MCGILL UNIVERSITY

ETHICAL AND LEGAL ASPECTS OF

RESEARCH INVOLVING HUMAN SUBJECTS

CONDUCTED IN THE FACULTY OF MEDICINE

AND AFFILIATED HOSPITALS

APPENDICES “A” THROUGH “L”

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Faculty of Medicine
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APPENDIX A
# MCGILL UNIVERSITY

## POLICY ON THE ETHICAL CONDUCT OF RESEARCH INVOLVING HUMAN SUBJECTS

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POLICY ON THE ETHICAL CONDUCT OF RESEARCH INVOLVING HUMAN SUBJECTS

PREAMBLE

A fundamental commitment of the University is to the advancement of learning through scholarly activities, including research involving human subjects. The University recognizes that such activities flourish only in a climate of academic freedom, and therefore is committed to safeguarding, among others, the freedom of inquiry and dissemination of research results. When the subjects of these activities are human beings these freedoms must be integrated with the responsibility to conduct the research in a manner that respects the dignity, rights and welfare, and above all protects from possible harm, the persons who are the subjects of the research.

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 supersedes any existing University policies with respect to the ethical review of human subject research.

Norms for the ethical conduct of human subjects research evolve continuously within a societal context, as investigators seek to satisfy and find balance among such basic principles as respect for human dignity, respect for free and informed consent, respect for vulnerable persons, respect for privacy and confidentiality, respect for justice and inclusiveness, minimizing harm, and maximizing benefit. 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.

1.0 RESPONSIBILITIES

Authority for ethics review according to this policy is established by the Board of Governors of the University. The ethical conduct of research involving human subjects is a responsibility that is shared by the various constituents of the University. Notwithstanding this shared responsibility, there are specific responsibilities that can be summarized as follows.

1.1 Responsibilities of the Administration

The Office of the Vice-Principal (Research) bears the responsibility for the implementation of the University's policies on research involving human subjects. It must provide for the appropriate administrative oversight and the necessary resources to ensure that the University's adopted practices and procedures are being adhered to and are in compliance with all applicable ethical requirements. The Office of the Vice-Principal (Research) is responsible for entering into
any agreements with other institutions, such as the McGill affiliated hospitals, to conduct the ethics review and approval of the research of McGill members.

Academic administrators such as Deans, Directors and Department Chairs, have a responsibility for the conduct of research carried out within their jurisdictions. They have a responsibility to be aware of ongoing research and a duty to create a climate for ethical practice in research by promoting widespread general awareness and knowledge of this policy and the need for ethics review.

1.2 Responsibilities of Researchers

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.

1.3 Responsibilities of Faculty Members as Supervisors of Student Researchers

All student research must be supervised by a faculty member who accepts responsibility for overseeing the ethical conduct of the student’s research project. The supervising faculty member has certain responsibilities even though the student may be the primary researcher. Supervisors must ensure that their students have the training and competence needed to carry out their responsibilities in an ethical manner. They must ensure that the students are aware of and familiar with the contents of this policy and of other applicable ethical guidelines that are relevant to their responsibilities. Once a student’s research project is approved, the supervisor must take further reasonable measures to ensure that the research is conducted in accordance with the provisions of this policy and other applicable ethical requirements. In the case of all undergraduate research, the supervisor has full responsibility to ensure that a student’s project receives the appropriate ethics approval. In the case of graduate or postdoctoral research, except for course research projects as described in Section 3.5, it is the joint responsibility of the faculty supervisor and the student to ensure that the project receives the appropriate ethics approval. Supervisors are required to co-sign the student’s submission to the REB to affirm their supervisory responsibilities.
1.4 Responsibilities of Student Researchers

Student research projects involving human subjects must receive the appropriate ethics review and approval before the research may begin. Although a student’s research must be supervised by a faculty member, this does not in any way relieve the obligation of the student to be familiar with and comply with the contents of this policy that are relevant to the student’s responsibilities. As stated in Section 1.3, it is the case of graduate or postdoctoral research, except for course research projects as described in Section 3.5, it is the joint responsibility of the faculty supervisor and the student to ensure that the project receives the appropriate ethics approval. As per Thesis Office guidelines, students will be required to include the ethics approval certificate when depositing their theses.

2.0 STRUCTURE

The overall responsibility for overseeing the ethical conduct of research involving human subjects is entrusted to the Office of the Vice-Principal (Research). The following bodies have been established for developing and implementing University policies and procedures related to human subject research.

2.1 Advisory Council on Human Research Ethics

The Advisory Council on Human Research Ethics (ACHRE) is the University body responsible for coordinating University-wide understanding of, and compliance with, the applicable requirements for the ethical conduct of research involving human subjects. The ACHRE reports to the Vice-Principal (Research) and must submit an annual report of its activities.

Membership

The ACHRE shall, at a minimum, consist of:
- the Chair, appointed by the Vice-Principal (Research) in consultation with the other members of the ACHRE, who shall be a faculty member who is knowledgeable in research ethics
- the Associate Vice-Principal (Research)
- the Chairs of the University REBs
- the Research Ethics Officer (Human Subjects), who will serve as Secretary
- one person representing community interests and concerns, who has no formal affiliation with the institution, appointed by the Vice-Principal (Research) in consultation with the other members of the ACHRE
- one graduate student or postdoctoral fellow, to be named by the PGSS

Other members may be appointed on an ad-hoc basis as deemed necessary to carry out the mandate of the committee.

Responsibilities

The ACHRE shall be responsible for:

- Advising and making recommendations to the Vice-Principal (Research) on policies and procedures to be established or modified, in order to ensure that all research involving human subjects conducted at or under the auspices of McGill University is carried out in a manner consistent with the highest ethical standards. The ACHRE will actively monitor the consistency
of these policies and procedures with other McGill policies, the Tri-Council Policy Statement Ethical Conduct of Research Involving Human Subjects, federal and provincial regulations, and all other applicable guidelines.

Reviewing and advising the Vice-Principal (Research) on the number, jurisdiction and responsibilities of the REBs at McGill University. Developing and reviewing policies, guidelines and procedures, in conjunction with the REBs, to promote consistency of procedures and policy interpretation.

Responding to any issues of concern raised by the REBs and providing ethical and legal expertise to the REBs as needed.

Collaborating with the Office of the Vice-Principal (Research) and the REBs to develop and implement educational resources and programs on the ethics of research involving human subjects, for faculty, staff and students.

Maintaining liaison with other organizations involved in the protection of human research subjects.

Creating subcommittees as required to carry out the business of the ACHRE.

Receiving the annual reports of the REBs and forwarding them to the Vice-Principal (Research).

Meetings

Meetings are at the call of the Chair, but not fewer than 2 times per year.

Quorum will be 50% of the membership. The Chair has the final authority to decide if the membership present is adequate for the proper conduct of the meeting.

Normally, decisions are arrived at by consensus. Only after reasonable efforts to reach a consensus have failed, decisions will be made on the basis of a simple majority vote of those members present.

Minutes will be taken of each meeting in sufficient detail to document attendance, decisions and dissents (when applicable including a record of voting), and a summary of the discussion of important issues.

2.2 Research Ethics Boards

The mandate of an REB is to determine the ethical acceptability of research involving human subjects, with the primary objective of protecting the rights and welfare of those subjects. Each REB reports to the ACHRE, and must submit an annual report of its activities.

The jurisdiction and number of REBs are established considering the range of research conducted at the University and consistent with appropriate workloads. Researchers usually submit their projects to their designated REB (see Appendix II). Researchers may consult with the REB Chair to determine if another REB may be more appropriate for the review of their research project. The REB Chair has the authority to refer a project to another more appropriate REB, in consultation with the Chair of the other REB.

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Membership

REBs will be maximally effective to the extent that their members are selected on the basis of their interest in, commitment to, and suitability for the role.

An REB shall, at a minimum, consist of five members, including both men and women, and have:
- members who are knowledgeable about the relevant ethical issues
- at least two faculty members who have broad expertise in the methods or in the areas of research that are covered by the REB; no REB may consist entirely of members of one discipline
- for biomedical research, at least one member who is knowledgeable in the relevant law but is not the legal counsel of the University; this is advisable but not mandatory for other areas of research
- at least one member who represents community interests and concerns, and has no formal affiliation with the Institution

The term of appointment for members will normally be 3 years, renewable, with staggered appointments. The Chair will be appointed by the Vice-Principal (Research) in consultation with the Deans of the relevant Faculties. The other members of an REB are to be appointed by the relevant Faculties/Schools/Departments according to their regular nominating procedures, in consultation with the Chair of the REB. The number of members to be nominated from each unit within the REB’s jurisdiction is to be determined by the Chair of the REB and should be approximately in proportion to the number of submissions from that unit. For REBs that cover a large number of units, REB membership should be rotated to ensure that all units submitting protocols have an opportunity to be represented. Other regular members may be appointed as deemed necessary by the REB Chair to carry out the mandate of the REB.

Alternate members may be appointed for each of the regular members so as not to prohibit the functioning of the REB in case of illness or other unforeseen circumstances.

When membership of an REB extends beyond 5 members, the community representation should increase proportionately.

The REB Chair may appoint ad hoc members or seek outside advice when reviewing a project that requires specific expertise regarding methodology, community or research subject representation, or other matters.

No member of an REB may participate in the review of any project in which the member has a conflicting interest, such as their own or their student’s project. Members must disclose to the REB possible conflicts of interest arising out of personal relationships, financial interests, multiple roles, or other factors. When the REB determines that a conflict exists, the member may be requested to provide information to the REB but may not be present during the consideration of the project.

Responsibilities

Each REB:

Is responsible for reviewing research projects involving human subjects in a manner consistent with this policy.
Has the authority to approve, require modification of, or disapprove research projects according to the requirements of this policy.

Is responsible for conducting the continuing review of ongoing research projects.

Has the authority to suspend or terminate approval of any proposed or ongoing research that is not being conducted in accordance with the REB's requirements or other ethical requirements.

Has the authority to suspend or terminate approval of any ongoing research that has been associated with unexpected serious harm to subjects or that it deems to pose an unacceptable risk of harm to subjects. In this regard, the REB Chair is authorized to act on behalf of REB members in exigent circumstances. Actions taken by the REB Chair in relation to exceptional circumstances should be brought to the full REB for ratification as soon as is practicable and in all cases, no later than 30 days after the action was taken.

Is responsible for promptly reporting the suspension or termination of approval of a research project to the principal investigator, the Vice-Principal (Research) and other institutional officials as deemed appropriate by the REB, providing a statement of the reasons for the action taken.

Is responsible for establishing and overseeing mechanisms for review of course research projects (as described in Section 3.5) in units within its jurisdiction.

Is responsible for serving as the initial appeals committee for any appeal taken by an individual against a decision of a department review of course research projects.

Receives and responds to any formal complaints or concerns made by any individual or organization regarding human subject research conducted under their jurisdiction and reports this promptly to the Vice-Principal (Research) and, as appropriate, to other institutional officials.

Acts as a resource to the University community on matters pertaining to the ethical conduct of research involving human subjects and can provide consultation to researchers at all stages of the application and review processes.

Is responsible for developing guidelines and procedures for implementing the requirements of this policy consistent with the needs of the relevant research disciplines served by the REB. These may be more, but not less, stringent than those described in the present policy. Such guidelines and procedures shall be formalized in writing and approved by the ACHRE.

Is responsible for informing the ACHRE of issues arising that may affect the review process of the REBs, or any other issues of concern that may affect University policy relating to research involving human subjects.

Meetings

The REB shall normally meet once a month or more frequently as needed.

As a minimum, a quorum of an REB must have one member with broad expertise in the methods or areas of research under review, one member who is knowledgeable about the relevant ethical issues, one member with no formal affiliation with the institution and, for biomedical research, one member who is knowledgeable in the relevant law. The Chair has the final authority to decide if the membership present is adequate for the proper conduct of reviews.
Researchers should be informed of the dates by which their projects must be received by the REB for consideration at the next scheduled meeting.

An REB should accommodate reasonable requests from researchers to participate in discussions of their proposals, but the researchers shall not be present when an REB makes its decisions. Normally decisions will be arrived at by consensus. Only after reasonable efforts to reach a consensus have failed, decisions will be made on the basis of a simple majority vote.

