



**REGULATORY FRAMEWORK
IN HEALTH RESEARCH AT THE
McGILL UNIVERSITY HEALTH CENTRE**

Document produced jointly
by the Division of Clinical Research of the
Research Institute of the McGill University Health Centre
and by the Research Ethics Office of the
McGill University Health Centre
in response to requirements set forth by the
*Plan d'action ministériel en éthique de la recherche
et en intégrité scientifique* (MSSS, June 1998) and by the
Fonds de la recherche en santé du Québec (FRSQ, April 2000)

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Foreword

The McGill University Health Centre (MUHC) represents the first and largest voluntary merger of university teaching hospitals in the country. Merged in 1999, the five partners of the MUHC include the McGill University Faculty of Medicine, three institutions serving adult patients (the Montreal General Hospital, the Royal Victoria Hospital which includes the Montreal Chest Institute, and the Montreal Neurological Hospital), as well as one institution serving children, the Montreal Children's Hospital, together with their respective research institutes, grouped together as the Research Institute of the MUHC. A leading edge academic health centre, the MUHC benefits from its association with one of the country's top medical schools, McGill University, integrating patient care, teaching and research, as its tripartite mission.

The present document entitled Regulatory Framework in Health Research at the McGill University Health Centre ⁽¹¹⁾ (*Cadre réglementaire de la recherche en santé au Centre universitaire de santé McGill*) was produced in response to the requirements set forth by the Ministry's Action Plan in Research Ethics and Scientific Integrity ⁽¹²⁾ (*Plan d'action ministériel en éthique de la recherche et en intégrité scientifique*) published by the *Ministère de la Santé et des Services Sociaux* in June 1998. It also meets the demands of the *Fonds de la recherche en santé du Québec*, in April 2000, addressed to the research establishments funded by the FRSQ, and requiring that they develop and implement a *Cadre réglementaire de la recherche en santé dans les établissements universitaires de santé du Québec* ⁽¹³⁾.

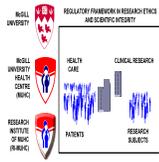
This Regulatory Framework is the grouping of policies, regulations and procedures, contracts and agreements ⁽¹⁻¹⁰⁾, most of which are already established and operating within the founding health institutions and research institutes that have become the MUHC, and which adhere to the guidelines of the *Plan ministériel* as well as to international guidelines pertaining to research ethics and scientific integrity. The development of the Regulatory framework was an opportunity to harmonize the Policies and Procedures ensuring the review of research projects, the transparency of research activities, the protection of human research subjects, the integrity of research ethics committees and control over investigational drugs, across the diversity of the MUHC and its Research Institute.

The development of the MUHC's regulatory framework is the result of an *ongoing* collaborative consultation process involving members of the Boards of Directors of the MUHC and its Research Institute, the Office of Research Ethics, the Office of Technology Transfer, and the Office of Clinical Contracts of the Research Institute of the MUHC, and the McGill University Faculty of Medicine. The adoption and implementation of the Regulatory Framework in Health Research at the MUHC is an ongoing process which will integrate novel guidelines in research ethics and scientific integrity as they will emerge.

Regulatory Framework in Health Research at the McGill University Health Centre: Summary

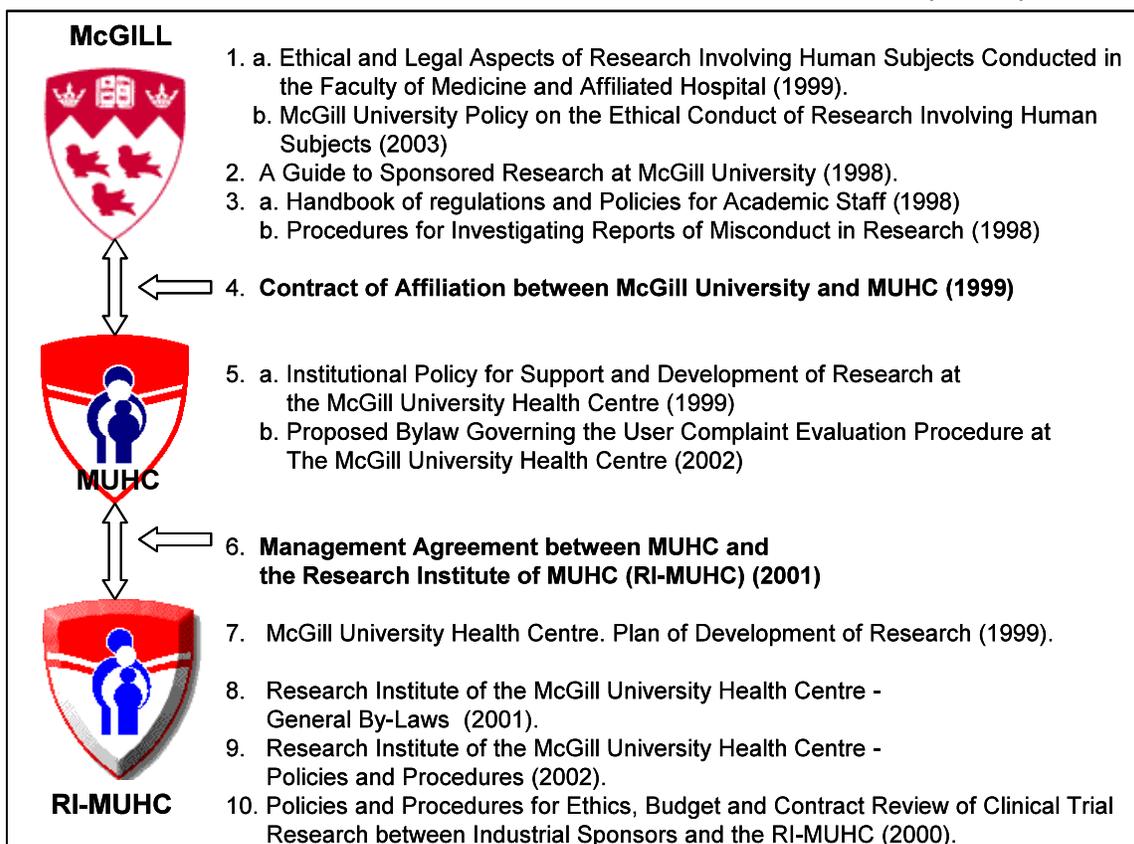
The *Cadre réglementaire de la recherche en santé au Centre universitaire de santé McGill*, in essence, comprises virtually all the policies and regulations (procedures, documents, contracts, agreements and resolutions) which apply in research ethics and scientific integrity, approved by (or submitted for approval to) diverse Boards and Committees at the MUHC and its Research Institute. These also comprise the whole spectrum of regulatory guidelines at the provincial, national and international levels, governing research ethics and scientific integrity. To meet the requirements set forth by the FRSQ and the MSSS, the Regulatory Framework in Health Research at the McGill University Health Centre is as follows:

The documents which laid the foundation of the Regulatory Framework are presented in Section 1, entitled *Foundation Documents of the MUHC's Regulatory Framework*. These documents are Policies and Procedures ratified by the McGill University Faculty of Medicine and by the Research Institute of the MUHC and which are integrated via a Contract of Affiliation between McGill University and MUHC and via an Agreement between the MUHC and the Research Institute of the MUHC. The contents of the foundation documents, pillars of this regulatory framework, are listed to substantiate the reaching of standards of excellence promoted by the Ministry's Plan and by international guidelines in research ethics and scientific integrity, ensuring the protection of human research subjects and the transparency in the management of research activities at the MUHC.



In Section 2, the measures dictated by the *Plan ministériel* for the health establishment to develop a *Cadre réglementaire en éthique de la recherche et en intégrité scientifique*, are addressed sequentially by referring to specific sections for the MUHC's Regulatory Framework in order to demonstrate its compliance with the Ministry's Plan.

REGULATORY FRAMEWORK IN RESEARCH ETHICS AND SCIENTIFIC INTEGRITY AT THE MCGILL UNIVERSITY HEALTH CENTRE (MUHC)



The Regulatory Framework in Health Research at the McGill University Health Centre, depicted in the diagram above, is based on the foundation documents. A first series of documents ⁽¹⁻³⁾ is constituted by the Policies and Procedures established by the McGill University Faculty of Medicine, and which govern: the ethical and legal aspects of research involving human subjects; the policies for Clinical Trials of investigational drugs and treatments sponsored by industry; and the regulations and policies dictated to investigators on scientific integrity (conflicts of interest, scientific or ethical misconduct).

A Contract of Affiliation between the McGill University and the MUHC ⁽⁴⁾ identifies, among other clauses, the obligation of the University to collaborate with the MUHC to promote high quality patient care, teaching and research. For its part, the MUHC has endorsed an Institutional Policy for Support and Development of Research at the MUHC ⁽⁵⁾, and, in order to fulfill its mission, the MUHC will institute efficient mechanisms to protect research, ensure its development, and maximize the impact of health research (basic biomedical research, clinical research, evaluative research, health care research, technology transfer). Thus, in conjunction with the McGill University Faculty of Medicine, the MUHC fully agrees to support its Research Institute.

In return, according to a Management Agreement between the McGill University Health Centre and the Research Institute of the McGill University Health Centre ⁽⁶⁾, the latter agrees to ensure the development of research within the MUHC and, in any particular project, the Research

Institute shall be responsible for compliance with the policies established by the McGill University Faculty of Medicine with regard to research ethics and scientific integrity ⁽¹⁻³⁾, by the *Fonds de la recherche en santé du Québec* (FRSQ), by the Canadian Institutes for Health Research (CIHR), as well as by all other regulatory agencies ensuring the protection of human research subjects.

The Research Institute has ratified a Plan of Research Development ⁽⁷⁾ identifying its mission and its research axes, has drafted General By-Laws ⁽⁸⁾ and has approved policies and procedures on Good Clinical Practice and control of investigational drugs ⁽⁹⁾ as well as Policies and Procedures governing the ethics, legal and financial reviews of research projects involving human subjects ⁽¹⁰⁾.

The documents laying the foundation of the *Cadre réglementaire de la recherche en santé au CUSM*, have been approved through resolutions by the Boards of Directors of the MUHC and its Research Institute. After the approval of the General By-Laws of the Research Institute of the MUHC ⁽⁸⁾ and of the Management Agreement between the MUHC and the Research Institute of the MUHC ⁽⁶⁾, the interactions governing the Regulatory Framework came into effect. The Regulatory Framework in Health Research at the MUHC was adopted by the Board of Directors of the MUHC on August 31, 2001.

**Foundation Documents of the Regulatory Framework in
Health Research at the McGill University Health Centre**

1.
 - a. McGill University Ethical and Legal Aspects of Research Involving Human Subjects Conducted in the Faculty of Medicine and Affiliated Hospitals – Policies and Procedures, McGill University Faculty of Medicine (1993): revised 1994, revised 1999, revised 2004, revised 2007.
 - b. McGill University Policy on the Ethical Conduct of Research Involving Human Subjects, approved by the Board of Governors, McGill University, Version 1 2003, Version 2 2007.
2. A Guide to Sponsored Research at McGill University, McGill University, 1998.
3.
 - a. Handbook of regulations and Policies for Academic Staff, McGill University, Montreal, 1998.
 - b. Procedures for Investigating Reports of Misconduct in Research, McGill University, 1998.
4. Contract of Affiliation between McGill University and MUHC, approved by the Board of Directors of the MUHC, November 22, 1999, signed November 26, 1999.
5.
 - a. Institutional Policy for Support and Development of Research at MUHC, approved by the Board of Directors of the MUHC, June 1999.
 - b. Proposed Bylaw Governing the User Complaint Evaluation Procedure at The McGill University Health Centre, approved by the Board of Directors of the MUHC, 2002.
6. Management Agreement Between the McGill University Health Centre and the Research Institute of the McGill University Health Centre, approved by the Board of Directors of the MUHC, August 2001
7. McGill University Health Centre. Plan of Development of Research. Document submitted to the FRSQ (1999). Emil Skamene, Scientific Director, RI-MUHC
8. Research Institute of the McGill University Health Centre - General By-Laws, approved by the Board of Directors of the MUHC, August 2001.
9. Research Institute of the McGill University Health Centre – Human Research Standard Operating Procedures (approved by the RI MUHC Board of Directors on June 19, 2008 and the MUHC Board of Directors on September 16, 2008)
10. Policies and Procedures for Ethics, Budget and Contract Review of Clinical Trial Research between Industrial Sponsors and the Research Institute of the McGill University Health Centre, revised October 24, 2000, approved by the Board of Directors of the MUHC, June 29, 2000.



1.1a McGill University Ethical and Legal Aspects of Research Involving Human Subjects Conducted in the Faculty of Medicine and Affiliated Hospitals.

McGill University Ethical and Legal Aspects of Research Involving Human Subjects Conducted in the Faculty of Medicine and Affiliated Hospitals - Policies and Procedures, 1993, Faculty of Medicine, McGill University; Revised April 1994, and August 1999 as a result of the Tri-Council Policy Statement; approved by the Board of Directors of the MUHC, May 26, 2000.
<http://www.medicine.mcgill.ca/research/irb/documents/P&P1999.Word6.doc>

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 - C Declaration of Helsinki; D Belmont Report;
 - E OPRR report 1991 (U.S.) Title 45, Code of Federal Regulations, Part 56; Title 21, Code of Federal regulations; Comparison of DHHS and FDA Regulation

- F *Code Civil du Québec, 1994*
- G *Loi sur les services de santé et les services sociaux L.R.Q
1991 Chapitre 42 (excerpts)*
- H *Acte respectant l'accès aux documents détenus par les organismes publics et la
protection de l'information personnelle (excerpts)*
- I List of REB Members
- J Procedures and Application Forms for Applicants and REBs.

Notes: The operating procedures of the MUHC Research Ethics Boards are based on this document. Prior to May 26, 2000 the operating procedures (*règles de fonctionnement*) were subject to the same McGill Policies and Procedures approved as noted above for each of the following hospitals : MCH, MCI, MGH, MNH and RVH. The operating procedures in force for the year 1999 were presented in the Research Ethics Boards Annual Report 1999.

McGill University and its teaching hospitals have all successfully obtained during 2003 individual Federal-wide Assurances (FWAs) from the US Office for Human Research Protection (OHRP). As required by these Federal-wide Assurances, the University and each Hospital must have side agreement signed and available for the OHRP should they request to see them. The Federal-wide Assurance replaces the old Multiple Project Assurance system that the University held for the hospitals, as well as the required Inter-Institutional Agreements that were signed previously between the Faculty and the Hospitals.

The MUHC holds an approved Federal-wide Assurance of Protection for Human Subjects (FWA) negotiated with the US Department of Health and Human Services (DHHS) on file with the Office for Human Research Protections. An approved FWA is mandatory to conduct research supported in whole or in part by the US Public Health Service (PHS). The nine MUHC REBs are registered under the FWA and provide review of PHS research according to the "Terms of the FWA for Institutions Outside the United States". The investigator may submit the US federally funded study for ethics review to an MUHC REB and have the funds administered by the RI-MUHC Accounting Office. However, the MUHC delegates to the Institutional Review Board (IRB) of the McGill University Faculty of Medicine the responsibility to review multicentre clinical trials to be conducted in McGill University affiliated hospitals, with one or more sites residing outside of the MUHC's jurisdiction.



1.1b McGill University Policy on the Ethical Conduct of Research Involving Human Subjects

McGill University Policy on the Ethical Conduct of Research Involving Human Subjects, 2003.
Faculty of Medicine, McGill University, approved by the Board of Governors of McGill University, April 28, 2003. <https://upload.mcgill.ca/rgo/McGillHSPolicy.doc>

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APPENDIX II - McGill Approved Research Ethics Boards

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Notes:

This policy articulates the administrative structures and procedures for the ethical review of human subject research at McGill University. The purpose of the procedures described in this policy is to promote and facilitate the conduct of human subject research in a manner consistent with the highest scholarly and ethical standards. This policy supercedes any existing University policies with respect to the ethical review of human subject research.

This policy is supplemented by a set of statements and guidelines regarding ethical research involving human subjects, documented in Appendix I. Researchers are directed to these documents for specific guidelines and regulations regarding the ethical conduct of research involving human subjects and discussion of issues such as privacy and confidentiality, free and informed consent, inclusion in research, research involving aboriginal peoples, clinical trials and human genetic research. Researchers are responsible for knowing about and adhering to the standards articulated therein.

All research projects involving the use of human subjects conducted at or under the auspices of McGill University require ethics review and approval by a McGill Research Ethics Board (REB) or an REB of a McGill affiliated hospital or an REB recognized by a formal agreement with the University, before the research may begin.

Researchers must be familiar with and comply with this policy and other ethical guidelines relevant to their research discipline. It is the responsibility of the researcher to obtain ethical approval as described in this policy for any project involving human subjects before starting the research. If there is any uncertainty about whether the research needs ethical review and approval, the researcher should consult the appropriate REB for advice.

All members of a research team who conduct research under the supervision of others also bear personal responsibility for the ethical conduct of research with human subjects. The Principal Investigator has the responsibility to ensure that the members of the research team comply with the provisions of this policy. Principal investigators should ensure that the members of the research team are aware of the contents of this policy and of other applicable ethical guidelines that are relevant to their responsibilities. Researchers must ensure that all individuals under their supervision have the training and competence needed to carry out their responsibilities in an ethical manner.



1.2 A Guide to Sponsored Research at McGill University

A Guide to Sponsored Research at McGill University, Published by the Faculty of Graduate Studies and Research, McGill University, Spring 1998.

<http://www.mcgill.ca/researchoffice/policies/sponsored/>

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- Policy on Ethics in Research and Research Training
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 - Internal Application for Contract
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 - Report of Invention
 - International projects checklist
-

Notes:

The Guide to Sponsored Research at McGill University addresses several issues of the *Plan ministérielle*, such as mandatory declaration of research activities, investigating reports of scientific and ethical misconduct, and managing conflicts of interest. This document also addresses the mandatory declaration of inventions or innovations by McGill University affiliated investigators seeking commercialization. The latter subject is part of the University Policy on Inventions and Patents developed by the Office of Technology Transfer (OTT) at the Faculty of Graduate Studies and Research, McGill University. The policy applies to McGill University affiliated hospitals, including the MUHC. The OTT has implemented a registry for inventions and procedures ensuring technology transfer, and reports annually to Scientific Directors in each of the MUHC's hospitals.

At the McGill University Health Centre, in compliance with the *Contract of Affiliation between McGill University and MUHC* ⁽⁴⁾ and with the *Management Agreement between the McGill University Health Centre and the Research Institute of the McGill University Health Centre* ⁽⁶⁾, all MUHC investigators must abide by the McGill University Policies and Procedures pertaining to the mandatory declaration of conflicts of interest in industry-sponsored research projects, and are subject to those disciplinary actions contemplated in cases of scientific misconduct when conflicts of interest have not been declared and/or resolved ^(2,3) (refer to Annex 2, p. 38-43, and Annex 3, p.63-65).

