remedial measures have often proven controversial*"[20]. This recognition of a need for change can be seen in the numerous conferences, debates, meetings occurring in this field mainly between academic members, institution members and decision makers. If almost everyone agrees on saying that research participants are protected overall, there is also a recognition of challenges Canadian governance of research ethics is facing. However, criticisms such as non-coherence of the system or systemic conflict of interest (COI) are put forward by some and denied or lessened by others. It's quite an euphemism to say that challenges are not identified in the same way by every actors and that consensus remains hard to build. Governance of research ethics has to

be analyzed from a global perspective and detachment from interests or supposed obvious certainties, in a way or another, has to be taken. That explains why governance of research ethics in Canada has often been compared with two other models[21], the American accreditation system[22] and the model developed by the Canadian Council for Animal Care[23]. In a way, one can say that these models have been used as benchmark, admitting mix blessing of both and analyzing whether or not some parts could be adapted.

Objectives – postulates and questions

After many discussions with my professional advisor, it was decided that I would focus on challenges Canadian governance is facing, challenges that could be found in Europe as well. Starting from a naive perspective, the goal was to become familiar with Canadian system and to be able, in a way, "to think out of the box". This study doesn't pretend to reinvent the wheel, but to question challenges identified from a different point of view. Following the words of Hoeyer, *"ethics regulation should […] be explored with an interdisciplinary approach that merges organization perspectives with cultural analysis as well as moral and political awareness"*[24], another objective was to focus on multi-disciplinary sources in order to keep a broad perspective. In doing so, this study aims at answering three main questions.

The first one rests upon the premise that research ethics in Canada is somehow organized in a way that may impact the goals of research ethics as described above. Based on this postulate, governance seems to be an appropriate concept to outline challenges Canada is facing. Research ethics here is addressed in a much broader way than only only being the result of ethics review. Thus, what in Canadian organization may generate issues for research ethics?

Issues resulting from these identified gaps in Canadian organization,will have to be discussed and analyzed. If empirical measures are difficult to find in this field, some other criteria have to be defined in order to correctly asses the implications. Thus, issues will be questioned in the light of criteria usually attributed to "good" governance. Also as said above, challenges that could occur in European Union were the ones interesting me the most. In that way, challenges resulting from structural processes that can also be fund in Europe will be questioned. This postulates that there are some issues that could, in a way, be present both in Canada and in Europe because of some similar processes of building research ethics. Lack of harmonization in research ethics, COI and difficult detachment between ethics and politics will the main concerns. Thus, what are the main challenges that Canadian governance of research ethics is facing?

Finally, the last objective of this study is to consider suggestions, recommendations and propositions made to improve the current situation in Canada and the adaptability of these possibilities in Europe. The objective is to understand how issues in Canada are likely to occur

in Europe, not necessarily in the exact same way, but according to some similar processes and how that could be prevented. What are the lessons we can learn from the current Canadian situation?

– Objectives in terms of public health perspective

In the end, this study aims at giving a global perspective on Canadian issues in research ethics. Research ethics interests public health in general. In fact, with the development of epidemiology and research on population, some specific issues are likely to be raised. That is why questioning the current situation could help resolve issues that are already present or that could be developed later on. In this study, private as well as public research involving human is considered, and it is worth specifying that there is no question of “ethically” good public research and bad private research.

Public health is indeed concerned with governance of research ethics as improvements in this field often rely on research process in general. Besides direct effects on participants health research may have, research may have more indirect influences on public health. Organizing and promoting a system that enhances protection of research participants and socially beneficial research is a common goal for both research ethics and public health.

Material and methods used

This study relies on two kinds of material: a mix and extended literature review and interviews conducted with identified actors involved in governance of research ethics.

– An extended literature review

It is worth noticing that Canada has, at least, two advantages. A great range of publications focuses on research ethics and is easily accessible. As a matter of fact, institutional bodies (NGO's, governmental bodies) often have clear and well-documented web sites giving precious information. Also, information are often available in English and in French which reduces some possible misreading and translation issues, especially in fields such as law or philosophy. Accordingly, a literature review seemed to be a good method to address this topic. Given the topic, sources of information were taken from the many fields crossing research ethics. Thus, both publications in specialized academic reviews[25] and policies, reports and initiatives from professional actors[26] were studied in order to answer the different objectives. For the legal and policy part, analyzes rely not only on specialized publications but mainly directly on laws and policies[27].The first step was to select sources of information available. This selection was mainly based on the relevance to the topic and the experience and the role when the information came from “professional” sources. My advisor helped me a lot in identifying pertinent publications and/or reports. Also two reports[28] were used as a starting point to build my bibliography. These reports are a mine of information and allowed me to get various perspective. Web sites of professional bodies were consulted in order to have precise

knowledge of their mandates and activities. The second step of this study was to read and analyze all the information gathered. Reading and analysis of the various publications were done according to the relevant methodology of the subject. Reports from professional bodies were helpful to identify the current challenges Canada is facing. They were used to gather factual information. They allowed also the identification of recommendations proposed. However, as many of them represent the view of actors involved in the process, caution was taken on some sensible subject (COI for instance). Publications in peer-reviewed journals were used to go into detail and to obtain sound analysis. Also, these publications were useful to encompass the topic from a global perspective.

The final step was crossing the results of the different analysis and the information resulting from the interviews in order to come to a synthesis. Information were discussed and weighted according to their origin, their scientific validity and their objectiveness. This synthesis was the basis for the redaction.

- Interviews

It was decided with my advisor that I would meet with some actors to get more precise view of the field. These interviews were conducted in order to put in perspective knowledge and information obtained during the literature review. Interviews were used to bring to light controversial issues and to see how different were challenges as perceived by actors and as identified in the literature review. I also used interviews to sort out some questions I had difficulties to answer only with the literature review. Relevant actors were identified on the basis of my advisor's expertise of the field and also on the basis of the literature review. The aim was to obtain a representative view of each actor involved in the governance of research ethics. Were thus contacted members from institutional bodies (CIHR, NSERC), governmental bodies (Health Canada, Industry Canada and Quebec government), NGOs (NCEHR), for-profit REB and academic researchers who were also part of REBs. However, the response rate was not sufficient enough to rely only on a field survey. I decided to conduct the interviews with the respondents according to qualitative methods. Interview guide (see annex 2) was built in a semi-directive way, with opened questions. Face-to-face meetings were preferred when possible. In average interviews lasted around one hour. For confidentiality reasons, names of respondents won't appear in this study. It is worth noticing that due to methodological reasons these interviews can't be used to build empirical and statistical knowledge or answer. Consequently, they are mainly used to shed new lights on the subject. They reflect personal and/or institutional point of views on governance of research ethics. Although they can't be considered scientifically relevant, they bring precious insights on the subject.

- Possible limitations and methodological bias

The main difficulties met, were the lack of pan-Canadian studies and, unsurprisingly, the lack of evidence-based data. If REBs issues and researchers' perception of research ethics are

quite well documented, only few analysis have considered Canadian governance of research ethics as a whole. This could blur the global perspective this study tends to adopt.

Also, research ethics is a quite “small” professional community. Published authors on this subject are not very numerous and this may then lead to publicize only some particular aspects of the subject. Caution has to be taken when analyzing authors' position and points of view because of some possible competing interests. Due to the length of my internship I was not able to get enough knowledge to avoid this bias. Furthermore, due to the field of the topic, objectivity is sometimes difficult to reach as the study is mainly based on a literature analysis. However, the extent of the literature and the interviews are supposed to lessen this bias.

Proposed framework

Results of the study will be presented and discussed in three parts. The analysis of Canadian governance of research ethics will be the focus of the first part. Presentation of the structure and the organization will shed light on how research ethics in Canada is governed. Relationships and links between each actors will be the main concern. The second part will discuss the challenges Canada is facing. Disadvantages of the decentralized model will be weighted. The political nature of research ethics will also be addressed. The final part, will be centered on the recommendations and the lessons that can be drawn. Proposed solutions will be analyzed. And finally, learnings from Canadian model will be questioned in the light of a European perspective.

Part I - Canadian organization of research ethics

This first part presents the organization of research in Canada and its implications on governance of research ethics. It is difficult to imagine research ethics totally independent from the research process and its structure. That is why it's not possible not to present the Canadian model. Research ethics is for a part framed by the organization of research (I) that could explain the governance of research ethics (II).

I- Organization of research in Canada: what influence on research ethics framework?

The presentation of Canadian organization of research (1) will put in light the ethical regulation of research (2).

1) Synthetic presentation of research in Canada

Research is usually understood as an activity targeting the acquisition of knowledge. It can be defined as "*a systematic investigation including research development, and testing and evaluation, designed to develop or contribute to generalizable knowledge*"[29]. Different functions are attributed to research. It is usually seen as "*a driver of social and economic development, innovation and national prosperity*"[30]. What can be called a "sub-sector" of research involves human participants. Research on humans has become more and more important and justified as we entered a society needing proof and evidence to act, all the more when research target is the improvement of human well-being or condition This sub-sector is very diverse regarding the fields concerned. In fact, social, behavioral, engineering, natural, medical and health sciences (at least) may necessitate research on humans. As different as they may seem, these fields have at least two points in common: involving human participants and following, more or less, the same research process. In Canada and elsewhere, this process can be cut in four stages: the research initiation, the research approval, the research conducting and finally the research completion[31]. This process, whatever the field, involves recurrent actors that have actions or functions at different stage of the process. Roles and functions are often blurred in research process. However, it is possible to build a typology of actors involved, typology mainly based on actors roles and interests.

- Researchers

They obviously are at the basis of the research process. They are the one leading and conducting the research. They are the expert in a given field and are supposed to produce knowledge and to set up "*scholarly standards*"[32]. But they are also part of a more global context. Besides their research activities, they have other necessities such as publishing or finding funding which create other obligations.

- Research institutions

In this broad category are included universities, research and teaching hospitals, pharmaceutical companies, think-tanks and government agencies. Needless to say that each type of institution has its own specificities and priorities. However, they all have in common the major role they play in research organization. They assure the promotion of scholarly standards in hiring, promoting and rewarding researchers, they set up priorities of research and, most of all, they have a crucial necessity of making sure they are credible and reliable. They rely on their reputation (both at scientific and ethical level) and they are one which can be hold responsible in case of legal proceedings.

- Research sponsors

Research sponsors are basically the one funding the research. They could be as diverse as research institutions and some research institutions can also be research sponsor. Their role is crucial in research. Indeed, they have strong incentives on the research process, thus they can give directions, promote or in turn prevent some research. Their main interests lay in the success of their endeavors and the credibility they project. Besides private sector companies and charities, major research sponsors are public-based. For instance, we can think of the three councils[33] which have the mandate to promote research all over Canada.

- Governments

Governments (federal and provincial)[34] play diversified role in research. They can promote and set up priorities in research (by funding, giving incentives...). They control, in a way, research activities as they can regulate, set rules in some areas[35] and they have an oversight role in some cases. However, roles given to the governments in Canada is quite complex and will be detailed all along this study.

- Interests groups

Interest groups such as NGOs, associations of consumers or patients, don't play a direct role in research but they could shape interests or research directions through different activities. They can influence all of the above actors via different ways of mobilization[36].

- Review Ethics Boards

Finally, REBs are devoted a particular function. They are responsible for the ethical oversight of research according to a particular process (which will be developed later on). Although they are given the same function, they are also diverse. They can either be in-house institution[37], specialized in a given topic[38] or in charge of studies conducted in a geographical area, and they can either be non-for profit or for profit. It is worth noticing that members composing REBs are also part of the categories above.

This (long but important) typology has the merit to shed light on the global process of research. There are many overlaps between actors and it shows how clear definition of roles,

functions and interests is difficult. Even if their main goal (perceived or supposed) is, at the end, the acquisition of knowledge oriented toward social and/or economic improvements, all these actors may respond to other sub-linear goals that could create competing interests. It would be very naive to regard research as a clear, defined field where actors have a precise role. Accordingly, research, especially the one involving human, has to be thought as a whole.