Only regular members (or their alternates when replacing the regular member) have a vote.

Regular attendance by REB members at meetings is required. Minutes must be taken of every meeting in sufficient detail to document attendance, decisions and dissent and the reasons for them (when applicable including a record of voting), and a summary of the discussion of important issues.

REB records must be kept for a minimum of three years beyond the termination of a project.

2.3 Research Ethics Boards of Affiliated Teaching Hospitals

The REBs of the affiliated teaching hospitals report directly to the Board of Directors of each of the hospitals and have their own policies and procedures. Researchers conducting human subject research at a hospital usually apply to the hospital REB for ethics review and approval. Multi-site projects conducted within the affiliated hospitals are normally reviewed by the Faculty of Medicine REB. The hospital REBs are recognized as acting on behalf of the University for conducting ethics reviews for McGill members conducting hospital-based research at any of the affiliated teaching hospitals. There shall be a written agreement between the University and the hospitals regarding the ethics review and approval of the research of McGill members.

The Faculty of Medicine coordinates the Research Ethics Committee of the Faculty (RECF). The RECF is a work group composed of the chair of the Faculty of Medicine REB and those of the affiliated hospitals, with the Associate Dean (Research) of Medicine acting as Chair. The purpose of the RECF is to provide a forum to address common issues across these REBs, and to discuss and share information and experiences regarding emerging ethical issues. The RECF will make recommendations for guidelines and procedures for the Faculty of Medicine and the affiliated hospital REBs to follow, and attempt to achieve, as far as possible, uniformity in function among these REBs. The Chair of the RECF will report to the ACHRE any issues of concern which pertain to University policy on research involving human subjects.

2.4 Confidentiality

The desirability of openness with respect to the business of the various committee meetings must be balanced by considerations of privacy of human subjects or of third parties, the confidentiality of proprietary data, the need to encourage free discussion at these meetings, and the desire to promote cooperation in carrying out the purposes of these committees.

Attendance at Meetings—Normally, regular REB and other committee meetings are closed to the University community and the general public. Exceptions may be made by each committee when warranted.
Minutes of Meetings – Normally, minutes of these meetings are only accessible to the committee members or other representatives of the University authorized by the Office of the Vice-Principal (Research).

Annual Reports – The Chair of each REB must submit an annual report to the Chair of the ARTRE, summarizing the nature and volume of the REB’s activities. These reports are made publicly available. Confidential matters should not be included in such reports, but should be conveyed separately.

Research Proposal – Each committee shall consider a research proposal and all accompanying information to be confidential documents.

3.6 RESEARCH REQUIRING ETHICS REVIEW

All research involving human subjects, conducted at or under the auspices of McGill University, must be reviewed and approved by the appropriate McGill approved REB.

3.1 Definition of Research

Research is defined as the systematic investigation to establish and communicate facts, principles, understandings or generalizable knowledge. Research involving human subjects may include, but is not limited to, projects where data are derived from:

1) the collection of information through any interaction or intervention with a living individual
2) the secondary use of data previously collected from human subjects
3) identifiable private information about an individual
4) human remains, cadavers, human organs, tissues and biological fluids, embryos or fetuses

The examples listed are not intended to represent an exhaustive inventory of activities requiring review. The REB may also determine that some activities apparently falling into these categories may be exempted from review. The researcher is responsible for consulting with the REB to clarify what types of activities must be reviewed and what exceptions may exist.

3.2 Scope of Review

The requirement for ethics review and approval by a McGill approved REB applies to:

- all research conducted by or under the supervision of any member of McGill University, whether the research is funded or non-funded, or conducted on University premises or elsewhere. For the purpose of this document, a member of the University is defined as including academic and non-academic staff, sessional instructors, students, visiting or adjunct scholars, postdoctoral fellows, paid and unpaid research associates and assistants, and any person in a like position, when acting in connection with their institutional role. This applies to new faculty even though their current research may have received ethics approval at a previous institution.
- all student research projects conducted as part of thesis or course requirements
- pilot studies and feasibility studies
• all research or subject recruitment conducted by organizations or individuals who are not members of McGill University while on University premises or using University facilities, equipment, or resources (including human resources)
• research that involves the use of the University’s non-public information to identify or contact human research subjects.

3.3 Research Projects in Which the Researcher is a Consultant

Research projects conducted by McGill members as part of consulting activities as defined by University regulations will need review and approval by the appropriate REB when:

a) McGill facilities, equipment, supplies, or support staff are used or
b) the research data collected will be disseminated in association with the University or

c) the researcher purports to represent the University in any way.

3.4 Research Conducted Off Campus

Institutional accountability requires that each institution is responsible for research carried out under its auspices no matter where the research is conducted.

Fieldwork Research - Research involving human subjects conducted in the field, whether in Canada or in foreign countries, must be reviewed and approved by the appropriate McGill REB before the research may begin. The investigator is responsible for being aware of any standard research protocol to be followed or ethical approvals to be obtained when dealing with particular groups or communities. The investigator is responsible for ensuring that all the required approvals have been obtained before starting the research, or for demonstrating to the REB why this is not feasible.

Research at Other Institutions - Research involving human subjects conducted by McGill members in other institutions must be reviewed and approved by the appropriate McGill REB before the research may begin, unless the institution’s REB has been recognized by a formal agreement, such as in the case of the REBs of the affiliated teaching hospitals. Researchers are also responsible for obtaining the necessary ethics approval from any ethics boards or authorities that oversee research at the other institutions. The investigator is responsible for ensuring that all the required approvals have been obtained before starting the research. When McGill members are conducting human subject research as part of a collaborative research team where the McGill member is the Principal Investigator, and the project will be conducted by a non-McGill collaborator, McGill REB approval is needed. In the case where the Principal Investigator is from another institution and has already obtained local REB approval, the McGill member must normally obtain McGill REB approval. However, the REB Chair has the discretion to expedite this review, based upon the nature of the project and the review of the other REB. The ACHRE may also develop guidelines specifying circumstances under which the approval of another REB constituted under the Tri-Council Policy Statement Ethical Conduct of Research Involving Human Subjects may be sufficient without further McGill review required.

Multi-Centre Research - Where multiple sites participate in the same research project, inter-institutional agreements may be developed and one REB designated to review the research. Although a delegated REB may approve a multi-centre project, the Institution in which the research will take place may, through its own REB, subsequently disapprove or decline to participate in the study. However, a project that has been disapproved by a
delegated REB may not subsequently be presented for review at the delegating institution’s REB. Where no agreement exists, review and approval must be sought from the appropriate local REB and the REB of each participating institution. REBs reviewing multicentre projects are expected to communicate any significant concerns they have about the rights and welfare of the subjects with the other REBs reviewing the same project.

3.5 Student Research

All student research involving human subjects, including but not limited to thesis, independent research projects, and postdoctoral research, must receive ethics review and approval as described in Section 4.1 before the research may begin. Some student research projects are conducted in courses that require students to collect data from human subjects, and these projects must also receive ethics review and approval. The intent of course research projects, however, is for the student to become more knowledgeable about the research process, rather than to contribute to generalizable knowledge, and the results of the data are not intended for publication or presentation outside the classroom. The REB may establish guidelines for delegating the review of course research projects to department review as described in Section 4.1. It is the responsibility of the course instructor to contact the REB if there is any uncertainty as to whether a course project needs ethics review or not. The applicable criterion for determining if ethics review is required is if an activity would be subject to ethics review in any other context, it is subject to review if it occurs in a teaching or training context. In the event that student research falls under the auspices of a research project that has already received ethics review and approval from a McGill approved REB, no further approval is necessary.

4.0 REVIEW OF RESEARCH

The review process is conducted in accordance with the guideline documents described in Appendix I. The type of review depends upon the anticipated level of risk posed to research subjects. Risks can include physical, psychological, or economic harms and can include injury to reputation or privacy. A project may be considered to involve minimal risk if the risk of harm anticipated is not greater, considering probability and magnitude, than those ordinarily encountered in the participant’s daily life.
4.1 Levels of Review

Full Review - The formal REB review process requires a convened meeting of the REB at which a quorum is present. REB Chair may designate any proposal for full review. Generally, proposals involving more than minimal risk, that involve deception, or where the subjects are vulnerable or captive populations, require full review.

Expedited Review - The REB Chair will examine submissions to assess their appropriateness for review through an expedited process. Proposals eligible for expedited review may be reviewed and approved by the REB Chair or a designated member. Individual REBs may choose to form a subcommittee to conduct expedited reviews. All expedited reviews must be reported to the full REB on a regular basis. Submissions that may be eligible for expedited review include, but are not limited to, projects that involve no more than minimal risk or projects that have been previously approved but to which the researcher wishes to make minor modifications.

Department Review - The REB may delegate the review of course research projects, as described in Section 3.5, to department review by an REB designated departmental representative or committee. Department review may not be used for any projects involving greater than minimal risk, or for projects that are part of a faculty member’s own research program. Jurisdiction of review is determined according to the department or faculty that offers the course, not by the department or faculty in which the student is registered. Department reviews must be reported to the full REB on at least an annual basis.

4.2 Scholarly Review as Part of Ethics Review

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, issue or phenomenon; it shall not be based on methodological biases or a preference for particular procedures.

4.3 Outcome of the Review Process

A decision on a submission can be categorized as follows:

a) Approved
b) The REB endorses the submission with conditions that must be met before final approval is granted.
c) The REB cannot make a decision based on the information provided and the decision is deferred pending receipt of additional information or major revisions. The REB will then re-review.

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The REB shall provide the researcher with a written summary of its grounds for a decision. Researchers have the right to request, and the REB has an obligation to provide, reconsideration of decisions based on the researcher's rebuttal to the concerns that were initially identified by the REB. The researcher has the right to appear and be heard in a meeting with the REB. The REB decision following reconsideration is final.

A decision of an REB to allow or disallow research on ethical grounds is final unless reversed by the REB upon reconsideration, pursuant to the standards in this policy. The instigation may however, refuse to allow certain types of research within its jurisdiction, even though it has been found to be ethically acceptable.

4.4 Appeals Process

A researcher who continues to dispute an REB decision after reconsideration by the REB may appeal that decision through the formal appeals process.

The Research Ethics Appeal Committee will serve as the final appeal committee whose decisions shall be final and binding in all respects for any appeal made by a researcher against a decision of an REB. The Appeal Committee will only hear appeals based on procedural error, conflicts of interest, or bias.

There shall exist two standing Appeal Committees, one serving the Faculty of Medicine REB, and the other serving the remaining REBs. Appendix IV contains the procedures for appeals applicable to the Faculty of Medicine. Appendix III contains the procedures applicable for all other appeals.

There shall be no recourse, grievances or review process of matters decided upon by the Research Ethics Appeal Committee pursuant to other regulations or policies of the University.

Researchers should recognize that decisions regarding appeals will be made in light of the primary objective of protecting the rights and welfare of the subjects.

4.5 Continuing Review

Ongoing research shall be subject to continuing ethics review based on the associated risks to the subjects. Normally, REBs will require annual reports on the status of all ongoing research projects. The greater the risk to the subject, the greater the scrutiny of the continuing review process. The design of this process will depend upon the particular circumstances of the project and might include but is not limited to:

a) requiring the researcher to submit status reports at various intervals as determined by the REB.

b) requiring the researcher to propose an appropriate monitoring mechanism.

c) requiring reports from an independent data and safety monitoring board.

The REB may require further monitoring activities or schedule audits of ongoing research projects, although it is not expected that the REB will be responsible for conducting these activities.

The REB should be promptly notified by the researcher when the project is terminated.
4.6 Modification of an Approved Project

Researchers proposing any significant changes to the research project must obtain the approval of the REB before proceeding with those changes, except when necessary to eliminate an immediate hazard to a subject. Such modifications may include, but are not limited to, changes in research design, subject population, or consent procedures. Other minor modifications should be reported on a regular basis including a change of project title, additional funding sources, change of principal or co-principal investigator(s) or other collaborators.

At the discretion of the Chair, these modifications may be approved by expedited review. However, significant revisions may require that the proposal be reviewed by the full committee.

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.

4.8 Conflicts of Interest

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.

4.9 Noncompliance

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.