The McGill University OTT, the MUHC and its Research Institute, maintain a collaborative agreement in hiring a human resource dedicated to the Institution (MUHC) and supported by the OTT staff. Intellectual property (IP) is shared by the McGill University, by the Research Institute of the MUHC, and by the investigator, and is assigned to the Institution with respect to commercialization.



1.3a Handbook of Regulations and Policies for Academic Staff

Handbook of Regulations and Policies for Academic and Librarian Staff, Published by the Faculty of Graduate Studies and Research, McGill University, Spring 1998.
<https://upload.mcgill.ca/secretariat/edition2001.doc>

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Chapter 1	Regulations Relating to the Employment of Academic Staff
Chapter 2	Regulations Relating to the Employment of Librarian Staff
Chapter 3	Regulations on Sabbatical Leaves, Guidelines for Leaves of Absence, Policy Concerning Sabbatical Leaves, Leaves of Absence and Tenure Consideration, Maternity Leave Regulations, Parental Leave Regulations
Chapter 4	Regulations Concerning the Retirement of Academic Staff and of Librarian Staff
Chapter 5	Regulations Concerning Complaints of Sexual Harassment
Chapter 6	Regulations on Research Policy
Chapter 7	Regulations on Consulting and Similar Activities by Academic and Librarian Staff
Chapter 8	University Policy on Inventions and Patents
Chapter 9	Policy on Conflict of Interest and Duty of Loyalty
Chapter 10	Regulations Governing Conflicts of Interest in Proprietary Research
Chapter 11	Policy on Conflicts of Interest in Academic Supervision and Evaluation
Chapter 12	Policy on Political Candidacy
Chapter 13	University Policy on the Non-Performance of Academic Duties During a Legal Strike
Chapter 14	Policy on Copyright of Written Works
Chapter 15	Code of Conduct for Users of McGill Computing Facilities
Chapter 16	Policy on Research Ethics
Chapter 17	Policy on Software Developed by McGill University Faculty, Academic Staff and Students

Notes:

The *Handbook of Regulations and Policies for Academic Staff* contains several clauses which are already present in the *Guide to Sponsored Research at McGill University*, but dictates more specific guidelines for academic staff with respect to managing conflicts of interest.



1.3b Procedures for Investigating Reports of Misconduct in Research

McGill University Faculty of Medicine Procedures for Investigating Reports of Misconduct in Research. Faculty Executive Approval September 15, 1998; Mandated by Vice Principal (Research) January 21, 1999. <http://www.med.mcgill.ca/research/>
(Click on *Misconduct in Sciences*)

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- 1 Scientific Misconduct (definitions)
- 2 Applicability
- 3 The Initial Report of Alleged Misconduct
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- 5 Investigation Committee
- 6 Actions by the University

Notes:

This document has been developed by the McGill University Faculty of Medicine (Approval on September 15, 1998) to ensure compliance with the policies set forth by the *United States Department of Health and Human Services* (PHS) pertaining to *Regulation on Handling Allegations of Scientific Misconduct* (42 CFR, Part 50, subpart A). Whereas these policies are not in conflict with the federal Tri-Council Policy Statement on "*Integrity in Research and Scholarship*" , they are however much more detailed.

The procedures presented in this document apply to all alleged cases of scientific misconduct by members of the Faculty of Medicine and affiliated institutions, including MUHC sites.



1.4 Contract of Affiliation between McGill University and MUHC



Contract of Affiliation between McGill University and McGill University Health Centre,
Approved by the Board of Directors of the MUHC, in accordance with a resolution adopted by its
Executive committee on November 22, 1999; Signed on November 26, 1999.
<http://ww2.mcgill.ca/muhc-ri/index.htm> (Click on *Policies, Regulations and Guidelines*)

Contents of the Contract

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- 10 Appointment of Medical or Scientific Staff
- 11 Management of the Contract
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- 13 Expenses
- 14 Conciliation
- 15 Term
- 16 Review Mechanism
- 17 Notice to Authorities
- 18 Effective Date

Notes:

The present document constitutes a Contract of Affiliation between the McGill University and the McGill University Health Centre, having as its goal the conduct of research and the training of certain students in the health field attending the University. The Contract engages the University to collaborate with the Centre to promote high quality patient care, teaching and research.



1.5a Institutional Policy for Support and Development of Research at the MUHC

Institutional Policy for Support and Development of Research at the MUHC, document approved by the Board of Directors of the MUHC, June 1999.

Summary of the Policy

- The Board of Directors affirms that research constitutes a crucial, integral part of the tripartite mission of the MUHC (clinical care, education, research).
- The MUHC endorses an Institutional Policy for Support and Development of Research, by instituting efficient mechanisms to protect, develop and maximize the impact of health research (basic, clinical, evaluative, and health care research, and technology transfer, etc).
- The organizational component of the MUHC which is responsible for its research mission is the Research Institute of the MUHC. The Scientific Director is responsible for the elaboration of the Plan of Development of Research along multidisciplinary programmatic axes. Such plan must be approved by the MUHC Board of Directors.
- Other topics addressed in the policy include:
 - Integration of Research and Clinical Care
 - Recruitment and Retention of Research Faculty
 - Research Space
 - Foundations and Research Institute
 - Clinical Research and Clinical Contracts
 - Participation of Research Institute on MUHC Committees
 - Review of Research Policies
 - MUHC Research Council
 - International Review Teams
 - MUHC Research Institute Advisory Board

Notes:

The MUHC has endorsed an Institutional Policy for Support and Development of Research at the MUHC ^(5a), by instituting efficient mechanisms to protect research, ensure its development, and maximize the impact of health research (basic biomedical research, clinical research, evaluative research, health care research, technology transfer). The Institutional Policy for Support and Development of Research at the MUHC was developed by the Scientific Director of the RI-MUHC in collaboration with the Executive Committee of the RI-MUHC, the Central Administrative Committee of the MUHC, the Advisory Board of the RI-MUHC, and with the Clinical Directors of the MUHC. This document integrates the mission of the RI-MUHC with that of the MUHC. Thus, in conjunction with the McGill University Faculty of Medicine, the MUHC fully agrees to support its Research Institute.



1.5b Bylaw Governing the User Complaint Evaluation Procedure at The McGill University Health Centre

Bylaw Governing the User Complaint Evaluation Procedure at The McGill University Health Centre, March 2002, document approved by the Board of Directors of the MUHC, April 25, 2002.

http://www.intranet.muhc.mcgill.ca/corporate/Policies/policy_patient_complaint.pdf

The purpose of this bylaw (User complaint evaluation procedure) is to set out the procedure for evaluating complaints by the MUHC, in compliance with the *Act respecting health services and social services* (R.S.Q., c. S-4.2). This Bylaw fulfills an important requirement of the *Plan d'action* with regards to the protection of human research subjects (*Section A, mesures 10-11*; sections 2.4.2 and 2.4.3 of the Regulatory Framework). “The person who accepts to participate in research activities must benefit from the same rights given to a user receiving health care and services. Accordingly, health care establishments conducting research activities must apply the following measures: ... 10) ensure that persons participating in research activities benefit from the same rights given to users receiving health care and services, including the user complaint evaluation procedure; 11) report on the complaints filed by these persons according to procedures established by the *Loi sur les services de santé et les services sociaux*.”.

Sections of the Bylaw

- 1 General Provisions
- 2 Making and Receiving a Complaint
- 3 Processing of a Complaint by the Local Commissioner for the Quality of Care and Services
- 4 Processing of a Complaint Regarding a Physician, Dentist, Pharmacist or Resident
- 5 User Complaint File
- 6 Annual Report on the Application of the Complaint Evaluation Procedure and the Improvement of the Quality of Services
- 7 Final Provisions

Excerpts from the Bylaw

A user may make a written or verbal complaint. This complaint must be sent to the local commissioner for the quality of care and services. The local commissioner for the quality of care and services is responsible for applying the user complaint evaluation procedure.

All healthcare workers must provide the user with the information needed to obtain quick access to the services of the local commissioner for the quality of care and services.

At the user's request, the local commissioner for the quality of care and services must provide all information regarding application of the complaint evaluation procedure. Moreover, he/she must inform the user of the protection afforded by law to any person who is involved in the evaluation of a complaint.

Accordingly, the Executive Director must take the necessary steps to ensure that information about making and processing complaints is available to the public. The Executive Director of the institution must send the Board of Directors, as soon as possible, any report or recommendations received from the local commissioner for the quality of care and services pursuant to this bylaw.

The local commissioner for the quality of care and services must send the Board of Directors an annual report specifically describing the number of complaints received, rejected on summary evaluation, evaluated or abandoned, as well as the grounds for these complaints. The annual report must indicate the duration of the evaluations, the follow-up taken and the number of and grounds for complaints leading to recourse with the patient ombudsman. The annual report must also contain the local commissioner for the quality of care and services's recommendations for improving the quality of care and services provided. The report may contain any other recommendation the local commissioner for the quality of care and services deems appropriate.

The medical examiner must send the Board of Directors and, where applicable, the council of physicians, dentists and pharmacists, an annual report specifically describing the number of complaints transferred to him/her, the number of complaints he/she rejected on summary evaluation, the number of complaints he/she redirected in compliance with Sections 33 and 41, as well as the grounds for the complaints evaluated. The annual report must also contain the medical examiner's recommendations for improving the quality of care and services provided. The report may contain any other recommendation the medical examiner deems appropriate. A copy of this report must be sent to the local commissioner for the quality of care and services.

The review committee must send the Board of Directors and, where applicable, the council of physicians, dentists and pharmacists an annual report specifically describing the number of requests it received, the grounds for these requests, the decisions it rendered, as well as the time required to evaluate these requests. The annual report may also contain the review committee's recommendations for improving the quality of care and services provided. The report may contain any other recommendation the review committee deems appropriate. A copy of this report must be sent to the local commissioner for the quality of care and services as well as to the patient ombudsman.

The local commissioner for the quality of care and services, the medical examiner or the review committee must intervene immediately and in the manner deemed most appropriate when informed that a person who has made or who intends to make a complaint has suffered reprisals of any nature.



1.6 Management Agreement between the MUHC and the Research Institute of the MUHC



Management Agreement between McGill University Health Centre and the Research Institute of the McGill University Health Centre, approved by the Board of Directors of the MUHC, August 2001. <http://ww2.mcgill.ca/muhc-ri/index.htm> (Click on *Policies, Regulations and Guidelines*)

Summary of the Agreement

This Agreement stipulates that: " In any particular project, the Institute will set up structures which will allow the MUHC Board to carry out it's responsibility for compliance with the McGill University Ethical and Legal Aspects of Research Involving Human Subjects Conducted in the Faculty of Medicine, as well as with the policies governing research, the FRSQ and the Canadian Institutes for Health Research, and those of all other agencies from which it receives research funding, as well as those of any other agency that regulates its research activities. "

This Agreement was approved by the Board of Directors of the MUHC in August 2001.



1.7 Plan of Development of Research of the RI-MUHC

McGill University Health Centre - Plan of Development of Research. Submitted to the FRSQ in 1999 by Dr. Emil Skamene, Scientific Director of the RI-MUHC, for the FRSQ's *Programme des Centres et Instituts de recherche*, as a document entitled *Centre universitaire de santé McGill. Plan de développement de la recherche*.

Table of Contents

Section 1	Mission of the Establishment and the Specificity of Research Institute
Section 2	Organizational Structure of the MUHC Research Institute
Section 3	Axes of Centre - Links of Research with Clinical Practice, Education and Technology Transfer
Section 4	Detailed Axes-based Plan of Development
Section 5	Summary of Plan of Development
Section 6	Financial Summary and Budget Proposal
Section 7	MUHC Budget Proposal

Notes: This document presents the mission, organizational structure, research axes and plan of development of research at the Research Institute of the MUHC.



1.8 Research Institute of the McGill University Health Centre General By-Laws

Research Institute of the McGill University Health Centre - General By-Laws,
approved by the Board of Directors of the MUHC, August 31, 2001,
revised October 11, 2001.

Contents of the By-Laws

1	General Provisions	2	Name
3	Head Office	4	Seal
5	Fiscal Year	6	Corporate Structure
7	Meetings of Members		
8	Members of the Board of Directors		
9	Officers		
10	Executive Committee		
11	Council		
12	Auditor		
13	Audit Committee		
14	Investment Committee		
15	Promissory Notes, Cheques, etc		
16	Contracts, Agreements, etc		
17	Amendments		

Notes :

The Research Institute of the McGill University Health Centre (RI-MUHC) is constituted by the grouping together of the investigators and of the administration of the research centres of the establishments that have become the MUHC:

1. Montreal General Hospital Research Institute (MGH-RI);
2. Research Institute of the Montreal Children's Hospital (RI-MCH);
3. Research Institute of Royal Victoria Hospital (RI-RVH);
4. Research Centre of the Montreal Chest Institute (RC-MCI);
5. Montreal Neurological Institute (MNI).

The Research Institute of the McGill University Health Centre is integrated with the Health Establishment (MUHC) and has acquired its own Board of Directors. Its administrative structure inherited of an expansion of the Board of Directors of the Montreal General Hospital Research Institute, resulting in the representation of the five research centres of the RI-MUHC on the Board of Directors.



1.9 Research Institute of the McGill University Health Centre – Human Research Standard Operating Procedures (2008)

*Research Institute of the McGill University Health Centre – Human Research Standard
Operating Procedures*

Table of Contents

- 1 Development, Approval and Review of SOPs
- 2 Qualifications, Training and Task Delegation of the Research Team
- 3 Security, Confidentiality and Retention of Essential Study Documentation
- 4 The Study Protocol
- 5 The Informed Consent Form
- 6 Assessment of Study Feasibility
- 7 Subject Recruitment Process
- 8 Subject Consent Process and Follow-up
- 9 Adverse Event Management
- 10 Management of Study Data
- 11 Biological Specimen Management
- 12 Experimental Drug Management
- 13 The Study Review Process
- 14 Health Canada Requirements for Research involving an Experimental Drug
- 15 On-going Communication with the REB
- 16 Conflict of Interest
- 17 Dealing with Protocol Deviations (Exceptions and Violations)
- 18 Quality Assurance and Monitoring
- 19 Preparation for an Audit or Inspection
- 20 Study Closure

The RI MUHC Human Research Standard Operating Procedures (SOPs) were created in order to ensure the protection of human subjects participating in research, as well as the protection of the research team responsible for the conduct of a study. They apply to research involving human subjects at the MUHC. However, depending on the nature of the study, not all of these SOPs are applicable to all studies involving human subjects.

The generic version of these SOPs were the result of a successful collaborative effort between the Fonds de Recherche en Santé du Québec (FRSQ), four Quebec universities (McGill University, Université de Montréal, Université de Sherbrooke, Université Laval) as well as the 19 FRSQ-funded research centres. The goal of this collaboration was to create quality assurance material for research activity involving human subjects that occurs in publicly funded institutions in Quebec and applicable to both academic research projects as well as pharmaceutical and device regulated clinical trials. They reflect the current best practices in human research in accordance with Provincial and Federal regulations and guidelines.

The RI MUHC Human Research SOPs were adapted from generic versions provided by the FRSQ and customized for research involving human subjects at the RI MUHC. These SOPs resulted from a collaborative effort of RI MUHC Clinical Research Coordinators; RI MUHC Administration including MUHC Research Ethics Office, MUHC Pharmacy, RI MUHC Office of Clinical Contracts, and MUHC Environmental Health and Safety; as well as RI MUHC Investigators. The SOPs incorporate the standards and regulations from:

- The International Conference on Harmonization (ICH) Guidelines for Good Clinical Practices, 1996;
- Health Canada Therapeutic Products Directorate Food and Drug Regulations for Clinical Trials. Division 5. Canada Gazette Part II, Vol. 135, No. 13, June 2001;
- The Tri-Council Policy Statement; Ethical Conduct for Research Involving Humans; Medical Research Council of Canada; Natural Sciences and Engineering Council of Canada; Social Sciences and Humanities Research Council of Canada, August 1998;
- The US Food and Drug Regulations, Code of Federal Regulations Chapter 21 Part 11, April 2003;
- Quebec Laws and Regulations
- Quebec Standards proposed by the Ministry of Health (MSSS) and the FRSQ
- Regulatory Framework in Health Research at the MUHC, updated November 2007



1.10 Policies and Procedures for Ethics, Budget and Contract Review of Clinical Trial Research between Industrial Sponsors and the Research Institute of the McGill University Health Centre

Policies and Procedures for Ethics, Budget and Contract Review of Clinical Trial Research between Industrial Sponsors and the Research Institute of the McGill University Health Centre, revised October 24, 2000, approved by the Board of Directors of the MUHC, June 29, 2000. <http://ww2.mcgill.ca/muhc-ri/index.htm> (Click on *Policies, Regulations and Guidelines*)

Table of Contents:

1. Role of the Office of Research Ethics (REO) in the review of industry-sponsored clinical trial research
2. Role of the Office of Clinical Contracts (OCC) in the administrative review process of industry-sponsored clinical trial research
3. Procedures for investigators seeking Ethics, Budget and Contract approvals to initiate industry-sponsored clinical trials research projects
4. Policies regarding review of Contracts (Clinical Trial Letters of Agreements)
5. Policies regarding Budget review of industry-sponsored clinical trials research
6. Authorized signatures for approval of Contracts and Budgets
7. Policy regarding overhead charges on Industry-Sponsored clinical research contracts
8. Montreal Neurological Hospital and Montreal Neurological Institute Policies

Notes:

The McGill University Health Centre delegates to its Research Ethics Boards (REBs) the responsibility to review, and ensure that ethical principles are applied to, research involving human subjects. The MUHC has nine REBs, supported by the Office of Research Ethics headed by Dr. Denis Cournoyer. The REBs review clinical research projects across the MUHC sites, and all these ethics committees report to the Board of Directors of the MUHC.

The evaluation of scientific merit of research projects sponsored by industry, particularly with regard to clinical trials of investigational drugs and innovative treatments, is a mandatory requirement for their approval by the research ethics committees. Depending on the MUHC hospital site reviewing the research projects, the scientific evaluation is performed prior, or simultaneously, to the ethics evaluation, either by a designated Scientific Committee, or by internal and external members invited to assess the scientific validity of the research projects simultaneously with ethical acceptability.

Since December 1, 2000, the Research Institute has implemented procedures to review all contracts underlying industry-sponsored research projects, prior to their approval and signatures, to ensure their compliance with institutional policies. The Office of Clinical Contracts reviews proposed study budgets and payment schedules to ensure that any monies destined to the institution, the investigators and their teams, as well as any compensations to research subjects, be the object of declarations prior to signature of contracts.

Briefly, the Office of Clinical Contracts reviews and executes Clinical Trial Agreements, reviews the corresponding budgets to assess direct and indirect costs, as well as the reimbursement to hospital departments for services provided in the course of the study, ensures the recovery of institutional overhead fees by the RI-MUHC, and offers administrative support to the Office of Research Ethics in the recovery of review fees from Sponsors for the Ethics, Legal and Financial reviews of projects. The Office of Clinical Contracts has appointed members in each site to coordinate financial and legal reviews of research contracts between Industry and the RI-MUHC.