Besides the respective place of actors, some indicators can give precious information on research in Canada. When talking about research involving humans, the first question that comes to mind is how many persons are concerned. Surprisingly, there is no available data in the literature. When asked, respondents were not able to provide me a figure. However, rough estimations have been made by NCEHR[39]. This report mentions the number of three million Canadian involved in research in universities. However, it also states that "*the number of human subjects involved in clinical trials, other medical or social research studies that are not based in universities but conducted in private clinicians' office or by governmental or non-governmental organizations is unknown*". Then, this is quite hard to have a precise idea of the real extent of research involving humans. It is nonetheless possible to refine that idea by studying research structure in Canada. Thus, based on Canada Statistics[40], it is possible to analyze the gross expenditure product in Canada by performing and funding sectors. The data analyzed are not specific to research involving human. They concern all types of research (divided in two parts: biomedical sciences and social sciences). However, they can be used to build a profile of main actors involved in research in Canada, supposing that the repartition of R&D expenditure in research involving human is similar to the overall research. This gives indications on how research is structured and which possible issues may emerge in terms of research ethics. The two major funding and performing sectors (so as in 2007) are business enterprise (respectively 48% and 54%) and higher education (15% and 35%). This have been true for the past decade. Also, it is worth noticing that business enterprise is funded at 16,5% by foreign sources (mainly USA) which can have impact in terms of regulation. Then both business enterprises (mainly pharmaceutical companies as well as private organization) and higher education (academic sphere) have a great influence in shaping and conducting research. Federal government plays also a major role when funding research (19%) meaning it may have influence over implementation of standards developed. Provinces have unequal weight in the balance which could explain the different structure they have implemented. Finally, clinical trials of drugs, devices and medical procedures have increased over the past decade[41]. And a shift has occurred, clinical trials are now realized mainly in community hospital and private physicians' offices privately funded whereas they were mainly conducted in academic centers[42]. Similarly to other developed countries, research is driven mainly by private businesses and academic sphere. This structure of research leads to a particular regulation framework.

2) Ethical process surrounding research : is the law sufficient for participants protections?

Research on humans is a problematic activity. Indeed, integrity of persons may be suspended in the name of a greater good. Against the Kantian imperative, "*act in such a way that you treat humanity, whether in your own person or in the person of any other, always at the same time as an end and never merely as a means to an end*"[43], research on humans has been (socially) progressively justified and legitimated, only on the strict condition that participants integrity, dignity, and autonomy is preserved and protected. As said above, ethics is one of the solutions to protect participants but is not the only one. That is why when starting this study, before focusing only on ethical regulation, I wondered if participants protection wouldn't be sufficiently insured by laws or legal norms.

To grasp Canadian legal system is in it-self a challenge when you aren't from a federal country! First, there is no specific legislation that covers research involving humans in it-self. However, indirectly some laws can be applied to research. Canadian system relies on two levels of jurisdiction: the federal laws and the provincial laws. Both of these levels have competencies to act and legislate in respective fields of application defined by the constitutional laws[44]. Research is a “gray” field, meaning that competencies given to both federal and provincial levels allow them to act, in some ways, over research. Thus, provinces and territories are competent as far as higher eduction is concerned (and we saw that higher education is an important actor in research) whereas criminal laws (regulating offenses against the physical or mental integrity of persons) are the competency of the federal level. This paradoxical situation, an in- between potential excess and a current lack of proper legislation, tends to reject law as the useful tool to protect participants[45]. Indeed, few lawsuits are reported[46]. To cut a long story short, protection of participants in research has never been directly attributed to the law. Traditionally, in the name of academic freedom, research has been self-regulated[47] and it is in this way that participants protection is currently thought and carried out. Accordingly, ethics review process is seen as the most effective way to accommodate two necessities: protection of participants and academic freedom.

In Canada, there is a global consensus on what should (theoretically) be ethics review. First, REBs are considered the core structure of ethics review system. Implementation of REBs has historically started in research institutions. This birth of an ethical movement can be explained by the progressive awareness of the academic sphere of possible abuses on participants, “good” research can have. Following the revelation of some scandals[48] and the recommendations of the declaration of Helsinki[49], large research institutions, exclusively in biomedical sciences, have created their own REBs. Their reasons were mainly to avoid entry of external regulation (such as law) in the academic and professional sphere[50]. Then, progressively, REBs have become the standard for almost every research institutions. It has to

be noticed that this implementation, at least at the beginning, has resulted mainly from the academic sphere and not initiated by policies coming from outside of academy. Several criteria frame the ethics review and the functioning of REBs. As stated in ethical guidelines such as the Declaration of Helsinki, both formal and substantial procedures apply to REBs. Independence, transparency and representativeness of REBs members are in order. As far as the content of the review is concerned, there is a general agreement on the fact that reviews should be both prospective and on-going. REBs tasks are mainly to make sure of the scientific validity of the research, the risk/benefits ratio, the subject selection, the free and informed consent materialized in the consent form.

However, in the past 30 years many factors have influence REBs and ethics review. In a report of the US Office of the Inspector General, *Institutional Review Boards: a time for reform*[51], are identified six main changes in research environment leading to major consequences on REBs (see annex 3). In short, factors such as scientific and technological innovations, commercialization and privatization, and globalization have greatly influenced the role attributed to REBs in developed countries. These factors have put great pressure on REBs. For instance, pressure for quicker reviews, increasing number of research protocols submitted or even "new" emerging ethical issues have conveyed many difficulties for REBs. Lack of time and of resources may have impacted the quality of reviews. The REBs-based system has, thus, been heavily criticized, leading to a reform of this model.

To conclude, protection of participants relies more and more on REBs. The initial role of REBs seems to have changed a lot, whereas REBs functioning remains the same. The development of REBs was initiated not necessarily in a coherent way and they have been gradually implemented in a voluntary way, at first, by institutions. However, some changes in research context have led various actors to organize and to frame this initial structure.

II - A (very) complex governance of research ethics

If REBs are the "daily" gatekeepers of participants' protection, they are nowadays integrated in a complex framework of policies, practices, and guidelines shaping research ethics. The concept of governance (1) allows to understand this current framework of research ethics in Canada (2).

1) Concept of governance[52]

"*There are almost as many ideas of governance as there are researchers in the field*"[53]. So why using this concept? During the literature review, almost every papers or reports mention the term "*governance of research ethics*". Even if professionals of this field use it daily, questioning this concept seemed necessary to really understand what it was about.

This trendy concept was first used in the World Bank vocabulary, in the 80's. It is "*the manner*

in which power is exercised in the management of a country's economic and social resources for development"[54]. Oriented towards the management of transitioning countries, the World Bank developed a list of "good" governance indicators such as accountability, government effectiveness, quality of regulation among others. Deriving from this initial definition, governance has been one of the concepts in the political sciences tool-box. However, one definition of governance seems particularly relevant for the context of research ethics. According to Hufty, "*governance refers to collective processes, formal and informal, that determine, in a given society, (…) both the way decisions are taken and how social norms and institutions are created*"[55]. This definition gives an analytical frame particularly relevant for research ethics.

Five elements compose this frame. First, there is the definition of a problem or an issue. In research ethics, the issues for good governance would be the promotion of ethical research which could imply the pursuance of socially beneficial research and the promotion and protection of the dignity and the well-being of the research subjects, both of which promote public trust[56]. The second element is the norms[57]. Norm has to be understood in its broader meaning and could be legal, formal or informal. They are games rules set up by the actors and their interactions. They result from deals, agreements, and decisions made by the actors according to some governance process. They are framed as reflecting collective expectations and for what is considered an appropriate behavior in a given society. The efficiency of a given norm is more important than its status. For instance, in research ethics a norm coming from a legitimate body is more likely to be followed than one resulting from a recognized "illegitimate" although legal body. Pluralism of norms could be a problem as it could be used for political means or power. The third component of governance is the actors[58]. They are every formal and informal stakeholders involved in a given situation. Depending on their resources, on their capacities and willingness to mobilize resources and on their efficiency to mobilize and interaction with other actors, actors have differentiated influence on the overall system. The strategic actors are the ones who have enough power to prevent or disturb the decision-making process. The fourth component is the meeting points[59]. They are the formal and informal places where actors, problems,norms and processes meet. Processes, fifth component, can be understood as the evolution of the all system. Processes[60] are usually shaped by the alternative and reciprocal interactions of norms, actors and problems redefinition on each others.

With this frame, governance can be analyzed as an object. Governance in itself in neither good or bad, it is. However, it can rise negative effects. Thus, if there were increased risks for research participants involved in research, it would be regarded as negative. That is why governance of research ethics will be analyzed through the goals defined above. Some indicators are often quoted to analyze the impacts of the current governance. Based on

several reports, accountability, oversight, transparency, clear government roles and responsibilities, clear relationships, clear structure and standards and clear public processes, mechanisms and participation are indicators usually quoted to consider governance as "good"[61]. A very interesting approach, developed by McDonald[62], has raised the "agency risk" where the agents (or actors) tend to pursue their own agenda independently of those of their organizations. In other words, McDonald questions the possibility for actors involved in research to deal with institutional and personal agendas such as promoting research, finding funding, or increase the institution prestige. Thus, the main issue here is to effectively put into effect the collective intention (that is the goals given to research ethics for instance). Obstacles to this implementation could then be the diverse agendas actors have in research ethics. That is why he concludes saying that good governance "*involves the translation of collective moral intentions into effective and accountable institutional actions*"[63]. Governance of research ethics in Canada, as in almost REB-based model, relies on the oversight of those REBs as they are devoted "*the primary governance mechanism or instrumentality used to ensure the ethical conduct of research involving humans*"[64]. Furthermore, it is as if major actors of research ethics (sponsors, researchers, institutions) behave as if their responsibilities were discharged on the REB approval (or refusal) process of a research. Ethical research has become more or less a synonym to review process of a given protocol. That is to say governance of research ethics in Canada has to be studied as a result of complex relationships between actors (REBs, researchers, research institutions, sponsors, regulators), with two-tiers agendas in some cases, relationships that occur according to both horizontal and vertical interactions. Given the particular position of REBs in this system, a great attention will focus on the norms, processes and interactions of actors on the REBs.

2) Governance of research ethics in Canada: a decentralized model leading to differentiated situations

Here are presented, the norms, processes and actors that shape Canadian governance of research ethics. It is important to precise that this study focus only on a pan-Canadian level to have a global overview of the governance.

REBs (primary actor) are mainly composed by volunteer researchers and research institutions members. Larger institutions mainly created their own in-house REBs. However, even if those REBs were a good start, some scandals raised concerns on the actual oversight of REBs and on the lack of REBs in some Provinces or institutions. REBs were created only on a voluntary basis, leading to a fragmented net of REBs here and there, a very loose and distended net accordingly to geographical location or funding institutions.

- Quebec case: a specific position within the pan-Canadian governance

The Poisson case[65], in Quebec, in 1994, focused the attention on possible drift of the current

system. This led to the redaction of the *Deschamp Report* in 1995[66] that reveals some severe dysfunctions in the REBs organization and practices. The Quebec Department of health and social services, in their *Plan d'action ministériel* in 1998, on research ethics and scientific integrity[67], took action to reorganize the current system. Two implications of great importance. The article 21 of the Civil Code of Quebec[68] was re-written and mandates a specific committee (the newly Central Ethics Review Board) to oversight research including legal incompetent minor and adults[69]. In this particular case, the Quebec government decided to take firm actions to regulate research. This is due to both the Poisson case, and the willingness of Quebec to show political specific actions, partly motivated by Quebec position within Canada.