Acknowledgement: Parts of this policy are adapted from the Tri-Council Policy Statement Ethical Conduct for Research Involving Humans and documentation developed by the University of Manitoba, University of Calgary, Brock University, and the University of Alberta.

Approved by Board of Governors, April 28, 2003
APPENDIX I

POLICY FRAMEWORK

Review and approval of the ethical acceptability of research projects involving the use of human subjects will be made in light of the following:

- Research must be conducted in a manner consistent with this present policy, Advisory Council on Human Research Ethics approved policies, procedures and guidelines, other applicable University policies, procedures and guidelines, the Tri-Council Policy Statement Ethical Conduct for Research Involving Humans and, as relevant, with federal and provincial laws.
APPENDIX II

MCGILL APPROVED RESEARCH ETHICS BOARDS

1) McGill Research Ethics Boards - The University currently has 5 Research Ethics Boards formally approved to conduct the ethics review of research involving human subjects in accordance with this policy. A researcher’s designated REB is usually determined according to the unit of the researcher’s primary academic appointment, although researchers may consult with the REB Chair to determine if another REB may be more appropriate for the review of their research project. Faculties and departments are assigned to specific boards as follows:

Faculty of Agricultural and Environmental Sciences Research Ethics Board – for members in the Faculty of Agricultural and Environmental Sciences

Faculty of Education Research Ethics Board – for members in the Faculty of Education

Faculty of Medicine Research Ethics Board (also referred to as the Institutional Review Board or the IRB) – for members in the Faculties of Medicine and Dentistry

University Research Ethics Board I – for members in Anthropology, CDAS, Economics, Geography, Political Science, Sociology, and in the Faculties of Engineering, Law, Management, Religious Studies and any other unit not specifically assigned to another board

University Research Ethics Board II – for members in Linguistics, Psychology, Social Work and the Faculty of Music

2) Affiliated Hospital Research Ethics Boards – As described in Section 2.3, the University recognizes the Research Ethics Boards of the affiliated hospitals as acting on behalf of the University for conducting ethics reviews for McGill members conducting research in the following affiliated hospitals:

- the McGill University Health Center
- the Douglas Hospital
- the SSMH Déвид General Hospital
- St. Mary’s Hospital Center
APPENDIX III

PROCEDURES FOR APPEALS OF DECISIONS OF RESEARCH ETHICS BOARDS SERVING ALL FACULTIES (EXCEPT THE FACULTY OF MEDICINE)

The Research Ethics Appeal Committee (henceforth "Appeal Committee") is established in accordance with Article 1.11 of the Tri-Council Policy Statement "Ethical Conduct for Research Involving Humans" to hear appeals of decisions of Research Ethics Boards (REBs) serving all faculties of McGill University, except the Faculty of Medicine.

1 Notice of Appeal

1.1 A Notice of Appeal must be filed with the Chair of the Advisory Council on Human Research Ethics (ACHIRE) within 6 months of the rejection of a project by an REB. The notice must clearly state the grounds upon which the appeal is filed.

1.2 The Chair of the ACHIRE shall determine that a definite impasse exists between the researcher and the REB whose decision has been appealed.

1.3 The Chair of the ACHIRE shall then charge the Chair of the Appeal Committee to call the committee to hear the case. The Chair of the ACHIRE shall ensure that all parties have copies of the notice of appeal.

2 Composition of the Appeal Committee

2.1 The Appeal Committee shall be named annually by the Vice-Principal (Research) in consultation with the President of the McGill Association of University Teachers or the designee of the President. Normally, no member should serve more than three consecutive terms.

2.2 The composition of the Appeal Committee shall be the Chair, who will be a Chair of one of the REBs, two faculty members who have experience serving on an REB, an individual knowledgeable about the relevant ethical issues, a lawyer, and a community member who is currently serving on a McGill REB. When the Principal Investigator making the appeal is a student, then the ACHIRE student member will also serve on the Appeal Committee. No member of the Appeal Committee hearing a particular appeal can be a member of the REB whose decision is being appealed, or can have been a member of the REB when the decision being appealed was made. The Vice-Principal (Research) will normally name alternate committee members who can substitute for any members who must be recused or cannot otherwise attend.

2.3 The whole committee must be present for a quorum to exist. The Appeal Committee shall appoint ad hoc experts as required.

3 The Appeal

3.1 It is not the intention that the appeal process should simply substitute the opinion of one group of reasonable individuals with that of another. The Appeal Committee shall therefore have the jurisdiction to hear appeals based only on failure to follow proper procedures, a conflict of interest or evidence of bias.

3.2 The appeal shall involve two distinct stages: (i) to determine whether grounds exist that would require that the protocol be considered anew and (ii) a de novo consideration of the protocol if grounds for appeal are established.
3.3 In the first stage, the mandate of the Appeal Committee is to determine whether the protocol received fair and reasonable consideration, and not to make a de novo decision on the ethical merits of the protocol.

3.3.1 The Appeal Committee shall receive for its consideration the notice of appeal, all the documentation provided to the REB, and the minutes of the REB regarding the project. The investigator shall appear expressly to present evidence to establish the grounds for appeal as outlined in 3.1. The Chair of the REB or representative shall also appear simultaneously. Each of the parties has the right to be assisted by an advisor who shall be a member of the McGill University community and will not receive any remuneration for acting as an advisor.

3.3.1.1 At the hearing, the investigator presents evidence to support grounds (article 3.1) that would invalidate the REB decision. The Chair of the REB responds. The Appeal Committee can question both parties. Each party is given a single opportunity for brief summation, with the investigator speaking last.

3.3.1.2 The Appeal Committee may elect to hear witnesses if, in its opinion, it is relevant to reaching a decision on the grounds of the appeal.

3.3.2 The Chair of the Appeal Committee shall provide a written decision of the Appeal Committee concerning the grounds of the appeal with copies to the investigator, the REB and the Chair of the ACHRE.

3.4 If the Appeal Committee finds that there has been a failure to follow proper procedures, or evidence to support a possible conflict of interest or bias, it proceeds to the second instance.

3.4.1 In a second meeting the committee shall undertake a de novo decision on the ethical merits of the protocol in question. All the documents made available to the initial REB and the relevant minutes of the REB are to be available to the Appeal Committee. The Appeal Committee must afford the investigator an opportunity to appear to answer questions.

3.5 The Appeal Committee shall meet within 30 days of receipt of the written notification of the appeal, and shall render a written decision on the grounds of appeal within 30 days of that meeting. If grounds are established, a written decision on the ethical merits of the protocol shall be provided within an additional 60 days.

3.6 The decision of the Appeal Committee is final and a written decision is provided to the investigator, the REB and the Chair of the ACHRE.

4 Responsibilities

4.1 The original Research Ethics Board assumes the sole responsibility for administering and monitoring a project approved by the Appeal Committee.

5 Reporting

5.1 The Chair of the Appeal Committee shall make an annual report on the activities of the Appeal Committee to the Vice-Principal (Research).
APPENDIX IV

PROCEDURES FOR APPEALS FROM THE DECISIONS OF RESEARCH ETHICS BOARDS IN THE FACULTY OF MEDICINE, MCGILL UNIVERSITY

March 1, 1999

The Research Ethics Appeal Committee of the Faculty (hereafter "Appeal Committee") is established in accordance with Article 1.11 of the Tri-Council Policy Statement "Ethical Conduct for Research Involving Humans" to hear appeals of decisions of Research Ethics Boards (hereafter "REBs") of the Faculty and of Affiliated Hospitals.

1 Notice of appeal

1.1 Notice of Appeal must be filed with the Associate Dean (Research) of the Faculty of Medicine within 6 months of the rejection of a protocol by a Research Ethics Board. The notice must clearly state the grounds upon which the appeal is filed.

1.2 The Associate Dean shall determine that a definite impasse exists between the researcher and the REB whose decision has been appealed.

1.3 The Associate Dean shall then charge the Chair of the Appeal Committee (or the Co-chair as appropriate) to call the Appeal Committee to hear the case. The Associate Dean shall ensure that all parties have copies of the notice of appeal.

2 Composition of the Appeal Committee

2.1 The Appeal Committee shall be named annually by the Dean of Medicine with consideration to recommendations received from the Research Ethics Committee of the Faculty. With the exception of the Chair of the Institutional Review Board, no member can serve more than three consecutive terms.

2.2 The composition of the Appeal Committee shall be as follows: The Chair shall be the current Chair of the Institutional Review Board of the Faculty of Medicine. The Dean of Medicine shall name the following members: three Chairs or alternates of hospital-based Research Ethics Boards, one of whom is designated as co-Chair; a lawyer and alternate; an ethicist and alternate; two community members and alternates from different Research Ethics Boards. The Co-chair shall act as Chair if the appeal is from a section of the Institutional Review Board. No members of the Appeal Committee hearing a particular appeal can be affiliated with that REB.

2.3 A quorum consists of the Chair (or Co-Chair), two hospital-based REB Chairs, a lawyer, an ethicist, and one community member. The appeal committee shall appoint ad hoc experts as required and described in the Tri-Council Statement "Ethical Conduct for Research Involving Humans".

3 The Appeal

3.1 It is not the intention that the appeal process should simply substitute the opinion of one group of reasonable individuals with that of another. The Appeal Committee shall therefore have jurisdiction to hear appeals based only on failure to follow proper procedures, a conflict of interest or evidence of bias.

3.2 The appeal shall involve two distinct stages; i) to determine whether grounds exist that would require that the protocol be considered anew and ii) a de novo consideration of the protocol if grounds for appeal are established.
3.3 In the first stage, the mandate of the Appeal Committee is to determine whether the protocol received fair and reasonable consideration, and not to make a de novo decision on the ethical merits of the protocol.

3.3.1 The Appeal Committee shall receive for its consideration the notice of appeal, all the documentation provided to the Research Ethics Board, and the minutes of the REB regarding the protocol. The investigator shall appear expressly to present evidence to establish the grounds for appeal as outlined in 3.1. The Chair of the REB or representative shall also appear simultaneously. The parties are not assisted by advisors.

3.3.1.1 At the hearing, the Investigator presents evidence to support grounds (article 3.1) that would invalidate the Research Ethics Board decision. The Chair of the REB responds. The Appeal Committee can question both parties. Each party is given a single opportunity for brief summation, with the Investigator speaking last.

3.3.1.2 The Appeal Committee may elect to have witnesses if, in its opinion, it is relevant to reaching a decision on the grounds of the appeal.

3.3.2 The Chair of the Appeal Committee shall provide a written decision of the Appeal Committee concerning the grounds of the appeal with copies to the investigator, the REB and the Associate Dean (Research).

3.4 If the Appeal Committee finds that there has been a failure to follow proper procedures, or evidence to support a possible conflict of interest or bias, it proceeds to the second instance.

3.4.1 In a second meeting the committee shall undertake a de novo decision on the ethical merits of the protocol in question. All the documents made available to the local REB and the relevant minutes of the REB are to be available to the Appeal Committee. The Appeal Committee must afford the researcher an opportunity to appear and answer questions.

3.5 The Appeal Committee shall meet within 30 days of receipt of the written notice of the appeal, and shall render a written decision on the grounds of the appeal within 30 days of that meeting. If grounds are established, a written decision on the ethical merits of the protocol shall be provided within an additional 60 days.

3.6 The decision of the Committee is final and a written decision is provided to the researcher, the REB and the Associate Dean Research of the Faculty of Medicine.

4 Responsibilities

4.1 The Institutional Review Board of the Faculty of Medicine and each Hospital Research Ethics Board, with the approval of the Board of Directors of the Hospital, agree that the decisions of the Appeal Committee are binding.

4.2 The original Research Ethics Board assumes the sole responsibility for administering and monitoring a protocol approved by the Appeal Committee.

5 Reporting

5.1 The Dean of Medicine shall make an annual report on the activities of the Appeal Committee to the Vice Principal Research.

5.2 Hospital-based Research Ethics Review Boards are responsible for reporting to the Board of Directors of their Hospital any Appeal Committee decisions relevant to their own function.
APPENDIX B
TRI-COUNCIL POLICY STATEMENT

Ethical Conduct for Research Involving Humans

Medical Research Council of Canada
Natural Sciences and Engineering Research Council of Canada
Social Sciences and Humanities Research Council of Canada

Canada
THIS APPENDIX CONTAINS ONLY THE SUMMARIES OF ARTICLES OF THE TRI-COUNCIL POLICY STATEMENT

YOU MIGHT WISH TO SUBSTITUTE THIS WITH YOUR COPY OF THE COMPLETE STATEMENT
SCOPE OF RESEARCH REQUIRING ETHICS REVIEW

The following which is adapted from the University of Alberta, General Faculty Council Policy Manual indicates the range of research projects or instances that should be reviewed by the REB.