The financial evaluation also addresses the issue of potential conflicts interest in budgets allocated for clinical trials: the Office verifies the *Clinical Investigator Financial Disclosure Form* required by the FDA (US Food and Drug Administration). If the Office perceives potential conflicts of interest or if industry-sponsored research contracts offer an incentive bonus (*finder's fee*) or excessive gratification for recruitment of subjects, the Office of Clinical Contracts must notify the Office of Research Ethics of such potential conflicts of interest.

2. Regulatory Framework in Research Ethics and Scientific Integrity: Measures Dictated by the *Plan ministériel*

Note: sections outlined in boxes are the recommendations of the FRSQ (in French) for implementation of the Ministry's Plan of Action in Ethics within health care establishments (sections 1 to 18)

2.1 Adoption of the Regulatory Framework

- 1) Les établissements et les organismes du réseau de la santé et des services sociaux où se déroulent des activités de recherche doivent adopter un cadre réglementaire pour les activités de recherche. Ce cadre devra établir des responsabilités explicites et un mode de fonctionnement équitable et transparent.
Le cadre devra s'harmoniser, à titre de référence, avec les lignes directrices des organismes de subvention québécois et le guide des trois conseils de recherche fédéraux. Au minimum, il devra contenir des normes particulières portant sur les éléments suivants :
 - La protection des personnes;
 - La déclaration obligatoire des activités de recherche;
 - Le traitement des cas d'inconduite scientifique et de manquement à l'éthique;
 - La gestion des conflits d'intérêts, de la double rémunération et de l'incorporation des chercheurs;
 - La gestion financière et le coût des projets de recherche;
 - La gestion des banques de données et des dossiers de recherche;
 - Le contrôle des médicaments d'expérimentation;
 - Le fonctionnement des comités d'éthique de la recherche

The Regulatory Framework in Health Research at the McGill University Health Centre, in essence, comprises virtually all the policies and regulations (procedures, documents, contracts, agreements and resolutions) which apply in research ethics and scientific integrity, approved by (or submitted for approval to) diverse Boards and Committees at the MUHC and its Research Institute. These also comprise the whole spectrum of regulatory guidelines at the provincial, national and international levels, governing research ethics and scientific integrity. The development of the MUHC's regulatory framework is the result of an *ongoing* collaborative consultation process involving members of the Boards of Directors of the MUHC and its Research Institute, the Office of Research Ethics, the Office of Technology Transfer, and the Office of Clinical Contracts of the Research Institute of the MUHC, and the McGill University Faculty of Medicine.

The documents laying the foundation of the *Cadre réglementaire de la recherche en santé au CUSM*, have been approved through resolutions by the Boards of Directors of the MUHC and its Research Institute. After the approval of the General By-Laws of the Research Institute of the MUHC ⁽⁸⁾ and of the Management Agreement between the MUHC and the Research Institute of the MUHC ⁽⁶⁾, the interactions governing the Regulatory Framework came into effect. The

Regulatory Framework in Health Research at the MUHC was adopted by the Board of Directors of the MUHC on August 31, 2001.

2.1.1 Protection of Human Research Subjects

The McGill University Health Centre, through its process of governance, delegates to its Research Ethics Boards (REBs) the responsibility to ensure that ethical principles are applied to research involving human subjects. All research projects conducted on human subjects under the MUHC's jurisdiction require approval, or deferral, by a MUHC REB, or, under certain conditions, by the McGill Faculty of Medicine Institutional Review Board (IRB), and must be conducted in compliance with regulatory guidelines and laws applicable in North America.

In accordance with the *Management Agreement between the McGill University Health Centre and the Research Institute of the McGill University Health Centre* ⁽⁶⁾ (approved by the Board of Directors of the MUHC, August 2001), for all research projects the Institute shall be responsible for compliance with the policies established by McGill University with regards to research ethics and scientific integrity ⁽¹⁻³⁾ (*McGill University Ethical and Legal Aspects of Research Involving Human Subjects Conducted in the Faculty of Medicine*), and with other guidelines of the regulatory framework established by governmental, regulatory and granting agencies, such as the FRSQ, the Tri-Council and the Canadian Institutes for Health Research.

Conducting genetic research and DNA banking raises specific questions concerning protection for the rights of research subjects, and respect for their private information held by the institution. Participation in such specialized research introduces the possibility to discover new information about the health of the person, the person's family history and the person's lifestyle. Investigators conducting genetic research at the MUHC must be familiar with the document "*Best Practices for Protecting Privacy in Health Research*" published by the Canadian Institutes of Health Research: <http://www.irsc.gc.ca/e/29072.html>

The free and informed consent discussion involving genetic research including collection of material for tissue banking and/or data repositories must be thorough and unhurried. Obtaining genetic information requires the person's written consent, and access to professional genetic counselling must be available to MUHC research subjects both pre- and post-signing of the consent document. The Faculty of Medicine IRB and the REBs of the McGill affiliated hospitals adopted "*Guidelines for a Consent Document for Genetic Research and DNA Banking*" published by Le Réseau de médecine génétique appliquée du FRSQ in force at the MUHC: <http://www.medicine.mcgill.ca/research/irb/documents/Genetic%20consent.doc>

In compliance with Section 1.2 of Annex 1b, *McGill University Policy on the Ethical Conduct of Research Involving Human Subjects, 2003*,

" Researchers have the primary responsibility to ensure that their research is carried out in an ethical manner. They are responsible for the protection of the rights and welfare of the human research subjects.

Researchers must be familiar with and comply with this policy and other ethical guidelines relevant to their research discipline. It is the responsibility of the researcher to obtain ethical approval as described in this policy for any project involving human subjects before starting the research. If there is any uncertainty about whether the research needs ethical review and approval, the researcher should consult the appropriate REB for advice."

2.1.2 Mandatory Declaration of Research Activities

The mandatory declaration of research is an issue regulated by several clauses contributing to the *Cadre réglementaire de la recherche en santé au CUSM*.

Obligation to comply with University Policies and Procedures in Research Ethics and Scientific Integrity: In compliance with the *Management Agreement between McGill University Health Centre and Research Institute of the McGill University Health Centre*⁽⁶⁾, the latter agrees to ensure development of research at the MUHC, and agrees, for any research project, to comply with the McGill University Faculty of Medicine policies pertaining to research ethics and scientific integrity⁽¹⁻³⁾.

Obligation for investigator to submit research protocol to Research Ethics Board in order to have approval to conduct research on human subjects: In compliance with Annex 1a, *McGill University Ethical and Legal Aspects of Research Involving Human Subjects Conducted in the Faculty of Medicine and Affiliated Hospitals – Policies and Procedures* (revised 2007; approved by the MUHC Board of Directors, May 22, 2007), section III. C p. 22, entitled *Summary of Investigator's Responsibilities*, stipulates that:

" An investigator wishing to conduct research on human subjects ... must submit a research protocol approved by a departmental chair, a departmental committee, or a specifically authorized individual within the Hospital, for review by the investigator's institutional REB. "

In compliance with Annex 1b, *McGill University Policy on the Ethical Conduct of Research Involving Human Subject, 2003*,

"All research projects involving the use of human subjects conducted at or under the auspices of McGill University require ethics review and approval by a McGill Research Ethics Board (REB) or an REB of a McGill affiliated hospital or an REB recognized by a formal agreement with the University, before the research may begin."

Interdiction to not declare research activities: The *Handbook of Regulations and Policies for Academic Staff*, McGill University, 1998 (Annex 3), stipulates that:

" The University does not allow its staff or students to be engaged in secret research on University premises or using University facilities ", Chapter 6, *Regulations on Research Policy*, paragraph 1.

This policy applies to MUHC hospitals affiliated to McGill University, given the obligation of RI-MUHC investigators to comply with University policies and procedures (Annex 6 of the Regulatory Framework in Health Research at the MUHC).

Obligation to declare clinical trial research activities: The mandatory declaration of research activities is also stipulated in Annex 14, letter sent to MUHC investigators in November 2000, stating that:

" At its June 29, 2000 meeting, the MUHC Board approved a minimum of 30% overhead fee applied on direct costs of industry sponsored clinical research contracts... All clinical trial projects carried out at the MUHC sites must be reviewed by the MUHC Office of Research Ethics and administered by one of the hospital entities, or reviewed by the McGill Faculty of Medicine IRB and administered by McGill University."

This policy is also promoted in Annex 10, *Policies and Procedures for Ethics, Budget and Contract Review of Clinical Trial Research between Industrial Sponsors and the Research Institute of the McGill University Health Centre* (revised October 24, 2000; approved by the

Board of Directors of the MUHC, June 29, 2000), this information being in the public domain on the RI-MUHC Web Site at <http://ww2.mcgill.ca/muhc-ri/index.htm> (Click on Policies, Regulations and Guidelines).

Obligation to declare inventions and patents: *The Handbook of Regulations and Policies for Academic Staff*, McGill University, 1998 (Annex 3), stipulates that:

" All members of the University are required to report all of their Innovations made in the course of carrying out University duties..." chapter 8, *University Policy on Inventions and Patents*, paragraph 6.

Obligation to declare research on human biological material:

At the MUHC research using human biological material is subject to the "Guidelines for management of data and tissue banks" described by "Amendment March 2007", as Appendix M to the policy document entitled: "McGill University Ethical and Legal Aspects of Research Involving Human Subjects Conducted in the Faculty of Medicine and Affiliated Hospitals - Policies and Procedures" that is Foundation Document 1.1a of the "Regulatory Framework in Health Research at the McGill University Health Centre".

Laboratory Directors at the MUHC are often approached by investigators interested in conducting research on human material (organ, tissue, blood, body fluids, or other substances) obtained during the course of care. The Office of Research Ethics offered clarification and guidelines concerning such requests. These guidelines stipulate that: " Any research project involving human subjects must be reviewed and approved by an MUHC Research Ethics Board (REB), or, under certain circumstances, by the Faculty of Medicine Institutional Review Board (IRB), when: the study is conducted within the MUHC; the recruitment to the study occurs within the MUHC; the study is conducted by MUHC staff, whether at an MUHC site or another site (Tri-Council Policy Statement, Article 1.2). The Quebec Civil Code, 1994 (QCC) imposes legal limitations to the use of human material for research purposes. Article 22 (QCC) requires that free and informed consent be obtained from every person from whom material will be used for research purposes. Article 24 (QCC) requires that consent to any type of research be given in writing. It follows from these two Articles, and other relevant codes and regulations, that specimens obtained during the course of a previous research study can be used for subsequent research only if the latter study falls within the scope of the original consent." Such new use of stored research specimens is also conditional to approval of an REB. Recognizing that the above-mentioned legal and ethical criteria for human subjects research may not be widely known or well understood, the MUHC Office of Research Ethics forwarded a memo to Laboratory Directors to ensure compliance with the law and regulations by requiring that investigators document valid approval of an MUHC REB before permitting the use of human material for research purposes (refer to Annex 15, May 10, 2000).

2.1.3 Investigating Reports of Scientific and Ethical Misconduct

Investigating reports of scientific misconduct is dealt with in Annex 3. (refer to Annex 3.a, chapter 9, p.63 *Policy on Conflict of Interest and Duty of Loyalty*, sections 3 and 4, "From Conflict of Interest to Professional Misconduct" and "Management of Conflicting Situations"; Annex 3.a, chapter 16, *Policy on Research Ethics*, sections 5 and 10, "The Duty of honesty and Integrity" and " Disciplinary Action and Grievance". Moreover, Annex 3.b deals rigorously with investigations on reports of scientific misconduct. This document was developed by the McGill

University Faculty of Medicine (approval on September 15, 1998) to ensure compliance with guidelines dictated by the United States Department of Health and Human Services (PHS) concerning Policies and Procedures for any alleged scientific misconduct (Regulation on Handling Allegations of Scientific Misconduct [42 CFR, Part 50, subpart A]). Whereas these policies are not in conflict with the federal Tri-Council Policy Statement on "Integrity in Research and Scholarship", they are however much more detailed. The procedures presented in this document apply to all alleged cases of scientific misconduct by members of the Faculty of Medicine and affiliated institutions, including MUHC sites.

Investigating reports of ethical misconduct is addressed in Section 4.9 of Annex 1b, McGill University Policy on the Ethical Conduct of Research Involving Human Subjects, 2003, pertaining to the Non Compliance with policies or procedures for research involving human subjects, as follows:

“Instances of noncompliance with policies or procedures for research involving human subjects should be brought to the attention of the Chair of the appropriate REB for review and resolution. When deemed appropriate, serious instances of noncompliance will be forwarded to the appropriate institutional officials for disposition.

Noncompliance can include, but is not limited to, failure to obtain prior REB approval before starting a research project, inadequate supervision of the research, failure to report adverse events or protocol changes to the REB, failure to provide ongoing progress reports, or significant deviation from the approved protocol.

Actions taken by an REB or the University administration, as appropriate, may include, but are not limited to, education measures, compliance audits, terminating or suspending REB approval of active studies, restrictions on the ability to serve as an investigator on research projects involving human subjects, freezing of research funds, or academic penalties in accord with the Code of Student Conduct and Disciplinary Procedures. Graduate students who do not have REB approval for projects involving human subjects risk non-acceptance of their thesis work. Any action taken by the REB or the University administration will be reported promptly, in writing, to the investigator.”

2.1.4 Managing Conflicts of Interest, Double-Billing and Spin-Off Companies

Managing "Double-Billing": The Research Institute has not implemented a formal mechanism to control "double-billing" of health care procedures that are required by research protocols (payments via the *Régie de l'assurance maladie du Québec* (RAMQ) and via the research funds). However, the Research Institute requires that honoraria of the clinical investigator be reimbursed through the Department to which the investigator is appointed, to ensure transparency of the remunerative process. A policy to be enforced will be to attach a memo along with payment, to sensitize the investigator to the fact that:

" Costs incurred for health care performed during industry-sponsored research projects must not be the object of double-billing. When health care procedures are covered by the RAMQ, the investigator may not invoice the Research Institute to obtain double remuneration from research funds. If the study budget has provisions for the investigator's remuneration (honorarium) for health care (e.g. physical exam), the clinical investigator shall not request additional payment via the RAMQ for these health care procedures."

Managing conflicts of interest: Section 4.8 of Annex 1b, McGill University Policy on the Ethical Conduct of Research Involving Human Subjects, 2003, addresses the issue of conflicts of interest, as follows:

“The researcher has a duty to inform the REB of any actual, potential or perceived conflicts of interest. A conflict of interest arises where the researcher has a material interest of any nature - personal, financial, career or otherwise – that may conflict with the researcher's duty of honesty and integrity. Conflicts may arise when the researcher serves dual roles (e.g. treating physician, teacher or employer, as well as researcher) and as such may unduly influence the subject to participate in the research. The REB has the responsibility to identify and seek clarification of situations where conflicts of interest may exist. REBs should be provided with the relevant details regarding the research projects, budgets, commercial interests, consultative relationships and any other information needed to allow them to properly identify and address possible conflicts of interest. When a significant real or apparent conflict of interest is brought to the attention of the REB, the researcher may be required to disclose the conflict to potential subjects, to abandon one of the interests in conflict, or to take some other action to address the conflict, as specified by the REB.

REB members must disclose to the REB possible conflicts of interest arising out of personal relationships, financial interests, multiple roles, or other factors. Members of an REB may not be present during the consideration of their own project or any other project in which the member has a conflicting interest.

This section does not attempt to address all matters relating to conflict of interest therefore, as appropriate, reference should also be made to existing University guidelines and regulations on conflict of interest.”

The MUHC has also developed a Policy and Procedure on Professional Conduct, approved by the Board of Directors of the MUHC, November 27, 1998, and available at http://www.intranet.muhc.mcgill.ca/corporate/Policies/policy_professional_conduct.html.

This policy aims at protecting the MUHC and officers, directors, employees, volunteers and medical and research staff against the possibility of real or apparent conflict of interest. “The contract which exists between each Individual and the MUHC by fact of employment or appointment requires an Individual to act in the best interests of the MUHC and to refrain from such conduct or activity which is opposed to the best interests of the MUHC or which constitutes a real or potential detriment to the well-being of the MUHC.” When becoming employed or appointed at the MUHC, the Investigator is asked to complete a Declaration form stating that “ I have read and understood the Policy and Procedure on Hospital conduct and do hereby certify my full compliance with its provisions”.

Although the Research Ethics Boards of the MUHC are not directly involved in reviewing contracts and budgets of industry-sponsored research projects, the issues raised by potential conflicts of interest, finder's fees or excessive gratification, are addressed in the application forms submitted by investigators to the REBs. The administrative assistants (OCC coordinators) reviewing study budgets must report potential conflicts of interest, if perceived during financial review, to the REB. Since December 1, 2000, the Research Institute has implemented procedures to review all contracts underlying industry-sponsored research projects, prior to their approval and signatures, to ensure their compliance with institutional policies. The Office of Clinical Contracts reviews proposed study budgets and payment schedules to ensure that any monies destined to the institution, the investigators and their teams, as well as any compensations to research subjects, be the object of declarations prior to signature of contracts (refer to Annex 10).

Furthermore, according to Article 21, sections 54.1 to 54.6, of the US Federal Code of Regulations (21 CFR Part 54.1 to 54.6), the Food and Drug Administration (FDA) of the United States requires that investigators conducting clinical trials complete and sign a *Clinical Investigator Financial Disclosure Form* appended to the contract, with obligation to declare any potential financial interests for the investigator, and/or for members of his family, in conducting the clinical trial and in its outcome. For example, the Clinical Investigator Financial Disclosure Form identifies, among the investigator's declarations, the following situations as potential conflicts of interest: financial compensations or honoraria separated from the study budget, compensation exceeding \$25,000 US, the holding of more than 500 shares in the Company, etc. This *extra-muros* regulatory framework offers additional protection to ensure that industry-sponsored research contracts are transparent with regard to excessive gratification rewarding the recruitment of research subjects.

The threshold of monetary sums to be declared in Financial Disclosure Forms for conflicts of interest in biomedical research, has been the object of a recent survey on 297 research centres in the United States (refer to the *New England Journal of Medicine*, 2000; 343:1621-6). The survey revealed considerable variation in the policies governing conflicts of interest in research centres as well as a general deficiency in maintaining a high level of scientific integrity. At the McGill University Health Centre, in compliance with its Contract of Affiliation with McGill University (Annex 4) and with its Management Agreement with the Research Institute of the MUHC (Annex 6), MUHC investigators must abide by the McGill University Policies and Procedures governing mandatory declaration of conflicts of interest in industry sponsored research and are subject to those disciplinary actions contemplated in cases of scientific misconduct arising when conflicts of interest have not been declared and/or resolved (refer to Annex 2 and Annex 3).