- At a pan-Canadian level

Given the constitutional allocation of matters of health care, property, civil rights and higher education to the provinces, fourteen governments (federal and the thirteen provinces and territories) have varying responsibilities over research activities. Thus, there are various layers of protection for research participants, depending on different factors. First, the type of research determines whether the research is federally regulated. Indeed, experimental drugs or devices for instance, fall under Health Canada supervision[70]. Also, the adoption of the *Personal information protection and electronic Act*[71] puts personal information and use of data as a competence of the federal level. Second, the protection depends on the location of the research, whether it is conducted within a public institution (university/hospital) or in private (community-based research, private CRO) and in which province or territory. Then a third factor, maybe the most important, the source of funding, divided in three categories, public, private and foreign have implications in terms of participant protection. And finally, the category of subjects have, in some provinces, particular implications (as in Quebec case). This creates a particularly complex network of rules and practices. A given research can fall under many various regulations (for instance a multi-site trials of a new substance) whereas another one can fall basically under no regulation (private-funded research conducted in physicians' office).

- the place of the Tri-Council Policy Statement (TCPS)[72]

A particular guideline has to be studied a little bit more in detail. Following a quite long process[73],the three major government funding agencies, the Canadian Institutes for Health Research (CIHR, previously Medical Research Council), the Natural Sciences and Engineering Council (NSERC) and the Social Science and Humanities Research Council (SSHRC) in Canada have agreed, in 1998, on the Tri-Council Policy Statement on ethical conduct for research involving human. The mechanism is quite simple. These agencies will fund a research only if the fund recipient complies with the TCPS. The first requirement for the funding is that the research institution has to have a REB in place. The Interagency Advisory Panel on Research Ethics (PRE)[74] via its Secretariat on Research Ethics (SRE), has the mandate to both improve and adapt the TCPS[75] and assure an oversight of REBs in place.

The oversight is mainly based on procedural aspects such as the REB composition and on institutions account book. In this mechanism, the institution in which research is conducted is responsible for setting up a REB and it is the said institution that has to deal with possible ethical issues emerging. The three agencies will suspend or even stop funding a research if some procedural aspects are missing (such as continuing review), but this mainly relies on the report of adverse event by the institution. It is clearly stated[76] that *"[the three agencies] are research funding agencies. [They] do not have a regulatory or a quasi-judicial mandate. [They] do not investigate allegations of non-compliance with Tri-Agency policies. Rather, [they] refer allegations [they] receive to the institutions where they are alleged to have occurred, for investigation. The institutions are required to report back their findings to [the agency] Ethics Office"*. Thus the actions the agencies can have are the followings: refusing to consider future grant applications for defined periods of time, placing a letter of reprimand in a researcher's file, declaring a researcher ineligible from applying for future funding for a defined time period or indefinitely, terminating remaining instalments of the grants, seeking a refund of all or part of the funds already paid as a grant or award for the research or scholarship involved within a defined time frame; and declaring a researcher ineligible to serve on agencies committees (e.g. peer review, advisory boards, etc.), reporting instances of possible illegal conduct to the appropriate authorities. This guideline, especially at its beginning was perceived as a leading guideline likely to harmonize the fragmented Canadian governance of research ethics. Indeed, TCPS was quite unique as all research involving human were put together. It was also seen as a policy likely to reach a large scale of research. This idea was reinforced with the Memorandum of Understanding on the Roles and Responsibilities in the Management of Federal Grants and Awards[77] (MOU) released in June 2002. But also, the most powerful aspect was the fact that an institution applying to one agency funding has to make all its research compliant with the TCPS. Furthermore, TCPS could be applied on a voluntary basis even for institutions or research not funded through one of the agency. The TCPS, was thus considered a tool to harmonize research all over Canada no matter the discipline of research.

- Rules and processes

Thus governance of research ethics in Canada reveals a "*concentration of structures for federally funded research [which] focus on standards setting and increasingly oversight activities. When other research hosts and funders are involved such as government or community-based or purely private research, few if any, research structures exist*"[78]. Regulation could be seen as both an obstacle and an opportunity. Indeed, it is considered an obstacle when it is perceived as imposed on a given organization. In turn, it will be regarded as an advantage when it is differentially imposed on other actors. Finally given the many types of actors involved[79], institutions, their members and every other stakeholders are likely to have both official agendas and unofficial agendas. Official agendas depending on the type of actors,

could be the promotion of public good, the acquisition of new knowledge, the profit maximization, whereas unofficial agendas could be personal career, reputation (of an institution for instance), financial incentives and so on. Amongst these actors, some NGO's have been created in order to improve the overall process (for instance when working on a possible accreditation system) or at a more local level (educational on-site vists for instance). This is notably the case of the National Council on Ethics in Human Research.

Norms and processes have to be analyzed at the light of potential conflicting agendas of actors. And, the current governance of research ethics can't be analyzed outside of the context of rapid scientific and technological improvements in a very globalized and increasingly privatized economy.

Conclusion

In this part, I focused on the presentation of the current governance of research ethics in Canada. Different factors, specific to the evolution of research as well as specific to Canada, have shaped this current situation. To conclude, current governance of research ethics is characterized by competing actors in terms of decision-making, creating a complex corpus of policies or regulations that is supposed to be implemented by REBs which are often under-resourced to do so. Consequently, disparities among research are observed in terms of ethics reviews. This matter of fact seems to challenge “good” governance to happen.

Part II – Main challenges Canadian governance faces

Words to comment Canadian governance of research ethics are often harsh. Hirtle[80], summarizing and quoting the conclusions of two reports[81], offers a great example. *"The current governance structure (…), "has been described by observers as a "mess", a reflection of overlaps and confusions that indicate a lack of truth in the partnership". Moreover, it is "not a single working group out the kinks of a new system but rather a hodgepodge of individual groups constantly eying at each other", (…) the current structure has "too many players intervening in evolving system,resulting in a confusion of roles and overlap of responsibilities*". In order to question this "mess", this part will rely on the analysis of two main dynamics. On the one hand, challenges can be seen as resulting mainly from interactions between strategic actors, influencing REBs actions (I).In this first dynamic attention will focus mainly on discrepancies between what should the process (good governance) result in and the current situation. On the other hand, the analysis will focus on the very nature of governance of research ethics (II). Thus, there will be questioned the "quality" of interactions of the actors.

I – A decentralized system: what is the price to pay?

This first part will aim at confronting the current governance to indicators of good governance when one wants to reach goals of research ethics. First, all research in same field should respond to the same criteria. This leads to the question of coherence and consistency of the system (1). Then, in a REBs-based system, oversight of REBs is a crucial issue (2). This questions the effectiveness of the process in place.

1) When standards are questioned

According to the process described above, standards oriented towards the promotion of socially beneficial research and towards the promotion and the protection of participants are supposed to be applied by the REBs. This is possible to question their scope of action, their coherence and consistency and their real influence on REBs.

- Scope of action

In Canada, many standards, no matter the origin, are set up to govern research ethics. To be credible, standards applied to research ethics must either apply to all research or be limited to some research where the limit would be seen as understandable and reasonable by the public and the actors involved[82]. Nonetheless, it is possible to wonder if all research are covered by ethics review and if not, what are the ones left aside. Literature tells us that the following kinds of research require a REB review. They are the followings: 1) research conducted at institutions receiving funding by any of the three national councils[83], 2) clinical trials[84], 3) research funded by bodies that have their own sets of standards[85] or research conducted by

individuals whose professional bodies have set up their own guidance[86], 4) research conducted by Health Canada[87], 5) research involving the disclosure of personal health information[88], 6) research involving incompetent minors and adults in Quebec[89], and 7) research whose authors want them to be published in a peer-reviewed journal[90]. This situation leaves aside a great number of research, research that would have been reviewed otherwise. The major issue at stake, is that are left aside, research conducted in physicians' office, in community-based organization, in industries and in other government branches. Also, some researchers whose research are not funded through any big institutions and are not conducted in academic might have trouble reaching a REB. In fact, institutional REBs often don't accept to take responsibility and accountability for research they don't host. Quebec, in 2008 has extended the mandate of its *Comité Central d'Ethique de la Recherche*[91], so that independent researchers working with any kinds of participants could access it. In other provinces, there is no such committee, leading to the conclusion that some research are simply not reviewed because of gaps in the REB network. While the scale of these research is unknown[92], having some research not being reviewed conveys gaps and lacks in governance of research ethics in the entire Canada. It's not possible to say that participants are similarly protected for similar research no matter the geographical location or the source of funding. There is a greater risk for participants to enter a not reviewed research[93]. But also, it creates diversified situations, influencing researchers' perception of research ethics as well as public trust.

- Coherence and consistency of standards promoted

When thinking of standards shaping research ethics in Canada, one word comes naturally to mind: patchwork. Indeed various layers of standards (administrative, legal, professional) build the very complex Canadian corpus governing research ethics. At least, one necessary condition for standards to be effective would be their consistency. This doesn't mean that every standards should be similar in every words and should bind every kinds of research in a similar way. Although all respondents recognized some slight discrepancies exist between some standards[94], they all told me that in the application of principles, there is no real competition between standards. Usually standards are adapted to the situation, the best one fitting applied[95].

However, if consistency of standards is not a huge deal when differences are slight, it can be problematic when regarding a controversial point. Clinical trials are a eloquent example. No less than four guidelines can be applied[96]: the TCPS, the Food and Drugs regulations, the International Conference on Harmonization of Technical Requirements for the Registration of Pharmaceuticals for Human Use (ICH) Harmonized Tripartite Guidelines[97] and the regulation coming from the US Food and Drugs Administration[98]. They all have their position over placebo use. No consensus, yet, has been reached on placebo use, internationally but also at Canadian level. There are two conflicting positions on placebo use in two standards, the TCPS

and the regulation coming from Health Canada and its Therapeutic Product Directory[99]. Despite a consensus-seeking roundtable (1998) and a national placebo initiative (2004)[100], this opposition still remains. Thus, double-standards are currently in place in Canada regarding this matter. Which standards should then be followed? This might create again discrepancies in governance of research ethics. In a multi-center research, this kinds of inconsistencies are a very huge deal. Downie gives an illustrating example. "*Ask almost anyone who has served on an REB how often they has a research respond to a negative review with a statement like: "but six other REBs passed the protocol as it was, why won't you?*""[101]. This creates, at the same time, pressure on REBs, and possible delays for the research to start. It may then have consequences in terms of effectiveness.

- Effectiveness of the standards

Standards can be seen as effective when they are actually applied and well-applied if possible. Researchers and above all REBs are the direct recipients of these standards. One can consider the standard to be effective when a given behavior has been changed in being compliant with the given standard. Not surprisingly, such data are difficult to obtain and to evaluate. Many variables[102] can explain changes (or not) in behaviors. Two studies[103], even if they are not significantly reliable[104] give an idea of the reception of standards by the REBs. Beagan concludes that "*some participants had no difficulty navigated amongst multiple sets of potentially-conflicting guidelines; other found the water exceedingly murky*"[105]. Also, the impact of competing guidelines, especially regarding discrepancies between the TCPS and and ICH guidelines, is seen by "*almost everyone [as] highly confusing and frustrating*"[106]. Besides, the NSERC study concluded that "*the level of awareness of the TCPS in this community is not as high as one might expec*t" and that "*the most striking finding (…) was the level of dissatisfaction whith how the TCPS is implemented and used at local leve*l"[107]. Lack of standards awareness and frustration of the REBs members seem to appear partly because of the proliferation of standards. As stated in the report *Moving Ahead*, this situation result in an "*inconsistent interpretation of existing policy and standards*"; and in the "*lack of clear guidelines and standards for REBs*"[108]. The multiplication of standards have differentiated consequences on REBs. The lack of consistency could lead to a double-standard research ethics, especially since these standards leave aside some parts of research involving humans. In terms of governance this situation reveals a lack of cohesiveness and comprehensiveness from a pan-Canadian perspective. As noted by Hirtle[109], "*the current multiplicity of standards of all types that are not coordinated may be at the root of some of the confusion in the research community about which standards apply to which situation and what to do in case of conflicting requirements"*.