- Whether the research is funded or not;
- Whether the funding is internal or external;
- Whether the subjects are from inside or outside the institution;
- Whether the subjects are paid or unpaid;
- Whether the research is conducted inside or outside Canada;
- Whether the research is conducted inside or outside the institution;
- Whether the research is conducted by staff or by students;
- Whether the research is conducted in person or remotely (e.g., by mail, electronic mail, fax or telephone);
- Whether the information is collected directly from subjects or from existing records not in the public domain;
- Whether the research is to be published or not;
- Whether the focus of the research is the subject;
- Whether the research is 'observational', experimental, correlational or descriptive;
- Whether a similar project has been approved elsewhere or not;
- Whether the research is a pilot study or a fully developed project;
- Whether the research is to acquire basic or applied knowledge; and
- Whether the research is primarily for teaching or training purposes or whether the primary purpose is the acquisition of knowledge.
ARTICLES INCLUDED IN TRI-COUNCIL POLICY STATEMENT: ETHICAL CONDUCT FOR RESEARCH INVOLVING HUMANS

For easy reference, the following is a comprehensive listing of all articles included in this document:

Article 1.1
(a) All research that involves living human subjects requires review and approval by an REB in accordance with this Policy Statement, before the research is started, except as stipulated below.

(b) Research involving human remains, cadavers, tissues, biological fluids, embryos or foetuses should also be reviewed by the REB.

(c) Research about a living individual involved in the public arena, or about an artist, based exclusively on publicly available information, documents, records, works, performances, archival materials or third-party interviews, is not required to undergo ethics review. Such research only requires ethics review if the subject is approached directly for interviews or for access to private papers, and then only to ensure that such approaches are conducted according to professional protocols and to Article 2.3 of this Policy.

(d) Quality assurance studies, performance reviews or testing within normal educational requirements should also not be subject to REB review.

Article 1.2
The institution in which research involving human subjects is carried out shall mandate the REB to approve, reject, propose modifications to, or terminate any proposed or ongoing research involving human subjects which is conducted within, or by members of, the institution, using the considerations set forth in this Policy as the minimum standard.

Article 1.3
The REB shall consist of at least five members, including both men and women, of whom:

(a) at least two members have broad expertise in the methods or in the areas of research that are covered by the REB;

(b) at least one member is knowledgeable in ethics;

(c) for biomedical research, at least one member is knowledgeable in the relevant law; this is advisable but not mandatory for other areas of research; and

(d) at least one member has no affiliation with the institution, but is recruited from the community served by the institution.

Article 1.4
(a) REBs shall be established by the highest levels of the institution, and cover as broad a range of research as is consistent with manageable workloads. Departmental REBs normally are not acceptable (except as discussed below for review of undergraduate research within course requirements). A multiplicity of REBs with small workloads within the same institution should be avoided.

[A.2]
(b) Large institutions may find it necessary to create more than one REB, usually to cover different areas of research. The jurisdiction of each REB should be clearly defined by the normal processes of governance within the institution, and a mechanism should be established to coordinate the practices of all REBs within the institution.

(c) Small institutions may wish to explore regional cooperation or alliances, including the sharing of REBs.

**Article 1.5**

(a) The REB shall satisfy itself that the design of a research project that poses more than minimal risk is capable of addressing the questions being asked in the research.

(b) The extent of the review for scholarly standards that is required for biomedical research that does not involve more than minimal risk will vary according to the research being carried out.

(c) Research in the humanities and the social sciences which poses, at most, minimal risk shall not normally be required by the REB to be peer reviewed.

(d) Certain types of research, particularly in the social sciences and the humanities, may legitimately have a negative effect on public figures in politics, business, labour; the arts or other walks of life, or on organizations. Such research should not be blocked through the use of harms/benefits analysis or because of the potentially negative nature of the findings. The safeguard for those in the public arena is through public debate and discourse and, as extenu, through action in the courts for libel.

**Article 1.6**

The REB should adopt a proportionate approach based on the general principle that the more invasive the research, the greater should be the care in assessing the research.

**Article 1.7**

REBs shall meet regularly to discharge their responsibilities.

**Article 1.8**

Minutes of all REB meetings shall be prepared and maintained by the REB. The minutes shall clearly document the REB’s decisions and any dissent, and the reasons for them. In order to assist internal and external audits of research monitoring, and to facilitate reconsideration or appeal, the minutes must be accessible to authorized representatives of the institution, researchers and funding agencies.

**Article 1.9**

REBs shall meet face-to-face to review proposed research that is not delegated to expedited review. REB review shall be based upon fully detailed research proposals, on where applicable, progress reports. The REB shall function impartially, provide fair hearing to those involved and provide reasoned and appropriately documented opinions and decisions. The REB shall accommodate reasonable requests from researchers to participate in discussions about their proposals, but not be present when the REB is making its decision. When an REB is considering a negative decision, it shall provide the researcher with all the reasons for doing so and give the researcher an opportunity to reply before making a final decision.

[A3]
Article 1.10 Researchers have the right to request, and REBs have an obligation to provide, reconsideration of decisions affecting a research project.

Article 1.11
(a) In cases when researchers and REBs cannot reach agreement through discussion and reconsideration, an institution should permit review of an REB decision by an appeal board, provided that the board be within the same institution and its membership and procedures meet the requirements of this Policy. No one has appeal boards are permitted.

(b) The Councils will not entertain any appeals of REB decisions.

Article 1.12 If an REB is reviewing research in which a member of the REB has a personal interest in the research under review (e.g., as a researcher or as an entrepreneur), conflict of interest principles require that the member not be present when the REB is discussing or making its decision. The REB member must disclose and explain the conflict of interest and offer evidence to the REB providing the conflict is fully explained to the REB, and the proposer of the research has the right to hear the evidence and to offer a rebuttal.

Article 1.13
(a) Ongoing research shall be subject to continuing ethics review. The report of the review should be in accordance with a proportionate approach to ethics assessment.

(b) As part of each research proposal submitted for REB review, the researcher shall propose to the REB the continuing review process deemed appropriate for that project.

(c) Normally, continuing review shall consist of at least the submission of a succinct annual status report to the REB. The REB shall be promptly notified when the project concludes.

Article 1.14 Research to be performed outside the jurisdiction or country of the institution which employs the researcher shall undergo prospective ethics review both (a) by the REB within the researcher's institution; and (b) by the appropriate REB, where such exists, which has authority in the country or jurisdiction where the research is to be done.

Article 2.1
(a) Research governed by this Policy (see Article 1.1) may begin only if (1) prospective subjects, or authorized third parties, have been given the opportunity to give free and informed consent about participation, and (2) their free and informed consent has been given and is maintained throughout their participation in the research. Articles 2.1(2). 2.8, 2.9, and 2.10 provide exceptions to Article 2.1(a).

(b) Evidence of free and informed consent by the subject or authorized third party should ordinarily be obtained in writing. Where written consent is culturally unacceptable, or where there are good reasons for not recording consent in writing, the procedures used to seek free and informed consent shall be documented.

[ A.4 ]
(c) The REB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirement to obtain informed consent, provided that the REB finds and documents that:

i. The research involves no more than minimal risk to the subjects;

ii. The waiver or alteration is unlikely to adversely affect the rights and welfare of the subjects;

iii. The research could not practically be carried out without the waiver or alteration;

iv. Whenever possible and appropriate, the subjects will be provided with additional pertinent information after participation; and

v. The waiver or altered consent does not involve a therapeutic intervention.

(d) In studies including randomization and blinding in clinical trials, neither the research subjects nor those responsible for their care know which treatment the subjects are receiving before the project commences. Such research is not regarded as a waiver or alteration of the requirements for consent if subjects are informed of the probability of being randomly assigned to one arm or another.

Article 2.2

Free and informed consent must be voluntarily given, without manipulation, undue influence or coercion.

Article 2.3

REB review is normally required for research involving unrealistic observation. However, research involving observation of participants in, for example, political rallies, demonstrations or public meetings, should not require REB review since it can be expected that the participants are seeking public visibility.

Article 2.4

Researchers shall provide to prospective subjects or authorized third parties, full and frank disclosure of all information relevant to free and informed consent. Throughout the free and informed consent process, the researcher must ensure that prospective participants are given adequate opportunities to discuss and contemplate their participation. Subject to the exceptions in Article 2.1(c), a written commitment of the free and informed consent process, researchers or their qualified designee representatives shall provide prospective subjects with the following:

(a) information that the individual is being invited to participate in a research project;

(b) A comprehensible statement of the research purpose, the identity of the researcher, the expected duration and nature of participation, and a description of research procedures;

(c) A comprehensible description of reasonably foreseeable harms and benefits that may arise from research participation, as well as the likely consequences of non-active, particularly in research related to treatment, or where invasive methodologies are involved, or where there is a potential for physical or psychological harm;

(d) An assurance that prospective subjects are free not to participate, have the right to withdraw at any time without prejudice to pre-existing arrangements, and will be given continuing and meaningful opportunities for deciding whether or not to continue to participate; and

(e) The possibility of commercialization of research findings, and the presence of any commercial or actual or potential conflict of interest on the part of researchers, their institutions or sponsors.
Additional information that may be required for some projects

1. An assurance that new information will be provided to the subject in a timely manner whenever such information is relevant to the subject's decision to continue or withdraw from participation;

2. The identity of the qualified designated representative who can explain scientific or scholarly aspects of the research;

3. Information on the appropriate resources outside the research team to contact regarding possible ethical issues in the research;

4. An indication as to who will have access to information collected on the identity of subjects, and description of how confidentiality will be protected, and unauthorized uses of data;

5. An explanation of the responsibilities of the subject;

6. Information on the circumstances under which the researcher may terminate the subject's participation in the research;

7. Information on any costs, payments, reimbursement for expenses, or compensation for injury;

8. In the case of randomized trials, the probability of assignment to each option;

9. For research on biomedical procedures, including health care interventions: information about (a) foregoing alternative procedures that might be advantageous to the subject, (b) which aspects of the research involve the use of procedures that are not generally recognized or accepted, and, (c) particularly in trials of therapeutic interventions, the care provided if the potential subject decides not to consent to participation in the study;

10. The ways in which the research results will be published, and how the subjects will be informed of the results of the research.
Article 2.5  Subject to applicable legal requirements, individuals who are not legally competent shall only be asked to become research subjects when:

(a) the research question can only be addressed using the identified group(s); and

(b) free and informed consent will be sought from their authorized representative(s); and

(c) the research does not expose them to more than minimal risks without the potential for direct benefits for them.

Article 2.6  For research involving incompetent individuals, the REB shall ensure that, as a minimum, the following conditions are met:

(a) The researcher shall show how the free and informed consent will be sought from the authorized third party, and how the subjects' best interests will be protected.

(b) The authorized third party may not be the researcher or any other member of the research team.

(c) The continued free and informed consent of an appropriately authorized third party will be required to continue the participation of a legally incompetent subject in research, so long as the subject remains incompetent.

(d) When a subject who was entered into a research project through third-party authorization becomes competent during the project, his or her informed consent shall be sought as a condition of continuing participation.

Article 2.7  Where free and informed consent has been obtained from an authorized third party, and in those circumstances where the legally incompetent individual understands the nature and consequences of the research, the researcher shall seek to ascertain the wishes of the individual concerning participation. The potential subject's dissent will preclude his or her participation.

Article 2.8  Subject to all applicable legislative and regulatory requirements, research involving emergency health situations shall be conducted only if it addresses the emergency needs of individuals involved, and then only in accordance with criteria established in advance of such research by the REB. The REB may allow research that involves health emergencies to be carried out without the free and informed consent of the subject or of his or her authorized third party if ALL of the following apply:

(a) A serious threat to the prospective subject requires immediate intervention; and

(b) Either no standard efficacy care exists or the research offers a real possibility of direct benefit to the subject in comparison with standard care; and

(c) Either the risk of harm is not greater than that involved in standard efficacy care, or it is clearly justified by the direct benefits to the subject; and
(d) The prospective subject is unconscious or lacks capacity to understand risks, methods and purposes of the research; and

(e) Third-party authorization cannot be secured in sufficient time, despite diligent and documented efforts to do so; and

(f) No relevant prior directive by the subject is known to exist, a dissent will prejudice his or her participation.