Managing Spin-Off Companies: There is an obligation to declare inventions (innovations) by investigators affiliated with McGill University, if they intend to commercialize such inventions. This is part of the University Policy on Inventions and Patents developed by the Office of Technology Transfer (OTT) at the Faculty of Graduate Studies and Research, McGill University. Such policy equally applies to McGill University affiliated hospitals, including the MUHC (refer to Annex 2, *A Guide to Sponsored Research at McGill University*, published by the Faculty of Graduate Studies and Research, McGill University, Spring 1998. The OTT has in place a registry of inventions and a process of technology transfer, and reports annually to the Scientific Directors of each MUHC hospital site. The policies governing enterprises or companies created *intra-muros* by investigators are in the following Annexes: Annex 2, *Guidelines for the Creation of Spinoff Companies*, and *Revised University Policy on Inventions and Patents*; Annex 3.a, chapters 8, 10 and 11, concerning *University Policies on Inventions and Patents*, and *Conflicts of Interest*; Annex 7, section 3.3, *Technology Transfer*; Annex 9, section 12, concerning *Inventions and Licenses*.

2.1.5 Management of Research Funds and Costs of Research Projects

Management of salary awards across the MUHC sites:

For all MUHC Hospital sites, the salary awards of investigators are managed by the administration of McGill University.

Management of research grants across the MUHC sites:

At the Montreal General Hospital and the Montreal Children's Hospital: Grant proposals require approval by the Scientific Director or by the Director of Administration. The management of basic research grants, as well as of clinical trials and research contracts, is ensured by the administration of the Research Institute of the MUHC, according to *Policies & Procedures of the Research Institute of the McGill University Health Centre* (refer to Annex 9, section 3). Clinical Trials Contracts and Research Contracts require the signature of authorized personnel of the Research Institute of the MUHC.

At The Royal Victoria Hospital and the Montreal Chest Institute: Grants have traditionally been managed by the administration of McGill University. Increasingly, grants are being administered by the Research Institute of the MUHC, and grant proposals require approval by the Scientific Director or by the Director of Administration. Clinical Trials Contracts and Research Contracts require the signature of authorized personnel of the Research Institute of the MUHC, and are managed by the Research Institute of the MUHC.

At the Montreal Neurological Hospital: Approval and management of basic research grants, clinical trials research contracts, and of investigators' salary awards, are all ensured by the administration of McGill University.

Management of research equipment: Given the recent merger of the five research centres grouped as the Research Institute of the MUHC, the inventory, equipment management policies and updating process across MUHC, are all in a developmental stage. At the RVH, MCI and MGH, the Departments of Biomedical Engineering hold an inventory of medical and research equipment at the MUHC. During the year 2000 "bug" alert, an inventory was also done on electronic equipment. A partial inventory has been made available in February 2001. The maintenance policy for this inventory has yet to be defined.

Policies on management of research equipment are in place at the *Research Institute of the McGill University Health Centre* (refer to Annex 9, section 5); the regulations address acquisition, ownership, security, maintenance and repairs, relocation and removal, of research equipment. Following incorporation of the Research Institute of the MUHC, these policies and procedures will be adapted to, and applied across, the MUHC. (refer to Annex 9, section 5, *Policies & Procedures of the Research Institute of the McGill University Health Centre*, (adapted from the *Montreal General Hospital Research Institute, Policies and Procedures, May 1998*).

2.1.6 Management of Research Data Bases and Medical Research Records

The management of research data and research medical records of human subjects participating in research activities is subject to the same protection and confidentiality provided for the medical records of users of health care and services, and must comply with the Policies and Procedures outlined in the The MUHC Security and Confidentiality Program available at: http://www.intranet.muhc.mcgill.ca/protection_information/

Oversight for research data repositories and tissue banks within the MUHC's jurisdiction is subject to the McGill policy entitled "Guidelines for management of data and tissue banks" described above at Article 2.1.2.

These Policies and Procedures ensure compliance with provincial and federal legislation with regards to confidentiality for health care and services user's medical records and electronic

storage of clinical data. Provincial legislation includes: *Commission d'accès à l'information: Lois et règlements*; *Commission d'accès à l'information: Exigences minimales relatives à la sécurité des dossiers informatisés d'utilisateurs du réseau de la Santé et des Services sociaux (avril 1992)*; An Act respecting Access to documents held by public bodies and the Protection of personal information (L.R.Q. A-2.1); Charter of human rights and freedoms (L.R.Q. C-12); An Act to establish a legal framework for information technology (Bill 161); *Loi sur les services de santé et les services sociaux* (L.R.Q. S-4.2); *Cadre Global de gestion des actifs informationnels appartenant aux organismes du réseau de la santé et des services sociaux - Volet sur la sécurité - Septembre 2002*.

The management of databases containing information on human research subjects (or on patients) must be compliant with information security and confidentiality frameworks, guidelines and regulations emanating from the Ministry of Health, the Réseau de Télécommunication Socio-santitaire (RTSS), the Regional Board and the MUHC.

The MUHC Security & Confidentiality Program has specific Policies and Procedures for: Storage and Transmission of Electronic Documents (Policy and Procedures - 5.14), to provide users of MUHC informational assets with guidelines and criteria for storage and transmission of electronic documents while ensuring the equitable and efficient use of limited MUHC informational assets; Verbal Consent for the Release of Patient Information (Policy and Procedures - 5.16), to define the requirements for documenting a patient's verbal consent to the release of information about the patient to a health care provider external to the MUHC for the purpose of ensuring continuity of care.

The patients' (or human research subjects') original medical records and other original source documents that are pertinent to a research study (clinical research project or clinical trial) may be made available for purpose of verification and monitoring, to authorized representatives of Clinical Research Organizations (CROs), Sponsors (Pharmaceutical Companies), the U.S. Food and Drug Administration or Health Canada, but permission for such access has been obtained in a written consent document before entering a patient in a study. Although the above-mentioned authorized representatives may have access to nominal information in source documents for purpose of verification and monitoring, the patients' research data transmitted to CROs, Sponsors or any regulatory agency, shall be coded and shall not include any nominal information.

With regards to management of research data and medical research records (source documents) of subjects participating in clinical research or clinical trials, these records must be locked confidentially in the investigator's office, with limited access, as stipulated in the informed consent documents.

At the MUHC the conduct of a research project including a therapeutic component requires that:

- i. a subject's participation in research be documented in the medical record by forwarding to the Medical Archives Department a copy of the signed consent document containing the Investigator's emergency contact telephone numbers, and the Confirmation of Participation in Research form;
- ii. entries in the subject's medical record describing the clinical evolution and events be similar to documentation that would occur outside of the research setting;
- iii. appropriate disclosure of the requirements for documentation in the medical record be made to a prospective subject during the free and informed consent procedure.

iv. the investigator give each study subject a wallet-size information card showing the MUHC or IRB study code; study drug(s), or medical device(s); and must include an emergency contact number.

The medical record of patients who participates as a subject of research should include documentation of the study entry criteria (inclusion and exclusion elements) if this is considered by the Research Ethics Board to be in the best interest of the subjects.

The retention of research records is subject to McGill Faculty of Medicine policy consistent with the Food and Drugs Act, and good clinical practices. At the MUHC the procedures are consistent with the “Calendrier de conservation des documents” in response to the Quebec Archiving Act, L.R.Q., A-21.1 articles 8, 9, and 35.

The MUHC Department of Medical Records is responsible for the maintenance of, the access to and the archiving of “Essential Research Documents” that form part of the medical record, and such documentation will be kept for the entire retention period in their original medium.

Essential research documents not maintained by the Sponsor, nor by the Sponsor-Investigator, nor by MUHC Department of Medical Records are retained by the Investigator in a manner consistent with the Food and Drugs Act, and the research protocol for a minimum of twenty five (25) years.

Original research documents specific and unique to the REB are retained for twenty five (25) years. Three (3) years following the Study Termination date recorded in the REB minutes, the REB file may be stored off-site from the MUHC. Copies of original documents are not retained.

2.1.7 Control of Investigational Drugs

Dispensation of investigational drugs: Annex 9, *Research Institute of the McGill University Health Centre, Policies and Procedure*, contains section 6 entirely dedicated to the conduct of clinical trials and to Good Clinical Practice (GCPs). Sub-section A12 entitled *Handling and Dispensing of Study Drug* stipulates that all investigational drugs must be stored, dispensed and accounted for by the hospital's Pharmacy. This regulation is currently in the process of being applied at all MUHC sites.

Recovery of costs incurred by the control of investigational drugs: The Pharmacy of The McGill University Health Centre, which has research staff specifically dedicated to control of investigational drugs, invoices the Research Institute for its services rendered on clinical trials research involving investigational drugs. This cost recovery is achieved in order to keep the integrity of the Pharmacy's operational budget allocated for health care services covered by the *Ministère de la santé et des services sociaux du Québec*.

Other policies found in the Research Ethics Boards' procedures (Annex 1; Annex 9, section 6) require that the administration of investigational drugs to research subjects be reported in the patients' medical records (section 2.1.6), and that adverse drug reactions or serious adverse events be reported to the research ethics committees.

2.1.8 Research Ethics Board Operating Procedures

The McGill University Health Centre, through its process of governance, delegates to its Research Ethics Boards (REBs) the responsibility to ensure that ethical principles are applied to research involving human subjects. The nine REBs listed below report directly to the Board of Directors of the MUHC.

<u>Name of Research Ethics Board</u>	<u>Acronym</u>
Biomedical A	BMA
Biomedical B	BMB
Biomedical C	BMC
Biomedical D	BMD
Genetics/Population Research/Investigator Initiated Studies	GEN
Neurosciences	NEU
Pediatrics	PED
Psychiatry/Psychology	PSY
Surgical Techniques/Medical Devices/Reproductive Technologies	SDR

As the MUHC is a large institution with multiple REBs, the Research Ethics Office (REO) was established to coordinate research regulatory compliance at the MUHC. The REO is supervised by the Director and the REO Compliance Officer who are responsible for introducing policy, harmonizing policy interpretation and standard operating procedures to create consistency of research ethics review, and research conduct at the MUHC.

REO responsibilities include providing direct administrative support for conduct of scientific and ethical review; representing MUHC on all matters of research regulatory compliance; proposing policy to the MUHC Board of Directors; implementing monitoring and educational programs to promote ethical research; and maintaining in good standing, federal assurances, provincial mandates and accreditation agreements.

REO serves to oversee development of the institution's Research Subjects Protection Program to maintain a culture of responsible conduct of research at the MUHC. REO serves as a resource and liaison for investigators, research administrators, regulatory authorities, and private and public sponsors of research, where the protection of the rights, and the well being of MUHC research subjects are concerned.

The Inter-Institutional Agreement (IIA) between McGill University and the MUHC allows for an MUHC REB to act as the REB of Record when McGill University Faculty members undertake research at the MUHC. The MUHC is delegated to act concurrently on behalf of the University to review and provide ongoing oversight for approved research studies as per §2.2.1. The McGill Faculty of Medicine Institutional Review Board (IRB) is mandated to conduct ethics review on behalf of the MUHC when a research study is conducted at more than one McGill affiliated hospital that includes a MUHC site. A MUHC staff with appropriate qualifications must be responsible for the study at the MUHC.

An Investigator appointed at McGill University without a MUHC appointment, who requests to conduct research at the MUHC, must include a MUHC staff as a member of the study team to represent the study locally. An Investigator with no MUHC or McGill appointment who requests

to conduct research at the MUHC, must assign a MUHC staff to be the MUHC Principal Investigator, responsible for all aspects of study review and conduct at the MUHC.

The MUHC participates in the Quebec Ministry of Health (MSSS) mechanism for review and oversight of Quebec multicentre research. The Coordinating Principal Investigator selected by the study sponsor to lead the research may or may not be the MUHC Investigator. However, the multicentre review system requires the MUHC Investigator to act as the Local Principal Investigator responsible for study conduct at the MUHC including submission for Site Specific Assessment reviews prior to initiating the study.

No research study shall be conducted at the MUHC in the absence of MUHC Authorization issued by the RI MUHC following appropriate research ethics review and approval, and favourable Site Specific Assessment (SSA) reviews. Research studies planned for conduct at the MUHC under the ethical oversight of a non-MUHC REB are subject to the same MUHC standards as studies reviewed and approved by the MUHC REBs.

The REO Compliance Officer acting in the capacity of the Human Protections Administrator (HPA) works with the MUHC Director General to negotiate the US Federalwide Assurance (FWA) with the US Department of Health and Human Services. The HPA is responsible to maintain in good standing the MUHC's FWA that is mandatory for the conduct of US federally sponsored research at the MUHC.

The McGill School of Nursing has approved policy and corresponding procedures to support certain student-designed research projects proposed for conduct at the MUHC. The projects are reviewed for scientific value and validity by a Scientific Committee of the School of Nursing. If approval for the scientific merit is provided, the proposals are submitted to the REO for assignment to an MUHC REB with competence to reasonably reflect the nature of the research. Such proposals are submitted identifying the student's supervisor as Principal Investigator, accompanied by the formal scientific review, and such studies will usually qualify for expedited review according to REB review criteria.

The REB operating procedures described at §2.2.1 are based on applicable regulations and laws governing human subjects' research and international principles of good clinical practice (GCP). If the REO receives a study proposal to which ethics review requirements do not apply, the REO Director may issue an exemption from ethics review.

The MUHC REBs work under the published guidelines of the "*Tri-Council Policy Statement*", and the "*Plan d'action ministériel en éthique de la recherche et en intégrité scientifique*", and in compliance with the "*Food and Drugs Act*", including the "*Food and Drug Regulations*", the "*Medical Devices Regulations*", and the "*Natural Health Products Regulations*", and act in conformity with standards set forth in the (US) "*Code of Federal Regulations*" governing human subjects research, and in a manner consistent with internationally accepted principles of good clinical practice (GCP).

The review and conduct of clinical trial research with investigational products is stipulated under Canadian law and authorized by Health Canada through issue of No Objection Letters (NOLs) to the product manufacturer or the sponsor of the clinical trial. Documentation of the NOL must be verified by the MUHC Investigator, and submitted to the REB, prior to review of the clinical trial.

A clinical trial conducted by an MUHC Investigator at a non-Canadian site must conform to the laws and regulations of the country where the research would be conducted. Written compliance

with GCP, and all other regulations governing the review and conduct of human subjects research at a non-Canadian site, must be provided to the MUHC Investigator, and confirmed to the satisfaction of the REB.

The Health Products and Food Branch Inspectorate is responsible to verify that Canadian research regulations and good clinical practices governing investigational health products are being applied appropriately through a program of compliance monitoring and enforcement activities. Additional regulatory requirements may apply to MUHC research that is subject to financial support, sponsorships, assurances and/or research agreements involving other federal jurisdictions. When any regulatory inspection involves research conducted at the MUHC, or research conducted elsewhere by a MUHC Investigator, the REO Director shall be notified by the Investigator, with sufficient notice to allow the Compliance Officer and/or other delegates to be present during the inspection meetings.

MUHC REBs maintain oversight for human subjects research including for studies subject to the Civil Code of Quebec, Article 21 involving legally incapacitated adults and minor children. An MUHC REB approval to conduct a study is valid at any MUHC site. REBs maintain scientific expertise to review specialized proposals such as for pediatric and psychiatric research. The Neurosciences REB is mandated to review research intended for conduct at the Montreal Neurological Institute.

It is an REB responsibility to determine if the risks of harm from research are reasonable in relation to any potential benefits to the participants and to society, and that risks are minimized to the extent possible, consistent with sound research design. It is not permitted to act upon a modification to an approved study without prior REB written approval for study amendment. The investigator will promptly notify the REB in writing should a reportable unanticipated problem or event occur in a research study.

A divergence or departure from the expected conduct of an approved study, described in the research protocol or research agreement, is a protocol deviation as defined at Section 2.2.1 (E)(1). The only departure from the protocol permitted without prior REB approval is one where urgent action is required to eliminate an apparent or immediate hazard to a study subject or others.

Reporting by the Investigator of adverse drug reactions (ADR), serious adverse events (SAE) and unanticipated adverse device effects (UADE) adheres to applicable regulations for notifying the REB of unanticipated problems involving study safety. An unanticipated problem or study event is “reportable” to the REB according to criteria in the research protocol and in local policy. The REB must receive details of the undesirable and detrimental experience only if the unanticipated problem or event is reportable by applicable regulations.

Reporting an SAE affecting the well being of an MUHC research subject does not depend on the sponsor’s conclusions, but rather on the Investigator’s judgment of the seriousness, expectedness, causality and/or frequency of the event.

Reporting of ADRs, SAEs and UADEs is time critical as defined under the Food and Drugs Act including the Food and Drug Regulations and Medical Device Regulations that conform with standards in the (US) Code of Federal Regulations and Good Clinical Practice: Consolidated Guideline” Topic Efficacy E6.

In compliance with Annex 1b, McGill University Policy on the Ethical Conduct of Research Involving Human Subjects, 2003, section 4.7 Adverse Events, “Researchers are obligated to

immediately notify the REB of any serious or unexpected adverse event experienced by a subject which occurs in connection with the project or if data analysis or other review reveals undesirable outcomes for the subjects.”

Unanticipated problems or events discovered during the course of the research may impact on the study’s “risk to benefit” assessment, and to ensure adequate protection of the subjects’ well being, the REB may need to reconsider approval for the study, or require modification to the study or revise the continuing review timeline based on such information.

The REO provides online access to guidance to explain the reporting criteria and to describe the procedures for notifying the REB of local and non-local reportable, spontaneous, and expected adverse events that are consistent with regulations for safety reporting.

2.2 Scientific, Ethics and Contract Reviews of Research Projects

2) Les recherches comptant sur la participation de sujets humains, de même que la recherche portant sur les embryons humains et la recherche en médecine génétique, doivent toutes être soumises à **l’examen d’un comité d’éthique**. Les projets de recherche doivent être soumis à un **examen de la qualité et de la pertinence scientifiques**.

Les établissements et les organismes du réseau de la santé et des services sociaux où se déroulent des activités de recherche doivent **s’assurer de la gestion financière rigoureuse** des projets et des activités de recherche.

2.2.1 Review by the Research Ethics Board

The MUHC Board of Directors delegates to the REBs the responsibility for review of the ethical acceptability and the scientific merit of all proposed research and modifications to approved research involving human subjects. REB oversight for an approved research study shall include continuing review at intervals established by the REB of Record, and shall be ongoing as long as the study activities are conducted at the MUHC. Ethical oversight shall conclude when the REB documents acceptance of the report of study completion or termination.

(A) Regulatory Authority

If disagreement involving applicable regulations should arise, the regulation providing the greatest level of protection for the rights and well being of the research subject shall apply.

1) Clinical trial research is conducted according to the Health Canada Regulatory Framework in compliance with the Food and Drugs Act, and as appropriate with the Food and Drug Regulations, the Medical Devices Regulations, and the Natural Health Product Regulations.