2) When oversight is at stake

Besides the "quality" of standards, oversight of review and implementation of REBs can challenge governance of research ethics. Oversight is a problematic question. On the one hand, it is seen as necessary to make sure ethics reviews are consistent with the standards. On the other hand, independence of REBs are a necessary condition for REBs to play their role. In a decentralized system, no central authority has the legitimacy and the power to realize such oversight. Oversight, when it exists, is conducted by the agency in charge of the policy and lays mainly on the overall process inside of a given institution. Thus, oversight from agencies or bodies whose policies or standards have to be applied relies mainly on some procedural rules (presence of REB in the institution, composition of members, and so on) and not at all on the content. For the three councils and other policy makers, the situation is quite simple. Institutions are responsible for the consistency of their REBs with the standards. Adverse events have to be reported but there is basically no oversight of what is approved. The same applies to the on-going studies review. This may lead to an "*ethical tunnel vision*"[110]. In other words, ethics review is associated with following rules and procedures as required by the funding agencies or regulators and implemented by the REBs. Ethics review is perceived as additional paperwork and REBs as another layer in a vast bureaucratic process. Ethics review is viewed more and more as a matter of verifying compliance with rules and procedures and not as a matter of evaluating the ethical acceptability of research by balancing the limits of development of new knowledge against the human risk involved[111]. Hirtle concludes "*REBs now evaluate the acceptable level of risks to which participants can agree to expose themselves to instead of evaluating the ethical acceptability if research or its overall value*"[112]. And this situation is all the more reinforced given the lack of resource and time pressuring the REBs. Ethics is then often viewed as "*a matter of efficiently processing applications for REB approval*" says McDonald and comparing with the scientific quality of research, "*the ethical quality of research involving human subject is given scant unsystematic attention*"[113]. In a paradoxical situation where there is "*simultaneous overregulation and underprotection (…), [this situation] has generated a trend in which researchers increasingly think of [REBs] as the ethics police*"[114]. Finally, this creates two kinds of effect. Ethics may be limited to a procedural review, emptying from its substance, which impacts the perception of researchers on REBs utility. Ethics process can be seen as a factor delaying the acquisition of new knowledge reinforcing the negative perception towards ethics review.

Current oversight of ethics review reveals another kind of issue. Compliance to a given standard should be compulsory. Compliance with the standards is, more or less, viewed as the condition for the researcher or the research institution to get the funding[116]. But also, in this process, these funding agencies which are also the standard-setting authorities, are supposed

to have power over the on-going review process. Thus, they can use, as a lever, funding incentives, to oversight the ethics process. That is to say, that such bodies have the power to stop funding a research if this one doesn't comply anymore with ethical standards. That is the usual process. However, this kind of process is not really transparent and is difficult to evaluate in practice. Several cases, certainly anecdotal, illustrate this issue[116]. To sum up quickly, it happened, at least twice, that funding agencies (CIHR and Health Canada), while informed of a breach, didn't withdraw the funding of the research, leaving a research that didn't comply with the standards going on. In the case of Health Canada and the CHEO clinical trials, this has resulted in a death of a child. The trials could have been shut down by Health Canada months before this death happened[117]. Here is questioned the ability/willingness of standards-setting authorities to properly enforce their own standards. In the case of the three councils, Weijner notes that "*to date, councils have failed to caution or suspend funding to any institution for failing to adhere to the Three Councils Policy Statement*"[118].

To conclude, while most breaches remain not serious, "*Canada has experienced a number of highly visible cases in which ethical breaches have occurred during research studies involving humans (…). None of these transgressions has led to sanction similar to those imposed in the United States, where federal research funding was discontinued ti research institutions until corrective action was taken*"[119]. Some authorities have taken action[120], but overall, in Canada oversight remains a problematic challenge for the overall governance of research ethics.

Challenges from these interactions clearly emerge. In terms of governance, Canadian current situation reveals concerns over its comprehensiveness, consistency, and oversight. Other challenges can also be identified in the very structure of relationships between actors in research ethics.

II – When ethics is politics

Qualifying the relationships and the interactions between actors in the field of research ethics is difficult. However, two recurrent issues in research ethics exist: possible conflicts of interest (1) and the lack of clear definition of roles and responsibilities (2).

1) Conflict of interest : an insolvable problem?

COI is a huge issue for research ethics. It might even be the most documented challenge governance is facing, yet no action has been actively taken at some levels. But first, what is a COI? The National Bioethics Advisory Commission states that *"independent review of research is essential because it improves the likelihood that decision are made free from inappropriate influences that could distort the central task of evaluating risks and potential benefits*"[121]. A COI would occur when, for instance, an actor is submitted to two, perceived or really, competing agendas, resulting in a decreased independence of the review. The main

problem with COI is that they are not perceived by everyone the same way. It is then very difficult to create provisions to avoid them if they are not identified as such. In turn, too much focusing on potential COI could also result in hiding or avoiding other issues. COI has then to be approached in a more realistic way, especially given the fact that research ethics is a quite small world in Canada. Three major kinds of COI can be identified at different levels of the governance of research ethics: within the REB, within institution and most interestingly within the system.

- Conflict of interest inside a REB

This first type of COI may be the more documented[122]. Indeed, REBs are staffed mainly by members of the same institution and are often researchers submitting their research to the very same REB. An overt COI could be seen in a researcher having a financial interest in the research submitted who is also a REB member. Rules on disclosure of competing interests[123] are usually well followed. Covert COI are more difficult to see. This occurs when a REB member feels he/she can be personally or professionally pressure to approve or disapprove a given study. This is for instance the case, when REB members may feel sensitive to priorities set up by the institution when reviewing the research proposals. And this is even reinforced with the current proximity, inside an institution, between the REB and the Office of Research Services in charge of promoting research. It has to be added that REB members are often nominated by/or according to the recommendation of the Vice President of Research whose mandate is to promote research.

- Institutional conflict of interest

Besides this classical COI, attention has focused also on institutional COI[124] A very interesting publication in the Journal of the American Medical Association[125] reviewed financial conflicts of interest in biomedical research. They found that "*one fourth of the investigators have industry affiliations and two-thirds of academic institutions hold parts ins start-ups that performed and sponsor research at the very same institution*". In Canada, one example is also often quoted, the Dr. Nancy Oliviery case[126]. In short, the researcher has noted a serious adverse event to a clinical tested drug. When she informed the company of this adverse event, she was threatened by the company with legal actions whether she discloses any information. The institution hosting the research was, at the time, negotiating with the company a consequent donation. An independent report concluded that "*the institution took no, or at the most, very limited action to support Dr. Olivieri and the decisions of REB until very late in the process*"[127]. This has a lot to do with the increasing commercialization of research. Of course that is not to say private research is always leading to participants abuses, but that is to balance the perceived benefits of such commercialization. Indeed, the JAMA study identifies some issues resulting from this movement. The research design may be likely to turn towards cheaper design in order to get easier positive results[128]. It also may have implication of what gets

disclosed and submitted for publication[129]. This outlines risks that may threaten academic freedom and ethical research when COI are generated by industrial/institutional collaboration[130].

- Systemic conflict of interest

The last type of COI described here, is well identified in Canadian governance of research ethics. It can be defined as a "systemic" COI as it occurs within in the governance system. A COI is systemic when it is a predictable result of the institution's standard operating procedures being used in pursuit of legitimate institutional objectives. This questions mainly the TCPS and the links with the three funding research agencies in Canada. The position of the three councils has been questioned on whether their mandate to promote and encourage research all over Canada is not in direct conflict with the goals of participants protection in the TCPS. In other words, "*national funding councils currently set up standards for research ethics and are responsible for enforcement of there standards and yet their mandate is the promotion of research*"[131]. This position has been contradicted by the report of the university of Ottawa. They said *"we reject that dichotomy. Our view is that all the primary groups involved in this process, the three councils, the universities and the researchers desire to promote ethical research and to see a system put into place that is both effective and fair*"[132]. This position directly echoes the difficult question raised in the first part of this study, that is to put good intention and good will into action. However, after the university of Ottawa report, the PRE and the SRE were created to steward development, interpretation and evolution of the TCPS. However, it should be mentioned,the PRE is named by the presidents of the three councils. That is why many calls have been raised to give the mandate to a group outside of the councils[133]. For instance, at a meeting of the CIHR Institute Advisory Boards were expressed concerns "*about the actual or perceived conflict of interest that arises when federal granting agencies set about to promote research and regulate the very research they promote*"[134]. This position was even acknowledge by the CIHR president in 2002[135] , and yet, no changes have been made. The same system is still in place. Also, one can notice that the SRE offices are in the same building as NSERC and SSHRC, which clearly does not draw a clear separation line between both. To conclude on this matter, "*we are likely to achieve progress in the governance of research in Canada only when control of the ethical standards for research is wrested from those who have a mandate to fund and promote research*"[136]. This has threatened legitimacy of TCPS and have increased resistances against it. COI, real or perceived, tends to reduce trust on the overall governance when they are released. A very tough question remains over the question of what should get disclosed or not. This could be avoid, at least partly, if the governance of research were perceived as legitimate and effective. Legitimacy is indeed a difficult issue of the current governance.

2) In the quest for leadership

Several words can be used to describe governance of research ethics. Among them: fragmentation, decentralization and leadership dilution. Obviously, those concepts shouldn't be understood only on a negative way. However, it is possible to notice that some issues governance is facing find their roots in the lack of clear leadership inside this field. This can be explained by different factors.

First, there is no unified, consistent and coherent approach of research ethics all over Canada. The complex constitutional division of legal powers certainly doesn't help to set up a unified approach in the field of research ethics. The number of issues raised by this field can legitimate the action of many actors. Also, one can notice the huge varieties of "ways of doing" all over Canada. Quebec's governance of research ethics is a good example. Furthermore, one can notice the willingness to shape a unified ethics review for all kinds of research. This has shed light on how complicated is this issue. "*The reaction from the social sciences and humanities and natural sciences and engineering was highly, perhaps even violently negative*"[137]. This reaction, still present, threatens greatly the chance for harmonization of ethics standards. More importantly, this lack of leadership can be seen as a result of a paradoxical situation. On the one hand, there is a "*current serious insufficiency of numbers of people in Canada trained in research ethics*"[138]. On the other hand, there is a multiplication of actors (understand bodies, agencies or other) who are part of the policy-making process. This paradoxical situation blurs the roles of actors and lessens the readability of the overall process. As noted by Downie[139], "*when the same individuals are involved in crafting organizational positions on a particular issue, there may be a deceptive (albeit unintentional) appearance of agreement among divergent organizations*". To go further, there is a risk of focusing only on some matters shaped by the interests of a limited amount of persons.

In addition of possible tensions occurring because of real or perceived conflicts of interest, overlapping actions, responsibilities and goals may threaten current governance. In a way, there is a dilution of clear responsibilities and delimitation of actors' respective scope of action. For instance, it is not clear who should be in charge of continuing review. While continuing review of research is generally admitted, roles, responsibilities and more importantly corresponding resources have not been appropriately transferred[140]. This could explain why ethics review is most often a singular event than a continuing review process[141]. It is as if there were a sudden proliferation of actors, at least in the past decade, trying to play a significant role in governance of research ethics but without taking respective responsibilities or adequate resource attribution. This situation creates undoubtedly confusion and makes even more difficult to build of possible leadership. Interests of actors involved logically shape the governance of research ethics. Interactions between these actors are all the more complicated

to understand as the overlapping roles and responsibilities of actors are not clearly defined. This explains the impression of incoherence and inconsistencies of the Canadian governance. To conclude on this issue, governance of research ethics in Canada suffers from a patchwork of actors playing many roles creating many rules games without any consultation or even cooperation (albeit unintentional) leading *in fine* to possible incoherences. Given the actors involved (government, funding agencies) and the related matters (research outcomes, benefits, health improvement among others) governance of research ethics is highly linked to politics (as discussed below). That is to say that this governance is a quite volatile reality, a result of a precarious equilibrium between forces at work.