Article 3.1
Subject to the exceptions in Article 1.1(c), researchers who intend to interview a human subject to secure identifiable personal information shall secure REB approval for the interview procedure used and shall ensure the free and informed consent of the interviewee as required in Article 2.4. As indicated in Article 1.1(c), REB approval is not required for access to publicly available information or materials, including archival documents and records of public interviews or performances.

Article 3.2
Subject to Article 3.1 above, researchers shall secure REB approval for obtaining identifiable personal information about subjects. Approval for such research shall include such considerations as:

(a) The type of data to be collected;

(b) The purpose for which the data will be used;

(c) Limits on the use, disclosure, and retention of the data;

(d) Appropriate safeguards for security and confidentiality;

(e) Any modes of observation (e.g., phonographs or videos) or access to information (e.g., sound recordings) in the research that allow identification of particular subjects;

(f) Any anticipated secondary use of identifiable data from the research;

(g) Any anticipated linkage of data gathered in the research with other data about subjects, whether those data are contained in public or personal records and

(h) Provisions for confidentiality of data resulting from the research.

Article 3.3
If identifying information is involved, REB approval shall be sought for secondary uses of data. Researchers may gain access to identifying information if they have demonstrated to the satisfaction of the REB that:

(a) Identifying information is essential to the research; and

(b) They will take appropriate measures to protect the privacy of the individuals to whom the data refer; and to minimize harm to subjects;

(c) They will not use the data for any purpose other than the purpose of the research; and

(d) They inform the appropriate REB of the purposes for which the data are to be used.

[ A.8 ]
Article 3.4 The REB may also require that a researcher’s access to secondary use of data involving identifying information be dependent on:

(a) The informed consent of those who contributed data or of authorized third parties; or

(b) An appropriate strategy for minimizing the subjects; or

(c) Consultation with representatives of those who contributed data.

Article 3.5 Researchers who wish to connect individuals to whom data refer shall seek the authorization of the REB prior to contact.

Article 3.6 The implications of approved data linkage in which research subjects may be identifiable shall be approved by the REB.

Article 4.1 Researchers and REB members shall disclose actual, perceived or potential conflicts of interest to the REB. REB members should develop mechanisms to address and resolve conflicts of interest.

Article 5.1 (a) Where research is designed to survey a number of living research subjects because of their involvement in genomic activities (e.g., in many areas of health research or in some social science research such as studies of child poverty or of access to legal clinics) that are not specific to particular identifiable groups, researchers shall not exclude prospective or actual research subjects on the basis of such attributes as culture, religion, race,ethnicity, or physical disability, sexual orientation, ethnicity,sex or age, unless there is a valid reason for doing so.

(b) This article is not intended to preclude research focused on a single living individual (such as in a biography) or on a group of individuals who share a specific characteristic (as in a study of an identifiable group of patients who happen to be all of one sex, colour or religion, or of a religious order which is restricted to one sex).

Article 5.2 Women shall not automatically be excluded from research solely on the basis of sex or reproductive capacity.

Article 5.3 Subject to the provisions in Articles 2.6 and 2.8, those who are not competent to consent for themselves shall not be automatically excluded from research which is potentially beneficial to them as individuals, or to the groups that they represent.

Article 6 (None)

Article 7.1 Phase I non-therapeutic clinical trials shall undergo both stringent review and continuous monitoring by an REB independent of the clinical trial sponsor.

Article 7.2 In combined Phase I/II clinical trials, researchers and REBs shall carefully examine the integrity of the first and informed consent process. Where appropriate, the REB may require an independent monitoring process.

Article 7.3 REBs shall examine the budgets of clinical trials to assure that ethical duties concerning conflict of interest are respected.

[ A 9 ]
Article 7.4 The use of placebo controls in clinical trials is generally unacceptable when standard therapies or interventions are available for a particular patient population.

Article 8.1 The genetic researcher shall seek free and informed consent from the individual and report results to the individual if the individual so desires.

Article 8.2 The researcher and the REB shall ensure that the results of genetic testing and genetic counselling records are protected from access by third parties, unless free and informed consent is given by the subject. Family information in databases shall be coded so as to remove the possibility of identification of subjects within the bank itself.

Article 8.3 Researchers and genetic counsellors involving families and groups in genetic research studies shall reveal potential harms to the REB and outline how such harms will be dealt with as part of the research project.

Article 8.4 Genetic researchers and the REB shall ensure that the research protocol makes provision for access to genetic counselling for the subjects, where appropriate.

Article 8.5 Gene alteration (including gene therapy) that involves human germ-line cells or human embryos is not ethically acceptable. Gene alteration for therapeutic purposes and involving human somatic cells may be considered for approval.

Article 8.6 Though the banking of genetic material is expected to yield benefits, it may also pose potential harms to individuals, their families, and the groups to which they may belong. Accordingly, researchers who propose research involving the banking of genetic material have a duty to satisfy the REB and prospective research subjects that they have addressed the associated ethical issues, including confidentiality, privacy, storage, use of the data and results, withdrawal by the subject, and future contact of subjects, families and groups.

Article 8.7 At the outset of a research project, the researcher shall discuss with the REB and the research subject the possibility and/or probability that the genetic material and the information derived from its use may have potential commercial use.

Article 9.1 Researchers shall obtain free and informed consent from the individual whose genotypes are to be used in research.

Article 9.2 In research, it is not ethical to use research ovum or sperm that have been obtained through commercial transactions, including exchange for service.
Article 9.3

It is not ethically acceptable to create, or intend to create, hybrid individuals by such means as mixing human and animal genes, or transferring somatic or germ cell nuclei between cells of humans and other species.

Article 9.4

It is not ethically acceptable to create human embryos specifically for research purposes. However, in those cases where human embryos are created for reproductive purposes, and subsequently are no longer required for such purposes, research involving human embryos may be considered to be ethically acceptable, but only if all of the following apply:

(a) The ova and sperm from which they were formed are obtained in accordance with Articles 9.1 and 9.2;
(b) The research does not involve the genetic alteration of human gametes or embryos;
(c) Embryos exposed to manipulations not directed specifically to their ongoing normal development will not be transferred for continuing pregnancy; and
(d) Research involving human embryos takes place only during the first 14 days after their formation, by combination of the gametes.

Article 9.5

It is not ethically acceptable to undertake research that involves exegesis, cloning human beings by any means involving somatic cell nuclear transfer, formation of animal/human hybrids, or the transfer of embryos between humans and other species.

Article 10.1

Research proposing the collection and use of human tissues requires ethics review by an REB. Among other things, the researcher shall demonstrate the following to the REB:

(a) That the collection and use of human tissues for research purposes shall be undertaken with the free and informed consent of competent donors;
(b) In the case of incompetent donors, free and informed consent shall be by an authorized third party;
(c) In the case of deceased donors, free and informed consent shall be expressed in a prior directive or through the acts of free and informed consent by an authorized third party.

A.11]
Article 10.2

For the purpose of obtaining free and informed consent, researchers who seek to collect human tissue for research shall, as a minimum, provide potential donors or authorized third parties information about:

(a) The purpose of the research;

(b) The type and amount of tissue to be taken, as well as the location where the tissue is to be taken;

(c) The manner in which tissue will be taken, the safety and invasiveness of acquisition, and the duration and conditions of preservation;

(d) The potential uses for the tissue including any commercial uses;

(e) The safeguards to protect the individual's privacy and confidentiality;

(f) Identifying information attached to specific tissue, and its potential variability; and

(g) How the use of the tissue could affect privacy.

Article 10.3

(a) When identification is possible, researchers shall seek to obtain free and informed consent from individuals, or from their authorized third parties, for the use of their previously collected tissue. The provisions of Article 10.2 also apply here.

(b) When collected tissue has been provided by persons who are not individually identifiable (anonymous and anonymized tissue), and when there is no potential harm to them, there is no need to seek donors' permission to use their tissue for research purposes, unless applicable law so requires.

Endnotes

1 Article 2.1(e) was adapted from Permission of Human Subjects, U.S. Dept. Of Health & Human Services, Title 45, Code of Federal Regulations, Part 46.11600.
June 22, 2001

Notification of passage of Schedule

Please be advised that the following Schedule was passed by Order-in-Council and appears in the Canada Gazette, Part II of:

**DATE:** June 20, 2001

Food and Drug Regulations-Amendment (Schedule No 1024) Clinical Trial Framework

**REGISTRATION:** SOR/2001-203

P.C.: 2001-1042

**PASSAGE:** June 17, 2001

Karen Reynolds
Policy Division/Dévision de la politique
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Her Excellency the Governor General in Council, on the recommendation of the Minister of Health, pursuant to subsection 30(1) of the *Food and Drugs Act*, hereby makes the annexed Regulations *Amending the Food and Drug Regulations (1024 — Clinical Trials)*.

* S.C. 1999, c. 33, s. 347
REGULATIONS AMENDING THE FOOD AND DRUG REGULATIONS (1024 — CLINICAL TRIALS)

AMENDMENTS

1. Paragraph C.01A.002(1)(c)* of the Food and Drug Regulations is replaced by the following:

(c) any activity with respect to a drug that is used only for the purposes of clinical testing in accordance with subsection C.05.006(1) or section C.08.005; and

2. Subsection C.03.202(2) of the Regulations is repealed.

3. Section C.03.208 of the Regulations is amended by adding the word "and" at the end of paragraph (n), by striking out the word "and" at the end of paragraph (o) and by repealing paragraph (p).

4. Part C of the Regulations is amended by adding the following after Division 4:

DIVISION 5

DRUGS FOR CLINICAL TRIALS INVOLVING HUMAN SUBJECTS

Interpretation

C.05.001. The definitions in this section apply in this Division.

"adverse drug reaction" means any noxious and unintended response to a drug that is caused by the administration of any dose of the drug (réaction indésirable à une drogue)

"adverse event" means any adverse occurrence in the health of a clinical trial subject who is administered a drug, that may or may not be caused by the administration of the drug, and includes an adverse drug reaction (incident thérapeutique)

"clinical trial" means an investigation in respect of a drug for use in humans that involves human subjects and that is intended to discover or verify the clinical, pharmacological or pharmacodynamic effects of the drug, identify any adverse events in respect of the drug, study the absorption, distribution, metabolism and excretion of the drug, or ascertain the safety or efficacy of the drug (essai clinique)

"drug" means a drug for human use that is to be tested in a clinical trial (drogue)

* SOR/98-7
* C.R.C., c. 870
"good clinical practices" means generally accepted clinical practices that are designed to ensure the protection of the rights, safety and well-being of clinical trial subjects and other persons, and the good clinical practices referred to in section C.05.010. (bonnes pratiques cliniques)

"import" means to import a drug into Canada for the purpose of sale in a clinical trial. (importer)

"Investigator's brochure" means, in respect of a drug, a document containing the preclinical and clinical data on the drug that are described in paragraph C.05.005(e). (brochure du chercheur)

"protocol" means a document that describes the objectives, design, methodology, statistical considerations and organization of a clinical trial. (protocole)

"qualified investigator" means the person responsible to the sponsor for the conduct of the clinical trial at a clinical trial site, who is entitled to provide health care under the laws of the province where that clinical trial site is located, and who is

(a) in the case of a clinical trial respecting a drug to be used for dental purposes only, a physician or dentist and a member in good standing of a professional medical or dental association; and

(b) in any other case, a physician and a member in good standing of a professional medical association. (chercheur qualifié)

"Research ethics board" means a body that is not affiliated with the sponsor, and

(a) the principal mandate of which is to approve the initiation of, and conduct periodic reviews of, biomedical research involving human subjects in order to ensure the protection of their rights, safety and well-being; and

(b) that has at least five members, that has a majority of members who are Canadian citizens or permanent residents under the Immigration Act, that is composed of both men and women and that includes at least

(i) two members whose primary experience and expertise are in a scientific discipline, who have broad experience in the methods and areas of research to be approved and one of whom is from a medical discipline or, if the clinical trial is in respect of a drug to be used for dental purposes only, is from a medical or dental discipline,

(ii) one member knowledgeable in ethics,

(iii) one member knowledgeable in Canadian laws relevant to the biomedical research to be approved,

(iv) one member whose primary experience and expertise are in a non-scientific discipline, and
(v) one member who is from the community or is a representative of an organization interested in
the areas of research to be approved and who is not affiliated with the sponsor or the site where
the clinical trial is to be conducted. (comité d'éthique de la recherche)

"serious adverse drug reaction" means an adverse drug reaction that requires in-patient hospitalization
or prolongation of existing hospitalization, that causes congenital malformation, that results in
persistent or significant disability or incapacity, that is life threatening or that results in death.
(reaction indésirable grave à une drogue)

"serious unexpected adverse drug reaction" means a serious adverse drug reaction that is not identified
in nature, severity or frequency in the risk information set out in the investigator's brochure or on the
label of the drug. (Réaction indésirable grave et imprévue à une drogue)

"sponsor" means an individual, corporate body, institution or organization that conducts a clinical trial.
(promoteur)

Application

C.05.002. (1) Subject to subsection (2), this Division applies to the sale or importation of drugs to
be used for the purposes of clinical trials involving human subjects.