- 2) Research reviewed and conducted at the MUHC must comply with the laws and regulations of Quebec.
- 3) All aspects of research involving review or conduct that are not governed by the laws of Canada or of Quebec, are subject to institutional policy, and shall conform to internationally accepted principles of good clinical practice and established professional ethical norms.
- 4) A clinical trial with an investigational product regulated by Health Canada and the US Food and Drug Administration will be reviewed and conducted at the MUHC according to the MUHC approved research agreement and the applicable regulations.
- 5) MUHC research activities involving human subjects sponsored in whole or in part by the US Public Health Service are conducted in compliance with the Federalwide Assurance for International Non-US Institutions negotiated by the institution.
- 6) Research designed in whole or in part to collect private information held by the records of the institution requires review by the REB. In compliance with Articles 19.1 and 19.2 of the *Loi sur les services de santé et les services sociaux* and Article 125 of the *Loi sur l'accès aux documents des organismes publics et sur la protection des renseignements personnels*, the research use of private information held by the records of the institution, also requires written consent of prospective subjects or authorization from the Director of Professional Services.

(B) Research Ethics Board of Record

The REB of Record is the legally constituted authority, competent to act as the primary entity mandated by the institution to provide necessary approvals, and to oversee the responsible conduct of MUHC human subjects research, and on behalf of institutions and individuals in other jurisdictions according to applicable Inter-Institutional Agreements and Independent Investigator Agreements.

There can be only one REB of Record for each study approved for conduct at the MUHC. The REB will accept responsibility for research ethics review according to local, federal, provincial, and international regulatory criteria for “engagement in research.”

Each new request for ethical review of human subjects research is submitted to the REO where the request is directed to an appropriate REB. If the REB Chair accepts the responsibility for review, the REB is designated as REB of Record for the study. If the REB Chair declines responsibility for review, the proposal is directed by the REO to another REB Chair to establish oversight responsibility. Authority for the REB of Record decision-making takes effect following either: Full Board deliberation [2.2.1(C)], or via an Expedited Review procedure [2.2.1(D)].

(C) Ethics Evaluation of Human Subjects Research

- 1) Convened Meetings of the Full Board

The REB membership will comply with the applicable regulatory requirements. Alternate Members will be appointed to ensure that the expertise required to form a quorum, legally defined by applicable regulations is consistently available to conduct Full Board Review.

Initial and ongoing reviews of human subjects research activities are conducted at convened meetings of the REB, at which a simple majority (fifty percent plus one) of the Members are present, and the required expertise is represented to constitute a quorum of the Committee. A Full Board Review decision takes effect following REB deliberation in the presence of quorum, when the Chair confirms the agreement of the majority of the members present. Should the quorum fail during a meeting, no further decisions requiring Full Board Review will be made until quorum is restored.

REB deliberates to determine if the proposed research interventions are scientifically and ethically sound, and acceptably safe, and to consider the Investigator's qualifications to conduct the study under the described conditions. The REB strives to apply fair and impartial decision making to every proposal accepted for review.

During the deliberation every effort is made to reach consensus for each decision requiring Full Board Review, whereby agreement is expressed by general consent or unanimous vote. In the absence of consensus, the decision is made and documented following a recorded vote to show those Members in favour, opposed or abstaining. Only the opinion of Members present for the deliberation will contribute to the decision. In the event that no majority decision is expressed by the Members present, the REB Chair will cast the deciding vote.

MUHC REBs may provide Full Board Review using a Primary Reviewer system to conduct Initial or Continuing Reviews, or to review proposed modifications to an approved study, or for ongoing activities such as review of unanticipated events involving risk to study subjects including adverse event reporting. The Chair may accept the task of Primary Reviewer or assign one or more REB Members as Primary or Secondary Reviewer(s) based on the Member's knowledge and familiarity with the research area. Primary and Secondary Reviewers will receive the complete set of study documents while other Members will receive a summary of the information. The Primary Reviewer will present the research, or the study report to the REB in the absence of the Investigator, and will lead discussion during the deliberation. Secondary Reviewer(s) will present additional information as needed for the REB to reach a decision.

The Primary Reviewer system may be used to conduct review of the complete application for research funding by a peer-review agency, where one or more studies are subject to REB review. Each study funded by the grant will be reviewed on its own merit, and within context of the research program described in the grant application.

2) Research Endorsement

Only Investigators with documented permission to conduct research at the MUHC known as "privilege to conduct research" may submit for MUHC research ethics review as per 2.3.2. Each Application for Initial Review will be co-signed by the Investigator's Departmental or Divisional Head. When the Investigator is the Departmental Head, "the Application" will be co-signed either by the Academic Departmental Chair or by the

Director of the RI MUHC. While there is no obligation to do so, an Investigator, or the Representative may present the research at an REB meeting, or by teleconference or videoconference. The Investigator will respond to every question and request for information from the REB, or their Representative concerning the research for the duration of the study.

All regulations governing the review of research, including from the Quebec Ministry of Health and Social Services require the REB to have access to complete study information. Therefore, if an MUHC REB is asked to review a research proposal that was rejected, or subjected to suspension or withdrawal of the ethical approval of another duly mandated REB, or if the investigator withdrew the research proposal from REB review, the MUHC REB will consider the reasons for the rejection, suspension, or termination of approval by the former REB. The MUHC REB will provide explicit reasons for accepting the proposal for review, as well as the reasons leading to any decision to provide approval for the study.

3) REB Records

The REB will create and maintain electronic and/or paper records of its review activities and decision-making, according to applicable regulation, and in sufficient detail to reconstruct events and to take measures appropriate to oversee the research. Original documents specific and unique to the REB will be retained in compliance with applicable regulatory requirements.

The REB research study file will be established upon receipt of the original Application for Initial Review and will contain all subsequent submissions, reports and correspondence to be retained for the duration of time required by law.

The approved minutes of Full Board convened meetings are recorded effectively to reconstruct the process of deliberation leading to the decision including attendance, summary of the discussion and outcomes, and a recorded vote as needed. The minutes will not be a literal reiteration of the process, but will document specific findings and important issues.

4) Review Materials

To promote the responsible conduct of research, ethical review requires submission of detailed proposals to allow the REB to arrive at informed decisions. REB Members will have access to all documents required for the REB to maintain compliance with provincial, federal and international regulations governing ethical review and oversight. Each research proposal or report on a research activity, submitted to an MUHC REB will be accompanied by the appropriate MUHC standard application or reporting form.

For each new proposal to be reviewed, REB Members will receive at least one week prior to the convened meeting, a set of documents that includes a research protocol appropriate to describe the study rationale and objectives with recent literature review and references, non-technical summary, study design and instrumentation, and methodology to explain recruitment and enrolment, treatment interventions and interactions, data collection and analysis, safety management, anticipated risks and benefits, statements of ethical oversight and of intent to publish, as well as descriptions of study resource utilization, publicity, financing and sponsorship, and all materials to be offered to a study subject or

their representative. Where appropriate, Members selected by the Chair will review documents to show results of prior and ongoing pre-clinical and clinical investigations including technical reports on medical devices, reports on biochemistry, pharmacology, toxicology, mechanism of action, and expected probability for side effects.

The set of documents described above is also required to conduct review by expedited procedures (2.2.1D), as appropriate, or to decide if the proposal is exempt from REB review, or is appropriate for MUHC REB review, or is subject to additional reviews, or whether verification of information is required from a source other than the Investigator.

5) Review Outcomes

No research activity subject to REB review may be conducted without prior written approval of the REB of Record, including planned revisions for the conduct of the study, except for a change to eliminate an immediate hazard as described at 2.2.1(E)(1) ii.

The REB will review research intended for conduct within the MUHC, and/or elsewhere by staff of the institution, and according to an Inter-Institutional Agreement or and Independent Investigator Agreement, where appropriate. The outcome of REB review involving a proposed or ongoing study will be either: to approve, to disallow, to propose modifications, to suspend approval, to terminate approval, or to keep “on file”. The Chair will ensure the decisions are recorded properly, and that Investigators are forwarded correspondence documenting the decisions as soon as possible.

The REB may provide recommendations for revisions or clarifications to the study that, if complied with will lead to final ethical approval for the research. The REB extends authority to the Chair, or another REB representative to review the appropriateness of the Investigator’s response to determine concurrence with the recommendations established at the convened meeting of the Full Board. The date concurrence is confirmed determines the date of final REB approval.

When all ethical and scientific concerns have been resolved to the satisfaction of the REB, (*cf.* « *Gazette officielle du Québec* ») final written REB approval will be forwarded to the Investigator, and to the institution confirming the study may be conducted. It is the Investigator’s responsibility to pursue all additional reviews required by the institution, and to advise the institution, if and when the study is initiated.

6) Ongoing Oversight

REB will follow established procedures to oversee the progress of ongoing research beginning with the decision to approve the study, until their acceptance of the report of study completion or termination is documented in the REB minutes.

REB will instruct the Investigator to notify them of all new information relevant to the study learned during the course of its conduct, and to respect deadlines for ongoing reporting. Regulations require certain research-related events such as Continuing Review and unanticipated problems involving risk to subjects to be reported according to specific timelines.

Minor revisions proposed for previously approved research may be reviewed in an expedited manner, prior to the next projected continuing review, and the outcome will be

reported to the Full Board at the following convened meeting. When a proposed revision is not minor the modification will be reviewed at a Full Board convened meeting.

Ongoing ethical oversight includes a substantive, meaningful Continuing Review conducted at an interval no greater than twelve months from the date of previous REB review and approval, or sooner if required by the REB. Ethics approval expires on the anniversary date of the previous REB approval. Continuing Review by the Full Board is required unless the research qualifies for expedited review as per 2.2.1(D)(8). When the Continuing Review of a study previously received approved via expedited review, the Chair will determine if new information or unanticipated problems made known since the previous review would disqualify further review by expedited procedures. Continuing Review will determine whether the previous review interval remains adequate to ensure ongoing protection of the rights and well being of study subjects, until the REB receives a written report of study completion or termination.

When Continuing Review of a study does not occur prior to the end of the approval period specified in writing by the REB, the ethical approval expires automatically, and research activities must stop. Continuation of the research after expiration of ethical approval is a violation of the regulations and the data collected during the interval of expired approval could be rejected. However, if the investigator is actively pursuing review with the REB, and the REB believes an over-riding safety concern or ethical issue is involved, they may permit the study to continue for the brief time required to complete the review process. No new subjects will be recruited or enrolled during this time. If ethical approval expires and the Investigator is not actively pursuing review, the study will be terminated by the REB. The Investigator may re-submit the study for Initial Review by the same REB only.

(D) Evaluation via Expedited Review of Research:

- 1) For purposes of REB oversight an expedited review of research requires that the evaluation be carried out by the REB Chair, or Co-Chair, or a designated experienced REB Member, or group of REB Members.
- 2) The outcome from deliberation via expedited review may result in REB approval for the research, or for the amendment proposed to approved research, but may not disallow the proposal.
- 3) When approval via expedited review cannot be provided, the research proposal, or amendment proposed to approved research will be considered at the next convened meeting of the REB at which a quorum of the Membership is present.
- 4) Evaluation via expedited review of a proposal may be considered when the research procedures fall within one of the following categories:
 - i. clinical studies of drugs and medical devices that do not require Health Canada registration of a Clinical Trial Application or Investigational Testing Authorization.
 - ii. collection of blood samples by finger stick, heel stick, ear stick or venipuncture.

- iii. collection of human material for research purposes acquired by non-invasive means.
 - iv. collection of human material or data acquired during the course of providing clinical care.
 - v. use of existing human material, or data obtained during the course of prior research when the secondary use falls within the scope of the original informed consent.
 - vi. collection of data from audio, video, digital or image recordings made for research purposes.
 - vii. research on individual or group characteristics or behaviour, or research using survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.
- 5) Initial evaluation via expedited review of a proposal to conduct research may be considered when:
- i. the collection of data is carried out through nothing more than non-invasive or non-intrusive means, whether or not subject consent is required;
 - ii. the probability and magnitude of discomfort, or disruption is no greater than that which is encountered in the daily life of the research subject; or
 - iii. the intervention meets the definition of minimal risk in the Tri-Council Policy Statement “Ethical Conduct for Research Involving Humans”.
- 6) Initial evaluation via expedited review of a proposal to conduct an experimentation may not be considered when the research involves legally incompetent persons, i.e. minor children or legally incompetent adults.
- 7) Evaluation via expedited review of an amendment proposed to approved research may be considered when:
- i. the proposal for research did receive approval of the REB, and
 - ii. the REB approval for the research was not withdrawn, did not expire or terminate, and
 - iii. the proposed modification is not expected to increase significantly the risk related to the study.
- 8) Continuing review via expedited review of research may be considered when:
- i. the report is submitted within the interval established by REB approval appropriate to the degree of risk, but not less than once per year, and
 - ii. the initial REB approval was provided via expedited review, or

- iii. there has been no significant change to the approved research since the previous REB review, or
 - iv. the research is permanently closed to the enrollment of new subjects, or
 - v. all subjects have completed all research-related interventions and the research continues only for long-term follow-up of subjects, or
 - vi. no new subjects have been enrolled and no new risks have been identified since the previous REB review, or
 - vii. the remaining research activities are limited to data analysis.
- 9) The outcome of the expedited review will be reported to the Investigator in correspondence summarizing the decision, and stipulating that the evaluation was conducted via expedited review. The formal decision will provide either: (i) REB approval, or (ii) the specific recommendations required to attain REB approval.
- 10) The outcome from a deliberation via expedited review must be reported at the next convened meeting of the REB, and be recorded in the minutes of the meeting, to permit the REB to maintain surveillance over the decisions made on its behalf.

(E) Evaluation of a Protocol Deviation:

- 1) For purposes of REB review and oversight of human subjects' research a divergence or departure from the expected conduct of an approved study as described in the research protocol, or study agreement is a "protocol deviation".

The term protocol deviation is widely used to describe any study event whereby the current REB approved research protocol was not followed, i.e., an event that breaks a protocol rule. A protocol deviation is evaluated by the REB in one of two subcategories: (i) protocol exception and (ii) protocol violation.

- i. Protocol exception is a minor divergence or departure from the expected conduct of a study that is not consistent with the current REB approved version of the research protocol, consent document or study addenda, that had been anticipated by the Investigator, and for which the REB may grant acceptance.
- ii. Protocol violation is a major divergence or departure from the expected conduct of a study that is not consistent with the current REB approved version of the research protocol, consent document or addenda, that had not been anticipated by the Investigator, and for which an REB decision on corrective action is required.

The only protocol violation permitted without prior REB approval is one where urgent action is required to eliminate an apparent or immediate hazard to a study subject or others.

The Investigator must forward without delay to the sponsor, and to the REB, a written explanation of the protocol violation describing the action taken, the outcome of the action and the corrective measures proposed to avoid repetition of the event.

The REB's view on the adequacy of the corrective measures will result in a decision to accept or reject the action taken, and will be communicated in writing to the Investigator.

Protocol violations will be discussed at a convened meeting of the Full Board to permit the REB to maintain surveillance over the event.

- 2) REB review of a protocol deviation is evaluated according to the following criteria:
 - i. The protocol deviation is considered a "protocol exception" when the action:
 - . has no substantive effect on the risk posed to a research subject or others; and
 - . has no substantive effect on the value of the data collected; and
 - . does not confound the scientific analysis of the study results; and
 - . did not result from wilful or voluntary misconduct on the part of an Investigator or a member of the Investigator's study team.
 - ii. The protocol deviation is considered a "protocol violation" when the action:
 - . constitutes a change in the conduct of the research that should have received prospective REB review and approval prior to implementing the change; or
 - . has harmed or posed a significant risk of harm to a research subject or others; or
 - . has damaged the scientific integrity of the data collected or confounded the scientific analysis of the study results; or
 - . resulted from wilful or voluntary misconduct on the part of an Investigator or a member of the Investigator's study team.
- 3) It is the responsibility of the Investigator to report a protocol deviation to the REB according to the following terms:
 - i. Protocol exceptions do not need to be reported to the REB. However, with a written rationale an Investigator may collect all protocol exceptions occurring since the previous REB review and submit the information in a summary document only at the time of continuing review.
 - ii. Protocol violations are reported to the REB without delay along with corrective action proposed by the Investigator to avoid repetition of the event.

If a similar protocol violation has occurred previously in the study, the Investigator will provide an amendment to the protocol designed to avoid repetition of the event.

If the protocol violation introduces new information that may affect a subject's willingness to continue in the study, all study subjects must be informed, and the REB may require the subjects to renew their consent in writing.

(F) Review of Publicity for Non-Published Research:

All publicly available information concerning a research study including a poster, flyer, newspaper advertisement, press release, electronic publicity, or recording must be reviewed by an MUHC REB, or where appropriate by the Faculty of Medicine IRB. Publicity for unpublished research also must comply with MUHC Public Relations and Communication (PRC) policy.

It is the Principal Investigator's responsibility to submit to the REB for review the PRC Media Clearance Form for Research, showing PRC approval for the format of the publicity. Review of the information concerning non-published MUHC research on internal or external websites is joint-responsibility of the PRC and the REB coordinated by the REO. (See also 2.3.3 below)

(G) Unanticipated Problems Involving Risk, Serious or Continuing Non-Compliance and Suspension or Termination of REB Approval:

Non-compliance with applicable law, regulations, directives and policies that govern the review and conduct of human subjects research constitutes a major risk to responsible oversight of the institution's research. The REB will follow impartial and accountable procedures to examine each allegation of serious or continuing non-compliance with scientific or ethical standards, and will act either to suspend or to terminate ethical approval for a research study, if judged necessary.

As described at Section 2.5.4, the REB has the option to evaluate or to request evaluation of any situation of potential non-compliance with research regulations, or other untoward event arising from the conduct of research.

If at last resort, an REB acts to suspend or to terminate ethical approval for a study, the explanation for withdrawing approval will be reported in writing by the REB to the Investigator, to the Institution, and when the research involves a federally regulated product, to Health Canada, and as appropriate to the US Food and Drug Administration, to the US Federal Department or Agency, and to international federal health regulators.

The REB will forward incident reports of established scientific or ethical misconduct as described at Section 2.3.4: "Investigating Reports of Scientific and Ethical Misconduct" within thirty (30) days of preparing the report.