This leads to the difficult question of the legitimacy of actors and its implications on standards. The model in place in Canada focuses on standards-setting to modify behaviors. It is well observed that in order to be implemented, standards have to either be “legally” binding (ie enforcement of those standards relies on a coercive authority) or willingly accepted as the result of a legitimate authority or in many cases, both. In the current situation, implementation of standards doesn't sufficiently rely on coercive enforcement (lack of oversight mainly). The standards-setting authorities must be recognized as legitimate by those whose behaviors are going to be affected, mainly researchers and REBs[142]. In research ethics traditionally, professional bodies were considered the more legitimate to set up standards and to control their own activities[143]. And in fact REBs are the emanation and the extension of professional bodies regulation. However, this kind of regulation has been criticized as being both judge and jury. Other standards have thus been set up by administrative government authorities with input professional. Even if those authorities have received help from the professional area, other stakeholders have criticized the legitimacy of such authorities. This is particularly true in the case of the social sciences and humanities community in front of the TCPS release. These reactions have broken into the authority of the TCPS. While TCPS was at the beginning perceived as a standard that would harmonized research ethics, one can notice that twelve years later, this ambition has not been met[144]. For other standards, clearly the lack of official recognition of standards-setting authority undermines their legitimacy.

This lack of recognition of a legitimate body to govern research ethics, makes it difficult to build leadership. Research ethics is thus governed by actors who are seen legitimate in a restricted area. This wouldn't be a problem is every areas of research involving human was covered, which is not the case. Although calling for (more or less) same principles and goals, in their actions and interactions, actors might thwart and invalidate their respective interests. This lack of leadership prevents the governance of research ethics from being driven in coherent direction. This has definitely some impacts on public trust.

Conclusion

Governance of research ethics faces many challenges. Effective and transparent processes as well as responsible and accountable actors are not (yet) in place. Although good elements are in place, majors difficulties lay on interactions of these elements and on contradictory actions. Governance of research ethics in Canada remains complex because of its "*decentralized and multi-sourced arrangements*"[145]. While it would be wrong to state that Canadian participants to research are definitely at risk, challenges identified may result in a loss of trust and confidence from the public to the research community. These concerns, although not evidence-based, have been recurrent for the past ten years. Several recommendations have been pushed forward.

Part III – Which lessons can be learned?

Once problems are identified, the next step is to address them. Several propositions have been made in Canada and are presented here (I). Also, learnings from Canadian situation may, in some ways, be adapted in other context, especially in Europe (II).

I- Overview of proposed recommendations

According to the literature review and to interviews conducted, two recommendations recurs everywhere. An accreditation system is seen as a way to harmonize and provide a leadership needed (1). At the same time, there seems to be a general agreement on building a culture of ethics that could overcome the current ethical tunnel vision (2).

1) Accreditation system

There is a quite general agreement on the need of an accreditation system[146]. Public authorities such as the House of Common as well as research ethics community have called for an accreditation system of REBs in Canada. An accreditation system *"is usually a voluntary program, sponsored by a non-governmental agency (NGO), in which trained external peer reviewers evaluate a health care organization's compliance with pre-established performance standards. Accreditation addresses organizational, rather than individual practitioner, capability or performance. Unlike licensure, accreditation focuses on continuous improvement strategies and achievement of optimal quality standards, rather than adherence to minimal standards intended to assure public safety »*[147]*.* Two models of accreditation are often taken as example. The US AAHRPP[148] is an non-profit organization created in 2001. Responding to increased public concerns for protecting research participants, AAHRPP accreditation seeks not only to ensure compliance with US federal regulations, but also to help organizations to reach higher performance standards. The CCAC, created in 1968 has the mandate "t*o work for the improvement of animal care and use on a Canada-wide basis*"[149]. This model has been internationally recognized and a lot of its guidelines have be adopted worldwide[150]. The CACC accredits Animal Care Committees all over Canada, local committees that are in charge for animal protection and surveillance.

Based on these two models, NCEHR[151] has created its own accreditation system. Basically, this system would rely on an independent council[152], an accreditation panel in charge of accrediting public and private organizations REBs, public and private organizations that conduct human research but do not have their own REB; and public and private organizations that offer non-institutional REB services to others. Additionally this Council would be in charge with overall responsibility for providing oversight, leadership and policy direction for issues related to human participants in research[153]. As developed in its task force report, the model

proposed by NCEHR is educational, flexible and adaptable, voluntary, transparent and accountable to stakeholders, peer reviewed, and based on various ethical standards. It was also recognized that it would focus first on biomedical research as the consensus on the need for such a model seems to be the strongest. The main advantages are the consistency it would give the research ethics governance, the resolution of the systemic COI of the current governance and the educational aspects. Besides, this accreditation program would be harmonized with existing policies (such as Quebec). It would aim at increasing public trust, promoting and facilitating collaborative research. All stakeholders have interest in this system. Research participants would have a greater confidence given the transparency of the process, researchers would benefit from the increased confidence of the public and from the decrease in "bureaucratic" procedure, institutions and sponsors would benefit from harmonized standards and procedure, regulators would then be discharged of a part of their duty of care for health and safety.

The Expert's Committee recommended "*a participant protection system which includes the accreditation of programs within organizations that conduct or review research with humans. As noted earlier, the Committee found that the accreditation structure and processes as proposed by NCEHR met its criteria and essentially have adopted them for this component of the Council's functions*"[154]. Furthermore a subcommittee, set up a deadline for a pilot study: "*this includes engaging experts and organizations in the field such as the Association for the Accreditation of Human Research Protection Programs. The pilot project should be in place by June 2009*"[155]. However, despite the quality of the model proposed, the general agreement on this accreditation system, the repetitive assurance from the government of the necessity of this model and even the support of Industry Canada, NCEHR has not received enough funds to implement this model, leading to the unfortunate temporary abandon of the said model.

2) Building a culture of ethics

Besides the accreditation system, a well-shared recognition lays on creating a research ethics culture[156]. This culture of research ethics could be seen as scattered-dab improvements to the current governance. Research process in this vision should be thought as a whole and local actions should be assessed from this global perspective. The advantage of these kinds of small steps is their chance to be actually enforced. As we have seen, there is a strong strength of inertia in the current governance and this creates resistances to global changes. Thus, some small changes could be implemented as well inside the current system. Several aspects are of concern, based on interviews and literature examples.

- Education

Education in research ethics is the main theme respondents stated when asked what would be the best way to improve research ethics in Canada. Some tutorials have been put on line by

the SRE and the unit of research ethics of Quebec. These tutorials, getting into diverse issues in research ethics, aim mostly at improving the knowledge of researchers, and try to reconcile them with REBs. Apparently, in October 2008, 35 399 individuals have completed the tutorial of the SRE which seems to be a good start[157]. However, these tutorials can't be sufficient. Some NGOs such as NCEHR or Canadian Association of Review Ethics Boards have developed courses and training for REBs members. Also, on-site visits in Canadian REBs, as for example the ones organized by NCERH, promote educational aspects of research ethics. Some local initiatives in universities or hospital[158] are also in place in order to promote education. But there is no national measurement to evaluate the outcomes of such initiatives[159]. However, education through local initiatives or courses given for future researches or researchers seems to be more and more recurrent in the proposed solutions.

- Professionalization of REBS

This issue remains quite controversial in Canada. There are for-profit REBs in Canada that review research protocols mainly coming from industry-funded research and mainly on "community-based" trials[160]. Indeed, in these cases researchers have often no choice but to access a for-profit REB, since institutional REBs refuse to take liability for external research. These for-profit REBs have been heavily criticized in the literature due to their potential COI with pharmaceutical companies. Lemmens has worked a lot on this issue. Thus on REBs, he recalls "t*hey have to inspire trust in medical research. This require that they do not only act independently, but also that they are seen to be independent. One can doubt whether this is the case in the current system of private review, where REBs are service provider ans depend to inordinate degree on the goodwill of their clients*"[161]. However, in Canadian context, they are also the only REBs that non instutional-funded researchers can have access to, except in the case of Quebec and Newfoundland where respectively the Central Committee of Research Ethics and the Provincal Health REB[162] can be reached by independent researchers. In my interview with a president of one of for-profit REBs in Canada, I insisted on the possible COI. His answers were actually very interesting. He insisted on the fact that "*there is an oversight coming from different actors, the US government, or Health Canada, but there is also some pressure from the sponsors as they can face criminal charges. Also there are independent audits that don't exist for public REBs*". He also outlined the advantages of for-profit REBs. "*Members of [for-profit REBs] are outstanding, they are coming the academic field mainly. It offers credibility to the institution. They don't cost more than hospital REBs, but really our main advantage is the time for reviews, we have twenty-seven staff full time and we manage to have six to eight meetings per month*"[163]. In front of the increasing responsibilities devoted to REBs and the lack of effective structure, the for-profit REBs could be a temporary solution in Canada, if an adequate oversight is ensured. Also, partnerships with institutions could be developed in order to help REBs coping with resources and time constraints.

- Involving participants and questioning the current perception of research

Although often seen as passive recipient, including participants or public representative could be helpful to improve research ethics. First, research participants could be asked feedback after being involved in research. This would allow researchers and institutions to possibly improve research and to consider participants not only as a number on a consent form. At the 2010 National Conference on research ethics[164], a whole session was devoted to participants' experience. For one hour, four participants exposed their feelings and perceptions of the research in which they were involved. The experience seemed to have been well welcomed by the public of this conference (mainly researchers or administrative people in charge of research ethics). Another way of increasing the public participation is in integrating them to REBs. Thus, many guidelines[165] require the presence of a “community representative” in the REBs. In NCEHR on-site visits, from 1998 to 2004[166], 67% of REBs had at least one community/public member. Definition of public /community is not precisely given in any of the guidelines. It refers to non-scientific member, a representative from the community served by the institution, a non affiliated person from outside the institution but who still uses the services of the organization, an outside consultant, an outsider[167]... The role of such members would then be to correct a natural tendency of scientist-based REB to take the point of view of investigators and thus to help promoting participants point of view[168]. Other roles have been given to this community member[169] such as building a bridge between the researchers and the general public or as guidance for the researchers on ethical issues relevant for the public. Also, a 2003 study[170] revealed that 94% of respondents (public members) said that their primary role was to improve the clarity and the language level of the consent form, and 53% stated that they see themselves as representatives and voices of the community. Thus, involving public more could have positive outcomes and could help creating more links between profane and scientist sphere. It would also be likely to improve trust in research involving human.

A last way to involve public would be the creation of a public association or movement for research participants. Such movements have been proven efficient, as for instance the movement of animal rights activists that led to the creation of CCAC. In the United States, human participants protection has been shaped as a major public concern leading the involvement of Congress members[171]. An association such as Public citizen[172] might also help promoting participants protection.

Many solutions may be put forward in order to promote research ethics. But could the Canadian model be a good comparison point for Europe?

II – How does it matter for Europe?

Some similarities between Canada and Europe in research ethics exist (1). Thus, in studying Canadian model, some issues in Europe could be addressed, or at least, some issues occurring in Canada could be prevented from occurring in Europe (2).

1) The danger of comparison

The analysis of Canadian governance can be a good starting point to reveal issues currently at stakes in research on human in general. Similarities exist between research organization in developed countries and the internationalization of research raises issues that have to be taken into account. Of course, each country has adopted its own mechanisms and has its specificities. Comparisons could be misleading if these particularities are not respected. However, in research ethics some principles seem to have reached a consensus. That's why it is particularly interesting to compare how countries have chosen to set them up or not. In this perspective, Canadian organization puts in light some issues that can be met at the European level. Only European Union will be considered here. Some initiatives have been taken on the behalf of the Council of Europe. Indeed, the Oviedo convention[173] could be taken into account, but too many countries haven't ratified it yet. This convention is the testimony of a willingness to take action but it still can't be yet regarded as an effective document. Two main similarities will be discussed here as the foundation of a comparison between Canada and Europe: the similar goals attributed to research and research ethics and some political similarities between these two entities.