(2) Except for paragraph C.05.003(d), subsections C.05.006(2) and (3), paragraphs C.05.010(a) to
(l), section C.05.011, subsections C.05.012(1) and (2), paragraphs C.05.012(f) to (d) and (f) to
(k), subsection C.05.012(4) and sections C.05.013, C.05.016 and C.05.017, this Division does not
apply to the sale or importation of a drug for the purposes of a clinical trial authorized under subsection
C.05.006(2).

Prohibition

C.05.003. Despite sections C.01.014, C.08.002 and C.08.003, no person shall sell or import a
drug for the purposes of a clinical trial unless

(a) the person is authorized under this Division;

(b) the person complies with this Division and sections C.01.015, C.01.036, C.01.037 to
C.01.040, C.01.040.2, C.01.064 to C.01.067, C.01.070, C.01.131, C.01.133 to C.01.136, and
C.01.435; and

(c) if the drug is to be imported, the person has a representative in Canada who is responsible for
the sale of the drug.
General

C.05.004. Despite these Regulations, a sponsor may submit an application under this Division to sell or import a drug for the purposes of a clinical trial that contains a substance the sale of which is prohibited by these Regulations, if the sponsor establishes, on the basis of scientific information, that the inclusion of the substance in the drug may result in a therapeutic benefit for a human being.

Application for Authorization

C.05.005. An application by a sponsor for authorization to sell or import a drug for the purposes of a clinical trial under this Division shall be submitted to the Minister, signed and dated by the sponsor's senior medical or scientific officer in Canada and senior executive officer and shall contain the following information and documents:

(a) a copy of the protocol for the clinical trial;

(b) a copy of the statement, as it will be set out in each informed consent form, that states the risks and anticipated benefits arising to the health of clinical trial subjects as a result of their participation in the clinical trial;

(c) a clinical trial attestation, signed and dated by the sponsor's senior medical or scientific officer in Canada and senior executive officer, containing:

(i) the title of the protocol and the clinical trial number,

(ii) the brand name, the chemical name or the code for the drug,

(iii) the therapeutic and pharmacological classifications of the drug,

(iv) the medicinal ingredients of the drug,

(v) the non-medicinal ingredients of the drug,

(vi) the dosage form of the drug,

(vii) the name, address and telephone number and, if applicable, the facsimile number and electronic mail address of the sponsor;

(viii) if the drug is to be imported, the name, address and telephone number and, if applicable, the facsimile number and electronic mail address of the sponsor's representative in Canada who is responsible for the sale of the drug,
(ix) for each clinical trial site, the name, address and telephone number and, if applicable, the facsimile number and electronic mail address of the qualified investigator, if known at the time of submitting the application,

(x) for each clinical trial site, the name, address and telephone number and, if applicable, the facsimile number and electronic mail address of the research ethics board that approved the protocol referred to in paragraph (a) and approved an informed consent form containing the statement referred to in paragraph (b), if known at the time of submitting the application, and

(xi) a statement

(A) that the clinical trial will be conducted in accordance with good clinical practices and these Regulations, and

(B) that all information contained in, or referenced by, the application is complete and accurate and is not false or misleading;

(d) the name, address and telephone number and, if applicable, the facsimile number and electronic mail address of any research ethics board that has previously refused to approve the protocol referred to in paragraph (a), its reasons for doing so and the date on which the refusal was given, if known at the time of submitting the application;

(e) an investigator's brochure that contains the following information, namely,

(i) the physical, chemical and pharmaceutical properties of the drug,

(ii) the pharmacological aspects of the drug, including its metabolites in all animal species tested,

(iii) the pharmacokinetics of the drug and the drug metabolism, including the biological transformation of the drug in all animal species tested,

(iv) any toxicological effects in any animal species tested under a single dose study, a repeated dose study or a special study in respect of the drug,

(v) any results of carcinogenicity studies in any animal species tested in respect of the drug,

(vi) any results of clinical pharmacokinetic studies of the drug,

(vii) any information regarding drug safety, pharmacodynamics, efficacy and dose responses of the drug that were obtained from previous clinical trials in humans, and

(viii) if the drug is a radiopharmaceutical as defined in section C.03.201, information regarding directions for preparing the radiopharmaceutical, the radiation dosimetry in respect of the
prepared radiopharmaceutical and a statement of the storage requirements for the prepared radiopharmaceutical;

(f) if the drug contains a human-sourced excipient, including any used in the placebo,

(i) information that indicates the human-sourced excipient has been assigned a drug identification number under subsection C.01.014.2(1) or, in the case of a new drug, issued a notice of compliance under subsection C.08.004(1), as the case may be, or

(ii) in any other case, sufficient information to support the identity, purity, potency, stability and safety of the human-sourced excipient;

(g) if the drug has not been assigned a drug identification number under subsection C.01.014.2(1) or, in the case of a new drug, a notice of compliance has not been issued under subsection C.08.004(1), the chemistry and manufacturing information in respect of the drug, including its site of manufacture; and

(h) the proposed date for the commencement of the clinical trial at each clinical trial site, if known at the time of submitting the application.

Authorization

C.05.006. (1) Subject to subsection (3), a sponsor may sell or import a drug, other than a drug described in subsection (2), for the purposes of a clinical trial if

(a) the sponsor has submitted to the Minister an application in accordance with section C.65.005;

(b) the Minister does not, within 30 days after the date of receipt of the application, send to the sponsor a notice in respect of the drug indicating that the sponsor may not sell or import the drug for any of the following reasons:

(i) that the information and documents in respect of the application

(A) were not provided in accordance with these Regulations, or

(B) are insufficient to enable the Minister to assess the safety and risks of the drug or the clinical trial, or

(ii) based on an assessment of the application, an assessment of any information submitted under section C.05.009 or a review of any other information, the Minister has reasonable grounds to believe that
(A) the use of the drug for the purposes of the clinical trial endangers the health of a clinical trial subject or other person,

(B) the clinical trial is contrary to the best interests of a clinical trial subject, or

(C) the objectives of the clinical trial will not be achieved;

(c) for each clinical trial site, the sponsor has obtained the approval of the research ethics board in respect of the protocol referred to in paragraph C.05.005(a) and in respect of an informed consent form that contains the statement referred to in paragraph C.05.005(b); and

(d) before the sale or importation of the drug at a clinical trial site, the sponsor submits to the Minister the information referred to in subparagraphs C.05.005(c)(ix) and (x) and paragraphs C.05.005(d) and (h), if it was not submitted in respect of that clinical trial site at the time of submitting the application.

(2) Subject to subsection (3), a sponsor may sell or import a drug for the purposes of a clinical trial in respect of

(a) a new drug that has been issued a notice of compliance under subsection C.08.004(1), if the clinical trial is in respect of a purpose or condition of use for which the notice of compliance was issued; or

(b) a drug, other than a new drug, that has been assigned a drug identification number under subsection C.01.014.2(1), if the clinical trial is in respect of a use or purpose for which the drug identification number was assigned.

(3) A sponsor may not sell or import a drug for the purposes of a clinical trial

(a) during the period of any suspension made under section C.05.016 or C.05.017; or

(b) after a cancellation made under section C.05.016 or C.05.017.

Notification

C.05.007. If the sale or importation of a drug is authorized under this Division, the sponsor may make one or more of the following changes if the sponsor notifies the Minister in writing within 15 days after the date of the change:

(a) a change to the chemistry and manufacturing information that does not affect the quality or safety of the drug, other than a change for which an amendment is required by section C.05.008; and
(b) a change to the protocol that does not alter the risk to the health of a clinical trial subject, other than a change for which an amendment is required by section C.05.008.

Amendment

C.05.008. (1) Subject to subsections (4) and (5), when the sale or importation of a drug is authorized under this Division and the sponsor proposes to make an amendment referred to in subsection (2), the sponsor may sell or import the drug for the purposes of the clinical trial in accordance with the amended authorization, if the following conditions are met:

(a) the sponsor has submitted to the Minister an application for amendment in accordance with subsection (3);

(b) the Minister does not, within 30 days after the date of receipt of the application for amendment, send to the sponsor a notice in respect of the drug indicating that the sponsor may not sell or import the drug in accordance with the amendment for any of the following reasons, namely,

(i) that the information and documents in respect of the application for amendment

(A) were not provided in accordance with these Regulations, or

(B) are insufficient to enable the Minister to assess the safety and risks of the drug or the clinical trial, or

(ii) that based on an assessment of the application for amendment, an assessment of any information submitted under section C.05.009 or a review of any other information, the Minister has reasonable grounds to believe that

(A) the use of the drug for the purposes of the clinical trial endangers the health of a clinical trial subject or other person,

(B) the clinical trial is contrary to the best interests of a clinical trial subject, or

(C) the objectives of the clinical trial will not be achieved;

(c) before the sale or importation of the drug, the sponsor submits to the Minister

(i) for each clinical trial site, the name, address and telephone number and, if applicable, the facsimile number and electronic mail address of the research ethics board that approved any amended protocol submitted under paragraph (3)(a) or approved any amended statement submitted under paragraph (3)(c), and
(ii) the name, address and telephone number and, if applicable, the facsimile number and electronic mail address of any research ethics board that has previously refused to approve any amendment to the protocol, its reasons for doing so and the date on which the refusal was given;

(d) before the sale or importation of the drug, the sponsor maintains records concerning

(i) the information referred to in paragraph C.05.005(h), and

(ii) the information referred to in subparagraph C.05.005(c)(ix), if any of that information has changed since it was submitted;

(e) before the sale or importation of the drug in accordance with the amended authorization, the sponsor ceases to sell or import the drug in accordance with the existing authorization; and

(f) the sponsor conducts the clinical trial in accordance with the amended authorization.

(2) For the purposes of subsection (1), amendments are

(a) amendments to the protocol that affect the selection, monitoring or dismissal of a clinical trial subject;

(b) amendments to the protocol that affect the evaluation of the clinical efficacy of the drug;

(c) amendments to the protocol that alter the risk to the health of a clinical trial subject;

(d) amendments to the protocol that affect the safety evaluation of the drug;

(e) amendments to the protocol that extend the duration of the clinical trial; and

(f) amendments to the chemistry and manufacturing information that may affect the safety or quality of the drug.

(3) The application for amendment referred to in subsection (1) shall contain a reference to the application submitted under section C.05.005 and shall contain the following documents and information:

(a) if the application is in respect of an amendment referred to in any of paragraphs (2)(a) to (e), a copy of the amended protocol that indicates the amendment, a copy of the protocol submitted under paragraph C.05.005(e), and the rationale for the amendment;

(b) if the application is in respect of an amendment referred to in paragraph (2)(f), a copy of the amended investigator's brochure or an addendum to the investigator's brochure that indicates the new information, including supporting toxicological studies and clinical trial safety data;
(c) if the application is in respect of an amendment referred to in any of paragraphs (2)(a) to (f) and, as a result of that amendment, it is necessary to amend the statement referred to in paragraph C.05.005(3), a copy of the amended statement that indicates the new information; and

(d) if the application is in respect of an amendment referred to in paragraph (2)(f), a copy of the amended chemistry and manufacturing information that indicates the amendment, and the rationale for that amendment.