2.2.2 Assessment of Scientific Merit and Relevance

The evaluation of scientific merit and relevance of research projects involving human subjects is addressed by The McGill University Policy on the Ethical Conduct of Research Involving Human Subjects, 2003, Annex 1.b, Section 4.2, as follows:

« When evaluating if the potential gains of the research warrant the costs and risks to be incurred by the subjects and where risk of potential harm to subjects exists, the REB must satisfy itself that the design of a research project is capable of addressing the questions being asked in the research. REBs may therefore require that research be peer reviewed, particularly when the research involves greater than minimal risk to subjects. In cases where the research has already passed acceptable peer review, such as through a funding agency or through a peer review process established within the University, the REB will normally accept documentation of those reviews as evidence that appropriate scholarly standards have been met. However, in cases where the REB has a good and defined reason for doing so, the REB reserves the right to request further *ad hoc* independent peer review. REB members may also conduct the review of scholarly validity during the course of ethical review, which would require that the REB has members with the necessary expertise to carry out a proper peer review of the research in question. REBs shall base their judgment about scholarly value on a global assessment of the degree to which the research

might further the understanding of a problem, issues or phenomenon; it shall not be based on methodological biases or a preference for particular procedures. »

The MUHC hospitals ensure the evaluation of scientific merit of research projects involving human subjects in compliance with the above Policy ^(1.b). Evaluation of scientific merit of research projects sponsored by industry, particularly with regard to clinical trials of investigational drugs and innovative treatments, is a mandatory requirement for their approval by the Research Ethics Boards. Depending on the MUHC hospital site reviewing the research projects, the scientific evaluation is performed prior, or simultaneously, to the ethics evaluation, either by a designated Scientific Committee, or by internal and external members invited to assess the scientific validity of the research projects simultaneously with ethical acceptability (refer to Annex 10). This evaluative process undergoing harmonization is expected to be standardized across the MUHC during the year 2001. Presently, the individuals or committees responsible for scientific evaluation at the MUHC are:

- Research Ethics Boards (on all sites) assisted by external reviewers (The Montreal General Hospital),
- Scientific Committees (Montreal Children's Hospital and Montreal Chest Institute),
- Departmental Director involved (Royal Victoria Hospital)

2.2.3 Contract Review and Budget Breakdown

The financial evaluation of research projects sponsored by industry is conducted by members of the Office of Clinical Contracts (OCC). The Office of Clinical Contracts reports to the Associate Director of Clinical Research of the RI-MUHC. The Executive Director of the OCC is Dr. Phil Gold, and the structure, composition and role of this office is outlined in Annex 10.

The review of clinical research contracts sponsored by industry is coordinated by members of the Office of Clinical Contracts (OCC). Briefly, the Office of Clinical Contracts reviews and executes Clinical Trial Agreements, reviews the corresponding budgets to assess direct and indirect costs, as well as the reimbursement to hospital departments for services provided in the course of the study, ensures the recovery of institutional overhead fees by the RI MUHC, and in the recovery of review fees from Sponsors for the Ethics, Legal and Financial reviews of projects.

The MUHC's Standard Contract Clauses presented to sponsors during contract review are outlined in section 4 of Annex 10, *Policy Regarding the Review of Contracts (Clinical Trial Letters of Agreements) at the MUHC*. This policy addresses institutional requirements with regards to Publication Rights, Intellectual Property, Indemnification, Applicable Law, etc. The policy is also coherent with that of McGill University for Industry-Sponsored contracts. The person approving and signing contracts on behalf of Institution (or delegating the authority to review and/or sign contracts on MUHC sites) is the Legal Counsel of the MUHC, Maître Barry Cappel.

2.3. Transparency of Research Activities

2.3.1 Mandatory Declaration of Research Activities

3) Instauration de la déclaration obligatoire, de la part des chercheurs, de
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toutes les activités de recherche qu'ils accomplissent et les soumettre aux normes scientifiques, financières et éthiques en vigueur.

See section 2.1.2 in this document, entitled *Mandatory Declaration of Research Activities*. Beyond the mandatory declaration of research activities by investigators, the nine REBs must submit an Annual Report to the Board of Directors of the MUHC and to the Executive Director of the MUHC. With regards to clinical trials research, a copy of the financial evaluation (budget breakdown) is forwarded to the Department of Professional Services.

2.3.2 Negotiating the Privilege to Exercise Research

4) Négocier le privilège de l'exercice de la recherche au moment du renouvellement des privilèges d'exercice dans l'établissement.

The negotiation of the privilege to exercise research involving human subjects at the MUHC is a responsibility shared by the Board of Directors of the MUHC, by the McGill University, by the REBs as well as by the Investigators.

The MUHC has developed a Policy and Procedure on Professional Conduct, approved by the Board of Directors of the MUHC, November 27, 1998, and available at http://www.intranet.muhc.mcgill.ca/corporate/Policies/policy_professional_conduct.html. This policy aims at protecting the MUHC and officers, directors, employees, volunteers and medical and research staff against the possibility of real or apparent conflict of interest, as follows:

“The contract which exists between each Individual and the MUHC by fact of employment or appointment requires an Individual to act in the best interests of the MUHC and to refrain from such conduct or activity which is opposed to the best interests of the MUHC or which constitutes a real or potential detriment to the well-being of the MUHC.”

When becoming employed or appointed at the MUHC, the Investigator is asked to complete a Declaration form stating “I have read and understood the Policy and Procedure on Hospital conduct and do hereby certify my full compliance with its provisions.” (http://www.intranet.muhc.mcgill.ca/corporate/Policies/form_professional_conduct.pdf)

The present policy and procedure applies to Individuals connected with the MUHC including members of Board committees, medical staff, management, volunteers, employees and research personnel, including consultants working on research grants, and constitutes part of the formal relationship between the Individual and the MUHC.

“It is the policy of the MUHC that all Individuals must avoid any conflict between their personal interests and those of the MUHC. It is not intended to interfere with the right of an Individual to engage in any activity outside of his employment or appointment that does not conflict with nor represent a potential conflict with the interests of the MUHC. Participation in political activities is excluded from this policy. Each Individual will be held responsible for ensuring that neither he

nor any member of his immediate family has any interest or engages in any activity that is in conflict with this policy. Notwithstanding this, if an Individual has any doubt as to any such interest or activity, it should be reported to the Assistant Secretary of the Board.”

McGill University also addresses the issue of the privilege of exercising research in its Policy on the Ethical Conduct of Research Involving Human Subjects, 2003, Annex 1.b, Section 1.2, as follows:

“Researchers have the primary responsibility to ensure that their research is carried out in an ethical manner. They are responsible for the protection of the rights and welfare of the human research subjects.

Researchers must be familiar with and comply with this policy and other ethical guidelines relevant to their research discipline. It is the responsibility of the researcher to obtain ethical approval as described in this policy for any project involving human subjects before starting the research. If there is any uncertainty about whether the research needs ethical review and approval, the researcher should consult the appropriate REB for advice.

All members of a research team who conduct research under the supervision of others also bear personal responsibility for the ethical conduct of research with human subjects. The Principal Investigator has the responsibility to ensure that the members of the research team comply with the provisions of this policy. Principal investigators should ensure that the members of the research team are aware of the contents of this policy and of other applicable ethical guidelines that are relevant to their responsibilities. Researchers must ensure that all individuals under their supervision have the training and competence needed to carry out their responsibilities in an ethical manner.”

The MUHC REBs must also contribute to negotiating the privilege to exercise research involving human subjects by ensuring that each project submitted for review is to be conducted by an experienced and qualified investigator, with sufficient human and material resources, to ensure Good Clinical Practice and safety for the research subjects.

2.3.3 Establishing Registries of Research Projects

5) Constituer un registre des projets de recherche.

The nine REBs of the MUHC, and the McGill University Faculty of Medicine IRB, hold registries of all clinical research projects involving human subjects submitted for their review.

Registering clinical research studies in a publicly accessible electronic registry is a measure to enhance research transparency and accountability by providing greater opportunity for informed decision-making. It is the responsibility of the Sponsor, or the Sponsor-Investigator to register randomized clinical research studies conducted at the MUHC in an internationally approved public registry, as coordinated by the RI MUHC Office of Clinical Research. It is the MUHC Principal Investigator’s responsibility to verify the study was registered completely and to provide the REB, or the REO with the unique identifying number assigned by the registry, to permit the study approval, or MUHC Authorization document to be forwarded to the Investigator.

Responsibility is shared by the RI MUHC, the PRC, the REB and the REO for the appearance of unpublished clinical trial research information on the MUHC web site and may include general clinical trial information and trial-specific information. The RI MUHC is responsible for design of the web site architecture, and the PRC will review the format for conformity with MUHC PRC policy. With permission of the study sponsor, the Investigator may submit the proposed web-content and format, for MUHC review according to the RI MUHC procedures. The REB of Record will review the proposed web-content to ensure the information is balanced and not misleading or coercive. The REO will ensure adherence to emerging regulations and voluntary standards.

Standards developed by the US Department of Health and Human Services for clinical trial web sites suggest that the framework: provide a comprehensive overview of clinical trials at the institution; disclose prominently a comprehensive privacy/confidentiality policy; disclose prominently significant financial relationships and provide key information in clinical trial listings.

The administration of the RI-MUHC has accounting registries receiving installments from industrial sponsors for the conduct of clinical trials research.

The administration of the RI-MUHC submits an annual report to the FRSQ, for infrastructure support via the *Programme des Centres et Instituts de recherche*, identifying all research projects sponsored by granting agencies with, or without, peer-review committees.

The Office of Clinical Contracts files a signed copy of all Clinical Trial Agreements (contracts) reviewed at the MUHC.

2.3.4 Investigating Reports of Scientific and Ethical Misconduct

6) Faire enquête sur les cas de manquement à l'éthique et les cas d'inconduite scientifique.

See section 2.1.3 in this document, entitled *Investigating Reports of Scientific and Ethical Misconduct*.

The institution will use impartial and accountable procedures to investigate every allegation of scientific or ethical misconduct in research conducted on the part of an Investigator or a Member of the Study Team. When called upon by an institutional or regulatory authority, the REO and the REB will assist all investigations of alleged scientific or ethical misconduct in research as described at 2.2.1(G).

As deemed appropriate by the MUHC Executive, incident reports of established scientific or ethical misconduct will be forwarded to: McGill University; the Investigator's professional organization; the Canadian and Quebec research funding agencies; the US federal research funding agencies; and the Office for Human Research Protections, US Department of Health and Human Services. As necessary, incident reports will be forwarded on behalf of the MUHC, by McGill University to the Office of Research Integrity, US Department of Health and Human Services.

2.3.5 Applying the Ministry's Policy on Research Contracts (Overhead Policy)

- 7) Appliquer la politique de la circulaire ministérielle du 31 mars 1995 intitulée « Contribution de l'entreprise privée dans le cadre d'activités contractuelles de recherche » (annexe 2).

The Overhead Fee, a percentage charged on the direct costs incurred in a research contract to cover indirect costs (*contribution additionnelle de l'entreprise privée*), is 30% (refer to Annex 10). Overhead charges of 30% are applicable to all research costs (salaries, direct costs of study, purchase of equipment, laboratory analyses, diagnostic tests, pharmacy costs, compensation to patients). However, the Review Fee of \$3,500 covering ethics, legal and financial evaluation of research projects, is not subject to overhead charges and is invoiced separately.

On June 29, 2000, the MUHC Board of Directors approved a minimum of 30% overhead fee applied on direct costs of industry sponsored clinical research contracts. The breakdown of this overhead (OH), when administered within the MUHC, is as follows: By Ministerial decree, 3 of the 30% to return to the MUHC to its global budget for infrastructure support (i.e. 10% of the OH); 18 of the 30% to the Research Institute to support research (i.e. 60% of the OH); 9 of the 30% to the Clinical Department to support research (i.e. 30% of the OH) (refer to Annex 10, section 5).

2.3.6 Reports on the Implementation of the Regulatory Framework and on Cases of Scientific or Ethical Misconducts

- 8) Rendre compte, dans leur rapport annuel, des actions prises pour mettre en place les mesures qui sont de leur responsabilité et rendre compte des enquêtes relatives aux cas de manquement à l'éthique ou aux cas d'inconduite scientifique.

On an annual basis each MUHC REB will submit a report on their activities to the MSSS in the specified format. Information concerning established scientific or ethical misconduct in research will be communicated to the MUHC Board of Directors, and to its Research Ethics Sub-Committee at the earliest opportunity. Other parties will be informed of established scientific or ethical misconduct in research according to Section 2.5.4, Subsection 3 for the "Disposition of Findings of QI Visits". Non-nominal information concerning established misconduct will be included in the REB's annual report to the MSSS.

The REO will monitor REB annual reporting to the MSSS to maintain in good standing the designation (*Approbation Ministérielle*) by the Quebec Minister of Health and Social Services for MUHC REBs to review research with legally incompetent persons, in compliance with Article 21 of the Quebec Civil Code.

2.4. Protections for Human Subjects of Research

The dignity, rights and well being of the research subject must prevail over any other interest, whether economic, scientific, or of the community, particularly when a conflict of interest associated with the research has been identified. This principle shall apply to all human subjects research reviewed and conducted at the MUHC, or reviewed and conducted elsewhere involving a staff of the MUHC.

2.4.1 Confidential Registries of Human Research Subjects

- 9) Identifier les personnes qui prêtent leur concours à des activités de recherche en respectant la confidentialité.

In order to protect subjects participating in research the MUHC requires explicit commitment from Principal Investigators conducting research with a therapeutic component, that they will maintain a registry with specific information required by MSSS, concerning all subjects participating in studies conducted under their leadership. Each potential subject must give consent for their information to be included in the registry, and be made aware institutional personnel, and representatives of the MSSS and other authorized parties to the research may access the registry. Retention of the person's information in the registry will not exceed twelve (12) months following the conclusion of the subject's participation in the research.

2.4.2 Rights of Human Research Subjects and Managing Their Complaints

- 10) Assurer aux personnes prêtant leur concours aux activités de la recherche les mêmes droits qu'aux usagers recevant des soins de santé ou des services sociaux, notamment à l'égard du mécanisme de traitement des plaintes.

The Rights of Human Research Subjects and Management of Their Complaints is addressed in The Proposed Bylaw Governing the User Complaint Evaluation Procedure at The McGill University Health Centre, March 2002, Section 1.5b of the Regulatory Framework (approved by the Board of Directors of the MUHC, April 25, 2002), available at http://www.intranet.muhc.mcgill.ca/corporate/Policies/policy_patient_complaint.pdf.

The purpose of this bylaw (User complaint evaluation procedure) is to set out the procedure for evaluating complaints by the MUHC, in compliance with the Act respecting health services and social services (R.S.Q., c. S-4.2). This Bylaw fulfills an important requirement of the *Plan d'action* with regards to the protection of human research subjects (*Mesures 10-11*; sections 2.4.2 and 2.4.3 of the Regulatory Framework, which stipulates that: "The person who accepts to

participate in research activities must benefit from the same rights given to a user receiving health care and services. Accordingly, health care establishments conducting research activities must apply the following measures: ... 10) ensure that persons participating in research activities benefit from the same rights given to users receiving health care and services, including the user complaint evaluation procedure; 11) report on the complaints filed by these persons according to procedures established by the *Loi sur les services de santé et les services sociaux*.”

In addition, the rights of human subjects participating in research, and the available resources for these subjects, or patients, wishing to enforce such rights, must be clearly stated in the informed consent forms reviewed and revised by the REBs of the MUHC.

2.4.3 Reports on Complaints by Human Research Subjects

11) Faire état des plaintes reçues par ces personnes selon les mécanismes prévus dans la Loi sur les services de santé et les services sociaux.

The Reports on Complaints by Human Research Subjects is addressed in The Proposed Bylaw Governing the User Complaint Evaluation Procedure at the MUHC:

http://www.intranet.muhc.mcgill.ca/corporate/Policies/policy_patient_complaint.pdf.

Section 6 of this Bylaw is dedicated to the “Annual Report on the Application of the Complaint Evaluation Procedure and the Improvement of the Quality of Services” as follows: “the Executive Director must take the necessary steps to ensure that information about making and processing complaints is available to the public. The Executive Director of the institution must send the Board of Directors, as soon as possible, any report or recommendations received from the local commissioner for the quality of care and services pursuant to this bylaw.” Also involved in the Report on the Application of the Complaint Evaluation Procedure are: the local commissioner for the quality of care and services, the medical examiner and the review committee.

The Local Commissioner for the Quality of Care and Services (LCQCS) coordinates the process to address a complaint made by a person volunteering to be a research subject at the MUHC. The LCQCS will inform the Director of the REO of complaints concerning human research activities. In the course of evaluating such complaints the LCQCS may also interact with the Director General and Chief Executive Officer, the MUHC Board of Directors, an ad hoc review committee, the Medical Examiner, and where appropriate the Council of Physicians, Dentists, and Pharmacists. The REO Director will inform the REB of Record of the nature of the complaint. The REB will include non-nominal information concerning each founded complaint in the annual report to the MSSS.

In the case of every founded complaint involving a research subject the LCQCS, in compliance with Foundation Document 5b “The Bylaw Governing the User Complaint Evaluation Procedure at the McGill University Health Centre”, will include the appropriate information in the Report and will organize transmission of the Report to the appropriate parties.

2.5. Governnance of Research Ethics Boards

2.5.1 Reporting of Research Ethics Boards to the Board of Directors

12) Les conseils d'administration verront à ce que les comités d'éthique de la recherche leur soient rattachés.

Canadian regulations specify that Research Ethics Boards (REBs) must be established by the highest levels of the institution. Through its process of governance the MUHC delegates to REBs the responsibility for oversight of research involving human subjects within its jurisdiction, and thus REBs are accountable directly to the MUHC Board of Directors.

When multiple REBs exist within an institution, Canadian regulations require a mechanism to be established to coordinate the practices of all the REBs. The Research Ethics Office (REO) was created to coordinate REB policies and standing operating procedures, and to provide administrative support to the multiple REBs of the MUHC.

2.5.2 Process of Appointment to Research Ethics Boards

13) Les conseils d'administration verront à nommer les membres des comités d'éthique.

The process to nominate and appoint REB Chairs, Members and Alternate Members is consistent with relevant law, regulatory guidelines and local policy. Appropriate candidates are recommended by the REB Chairs to the REO Director who places the individuals in nomination to the Board of Directors.

The appointments of individuals to serve on REBs are made exclusively by the Board of Directors of the MUHC for a term of three years. The mandate is renewable, subject to mutual agreement and continued endorsement by the Board of Directors.

When a new Member is appointed to an REB, the person's curriculum vitae is forwarded to the Minister of Health, accompanied by the supporting Board of Directors resolution.

It is the intention of the Board of Directors to allow all current and future Members in good standing of the nine MUHC REBs, to act as Alternate Members on any MUHC REB, as required from time to time.

Neither members of the institutional Board of Directors, nor the Legal Counsel, nor Directors of the Research Institute may be appointed to an REB.

Effective community representation on an REB is considered essential, therefore, as the size of the REB increases beyond the minimum composition, the number of community members should increase proportionately to maintain community representation of at least 20%.

An REB Member may be dismissed by the Board of Directors for any of the following:

- (i) for reasons of a serious nature considered incompatible with a Member's function;
- (ii) if declared incompetent, or placed under tutorship or curatorship;
- (iii) if the Member no longer possesses the required qualification;
- (iv) if the Member regularly misses meetings without appropriate justification.

In agreement with a decision of the *Commission d'accès à l'information* the identity of MUHC REB Members is not considered to fall within the public domain. REB Members are not identified to media or others who might request such information. However, REB Members are identified on formal membership rosters showing the entire composition of each REB that may be shared with research sponsors, government agencies, and in fulfilment of regulatory obligations. No individual REB Member is to be associated with the formal decision-making for a specific research proposal.

2.5.3 Training of Research Ethics Boards' Members and Professional Staff

14) Les conseils d'administration verront à exercer leurs responsabilités vis-à-vis de la formation en éthique pour les membres des comités d'éthique et les professionnels qui sont à leur emploi.