- Goals attributed to research and research ethics

Research ethics in Canada is perceived as a way to ensure protection of human participants and promoting socially beneficial research in a climate of trust between all the stakeholders. Research is seen as a driver of social and economical improvements. Similar goals and perception can be found at the European Union level, at least at the institutional level. Research in Europe, since the treaty of Amsterdam[174] has become a legal and political obligation for European Union. The European Commission on its website states that "*the individual and collective wellbeing of citizens depends on the quality and relevance of research and technological developments*". This position has been reinforced with the Lisbon strategy, that is to say *""the most competitive and dynamic knowledge-based economy in the world capable of sustainable economic growth with more and better jobs and greater social cohesion, by 2010"*[175] and the entry into force of the Treaty of Lisbon[176] the 1st December 2009. According to the article 179 of the European treaty[177], "*the Union shall have the objective of strengthening its scientific and technological bases by achieving a European research area in which researchers, scientific knowledge and technology circulate freely, and encouraging it to become more competitive, including in its industry, while promoting all the research activities*

deemed necessary by virtue of other Chapters of the Treaties". Thus, research in Europe is framed by the seventh framework program (FP7, 2007-2013). The budget devoted to research is fifty billion euros over five years. The budget of research is currently around 2% of European GDP, approximatively the same compared to Canada. European Union also promotes research ethics. For instance the European commission has given to research ethics the goal "*to ensure freedom of research and the need to work in the interest of the physical and moral integrity of individuals*". These values are for instance present the European Charter of Fundamental Rights[178]. One of the tasks of the Commission is to analyze, through ethical reviews, whether these values are respected in the research activities funded under the Framework Program. But also, these values are also promoted in the Science and Society Action Plan[179]. The chapter three of this action plan is devoted to ethics. Given these elements, it is quite logically that we can conclude that European Union has more or less given the same value to research ethics.

– Similar political organization and research ethics governance

It could be strange to compare two political entities that don't have the same legal status. Indeed, Canada is a sovereign state whereas European Union is a community of countries that have chosen to delegate some of their national competencies at a supra-national level. If the European Union is a unique political entity, some similarities with Canada can be drawn. Indeed, as we have seen Canada is a federal state with two levels of government. European Union is certainly not a federal entity, at least not yet, but some of the policies have been heavily harmonized and can almost be regarded as such. In the case of research, the state members have kept their competency but the European Union tends to unify research and to promote more and more cooperation. Both European Union and Canadian federal level are not directly competent for research, but they have direct interests in promoting research. Thus, in a way, Provinces and national state members have also similar competencies. It is true, however, that the comparison would need to be further detailed. As far as research ethics is concerned, some similarities exist. Indeed, state members of the EU have their own organization so as Canadian provinces and territories. Almost all have REB-based[180] governance of research ethics. However, disparities between member states exist, so are they in Canadian Provinces. Thus, in both case, there is a willingness to harmonize the governance in some part of research[181], but with local diversified situation, going from regulatory-based (Quebec and France) to very decentralized one (Ontario and the United Kingdom). As in Canada a proper regulation over the Clinical trials on drugs relies on a administrative agency (EMA for European Union).

2) Learnings for Europe

Given the similarities with the Canadian system, some concerns should be considered in

Europe as well. Two main points will be developed. This doesn't give proper solutions but focuses on some issues already debated in Canada that could have their place in Europe.

- inclusion of social sciences and humanities

First, one really interesting point when studying the Canadian system, was the will to integrate all kinds of research involving humans. As we saw, this issue is quite complex. Resistances to the TCPS were mainly coming from this field of research. Burgess[182], gives a quite good idea on how violently the historian field reacted to the 1996-1998 period of review and drafting of the TCPS. She describes it as "*combat against the code*", and explains very well the hostility and mistrust the TCPS faces in social sciences and humanities communities.

This situation is quite similar in Europe. Indeed, a debate is taking place in front of recurrent issues in social sciences. Following recent trials[183] in France involving social and political researchers, the question of regulation of this field is pushed forward almost everywhere in Europe. Among other concerns, there is a criticism towards the model prevailing in ethical regulation, that is the biomedical model that wouldn't fit social sciences[184]. The freedom of research is pushed forward and the risk of censorship of some controversial issues, especially in sociology and political sciences. The obligation of preliminary consent of the subject is criticized heavily [185]. Some social scientists see in this practice a potential drift of studying only consensual objects and their freedom of studying human relationships in every possible way threatened. This concern is well documented in Canada[186] since the application of the TCPS and in the US[187] as well. To sum up this position, what is the most feared is the regulation, only according to a procedural way, of such research.

However, in front of this position quite specific to French-speaking researchers, one can notice the development of a compulsory ethical evaluation of research supported by both European institutions[188], and scientific journals. Furthermore, there is a generalization of the North-American approach to ethical review of social sciences, as explained by Fassin, "*via a transnational circulation of scientific good practices models*"[189]. Thus, some calls[190] have been raised to review social sciences when they study health-related issues.

In front of the current fragmented situation in Europe, an analysis of Canadian current system would be appropriate and needed. Given the fact that these questions have been raised in Canada for the past decade, Europe could learn a lot on this issue from Canadian model.

- Globalization of research and its implications in Europe

As in Canada, European research ethics is facing several issues resulting from a current globalization of research. With the 2001 directive, European Union has showed its willingness to unify and harmonize interventional trials. This directive also tries to facilitate multi-center research that have increased heavily the past two decades. Furthermore European networks have been developed greatly in the past decade. For instance the Forum of National Ethics

Councils[191] or EUREC[192] try to steer a European movement. Also, the current Framework Program requires the integration of ethics into all EU-funded research. And indeed, "*the European Commission has taken a pro-active role to facilitate both the embedding of ethics in research policies and has promoted research ethics within and beyond the European Union*"[193]

However this directive has met many national criticisms and resistances throughout Europe[194]. As noted in a recent workshop on research ethics committees and research review in Europe, "*although the Directive 2001/20/EC gave provisions for a better harmonization of their practice between member states, including the single opinion per member state, inconsistent provisions and divergent implementation in the member states resulted in a suboptimal situation, especially for investigators and sponsors in multinational studies, and under some circumstances in unnecessary burden for research ethics committees"*[195]. It was also acknowledged that "*in 2006, 10% of the FP6 proposals that underwent ethics review raised serious ethical and social issues*"[196]. Here, are directly concerned issues emerging from multi-centers trials. The (re)definition of REBs role and responsibilities seems necessary and needs to be promoted at a European level. Also, it should be added, that this directive and the current movement of harmonization only concern interventional trials leaving outside a great part of research. Thus as in Canadian system[197], this could create inequalities within European Union. An accreditation system of REBs throughout Europe could be a solution. Some calls in this way have been raised[198]. Thus, Canadian current situation could be helpful to Europe, in order to prevent some problems to occur.

Conclusion

What shouldn't be forget is the complex place devoted to research ethics in both Europe and Canada. Indeed, ethics is seen as a way to make sure research involving humans are consistent with some ethical principles that seem to have reached a general consensus. But in these both models, ethics could be pressured by different competing interests. Research ethics is at the confluence of different worlds: academics, politics and industries. These three worlds have to acknowledge each other in order to really promote ethical research. What will be increasingly be at stakes for the next years will be to prevent a "balkanization" of research ethics, within Europe but also at a more global level. Current issues in governance of research ethics need to be addressed in order to prevent drifts all over the world.

Conclusion

When doing this study, people often asked me “but is there something going really wrong?” or also “are there a lot of person whose life is threatened by research? “. Hopefully no or at least we can suppose so.

However, findings of this study show that structure in it-self reveals problematic questions. Proximity between various stakeholders who have vested interests in research and research ethics has to be re-think in order to enhance efficient ethical research. Responsibilities laying REBs, responsibilities that are not followed by appropriate resources explain possible drifts in the Canadian Governance. It is not possible to say that each participant is treated the same way in similar research. This could result in possible exploitation of the more vulnerable populations.

If ethics is mainly promoted and implemented by individual behaviors, it is also the result of a more global system (perception of research and science for instance). Both of these levels have to be targeted by specific actions in order to improve the implementation of research ethics. Initiatives taken show the willingness to address the current situation.

Both Europe and Canada are concerned, all the more with the increasing globalization and commercialization of research. Responses that have to be taken should balance all the respective interests of stakeholders involved. A comprehensive model has to be reached to avoid disparities within developed areas and also in-between developing/developed countries.

Gradual implementations are likely to modify and improve behaviors, perception and process on a long term period. It is necessary to restore trust and legitimacy of decision-makers to have a meaningful impact on the overall system.

Finally, between ethics and research, although they might have antagonist interests, it is not an “either/or choice. Both of these values are necessary and they should be think together at a more global scale to articulate both of them.

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Conference

2010 National conference, *Globalization in human research ethics: today and for the future*, February 20-21 2010, NCEHR, Ottawa.

Interviews

President of a for-profit REB, Thursday 11th of March 2010, phone call, 1h15, in English

Member of the Quebec Department of Health and Social Services, Ethics unit, Friday 12th of March 2010, phone call, 1h15, in French

Member of the Secretariat on Research Ethics, Tuesday 23rd of March 2010, face-to-face meeting, 1h30, in English

Member of CHIR ethics unit, Wednesday 7th of April 2010, face-to-face meeting, 1h30, in French

Websites (all accessed at the later on June 2010)

The Canadian Council on Animal Care

http://www.ccac.ca/

European websites

http://eur-lex.europa.eu/fr/index.htm

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Expert committee for research involving humans

http://www.hrppc-pphrc.ca/english/experts.html

Health Canada

http://www.hc-sc.gc.ca/index-eng.php

National Council on Ethics in Human Research

http://www.ncehr-cnerh.org/

Panel on research ethics

http://pre.ethics.gc.ca

Quebec Health and social services departement

http://www.msss.gouv.qc.ca/

Three councils

http://www.cihr.ca http://www.nserc-crsng.gc.ca http://www.sshrc.ca/

List of annexes

Annex 1 – References

Introduction

1) H.K. Beecher. *Ethics and clinical research*. The New England Journal of Medicine, 1966, 274: 1354–1360.

2) Also called in the United States Institutional Review Boards, but as the study focuses on Canada, Review Ethics Board will be preferred.

3) For instance the Tuskegee study is often quoted, see J. H. Jones, *Bad Blood: The Tuskegee Syphilis Experiment* (New York: Free Press, 1993) . We can also think of some more recent cases such as the Gelsinger case, see Mary R. Anderlik & Nanette Elster, *Currents in Contemporary Ethics* (2001) 29 J.L. Med. & Ethics 220 or in Canada, the Dr. Olivieri case, see R.A. Phillips & J. Hoey, *Constraints of Interest: Lessons at the Hospital for Sick Children* (1998) 159 Can. Med. Assn. J. 955 at 955.

4) In this study research “subjects” or research “participants” equally used.

5) Principles used here are emerging from a Western reflexion, their universality can be of course questioned. For more references, see *The Belmont Report: Ethical Principles and Guidelines for the protection of human subjects of research*,The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research April 18, 1979 or TL. Beauchamp, & JF Childress, (1983) *Principles of biomedical ethics*. Oxford University Press

6) This is mainly due to industrialization and the evolution of techniques. A good indicator is the shift in the funding of research. Nowadays, biomedical research is primarily funded by industries or companies, whereas it was publicly founded before. This could have great implications on the way ethics is thought and implemented

7) Agencies such the Food and Drug Administration in the United States, the Therapeutic Product Directorate within Heatlh Canada or the Agence Française de Sécurité Sanitaire des Produits de Santé deliver marketing approvals for new drugs or new medical devices.