(4) If the sponsor is required to immediately make one or more of the amendments referred to in subsection (3) because the clinical trial or the use of the drug for the purposes of the clinical trial endangers the health of a clinical trial subject or other person, the sponsor may immediately make the amendment and shall provide the Minister with the information referred to in subsection (3) within 15 days after the date of the amendment.

(5) A sponsor may not sell or import a drug for the purposes of a clinical trial

(a) during the period of any suspension made under section C.05.016 or C.05.017; or

(b) after a cancellation made under section C.05.016 or C.05.017.

Additional Information and Samples

C.05.009. If the information and documents submitted in respect of an application under section C.05.005 or an application for amendment under section C.05.008 are insufficient to enable the Minister to determine whether any of the reasons referred to in paragraph C.05.006(1)(b) or C.05.308(1)(b) exist, the Minister may require the sponsor to submit, within two days after receipt of the request, samples of the drug or additional information relevant to the drug or the clinical trial that are necessary to make the determination.

Sponsor's Obligations

Good Clinical Practices

C.05.010. Every sponsor shall ensure that a clinical trial is conducted in accordance with good clinical practices and, without limiting the generality of the foregoing, shall ensure that

(a) the clinical trial is scientifically sound and clearly described in a protocol;

(b) the clinical trial is conducted, and the drug is used, in accordance with the protocol and this Division;
(c) systems and procedures that assure the quality of every aspect of the clinical trial are implemented;

(d) for each clinical trial site, the approval of a research ethics board is obtained before the clinical trial begins at the site;

(e) at each clinical trial site, there is no more than one qualified investigator;

(f) at each clinical trial site, medical care and medical decisions, in respect of the clinical trial, are under the supervision of the qualified investigator;

(g) each individual involved in the conduct of the clinical trial is qualified by education, training and experience to perform his or her respective tasks;

(h) written informed consent, given in accordance with the applicable laws governing consent, is obtained from every person before that person participates in the clinical trial but only after that person has been informed of

(i) the risks and anticipated benefits to his or her health arising from participation in the clinical trial,

(ii) all other aspects of the clinical trial that are necessary for that person to make the decision to participate in the clinical trial;

(i) the requirements respecting information and records set out in section C.05.012 are met; and

(j) the drug is manufactured, handled and stored in accordance with the applicable good manufacturing practices referred to in Divisions 2 to 4 except sections C.02.019, C.02.025 and C.02.026.

Labelling

C.05.011. Despite any other provision of these Regulations respecting labelling, the sponsor shall ensure that the drug bears a label that sets out the following information in both official languages:

(a) a statement indicating that the drug is an investigational drug to be used only by a qualified investigator;

(b) the name, number or identifying mark of the drug;

(c) the expiration date of the drug;

(d) the recommended storage conditions for the drug;
(e) the lot number of the drug;

(f) the name and address of the sponsor;

(g) the protocol code or identification; and

(h) if the drug is a radiopharmaceutical as defined in section C.03.201, the information required by subparagraph C.03.202(1)(b)(vi).

Records

C.05.012. (1) The sponsor shall record, handle and store all information in respect of a clinical trial in a way that allows its complete and accurate reporting as well as its interpretation and verification.

(2) The sponsor shall maintain complete and accurate records to establish that the clinical trial is conducted in accordance with good clinical practices and these Regulations.

(3) The sponsor shall maintain complete and accurate records in respect of the use of a drug in a clinical trial, including:

(a) a copy of all versions of the investigator's brochure for the drug;

(b) records respecting each change made to the investigator's brochure, including the rationale for each change and documentation that supports each change;

(c) records respecting all adverse events in respect of the drug that have occurred inside or outside Canada, including information that specifies the indication for use and the dosage form of the drug at the time of the adverse event;

(d) records respecting the enrollment of clinical trial subjects, including information sufficient to enable all clinical trial subjects to be identified and contacted in the event that the sale of the drug may endanger the health of the clinical trial subjects or other persons;

(e) records respecting the shipment, receipt, disposition, return and destruction of the drug;

(f) for each clinical trial site, an undertaking from the qualified investigator that is signed and dated by the qualified investigator prior to the commencement of his or her responsibilities in respect of the clinical trial, that states that

(i) the qualified investigator will conduct the clinical trial in accordance with good clinical practices, and
(ii) the qualified investigator will immediately, on discontinuance of the clinical trial by the sponsor, in its entirety or at a clinical trial site, inform both the clinical trial subjects and the research ethics board of the discontinuance, provide them with the reasons for the discontinuance and advise them in writing of any potential risks to the health of clinical trial subjects or other persons;

(g) for each clinical trial site, a copy of the protocol, informed consent form and any amendment to the protocol or informed consent form that have been approved by the research ethics board for that clinical trial site; and

(h) for each clinical trial site, an attestation, signed and dated by the research ethics board for that clinical trial site, stating that it has reviewed and approved the protocol and informed consent form and that the board carries out its functions in a manner consistent with good clinical practices.

(4) The sponsor shall maintain all records referred to in this Division for a period of 25 years.

Submission of Information and Samples

C.05.013. (1) The Minister shall require a sponsor to submit, within two days after receipt of the request, information concerning the drug or the clinical trial, or samples of the drug, if the Minister has reasonable grounds to believe that

(a) the use of the drug for the purposes of the clinical trial endangers the health of a clinical trial subject or other person;

(b) the clinical trial is contrary to the best interests of a clinical trial subject;

(c) the objectives of the clinical trial will not be achieved;

(d) a qualified investigator is not respecting the undertaking referred to in paragraph C.05.012(3)(f); or

(e) information submitted in respect of the drug or the clinical trial is false or misleading.

(2) The Minister may require the sponsor to submit, within seven days after receipt of the request, any information or records kept under section C.05.012, or samples of the drug, in order to assess the safety of the drug or the health of clinical trial subjects or other persons.

Serious Unexpected Adverse Drug Reaction Reporting

C.05.014. (1) During the course of a clinical trial, the sponsor shall inform the Minister of any serious unexpected adverse drug reaction in respect of the drug that has occurred inside or outside Canada as follows:
(a) if it is neither fatal nor life threatening, within 15 days after becoming aware of the information; and

(b) if it is fatal or life threatening, within seven days after becoming aware of the information.

(2) The sponsor shall, within eight days after having informed the Minister under paragraph (1)(b), submit to the Minister a complete report in respect of that information that includes an assessment of the importance and implication of any findings made.

(3) Sections C.01.016 and C.01.817 do not apply to drugs used for the purposes of a clinical trial.

Discontinuance of a Clinical Trial

C.05.015. (1) If a clinical trial is discontinued by the sponsor in its entirety or at a clinical trial site, the sponsor shall

(a) inform the Minister no later than 15 days after the date of the discontinuance;

(b) provide the Minister with the reason for the discontinuance and its impact on the proposed or ongoing clinical trials in respect of the drug conducted in Canada by the sponsor;

(c) as soon as possible, inform all qualified Investigators of the discontinuance and of the reasons for the discontinuance, and advise them in writing of any potential risks to the health of clinical trial subjects or other persons; and

(d) in respect of each discontinued clinical trial site, stop the sale or importation of the drug as of the date of the discontinuance and take all reasonable measures to ensure the recovery of all unused quantities of the drug that have been sold.

(2) If the sponsor has discontinued the clinical trial in its entirety or at a clinical trial site, the sponsor may resume selling or importing the drug for the purposes of a clinical trial in its entirety or at a clinical trial site if, in respect of each clinical trial site where the sale or importation is to be resumed, the sponsor submits to the Minister the information referred to in subparagraphs C.05.005(b)(iv) and (a) and paragraphs C.05.005(d) and (b).

Suspension and Cancellation

C.05.016. (1) Subject to subsection (2), the Minister shall suspend the authorization to sell or import a drug for the purposes of a clinical trial, in its entirety or at a clinical trial site, if the Minister has reasonable grounds to believe that

(a) the sponsor has contravened these Regulations or any provisions of the Act relating to the drug;
(b) any information submitted in respect of the drug or clinical trial is false or misleading;

(c) the sponsor has failed to comply with good clinical practices; or

(d) the sponsor has failed to provide

(i) information or samples of the drug as required under section C.05.009 or C.05.013, or

(ii) information or a report under section C.05.014.

(2) Subject to section C.05.017, the Minister shall not suspend an authorization referred to in subsection (1) unless

(a) the Minister has sent to the sponsor a written notice of the intention to suspend the authorization that indicates whether the authorization is to be suspended in its entirety or at a clinical trial site and the reason for the intended suspension;

(b) the sponsor has not, within 30 days after receipt of the notice referred to in paragraph (a), provided the Minister with information or documents that demonstrate that the authorization should not be suspended on the grounds that

(i) the situation giving rise to the intended suspension did not exist, or

(ii) the situation giving rise to the intended suspension has been corrected; and

(c) the Minister has provided the sponsor with the opportunity to be heard in paragraph (b).

(3) The Minister shall suspend the authorization by sending to the sponsor a written notice of suspension of the authorization that indicates the effective date of the suspension, whether the authorization is suspended in its entirety or at a clinical trial site and the reason for the suspension.

(4) If the Minister has suspended an authorization, the Minister shall

(a) reinstate the authorization in its entirety or at a clinical trial site, as the case may be, if within 30 days after the effective date of the suspension the sponsor provides the Minister with information or documents that demonstrate that the situation giving rise to the suspension has been corrected; or

(b) cancel the authorization in its entirety or at a clinical trial site, as the case may be, if within 30 days after the effective date of the suspension the sponsor has not provided the Minister with the information or documents referred to in paragraph (a).

C.05.017. (1) The Minister shall suspend an authorization to sell or import a drug for the purposes of a clinical trial, in its entirety or at a clinical trial site, before giving the sponsor an opportunity to be
heard if the Minister has reasonable grounds to believe that it is necessary to do so to prevent injury to the health of a clinical trial subject or other person.

(2) The Minister shall suspend the authorization by sending to the sponsor a written notice of suspension of the authorization that indicates the effective date of the suspension, whether the authorization is suspended in its entirety or at a clinical trial site and the reason for the suspension.

(3) If the Minister has suspended an authorization, the Minister shall

(a) reinstate the authorization in its entirety or at a clinical trial site, as the case may be, if within 60 days after the effective date of the suspension the sponsor provides the Minister with information or documents that demonstrate that the situation giving rise to the suspension did not exist or that it has been corrected; or

(b) cancel the authorization in its entirety or at a clinical trial site, as the case may be, if within 60 days after the effective date of the suspension the sponsor has not provided the Minister with the information or documents referred to in paragraph (a).

5. Section C.08.003.1⁴ of the Regulations is replaced by the following:

C.08.003.1. The Minister may examine any information or material filed with the Minister by any person pursuant to Division 5 or section C.08.002, C.08.002.1, C.08.003, C.08.005 or C.08.005.1 to establish the safety and effectiveness of the new drug for which the submission or supplement has been filed.

6. (1) The portion of subsection C.08.005(1)⁴ of the Regulations before paragraph (a) is replaced by the following:

C.08.005. (1) Subject to subsection (1.1) and notwithstanding sections C.08.002 and C.08.003, a manufacturer of a new drug may sell it to a qualified investigator to be used solely for the purpose of clinical testing to obtain evidence with respect to the safety, dosage and effectiveness of that new drug, when the following conditions are met:

(2) Section C.08.005 of the Regulations is amended by adding the following after subsection (1):

(1.1) This section applies only in respect of a new drug for veterinary use.

7. (1) The portion of subsection C.08.005.1(1)⁴ of the Regulations before paragraph (a) is replaced by the following:

⁴ SOR/95-411
⁴ SOR/87-511
C.08.005.1. (1) Every manufacturer who files a new drug submission, an abbreviated new drug submission, a supplement to a new drug submission, a supplement to an abbreviated new drug submission, or a supplement for the clinical testing of a new drug for veterinary use shall, in addition to any information and material that is required under section C.08.002, C.08.003 and C.08.005, include in the submission or supplement

(2) Subsection C.08.005.1(6) of the Regulations is replaced by the following:

(6) Every manufacturer who has filed a new drug submission, an abbreviated new drug submission, a supplement to a new drug submission, a supplement to an abbreviated new drug submission or a supplement for the clinical testing of a new drug for veterinary use, and has any relating clinical case reports or raw data that were not included therein, shall keep those reports or data and shall, within 30 days after receiving a written request from the Minister, submit them to the Minister.