As described by the «*Plan d'action ministériel en éthique de la recherche et en intégrité scientifique*» MSSS, Qc (1998), it is the responsibility of the Board of Directors to ensure that educational activities in research ethics are available for members of Research Ethics Boards and professional employees. The Office of Research Ethics (REO) is mandated to coordinate the practices of REBs within the MUHC including information concerning educational opportunities.

It is understood that the provision of ongoing education in research ethics for the MUHC research community, is essential to maintain a culture of compliance with regulatory codes, and with institutional policies and procedures relevant to the protection of human subjects. Education activities are part of the Quality Assurance (QA) and Education in Research Ethics Program described at §2.5.4. An overview of the range of educational activities available to the MUHC research community is included in the MUHC Research Ethics Boards and Research Ethics Office Annual Report.

2.5.4 Ethics Follow-Up on Ongoing Research Projects

15) Les comités d'éthique de la recherche verront à préparer et mettre en place un mécanisme de suivi éthique pour les projets de recherche en cours.

The goal of the Quality Assurance (QA) and Education in Research Ethics Program is to work constructively with investigators and research staff to improve the quality and the ethical integrity of research involving human participants at the MUHC. It operates under the jurisdiction of the Research Ethics Office (REO), which supports the work of the institution's Research Ethics Boards (REBs). The REBs in turn, derive their authority from the MUHC Board of Directors. The QA and Education Program supports the REBs by assisting them to follow ongoing studies in accordance with the Guide d'éthique de la recherche et d'intégrité scientifique FRSQ (2003), Partie 2 (27)

Le CÉR convient avec le chercheur d'un mécanisme de suivi plus ou moins rapproché, selon la nature du projet, sa complexité, la fréquence et la gravité des risques qui y sont associés, et les caractéristiques des sujets.

L'objet du suivi et de s'assurer que :

- *La dignité, le bien-être et les droits des sujets sont protégés ;*
- *Le projet de recherche se déroule conformément à ce qui a été autorisé par le CÉR*

Le suivi n'a pas à être exercé directement par le CÉR ; celui-ci peut confier cette tâche à des personnes qui lui sont extérieures ou à une autre instance. La personne ou l'instance à laquelle est confiée la tâche du suivi se rapporte au CÉR.

The QA and Education Program consists of two components

1. Educational Activities
2. Quality Improvement (QI) visits.

Both components are educational in nature and are intended to promote a culture of respect for the highest ethical conduct among all members of the research community. It strives to achieve this goal by promoting an attitude of respect for the rights and well being of human participants by providing education on the relevant regulations and policies governing research and by ensuring they are applied.

It should be noted that the primary person responsible for the conduct of a study is the principal investigator, who in turn shall be responsible for the oversight of co-investigators as well as staff. Although the Quality Assurance Officer may make recommendations to the REB of Record regarding improvements to the conduct of a study (e.g., training, delegations of tasks, etc.), the principal investigator is ultimately accountable to the REB of Record and to the authorities of the MUHC and the RI-MUHC for the conduct of the study in question.

This policy is consistent with McGill University's Policy on the Ethical Conduct of Research Involving Human Participants.

(A) EDUCATIONAL ACTIVITIES

As an institution devoted to the advancement of medical knowledge, the MUHC is home to a wide range of health research from basic science to clinical studies. As the complexity of research grows and new ethical dilemmas arise, the content and situational interpretation of ethics guidelines and regulations constantly evolve. The MUHC REO is committed to keeping its research professionals abreast of these developments both in their initial training and through continuing education. The Office of Research Ethics (REO) of the MUHC is committed to contributing its own expertise in the

field of ethics to support all members of the MUHC research community investigators, research coordinators, study staff, REB members and research ethics support staff , in accordance with the Guide d'éthique de la recherche et d'intégrité scientifique (2003), Partie 2 (29)

L'établissement prévoit des activités de formation destinées aux membres du CÉR, aux chercheurs et à l'ensemble du personnel.

Educational activities are tailored to meet both specific and general needs. These include:

- One-on-one consultations
- Group sessions and workshops
- Web pages and online training modules
- Conferences
- Professional development initiatives

These activities may draw upon external resources (e.g., from federal or provincial agencies).

An extensive educational policy that brings to the forefront excellence in research ethics is under development.

Responsibility of the Quality Assurance Officer:

Under the oversight of the Director of the REO, the Quality Assurance Officer will administer the education initiative of the QA and Education Program and liaise with McGill University and other institutions to foster the development of Quality Assurance and Education programs of the highest standard in research ethics.

The Director of the REO, in consultation with the Chairs of the REBs, may make certain elements of the Education Program compulsory for those investigators who wish to apply for initial or continuing ethics review of a study, as well as for study staff and others involved in the conduct of research with human participants or with the administration of the REBs.

(B) QI VISITS

1) Responsibility of the Quality Assurance Officer:

The Quality Assurance Officer is responsible for the conduct of QI Visits. The purpose of this component of the Program is to actively review the conduct of research at MUHC that involves human research participants. The Quality Assurance Coordinator supports the Quality Assurance Officer by conducting and writing reports for the Routine (not-for-cause) QI Visits.

QI Visits entail:

- i. Reviewing all documentation and data connected to the study under examination, collecting any and all necessary data to ascertain whether the study meets all pertinent external and internal regulatory standards and ethical guidelines, as well as study-specific requirements imposed by the REB.
- ii. Interviewing study investigators, co-investigators, coordinators, research nurses, technicians and other personnel employed to perform tasks related to the study and, where permitted and appropriate, study participants in order to gain additional

information about the conduct of the study. Of note, representatives of the study sponsor are not to be involved in QI visit;

- iii. In the case of Routine (not-for-cause) QI Visits, reporting in writing of the findings and recommendations simultaneously to the study investigator and the REB of Record. These visits will be educational in focus in that they will seek to remedy problems in a collegial fashion while at the same time identify common errors that can be addressed in the educational materials.
- iv. In the case of Directed (for-cause) QI Visits, reporting findings and recommendations to the authority having required the Visit and to the REB of Record, while also reporting the findings (without recommendations) simultaneously to the investigator and inviting comments prior to, or in conjunction with, the REB review;
- v. In the course of the Routine QI Visits, providing guidance to study investigators and research staff on relevant regulations and ethics guidelines in a supportive and educational fashion;
- vi. In the event of discovering a study that apparently operates without valid ethics review, reporting the matter promptly to the Director of the REO, who will assign the study for review to an appropriate REB (normally the REB that would have reviewed the study initially).

2) Selection of Studies for QI Visits:

- i. For Routine (not-for-cause) QI Visits, active studies will be selected randomly from each REB's database by the Quality Assurance Officer with the assistance of an MUHC-affiliated statistician;
- ii. Directed (for-cause) QI Visits shall be justified by an allegation or reasonable suspicion of misconduct or serious deficiency in the ethical conduct of a study involving human participants – any person making such allegations in good faith shall have their disclosure kept in confidence, where possible, and shall be protected from unreasonable disciplinary action by the administration of the MUHC and the RI-MUHC;
- iii. Any combination of two of the following shall have the full authority to mandate a Directed (for-cause) QI Visits: the chair of the REB of Record; the REB of Record by resolution of the full board; the Director of the REO; the Associate Director of Clinical Research of the RI-MUHC, the Scientific Director of the RI-MUHC; the Director of Professional Services of the MUHC; the Director of the Montreal Neurological Institute (for MNI-related studies or staff); an Ombudsman of the MUHC; a Medical Examiner of the MUHC; the Dean of the Faculty of Medicine of McGill University (for studies involving Faculty of Medicine staff); the CEO of the MUHC; the Board of Directors of the RI-MUHC; the Board of Directors of the MUHC;
- iv. When a report of administrative misconduct (e.g., financial misconduct) is forwarded by the Director of the Research Ethics Office to the appropriate

institutional authority, that institutional authority shall disclose the final resolution of the administrative misconduct (e.g., disciplinary action) in writing to the Director of the Research Ethics Office within 30 days of the final determination. The Director of the Research Ethics Office will in turn promptly inform the REB of Record of the findings and the REB may consider any potential ramifications relating to the administrative misconduct on the well-being of the human participants for the study in question;

- v. The decision for a Directed for-cause QI Visit is not, in itself, subject to appeal.

3) Disposition of Findings of QI Visits

The REB of Record is the principal authority concerned with the ethical conduct of studies under its oversight. The Quality Assurance Officer or Coordinator will provide what guidance he or she deems appropriate to Investigators and Research Staff for minor problems discovered on site. For further guidance see QA and Education Program Addendum 1. Disposition of Findings from the REB of Record will occur as follows:

- i. For matters involving the protection of human participants, whether serious or not, the REB of Record will recommend and enforce appropriate changes to the conduct of a study (detailed in Section 4 below), and will report directly on these matters to the Board of the MUHC as required by the Plan d'action Ministériel en éthique de la recherche et en intégrité scientifique (1998) as well as the Tri-Council Policy Statement: Ethical Conduct for Research involving Humans (2003 [1998]);
- ii. For serious problems as defined in Section 6 and for matters other than those directly involving the protection of human participants (e.g., scientific integrity, financial misconduct, or other administrative deficiencies), the Chief Operating Officer of the RI-MUHC (for matters involving administrative or financial misconduct), the Associate Director for Clinical Research of the RI-MUHC, the Scientific Director of the RI-MUHC and the Director of Professional Services of the MUHC, the Director of the Montreal Neurological Institute (for MNI-related studies or staff), as well as the Department Chair and Dean of the McGill Faculty of Medicine (for studies involving Faculty of Medicine staff) will be informed of the findings of the QI Visit Report in a timely manner by the Director of the REO; in addition, the Director of the REO may at his discretion inform the department and/or division head of the investigator(s) concerned;
- iii. For serious breaches of regulations and/or guidelines, sponsors, external funding agencies, as well as governmental oversight agencies will be informed, where required by law or regulations, by the responsible authority of the MUHC or McGill University Faculty of Medicine;
- iv. For serious problems as defined in section 6 below, the Scientific Director of the RI-MUHC and/or the Director of Professional Services of the MUHC, as well as the Dean of the McGill Faculty of Medicine (for studies involving Faculty of Medicine staff), the Director of the Montreal Neurological Institute (for MNI-related personnel), may require corrective action other than that required by the REB of Record, but they may not overrule the corrective action required by the

REB. Any corrective action they require will be reported to the Chair of the REB of Record for the REB's consideration in terms of the continuity of the study in question.

- v. For any resolution of the REB of Record having a possible impact on study personnel, the Director of the REO shall be informed by the Chair of the REB of Record of this resolution within seven days of the passing of the resolution. The Director of the REO will then inform the Human Resources Manager of the RI-MUHC in a timely manner of the REB resolution.

4) Post-QI Visit Actions

- i. For Routine (not-for-cause) and Directed (for-cause) Visits, the Quality Assurance staff will prepare a report with findings and recommendations under the Quality Assurance Officer's supervision. In the case of routine Visits, the findings and recommendations will be submitted simultaneously to the Investigator and the REB of Record. In the case of Directed Visits, the investigators will receive copy of the QA findings, but not the recommendations. The Investigator may, at his or her discretion, write a response to these findings and recommendations and submit this response to the REB of Record. Once the REB of Record has reviewed the report and has decided what, if any, recommendations shall be implemented, the Chair of the REB of Record will correspond with the Investigator, with a copy of this correspondence going to the Quality Assurance Officer. If it is deemed necessary by the REB of Record, the Quality Assurance Officer may follow-up with the Investigator and his or her staff to ensure compliance with any REB requirements for the study.
- ii. The investigator is required to keep the QI report and REB correspondence related to the QI Visits separate from the study files. The QI visits findings/reports and related correspondence are not to be divulged to the study Sponsor and/or its representatives. However, this provision does not limit the obligation of the REB and of the institution to report cases of ethics or scientific misconduct to responsible authorities, as required by law or regulation (see article 3 iii above)
- iii. Where serious violations of ethical guidelines or regulations (see section 6 below for definitions) have been discovered during a Routine or Directed QI Visit, the REB of Record will exercise diligence with all due haste. This may require that the Chair of the REB of Record call a meeting of the REB specifically to review the QI Visit findings. At the very least, serious findings in a QI Visit Report will be discussed as a principal agenda item at the next regularly scheduled meeting of the REB. The Investigator will have the right to present his or her case directly before the REB of Record in person or through an appointed representative. Upon receiving the report of serious findings from the Quality Assurance Officer, the REB of Record will assess the violations and may make the following determinations:

- a) The Investigator may be permitted to continue the study but will be required to respond to the findings in the report with a strategy for corrective actions in writing within thirty (30) days to the REB of Record to correct the violations identified. The REB of Record may approve, change, or reject the proposed strategy. If a strategy for corrective actions is approved, the REB of Record will require that the Quality Assurance Officer perform a follow-up Directed QI Visit within sixty (60) days to ensure that all violations have been resolved. If the REB of Record is then satisfied that the violations have been rectified, the matter will be reported in writing by the Chair of the REB of Record to the chain of authority named in paragraph (d) below within five (5) working days of the determination by the REB that the study status was corrected and that it will be permitted to continue. If the REB of Record, subsequent to the follow-up Directed QI Visit, is not satisfied that all conditions for correction have been met, paragraphs (b) or (c) below will apply at the REB's discretion.
 - b) The REB of Record may withdraw its approval for the study until the violations have been resolved to the satisfaction of the REB.
 - c) The REB of Record may permanently withdraw its approval for the study and other studies conducted by the investigator, if deemed appropriate.
 - d) The Chair of the REB of Record will inform the Director of the REO of the REB decision within 7 days of this decision. The Director of the REO will report the REB's findings and decisions in writing within five (5) working days to the Board of the MUHC, the Associate Director for Clinical Research of the RI-MUHC, the Scientific Director of the RI-MUHC, the Director of Professional Services of the MUHC, the Dean of the Faculty of Medicine of McGill University (for studies involving Faculty of Medicine staff), the Director of the Montreal Neurological Institute (for MNI-related personnel), and, as required by law, regulations or contractual obligations, to the sponsor, concerned external agencies, or Minister of Health and Social Services of the province of Quebec.
 - e) The Scientific Director of the RI-MUHC or his delegate will call a meeting of senior management personnel in the reporting chain in paragraph (d) above and other persons of interest at his or her discretion within 30 working days of receipt of the written report of the Director of the REO to determine what, if any, further measures will be taken from an administrative viewpoint. The Scientific Director may invite the investigator, the Chair of the REB of Record, the Director of the REO, and/or the Quality Assurance Officer to attend part or all of this meeting as he deems appropriate. The Scientific Director will provide a written report on the decisions rendered at this meeting to the Chair of the REB of Record, the Chief Executive Officer (CEO) of the MUHC, the Board of the RI-MUHC, and the Board of the MUHC within ten (10) working days.
- iv. The Quality Assurance Officer will ensure that full records of all QI Visits will be kept for a period of three years after the QI Visit in the case of Routine Visits without serious violations, and for a period of six years after the QI visit in the case of all Directed Visits and those Routine Visits with findings of a serious nature. Access to these records will be restricted to persons authorized by the

Director of the REO or the Chair of the REB of Record. Access to these records will be restricted to persons authorized by the Director of the REO or the Chair of the REB of Record.

5) Process of Appeal for REB Actions

Pursuant to McGill University's *Policy on the Ethical Conduct of Research Involving Human Participants* there is a process for appeals of REB decisions. In the event that an investigator or other interested party disagrees with the decision of an REB with regards to the disposition of a QI Visit, this appeals process shall be invoked, where applicable.

6) Definition of Serious and Minor Violations in QI Visit Findings

The global concern of the QA and Education program is the protection of the human participants. By protecting the human participant, we protect the investigator, his/her staff, as well as the institution. Various regulatory standards are in force that have developed over the years to ensure the highest level of participant protection. The lists provided below of "serious" and "minor" violations are drawn from the regulatory framework that governs research at our institution. Many of the violations listed are primarily of an administrative nature, while others have a more direct bearing on the safety and well-being of the research participant. When assessing these findings in the context of a QI Visit, the REB of Record as well as the management of the institution should aim for the highest level of participant protection while at the same time distinguishing between administrative and human protection violations on an incremental scale of seriousness.

For the purposes of disposition of findings so that the REB of Record and the Quality Assurance Officer have guidelines for the differentiation between serious and relatively minor violations, categorization of potential findings has been provided in subsections i, ii, and iii below. These lists are not exhaustive, and in the context of various studies, some violations that may fall in one or another list may in fact need to be dealt with more or less judiciously. Any findings that are not listed below shall be assessed on a case-by-case basis by the REB of Record, which will determine whether they are to be considered "serious" or "minor" in the context of the particular study.

The REB of Record, in the first instance, has the discretion to assess the context of a particular study when determining the disposition of findings of a QI Visit, although any problem that is identified as a "serious violation" on the list below must be reported to the Board of the MUHC and the institutional authorities designated above, even if the recommendation of the REB of Record is to judge the problem as less serious than it would normally be assessed in other studies.

Minor problems may be rectified through a plan established between the Investigator and the REB of Record, taking into account the recommendations made by the Quality Assurance Officer.

i. Serious Human Participants' Protection Violations:

- a) The regulatory requirements for the conduct of the study have not been met

- b) Study is being conducted without valid MUHC/McGill REB approval
- c) Participant enrolment/recruitment occurs while the study is on hold or approval has lapsed
- d) Failure to report serious protocol violations to the REB
- e) Failure to report serious protocol violations to the sponsor
- f) Failure to obtain REB approval for amendments or study modifications to the study protocol
- g) A greater number of participants are enrolled than have been approved by the REB (subject to REB interpretation)
- h) Failure to obtain consent/assent from a participant
- i) Use of an invalid consent/assent form (subject to REB interpretation)
- j) Consent/assent forms are not signed by the participant or a legal representative
- k) Failure to adhere to the protocol approved by the REB
- l) Major safety hazards at research site (e.g., lack of safety or emergency medical equipment)
- m) Improper storage of biological specimens, drugs or devices
- n) Lack of appropriate security for identifiable information
- o) The Investigator has delegated responsibility inappropriately (e.g., to unqualified/unlicensed personnel)
- p) Failure to file a brief summary of the study along with a copy of the signed informed consent form on the participant's hospital chart

ii. Serious Administrative Violations:

- a) Consent forms are missing
- b) Failure to report a Serious Adverse Event (SAE) to the REB and/or sponsor within the time limits required by the regulations and MUHC policy
- c) Source documents (e.g., collected nominal data) are missing
- d) Notes to file are not signed and dated
- e) Investigator(s) and/or staff are unwilling to cooperate with Quality Assurance Officer in providing information or answering questions.
- f) Failure to submit the Continuing Review within the timeframe required by the REB (subject to REB interpretation)
- g) A consent form has been backdated by a study representative
- h) There is not a study file for each participant

iii. Minor Administrative Violations:

- a) The documentation required by the regulations is incomplete or misplaced (a document that is misplaced for more than 15 days subsequent to the initial QI Visit will be considered "missing" and will constitute a serious violation)
- b) There are incomplete logs (i.e. monitoring, staff signature, enrolment)
- c) REB correspondence (approval letters, report etc.) is not on file
- d) Failure to close the study with the REB
- e) Failure to obtain REB approval for administrative changes (e.g. changes in study staff)
- f) Failure to report minor protocol exceptions to the REB or sponsor

- g) Original/approved consent/assent forms are not on file but can be located post-QI Visit
- h) Failure to offer a copy of the consent/assent form to the person signing
- i) The consent form is not signed by the person administering the informed consent procedure
- j) The consent form is not dated or has been dated by someone other than the person required to date the form
- k) Failure to document that a copy of the consent was offered to the participant
- m) There is no checklist of eligibility criteria
- n) Failure to obtain REB approval for administrative/editorial changes to the study protocol
- o) Photocopies are present where originals are required
- p) The Source document(s) or other collected nominal data are incomplete
- q) Entries have not been made in ink
- r) Crossing-outs are not initialed and dated
- s) The Source documents are not filed in a consistent fashion
- t) Delegation of responsibilities is not documented

2.5.5 Annual Reports of the Research Ethics Board to the Board Of Directors

16) Les comités d'éthique de la recherche doivent faire annuellement rapport au conseil d'administration des responsabilités qui leur ont été confiées.