8) Directive 20/2001/CE on *the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use*, effective in 2004 and followed by the directive 28/2005/CE on *laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorization of the manufacturing or importation of such products*, which sets up the GCPs as the recognized guideline.

9) European Union only will be considered in this study. Indeed, European Union in some ways can be compared to Canada because of its political processes. On the contrary, Europe of the Council of Europe is less likely to be able to be a great player in this field.

10) B.A Brody, *The ethics of biomedical research: an international perspective*, New York, Oxford university press, 1998, p. 36.

11) Such as the use of placebo-control for instance.

12) K. Hoeyer, *ethics regulation in the field of medicine: a historical sketch*, Harvard health policy review; volume 8, N°1, 2007:5-15

13) Many guidelines agree on the fact that a REB should be composed of both scientific and non scientific members for instance.

14) The ethical review of a study should be both prospective and continuing, accordingly to the level of risk.

15) On REBs see for instance: H.Edgar & D.J.Rothman*, the Institutional Review Boards and beyond: future challenges to the ethics of human experimentation,* (1995) 73/4 The Milbank Quaterly 489, or T.Lemmens & A Thompson (2001) *Non institutional commercial review boards in North America*, Ethics and Human Research **23**:2 , pp. 1-12 , p.12

16) M. Owen, C. Emerson, P. Kolopack, N. Preto, H. Sampson, A. Townsend, D.Willison, R.L. Woodgate, *Informing Governance Through Evidence-Based Research on REBs: Challenges and Opportunities*, Health Law Review Volume 17, 2 & 3 (2009) p.41. This article sums up the state of applied researches on REBs.

17) For instance, M. Hirtle, *The governance of research involving human participants in Canada*, Health Law Journal, vol. 11, 2003: 137-52

18) The scope of action can be restricted to a given structure (a hospital REB for instance), to a given discipline or even to a given geographical location.

19) D.J. Jones, *Issue identification paper: governance of research involving human subjects,* at section 3.12, report to Health Canada, 2002, M. McDonald & al.,*The governance of health research involving human subjects*, Law Commission of Canada, 2000, at Section B- 1, Center on governance, University of Ottawa, *Governance of the ethical processes for research involving human*, Ottawa, University of Ottawa, March 2000, Organization for Economic Cooperation and Development, *Public management policy, brief n°9: government of the future* (OECD, 2001).

20) The Experts Committee for Human Research Participant Protection in Canada, *Moving Ahead: Final Report*, Ottawa, 2008, p.10.

21) For instance see: The Experts Committee for Human Research Participant Protection in Canada, *Moving Ahead: Final Report*, Ottawa, 2008, for a comparison with the American system and C. Schuppli & M. McDonald, *Contrasting Modes of Governance for the Protection of Humans and Animals in Canada: Lessons for Reform*, Health Law Review Volume 13, (2005):97-106 on the CCAC model.

22) The Association for the Accreditation of Human Research Protection Programs in the United States, a non-profit organization created in 2001 to accredit, accordingly to federal legislation, research organizations.

23) Created in 1968, at the animal protection communities and the Medical Research Council's instigation. The CCAC is a non-profit body, “responsible for setting and maintaining standards for the care and use of animals used in research”. http://www.ccac.ca/en/About_CCAC/About_CCAC_Mandate.htm , accessed June 2010.

24) K. Hoeyer, *op.cit.,* p.14.

25) Health Law Review, Harvard health policy review, the Journal of Law, Medicine and Ethics, McGill Law Journal among others.

26) Various initiatives were of great interest such as the many Quebec government reports, the Sponsors' Table for Human Research Participant Protection in Canada,the report requested by the Law Commission of Canada in late 1998.

27) Such as the Civil code of Quebec, Criminal code of Canada, the Constitution of Canada, Tri-Councils Policy Statement among others.

28) M. McDonald & al.,*The governance of health research involving human subjects*, Law Commission of Canada, 2000; The Experts Committee for Human Research Participant Protection in Canada (2008) *Moving Ahead: Final Report*, Ottawa

Part I – Canadian organization of research ethics

29) As defined in the US legislation, see Code of federal regulation Title 45 part 46, 102

30) National Council on Ethics in Human Research, *Promoting Ethical Research with Humans: Report of the Task Force for the Development of an Accreditation System for Human Research Protection Programs*, Ottawa, 2006, p.20

31) Mac Donald, *HRIHS: process and context*, in M. McDonald et al.,*The governance of health research involving human subjects*, Law Commission of Canada, 2000, p44.

32) *Ibid* p.48.

33) The three councils are the three main agencies in charge of funding research all over Canada. The Canadian Institutes of Health Research (CIHR), Natural Sciences and Engineering Research Council (NSERC) and the Social Sciences and Humanities Research Council (SSHRC) fund research according to their field of competencies.

34) Canada is a federation of provinces and territories. Federal and provincial governments are given different roles and competences that can sometimes overlap or complete each other.

35) Federal government has the control over the approval of new pharmaceuticals and medical devices. See Department of health, *Regulations amending the food and drug regulation (1024 - Clinical trials)*, Canada Gazette part 1, 2000,p.227.

36) Mobilization may involve lobbying, demonstration, publicization, petition and so on.

37) For instance, Health Canada has its own REB.

38) For instance, the Ontario Cancer Review Ethics Board (OCREB) which is specialized in research on cancer.

39) National Council on Ethics in Human Research, 2006, *op. cit.*, p. 20

40) Statistics Canada, 2009, *Gross Domestic Expenditures on Research and Development in Canada (GERD), and the Provinces National Estimates 1998 to 2009 and Provincial Estimates 2003 to 2007*, Catalogue no. 88-221-X, vol. 2, no. 1

41) National Council on Ethics in Human Research, 2006, *op.cit*., p20

42) *Ibid*, p.20

43) I. Kant; *Grounding for the Metaphysics of Morals*, 3rd ed., Hackett, 1993, p. 36

44) Articles 92 and 93, the Constitution Act, 1867

45) Of course it depends on the offenses resulting from research. Death of a person would be legally reprehensible.

46) For a good analysis on courts ruling see J. L . Gold, *Watching the Watchdogs: Negligence, Liability, and Research Ethics Boards*, Health law Journal, 2003, vol. 11: 153-176, and on jurisdictional points : J. Llewellyn, J. Downie, and R. Holmes, Protecting *Human Research Subjects: A Jurisdictional Analysis*, Health Law Journal, 2003 Special Edition, 207-42

47) Through code of conducts, deontological codes, scientific reviews, ethics review and so on.

48) H.K. Beecher, *op. cit.*

49) Declaration of Helsinki, *Ethical principles for medical research involving human subjects,* 59th WMA general assembly, World Medical Association, Seoul, 2008.

50) A. Campbell & K. Cranley Glass, *The legal status of clinical and ethics policies, codes and guidelines in medical practice and research*, McGill Law Journal, 2001, vol. 46: 473-89.

51) Department of health and human services, US Office of the Inspector General, *Institutional Review Boards: a time for reform,* 1998,p.5*.*

52) For a really good discussion on governance see M. Hufty, *La gouvernance est-elle un concept opérationnel ? Proposition pour un cadre analytique*, in Fédéralisme Régionalisme, Volume 7 (2): 2007

53) P. Björk et H. Johansson, *Towards Governance Theory : In Search for a Common Ground*, IPSA Papers, 2001

54) World Bank, *Governance and Development*, Washington, IBRD, 1992

55) M. Hufty, *op.cit*., p. 10

56) M. McDonald, *Canadian Governance of Health Research Involving Human Subjects: Is Anybody Minding the Store?,* Health Law Journal, vol 9, 2001, p4

57) Norms in research ethics, for instance, could be the standards developed by the regulators.

58) Actors can be REBs, researchers, research institutions, governments, administrative bodies, courts, peer-reviews, public, research participants and so on.

59) Meeting points can be conference, political meetings, task forces, forum and so on.

60) Processes can be ethical review, how standards are usually constructed.

61) See above note 19.

62) M. McDonald, *Canadian Governance of Health Research Involving Human Subjects: Is Anybody Minding the Store?,* Health Law Journal, vol 9, 2001, he bases his approach on A. Buchanan, *Toward a theory of the ethics of bureaucratic organizations*, 6:4 Business Ethics, 1996.

63) McDonald, *ibid*, p.5.

64) McDonald, *ibid,* p.5

65) H. Doucet, *Développement des concepts et des enjeux en éthique de la recherche*, Pistes, vol 3, mai 2001

66) Commission Deschamps, *Rapport sur l'évaluation des mécanismes de contrôle en matière de recherche clinique au Québec,*1995

67) Gouvernement du Québec. Ministère de la Santé et des Services sociaux, *Plan d'action ministériel en éthique de la recherche et en intégrité scientifique*, Québec, 1998

68) Civil Code of Quebec, article 21

69) Its mandate has been recently enlarged as it now includes all possible research on every possible subjects, for researchers who wouldn't have easy access to a REB.

70) Health Canada regulates research falling under the regulations under development within *Assisted human reproduction Act*, S.C. 2004, c.2, the *Natural health product Regulations,* SOR/2003-196, the *Medical device Regulations,* SOR/1998-282 and the *Food and drug Regulations,* C.R.C.,

c.870.

71) *Personal information protection and electronic Act*, S.C. 2000, c.5

72) Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada and Social Sciences and Humanities Research Council of Canada, *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS)*, 1998 (with updates of May 2000 and September 2002),Ottawa:Tri-Council, 1998

73) M. McDonald*, From Code to Policy Statement: Creating Canadian Policy for Ethical Research Involving Humans*, Health Law Review, 2009, Vol. 17:12-25, p.20

74) Created by the three councils to to support the development and evolution of their joint research ethics policy. For more information see http://pre.ethics.gc.ca/eng/panel-group/about-apropos/, access June 2010.

75) While created to be a living and evolving document, ten years later and after many rounds of consultation, the second edition hasn't been released yet.

76) On CIHR website for instance, http://www.cihr.ca/e/37833.html, acces june 2010.

77) The MOU describes the basic requirements for obtaining and maintaining institutional eligibility to administer research funds. See, http://www.nserc-crsng.gc.ca/NSERC-CRSNG/Policies-Politiques/MOURoles-ProtocolRoles/index_eng.asp., access June 2010.

78) M. Hirtle, *op. cit*. note 7, p 140. Except the Alberta College of Physicians and Surgeons, which has established oversight for physicians who in their private capacities conduct pharmaceutical and other types of research.

79) Including research institutions (universities, health centers, hospitals), pharmaceutical companies, and medical offices; domestic (Tri-Councils) and foreign (NIH) institutions that sponsor research, health charities, regulatory bodies and governments applying standards from provincial, federal and international levels; and professional groups (Canadian Medical Association for instance).

Part II – Main challenges Canadian governance faces

80) M. Hirtle, *op. Cit.*, note 7, p149

81) Center on governance, University of Ottawa, Governance of the ethical processes for research involving human, Ottawa, University of Ottawa, March 2000 and M. McDonald & al.,The governance of health research involving human subjects, Law Commission of Canada, 2000

82) See the recommendations of the National Bioethics Advisory Commission, Ethical and Policy issues in research involving human participants: summary , Bethesda ML, National Bioethics Advisory Commission 2001, 2

83) Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS), *op.cit.*

84) Food and drug Regulations, C.R.C., c.870, ss G05.003(5), G.05.002.

85) For instance, Alberta Heritage Foundation

86) For instance, the College of Physicians and Surgeons of Alberta

87) But also, the National Defence, Correctional service Canada, the Space Agency and the International Development Research Center that have signed the TCPS.

88) Personal Health information Protection Act, S.O. 2004, c.3

89) Civil Code of Quebec, article 21

90) Many peer-reviewed jourals require ethics review.

91) “Depuis le 1er janvier 2008, le CCÉR a vu son mandat être élargi par le ministre à toutes les catégories de sujets de recherche. Ainsi, un chercheur dont l'établissement ne dispose pas d’un CÉR peut maintenant soumettre son projet au CÉR central même s’il n’implique que des majeurs aptes”. http://ethique.msss.gouv.qc.ca/site/ccer.phtml , access June 2010.

92) According to the budget analysis, the three councils fund 10% of the research, a strict estimation would conclude that only 10% of research involving humans are concerned. However, more precise estimations state the the TCPS concerns 60% of research, still leaving outside of its reach 40%.

93) J.Downie, Contemporary Health Research: A Cautionary Tale (2003) Health Law Journal, Special Edition 1-20 and M. McDonald, Canadian Governance of Health Research Involving Human Subjects: Is Anybody Minding the Store?, Health Law Journal, vol 9, 2001. They mention the fact that with no review participants are more likely to be deceived and/or exploited. They also state the risk of additional costs for communities.

94) It was mainly the case when comparing Quebec's standards and TCPS requirements

95) The example given was the rule of composition of a REB. If one regulation states that the minimum number of members has to be 5 and in another one 8, these two standards can't be seen as contradictory. Indeed the more stringent one has to be applied (in this case 8).

96) Five if we consider the Declaration of Helsinki.

97) Good Clinical Practices (GCP), The International Conference on Harmonization of Technical Requirements for the Registration of Pharmaceuticals for Human Use (ICH), 1996.

98) Applications for FDA Approval to Market a New Drug, 5 CFR § 314.126(b)(2)(i)2002. FDA recognized placebo-controlled study as a gold standard. Approval of FDA is required for a drug to enter the US market.

99) TCPS has as standards the clinical equipoise whereas Health Canada, that has signed the ICH-GCP, has more permissive use of placebo control.

100) See H. Sampson, D. Pullman & C. Weijer, *Research governance lessons from the National Placebo Initiative*, Health Law Review, 2009, vol.17:26-32

101) J.Downie, *Contemporary Health Research: A Cautionary Tale* (2003) Health Law Journal, Special Edition 1-20 p7

102) Such as the lack of resources, the turnover in REBs among others. For a in-deepth discussion, see G. Legault, *Du souci moral à la saine gestion: l'enjeu des politiques de la recherche sur des humaines*, 2:2 Ethique publique. Revue internationale d'éthique sociétale et gouvernementale, 2000, 23.

103) B. Beagan, *Ethics review for human subjects research: interviews with members of research ethics boards and national organizations* in M. McDonald et al.,*The governance of health research involving human subjects*, Law Commission of Canada, 2000, pp173-238 and the Interagency Advisory Panel on Research Ethics, *NSERC community whose research involves human subjects: results of a survey about their needs and supports in research ethics*, 2003

104) They were both realized shortly after the release of the TCPS and they are not statistically significant. However, they provide a qualitative analysis that gives interesting information.

105) Beagan, *op.cit.*, p204

106) Beagan, *op.cit.*, p. 206

107) PRE, *op. cit.*, p.25

108) The Experts Committee for Human Research Participant Protection in Canada, *op. cit*. p30

109) Hirtle, *op. cit*. p.148

110) McDonal, *op. cit.*, p.294

111) B. Legault, *op. cit.*

112) Hirtle, *op. cit*., p.145

113) McDonald, *op. cit*., p.295

114) C.K. Gunsalus & al., *Mission creep in the IRB world*, Science, 2006, 312:1441

115) It is worth noticing that this process leaves aside once again, research that are not reached by standards, and especially TCPS.

116) C. Weijer, *Placebo trials and tribulations*, 2002, 166 Can. Med. A. J. 603, on CIHR and Downie, *op. cit*. p.9 and CBC investigations

117) Downie, *op. cit*., p..9

118) C. Weijer, *op. cit*., p. 603

119) NCEHR, *op. cit*., p. 21

120) In december 2004, Quebec has reinforced its oversight process, see. S. Audy, *La surveillance continue del'éthique des projets de recherche: problématique et repères éthiques*, CLERUM, Montreal, 2002.

121) National Bioethics Advisory Commission, *op. cit.*

122) Downie, *op. cit*.

123) TCPS, article 1.2, the researcher or the supervisor can't assist the REB meeting and be present in the decision-making process.

124) A. Wood, C. Grady and E. Emanuel, *the crisis in human participants research: identifying the problems and proposing solutions,* President's commission Bio-ethics

125) J. E Bekelman, Y. Li and C.P. Gross, *Scope and impact of financial conflicts of interest in biomedical research, a systematic review,* 2003, 289 JAMA, 454

126) Hugely documented in Canadian literature, for instance Downie and Baird industry and the acadamy

127) J. Thompson, P. Baird and J. Downie, *The Olivieri report: the complete text of the report of the independent inquiry commissioned by the Canadian Association University Teachers,*Toronto: James Lorimer and Company, 2001

128) The use of placebo control for instance. It has be noted that it is not only specific to industry-funded research, as the US FDA considers placebo-control as the gold-standard.

129) The JAMA study showed an association between industry sponsorship and data-sharing as well as a significant association between industry-sponsorship and pro-industry conclusions.

130) Downie, *op. cit.* , p.13

131) Downie, *op. cit.*, p.14

132) Center on governance, University of Ottawa, *op. cit*., p.16

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Annex 2 – Interview guide

On your workplace

Present your organization
What is your annual budget? How many research participants?
What norms are you submitted to?/ What are the policies you set up? For which kind of research? According which process?
Which what other do you work/have links with? How do you work with them? Where do you meet? How often?

On research and research ethics in Canada
To have a more precise idea on how research ethics is implemented in Canada.
What assessment can be done?
Figures

What are, for you, the main goals of research ethics? Are there abuses that you know of?
How would you describe research ethics in Canada? (Organization, main actors, network, how many people involved?)
What are the main strengths? (Protection of participants, effectiveness...)
What are the main weaknesses? (Lack of coherence, redundancy…)

On governance of research ethics in Canada
Identification of the main problems and their impacts on participants and research.
How policies are built?
Solutions that can be proposed
Resistances

How would you describe the governance of research ethics in Canada? (non-system? A need for changes?) Do you think it's effective? Why?
Who are the main actors? What are their links? How do they work together?
What would you say about research ethics policies in Canada? What is the place of TCPS? How would you regard an accreditation system?
What are the main problems you can identify? What are your suggestions?
How would you evaluate governance? What in term of competitiveness?
What could be the US view on Canadian governance? Would you say the US regulations has authority on Canadian REBs?
Are authority and surveillance issues ?

Annex 3 - A changing environment for REBs

Department of health and human services, US Office of the Inspector General, *Institutional Review Boards: a time for reform,* 1998,p.5

A changing environment for IRBs		
Change	**Explanation**	**Key implications for IRBs**
Expansion of managed care	Emphasis on cost control and competition. Squeeze on research support for academic health center	Pressures to accommodate research sponsors who can provide research-related revenues for the parent institution. Increased difficulty in obtaining staff and other resources. More pressure on staff physicians to generate income, with less time available for voluntary commitments to IRBs.
Increased commercialization of research	Heightened industry role in sponsoring research. Sponsor emphasis on rapid product development.	Institutional and sponsor pressures for quick reviews. Sponsor shopping for customer focused IRBs. Added complexity on issues involving liability, academic freedom, and patient disclosure.
Proliferation of multi-center trials	Proliferation of trials spread across hundreds of sites, even across the world.	Diminished influence of “local” review. Flood of adverse-event reports to review. Lack of access to significant information concerning the status of ongoing research.
New types of research	Advances in biomedical research in the areas of gene-testing and gene therapy; increased research on mental health issues.	Need for new, highly specialized areas of expertise. Emergence of thorny ethical issues involving informed consent and appropriate research. Increased importance of having non-institutional board members.
Increased number of proposals	Intensified efforts to obtain government funding and to develop new products.	Significant increase in workloads. Without sufficient increases in staff and/or efficiency, less time is available to review initial protocols and to conduct continuing reviews of approved research.
Rise of patient consumerism	Increased consumer demand for access to research.	Presents major challenges in: Ensuring equitable recruitment of subjects Ascertaining local attitudes and values. Maintaining distinctions between therapy and research.

Summary

Background

Research ethics frames to protect participants and to promote fair and socially beneficial research. In Canada, there is no standardized oversight of research involving humans. Governance of this field is fragmented around various, actors, norms and processes. Challenges rise from this complex context.

Materials and methods

Research ethics is rarely evidence-based neither are governance processes. A qualitative approach was chosen. Primary analysis relies on institutional informations, laws and policies. Reports were used to have factual information on global processes and interactions. Peer-reviewed publications were used for in-depth analysis on precise points. Interviews with leading actors were conducted to validate, invalidate or re-frame conclusions and hypothesis drawn in the literature review.

Findings

Current governance of research ethics in Canada leaves some kinds of research with no ethics review. There is no leading standard or policy that apply to similar kinds of research. Standards are sometime contradictory leading to differentiated applications and frustration among the research community. The overall system relies on review ethics boards that are not resourced enough to assume all responsibilities they are given. Systemic conflict of interest shades over the legitimacy of the main guideline. Resistances of various actors appear, making difficult good governance of research ethics at pan-Canadian level. Initiatives exist at local level but remain inefficient on global scale. Similar structures and processes exist in Europe which may create similar challenges.

Future directions

Accreditation system of REBs is one possible solution. Biomedical research should be targeted first and social sciences have to develop their own model. Leadership and legitimacy have to be build to restore trust in research.

Keywords: research ethics – governance – review ethics boards – conflict of interest – legitimacy – Canada/Europe comparison.

Résumé

Contexte

L'éthique de la recherche encadre la recherche impliquant des êtres humains afin de les protéger tout en favorisant une recherche socialement juste et efficace. Au Canada, les recherches ne sont pas toute encadrées ni surveillées de la même façon. La gouvernance est fragmentée et construite autours de nombreux acteurs, de normes et de procédés. De nombreux défis émergent de cette situation.

Méthodes

Une approche qualitative a été favorisée en raison de la problématique étudiée. Elle repose sur une revue de littérature. Les sources primaires sont composées des informations institutionnelles ainsi que des lois et politiques. Les sources secondaires ont permis d'appréhender la problématique dans son ensemble et de construire hypothèses et analyse. Des entretiens semi-directifs ont été réalisés avec les acteurs principaux afin d'infirmer, valider ou modifier les conclusions obtenues à la suite de la revue de littérature.

Résultats

La gouvernance actuelle de l'éthique de la recherche laisse un nombre important de recherche sans surveillance. Aucun standard ou politique ne parvient à s'imposer comme légitime à l'ensemble des recherches. Ces standards sont parfois contradictoires, ce qui peut conduire à une application différenciée ainsi qu'à une frustration des membres de la communauté scientifique. Trop de responsabilités sont déchargées sur les Comités d'Ethique de Recherche que ne disposent pas de ressources suffisantes pour les assumer. Un conflit d'intérêt systémique entache la légitimité de l'EPTC, pourtant perçus à ses débuts comme à même d'harmoniser la gouvernance. Différentes stratégies sont élaborées par les acteurs rendant difficile une bonne gouvernance à l'échelle canadienne. Des initiatives locales existent mais sont inefficaces à une échelle globale. Des structures et procédés similaires se mettent en place en Europe ce qui peut laisser supposer que certains enjeux canadiens peuvent avoir un écho en Europe.

Recommendations

Le système d'accréditation est une réponse possible et devrait se concentrer en priorité sur la recherche biomédicale. Les sciences sociales doivent construire leur propre modèle. La légitimité et la confiance doivent être restaurées.

Mots-clefs: éthique de la recherche – gouvernance - comité d'éthique de la recherche – conflit d'intérêt – légitimation – comparaison Canada/Europe.