MUHC REBs are accountable directly to the Board of Directors and in keeping with their responsibility for oversight of research involving human subjects, will report annually to the Board concerning those research activities falling within their jurisdictions.

The Board of Directors of the MUHC requires that the REBs submit an Annual Report to the Minister of Health in the format requested by the MSSS.

The REO in fulfilment of its mandate to coordinate the practices of the MUHC REBs will submit to the Board of Directors a combined annual report consisting of the REBs' Annual Reports to the Minister of Health, and specific information reflecting the operational plan, budget and administrative resources necessary to meet the requirements imposed upon the MUHC by law and regulation, including the monitoring of research and the training for investigators and research staff in the responsible conduct of research.

2.6. Investigational Drugs

2.6.1 Control of Investigational Drugs

17) Soumettre les médicaments d'expérimentation au même type de contrôle que celui prévu pour les médicaments d'ordonnance, conformément aux dispositions des articles 116 et 117 (annexe I) de la Loi sur les services de santé et les services sociaux.

Policy to require inclusion of research information in the medical record of a patient is set out in the *MUHC Research Institute, Policies and Procedures* (refer to Annex 9) that will become the policy of the RI-MUHC following its incorporation.

The policy is as follows:

“For studies involving a drug trial or invasive procedures (as determined by the Research Ethics Committee or Clinical Trials Committee), study participants will be asked to obtain a medical record number (if not already available). If the participant is a "private" patient, a signed copy of the letter to the admitting office (attached to the approval letter) should be given to the participant so that he/she can obtain a medical record number. The investigator(s) will be required to forward a copy of the consent form (if appropriate), and a research subject identification study summary form to The Medical Record Department of each participant.”

2.6.2 Introducing New Medication in Research Protocols

18) Au cours de l'évaluation éthique des projets, porter une attention toute particulière aux conséquences pour les participants de l'introduction de nouveaux médicaments dans le cadre des protocoles de recherche. Pour faciliter l'évaluation de ces conséquences, un travail de révision des processus décisionnels pour la couverture des médicaments coûteux est en cours au Ministère.

A Research Ethics Board will, during the course of its review of a study proposed to test investigational drug(s), evaluate the proposed use of the drug(s) from the perspective of minimizing potential adverse effects to the research subject, and from the perspective of the future availability of the new medication.

2.6.3 Investigational Drugs for Minors or Incapacitated Adults:

Application of Clauses of Article 21 of the Civil Code of Quebec

The policies at the MUHC governing research in medical emergency situations are based on Article 21 of the *Code Civil du Québec*, such as decreed in the *Plan d'action ministériel en éthique de la recherche et en intégrité scientifique* (June 1998) and are in agreement with Article 2.8 of the Tri-Council Policy Statement on the Ethical Conduct for Research Involving Humans. The Belmont Report is a set of ethical principles that acts as an accepted international standard to guide the conduct of human subjects' research that defines the following:

“Research designates an activity designed to test an hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge (expressed, for example, in

theories, principles, and statements of relationships". The Belmont Report in addressing the topic of innovative therapy, states that:

"Innovation does not, in and of itself, constitute research. The fact that a procedure is experimental, in the sense of new, untested or different, does not automatically place it in the category of research. Radically new procedures of this description should, however, be made the object of formal research at an early stage in order to determine whether they are safe and effective."

The Civil Code of Quebec, Article 21 states that "Care considered by the Ethics Committee of the hospital concerned to be innovative care required by the state of health of the person submitted to it, is not an experiment." and which now reads in the amendment to Article 21 as follows : " An intervention considered by the Ethics Committee of the hospital concerned to be innovative care required by the state of health of the person submitted to it, is not an experiment". Although a standard procedure is not in place, the final decision allowing the use at the MUHC of a treatment considered as "innovative" typically calls for an ethics and scientific review, or consultation, involving the Clinical Ethics Committee and Research Ethics Committee, as well as for an evaluation of utilisation of institutional resources by administrative authorities (Director of Professional Services and Departmental Director). (Refer to Annex 1).

3. References

1. McGill University Ethical and Legal Aspects of Research Involving Human Subjects Conducted in the Faculty of Medicine and Affiliated Hospitals – Policies and Procedures , McGill University Faculty of Medicine, revised 1999.
2. A Guide to Sponsored Research at McGill University, McGill University, 1998.
3. 3.a Handbook of Regulations and Policies for Academic Staff, McGill University, Montreal, 1998.
3.b Procedures for Investigating Reports of Misconduct in Research, McGill, University, 1998.
4. Contract of Affiliation between McGill University and MUHC, approved by the Board of Directors of the MUHC, November 22, 1999, signed November 26, 1999.
5. Institutional Policy for Support and Development of Research at MUHC, submitted for approval by the Board of Directors of the MUHC, June 1999.
6. Agreement Between the McGill University Health Centre and the Research Institute of the McGill University Health Centre, Draft version, August 26, 2000, pending approval by the Board of Directors of the MUHC.
7. McGill University Health Centre. Plan of Development of Research. Document submitted to the FRSQ (1999), by Dr. Emil Skamene, Scientific Director, RI-MUHC.
8. Research Institute of the McGill University Health Centre - General By-Laws, Draft version, August 25, 2000, document submitted to the Board of Directors, October 18, 2000, pending approval by the Board of Directors of the MUHC.

9. Montreal General Hospital Research Institute, Policies and Procedures, May 1998. Document to be adapted to Policies and procedures of the RI-MUHC in 2001.
10. Policies and Procedures for Ethics, Budget and Contract Review of Clinical Trial Research between Industrial Sponsors and the Research Institute of the McGill University Health Centre, revised October 24, 2000, approved by the Board of Directors of the MUHC, June 29, 2000.
11. Regulatory Framework in Health Research at the McGill University Health Centre (*Cadre réglementaire de la recherche en santé au Centre universitaire de santé McGill*) February 2001, submitted for approval to the Board of Directors of the MUHC, June 2001 (*present document*).
12. *Plan d'action ministériel en l'éthique de la recherche et en intégrité scientifique*, published by the *Ministère de la Santé et des Services Sociaux* (June 1998).
13. *Cadre réglementaire de la recherche en santé dans les établissements universitaires de santé du Québec*, April 2000. Working Document published by the FRSQ, 4th version, May 2000
14. Policy on Overhead and Contract Review Fee on Industry Sponsored Clinical Research Contracts,
Document approved by the Board of Directors of the MUHC, June 29, 2000, circulated to MUHC investigators October 17, 2000.
15. Ethical and legal requirements for conduct of research using human material obtained during the course of providing care (clinical testing). Memo addressed to Clinical Laboratory directors, MUHC, by Dr. Denis Cournoyer, Director, Office of Research Ethics, MUHC, May 10, 2000.
16. McGill University Health Centre - Research Ethics Boards - Annual Report 1999.

Appendix 1: QA and Education Program Addendum: MUHC Guidelines for the Management of Serious Ethical Violations Involving Human Participant Research

The following recommendations are not be considered binding upon the REB, but are guidelines to assist the REB in resolving cases involving allegations of ethical misconduct. The REB is ultimately responsible for exercising its judgment according to the facts and context of each given allegation. The following recommendations apply only to those cases involving serious ethical violations as defined in the MUHC QA and Education Program policy, section B6.i and ii. REBs are encouraged to seek the guidance of the Office of Research Ethics throughout this entire process. Any actual disciplinary measures must be imposed by the appropriate institutional authority – the REB’s jurisdiction is limited to removing approval for any study or studies concerned – the guidelines below contain suggested ways in which the REB of Record could advise the institution in terms of appropriate post-review action.

1. For cases involving first-time violations of primarily an administrative nature, where no participants were actually put at risk by the violation, the REB should request that the Quality Assurance (QA) Officer to provide on-site education and follow-up review with the investigator and research staff in question. Wherever possible, the study should be permitted to continue, or be restored to approved status once the violations have been rectified.
2. For cases involving first-time violations of a nature in which participants were actually placed at risk, the REB should suspend approval for the study in question, as well as for other studies under the same principal investigator. The REB should request that the QA Officer to provide on-site education and a directed review of every study on which the investigator in question is principal investigator. If further problems are found, the QA Officer will provide to the REB of Record a recommended strategy for rectification of the problems in question. The REB may at its discretion continue to suspend some or all of the studies in question until such time as the problems found are resolved to its satisfaction. The REB may also require the QA Officer to perform a directed review on the study in question or other studies under the same principal investigator within six months after the resolution of the problem(s) in question to ensure compliance. If further serious problems are uncovered at that time, the studies of the principal investigator in question should have their approval removed, and the REB should advise the institution to require that the investigator in question be restricted from applying for ethics approval for at least one year from that date, and should at that time provide proof of appropriate training taken by himself or herself in Good Clinical Practices as well as Research Ethics in courses approved by the REB, upon recommendations by the QA Officer.
3. For cases involving repeat offences of an administrative nature in which participants were not put at risk, the REB of Record should recommend to the institution that the investigator in question should be placed on probation by the institution for one year, during which time he or she should be required to take approved training in Good Clinical Practices and Research Ethics in courses approved by the REB, upon recommendations by the QA Officer. He or she should also be participant to a directed review of one or more studies to ensure compliance. Where further serious problems are found, the REB may at its discretion suspend or remove approval for some or all of the studies under this principal investigator until it is satisfied that the underlying competence issues have been resolved.

4. For cases involving repeat offences of a serious nature involving actual risk to human participants, the REB may at its discretion advise the institution to forbid the investigator in question from conducting research involving human participants as a principal investigator or co-investigator for a period of up to three years. At the end of the disciplinary ban, this investigator should be on probation for not less than one year, and should be required to take remedial training and be subject to directed reviews of all studies on which he or she is principal or co-investigator during that probation period. Where further serious violations are discovered during this probation period, the REB may at its discretion advise the institution to impose a lifetime ban upon the investigator in question from conducting human research at the MUHC.

5. For the purpose of these guidelines, “scientific misconduct” is defined broadly to include falsification of study results (e.g., through fabrication or omission of data), attempting to conceal serious adverse events, gross malpractice in the care of human participants, attempting to conduct a study involving human participants without ethics approval, misappropriation of biological specimens for unauthorized use (e.g., unauthorized genetic testing), assigning unqualified personnel for tasks that may place a human participant at risk, misappropriation of study data or nominal participant information, and other violations that would call into question the scientific integrity of a study. Where an REB has good reason to believe that scientific misconduct has occurred, all studies under the principal investigator in question should be suspended and subjected to directed review by the QA Officer, and the matter should be reported at once to the Scientific Director of the RI-MUHC, the Director of Professional Services of the MUHC, and the Dean of the McGill University Faculty of Medicine (for faculty-affiliated investigators), and others as required in Section 2.5.4 of the Regulatory Framework, for their disciplinary follow-up. If the scientific misconduct is confirmed to have occurred and the investigator in question is permitted to remain on staff at the MUHC, the REB may at its discretion advise the institution to forbid the investigator in question from conducting human participants research for a period of up to three years, after which time the investigator should be placed on probation and monitored in a process similar to guideline number 4 above. Repeat offences of scientific misconduct should result in the institution imposing a lifetime ban on conducting research involving human participants at the MUHC.

Appendix 2: Summary of Amendments to the Regulatory Framework in Health Research

September 2003 Version

The Regulatory Framework in Health Research at The McGill University Health Centre comprises a series of foundation documents which are Policies and Procedures ratified by the McGill University Faculty of Medicine, and by the Board of Directors of the MUHC and its Research Institute. The Amendments proposed apply to the February 2001 version of the Regulatory Framework adopted by the Board of Directors of the MUHC on August 31, 2001, and are classified as follows:

1. Amendments to incorporate resolutions of the Board of Directors of the MUHC made on August 31, 2001, approving: the Management Agreement between the MUHC and the RI-MUHC; the General By-Laws of the Research Institute of the MUHC; Regulatory Framework in Health Research at the McGill University Health Centre.
2. Amendments to include the document entitled “McGill University Policy on the Ethical Conduct of Research Involving Human Subjects” (Approved by the Board of Governors of McGill University, April 28, 2003) as one of the Foundation Documents of the MUHC’s Regulatory Framework (to be referred to as Annex 1.b).
3. Amendments to include excerpts of the document entitled “McGill University Policy on the Ethical Conduct of Research Involving Human Subjects” (Approved by the Board of Governors of McGill University, April 28, 2003) referred to as Annex 1.b.
4. Amendments to include the document entitled “Proposed Bylaw Governing the User Complaint Evaluation Procedure at The McGill University Health Centre” (March 2002 version, approved by the Board of Directors of the MUHC, April 25, 2002) as one of the Foundation Documents of the MUHC’s Regulatory Framework (to be referred to as Annex 5.b).
5. Amendments to include excerpts of the document entitled entitled “Proposed Bylaw Governing the User Complaint Evaluation Procedure at The McGill University Health Centre” (March 2002 version, approved by the Board of Directors of the MUHC, April 25, 2002) referred to as Annex 5.b, in Section 2.4.2 “Rights of Human Research Subjects and Managing Their Complaints” and Section 2.4.3 “Reports on Complaints by Human Research Subjects.”
6. Amendment to mention in Section 1.1a that the “MUHC holds an approved Federal-wide Assurance of Protection for Human Subjects (FWA) negotiated with the US Department of Health and Human Services (DHHS) on file with the Office for Human Research Protections (OHRP)”.
7. Amendments to refer to the document entitled “McGill University Ethical and Legal Aspects of Research Involving Human Subjects Conducted in the Faculty of Medicine and Affiliated Hospitals – Policies and Procedures” as Annex 1.a (formerly referred to as Annex 1).

8. Amendments to refer to the document entitled “Institutional Policy for Support and Development of Research at MUHC” as Annex 5.a (formerly referred to as Annex 5).
9. Amendments to refer to the Montreal General Hospital Research Institute as the Research Institute of the McGill University Health Centre, except when referring to the entity before its change of name.
10. Amendments to delete the former Logo of the Montreal General Hospital Research Institute and to replace it with a Logo of the McGill University Health Centre.
11. Amendments to refer to the “*Management* Agreement between the McGill University Health Centre and the Research Institute of the McGill University Health Centre” instead of the “Agreement between the McGill University Health Centre and the Research Institute of the McGill University Health Centre”.
12. Amendments to refer to the MUHC Policy and Procedure on Professional Conduct, approved by the Board of Directors of the MUHC, November 27, 1998, in Section 2.1.4 on “Management of Conflict of Interest”, and in Section 2.3.2 “Negotiating the Privilege to Exercise Research”.
13. Amendment to Section 2.1.5 to mention that the Research Institute of the MUHC is currently managing the funds of Clinical Trials Contracts and Research Contracts for the RVH, MCI, MCH as well as for the MGH.
14. Amendment to Section 2.1.6 on the “Management of Research Data Bases and Medical Research Records” to indicate compliance with the Policies and Procedures outlined in the The MUHC Security and Confidentiality Program; to indicate measures of confidentiality involved during monitoring of source documents by external agencies; to indicate in the medical record the participation of a research subject.
15. Amendments to refer to the MUHC Ethics Committees as MUHC Research Ethics Boards.
16. General Administrative Amendments to update the links to the Web sites allowing the access to documents of the Regulatory Framework.
17. General Administrative Amendments to actualize statements in the Regulatory Framework.

May 2005 Version

The May 2005 version incorporates the resolutions of the Board of Directors of the MUHC made to the following sections (on the following dates):

- 2.2.1 Review by the Research Ethics Board (June 21, 2004);
- 2.5.1 Research Ethics Boards Reporting Structure (June 21, 2004);
- 2.5.2 Nomination, Appointment and Dismissal of REB Members (June 21, 2004);
- 2.5.4 Quality Assurance in Research Ethics Program (March 10, 2005);
- 2.6.2 Introducing New Medication in Research Protocols (June 21, 2004)

November 2007 Version

The November 2007 version incorporates the resolutions approved by the Board of Directors of the MUHC made to the following sections (on the following dates):

- 2.5.2 Nomination, Appointment and Dismissal of REB Members (October 26 and December 7, 2006)
- 2.1.2, Mandatory Declaration of Research Activities, 2.1.6 Management of Research Data Repositories, Tissue Banks and Documentation in Medical Records, 2.1.8 Operating Procedures of the Research Ethics Boards, 2.5.5 Research Ethics Board Annual Reporting (March 26, 2007)
- 1 Foundation Documents of the MUHC Regulatory Framework, 2.1. Protection of Human Research Subjects, Mandatory Declaration of Research Activities, 2.1.6 Management of Research Data Repositories, Tissue Banks and Documentation in Medical Records, 2.1.8 Operating Procedures of the Research Ethics Boards, 2.2.1 Review by the Research Ethics Board, 2.3.3 Establishing Registries of Research Projects, 2.3.4 Investigating Reports of Scientific and Ethical Misconduct, 2.4.1 Confidential Registries of Human REsearch Subjects, 2.5.2, Nomination, Appointment and Dismissal of REB Members (October 29, 2007)

November 2008 Version

The November 2008 version incorporates the resolutions approved by the Board of Directors of the MUHC made to the following sections (on the following dates):

- 2.2.1B Research Ethics Board of Record, 2.2.1C The Course of REB Review, 2.2.1 G Unanticipated Problems Involving Risk, Serious or Continuing Non-Compliance and Suspension or Termination of REB Approval, 2.3.4 Investigating Reports of Scientific and Ethical Misconduct, 2.3.6 Reports on the Implementation of the Regulatory Framework and on Cases of Scientific or Ethical Misconducts, 2.4.3 Reports on Complaints by Human Research Subjects, 2.5.4 Ethics Follow-Up on Ongoing Projects (November 10, 2008), Appendix 1 (November 10, 2008)
- Appendix 1.9: The RI MUHC Human Subject Standard Operating Procedures replace the existing Policies and Procedures (September 16, 2008)