8. Subsection C.08.006(3) of the Regulations is replaced by the following:

C.08.006. (1) For the purposes of this section, evidence or new information obtained by the Minister includes any information or material filed by any person pursuant to Division 5 or section C.08.002, C.08.002.1, C.08.003, C.08.005 or C.08.005.1.

9. Paragraph C.08.009(1)(a) of the Regulations is replaced by the following:

(a) to notify the manufacturer of a new drug for veterinary use that the sale of that drug to qualified investigators is prohibited, or

10. Paragraph C.08.017(b) of the Regulations is replaced by the following:

(b) report immediately to the Director all serious adverse drug reactions associated with the use of the new drug.

TRANSITIONAL

11. An application concerning the sale of a drug for human use for the purposes of a clinical trial that is received under Division 8 of the Food and Drug Regulations before September 1, 2001 is subject to those Regulations and any procedures established under those Regulations as they read at the time the application was received.

COMING INTO FORCE

12. These Regulations come into force on September 1, 2001

†SOR/81-333
APPENDIX D
11. No person may be made to undergo care of any nature, whether for examination, specimen taking, removal of tissue, treatment or any other act, except with his consent. If the person concerned is incapable of giving or refusing his consent to care, a person authorized by law or by mandate given in anticipation of his incapacity may do so in his place.

12. A person who gives his consent to or refuses care for another person it bound to act in the sole interest of that person, taking into account, as far as possible, any wishes the latter may have expressed. If he gives his consent, he shall ensure that the care is beneficial notwithstanding the gravity and permanence of certain of its effects, that it is advisable in the circumstances and that the risks incurred are not disproportionate to the anticipated benefit.

13. Consent to medical care is not required in case of emergency if the life of the person is in danger or his integrity is threatened and his consent cannot be obtained in due time. It is required, however, where the care is unusual or has become useless or where its consequences could be intolerable for the person.

14. Consent to care required by the state of health of a minor is given by the person having parental authority or by his tutor. A minor fourteen years of age or over, however, may give his consent alone to such care. If his state requires that he remain in a health or social services establishment for over twelve hours, the person having parental authority or tutor shall be informed of that fact.

15. Where it is ascertained that a person of full age is incapable of giving his consent to care, consent is given by his mandatory, tutor or curator. If the person of full age is not so represented, consent is given by his spouse or, if he has no spouse or his spouse is prevented from giving consent, it is given by a close relative or a
person who shows a special interest in the person of full age.

16. The authorization of the court is necessary where the person who may give consent to care required by the state of health of a minor or a person of full age who is incapable of giving his consent is prevented from doing so or, without justification, refuses to do so; it is also required where a person of full age who is incapable of giving his consent categorically refuses to receive care, except in the case of hygienic care or emergency.

The authorization of the court is necessary, furthermore, to cause a minor fourteen years of age or over to undergo care he refuses, except in the case of emergency if his life is in danger or his integrity threatened, in which case the consent of the person having parental authority or the tutor is sufficient.

17. A minor fourteen years of age or over may give his consent alone to care not required by the state of his health; however, the consent of the person having parental authority or of the tutor is required if the care entails a serious risk for the health of the minor and may cause him grave and permanent effects.

18. Where the person is under fourteen years of age or is incapable of giving his consent, consent to care not required by his state of health is given by the person having parental authority or the mandatory, tutor or curator; the authorization of the court is also necessary if the care entails a serious risk for health or if it might cause grave and permanent effects.

19. A person of full age who is capable of giving his consent may alienate a part of his body inter vivos, provided the risk incurred is not disproportionate to the benefit that may reasonably be anticipated.

A minor or a person of full age who is incapable of giving his consent may, with the consent of the person having parental authority, mandatory, tutor or curator and with the authorization of the court, alienate a part of his body only if that part is capable of regeneration and provided that no serious risk to his health results.

20. A person of full age who is capable of giving his consent may submit to an experiment provided that the risk incurred is not disproportionate to the benefit that can reasonably be anticipated.

21. A minor or a person of full age who is incapable of giving consent may not be submitted to an experiment if the experiment involves serious risk to his health or, where he understands the nature and consequences of experiment, if he objects.

Moreover, a minor or a person of full age who is incapable of giving consent may be submitted to an experiment only if, where the person is the only subject of the experiment, it has the potential to produce benefit to the person's health or only if, in the case of an experiment on a group, it has the potential to produce results capable of conferring benefit to other persons in the same age category or having the same disease or handicap. Such an experiment must be part of a research project approved and monitored by an ethics committee. The competent ethics committees are formed by the Minister of Health and Social Services or designated by the Minister among existing research ethics committees; the composition and operating conditions of the committees are determined by the Minister and published in the Gazette officielle du Québec.

Consent to experimentation may be given, in the case of a minor, by the person having parental authority or the tutor and, in the case of a person of full age incapable of giving consent, by the mandatory, tutor or curator. Where a person of full age suddenly becomes incapable of consent and the experiment, insofar as it must be undertaken promptly after the
appearance of the condition giving rise to it, does not permit, for lack of time, the designation of a legal representative, consent may be given by the person authorized to consent to any care the person requires; it is incumbent upon the competent ethics committee to determine, when examining the research project, whether the experiment meets that condition. Care considered by the ethics committee to be innovative care required by the state of health of the person concerned does not constitute an experiment.

22. A part of the body, whether an organ, tissue or other substance, removed from a person as part of the care he receives may, with his consent or that of the person qualified to give consent for him, be used for purposes of research.

23. When the court is called upon to rule on an application for authorization with respect to care or the alienation of body part, it obtains the opinions of experts, of the person having parental authority, of the mandatory, of the tutor or the curator and of the tutorship council; it may also obtain the opinion of any person who shows a special interest in the person concerned by the application.

The court is also bound to obtain the opinion of the person concerned unless that is impossible, and to respect his refusal unless the care is required by his state of health.

24. Consent to care not required by a person's state of health, to the alienation of a part of a person's body, or to an experiment shall be given in writing.

It may be withdrawn at any time, even verbally.

25. The alienation by a person of a part or product of his body shall be gratuitous; it may not be repeated if it involves a risk to his health.

An experiment may not give rise to any financial reward other than the payment of an indemnity as compensation for the loss and inconvenience suffered.

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42. A person of full age may determine the nature of his funeral and the disposal of his body; a minor may also do so with the written consent of the person having parental authority or his tutor. Failing the expressed wishes of the deceased, the wishes of the heirs or successors prevail; in both cases, the heirs and successors are bound to act, the expenses are charged to the succession.

43. A person of full age or a minor fourteen years of age or over may, for medical or scientific purposes, give his body or authorize the removal of organs or tissues therefrom. A minor under fourteen years of age may also do so with the consent of the person having parental authority or of his tutor. These wishes are expressed verbally before two witnesses, or in writing, and may be revoked in the same manner. The expressed wishes shall be followed, except for a compelling reason.

44. A part of the body of a deceased person may be removed in the absence of knowledge or presumed knowledge of the wishes of the deceased, with the consent of the person who could give consent to care or could have given it. Consent is not required where two physicians attest in writing to the impossibility of obtaining it in due time, the urgency of the operation and the serious hope of saving a human life or of improving its quality to an appreciable degree.

45. No part of the body may be removed before the death of the donor is attested by two physicians who do not participate either in the removal or in the transplantation.

46. An autopsy may be performed in the cases provided for by law or if the deceased had already given his consent thereto; it may also be performed with the consent of the person who was or would have been authorized to give his consent to care. The person requesting the autopsy or having given his consent thereto has a right to receive a copy of the report.

47. The court may, if circumstances justify it, order the performance of an autopsy on the deceased at the request of a physician or any interested person; in the latter case, it may restrict the release of parts of the autopsy report. The coroner may also order the performance of an autopsy on the deceased in the cases provided for by law.

48. No person may embalm, bury or cremate a body before an attestation of death has been drawn up and six hours have elapsed since that was done.

49. Subject to compliance with the prescriptions of law, it is permissible to disinter a body on the order of a court, on the charge of destination of its burial place or in order to bury it elsewhere or to repair the sepulture. Disinterment is also permissible on the order of a coroner in accordance with the law.
Draft Bill
An Act to amend the Civil Code as regards medical research

Tabled by
Mr. Serge Ménard
Minister of Justice

Québec Official Publisher
1997

EXPLANATORY NOTES

This draft bill amending the Civil Code provides that an experiment on a minor or a person of full age who is incapable of giving consent may only be carried out within the framework of a research project approved by an ethics committee designated or formed by the Minister of Health and Social Services and under conditions determined by the Minister.
Moreover, the draft bill provides for the possibility for other persons than the tutor, curator or mandantary of a person of full age to give the necessary consent in the case of certain biomedical research projects. Finally, ethics committees are empowered, in lieu of the court, to approve experiments conducted on a single subject who is either minor or of full age but incapable of giving consent.

LEGISLATION AMENDED BY THIS DRAFT BILL:
- Civil Code of Québec;

Draft Bill

AN ACT TO AMEND THE CIVIL CODE AS REGARDS MEDICAL research

THE PARLIAMENT OF QUÉBEC ENACTS AS FOLLOWS:

1. Article 20 of the Civil Code (1991, chapter 04) is amended by adding, at the end, the following paragraph:

   "A minor or a person of full age who is incapable of giving consent may not be submitted to an experiment except in the absence of serious risk to his health and of objection on his part if he understands the nature and consequences of the act; the consent of the person having parental authority or of the mandantary, tutor or curator is necessary."

2. Article 21 of the said Code is replaced by the following article:

   "21. Any experiment on a minor or a person of full age who is incapable of giving consent, or on a group of minors or of such persons, may only be carried out within the framework of a research project approved by an ethics committee designated or formed by the Minister of Health and Social Services and under conditions determined by the Minister. Moreover, the experiment must have the potential to produce a benefit to the health of the person concerned or, if it is conducted on a group, to the health of persons of the same age group or having the same illness or handicap of the persons submitted to the experiment.

   In the case of a biomedical research project which presupposes that it will be implemented in emergency situations, the committee may, when approving the project, provide that if a person of full age who is to be submitted to the experiment is incapable of giving consent owing to a sudden and temporary condition, consent may be given by the person qualified to give consent to care required by the person's state of health.

   Care considered by the ethics committee to be innovative care required by the state of health of the person who submits to it is not an experiment."

3. Article 23 of the said Code is amended by replacing the words "with respect to care, the alienation of a part of the body, or an experiment" in the first paragraph by the words "with respect to care or the alienation of a body part".
4. Article 776 of the Code of Civil Procedure (R.S.C., chapter C-25) is amended by replacing the words “with respect to care, the alienation of a part of the body or an experiment” in the first paragraph by the words “with respect to care or the alienation of a body part”.

5. Article 777 of the said Code is amended by replacing the words “treatment, specimen taking, removal of tissue or experiment” in the first paragraph by the words “treatment, specimen taking or removal of tissue”.

6. This Act comes into force on (insert here the date of assent to this Act).
APPENDIX E
Regulation respecting the organization and administration of institutions and regional boards
As Act respecting health services and social services and amending various legislation
(1981, c. 42, s. 505, pars. 1, 2, 3, 5 to 21, 23 to 28, s. 506 and s. 511)

CHAPTER I
ADMINISTRATION OF INSTITUTIONS AND REGIONAL BOARDS

DIVISION I
BYLAWS ADOPTED BY AN INSTITUTION

1. A public institution or a private institution under agreement shall adopt by-laws with respect to the following, where they are under its jurisdiction:

(9) the organization of teaching and research;

CHAPTER IX
EXPERIMENTAL MEDICINES

91. An institution referred to in section 117 of the Act may, within the framework of its clinical and basic research activities, provide experimental medicines or existing medicines for which a notice of compliance has not been issued by the Minister of Health and Welfare pursuant to the Food and Drugs Act (R.S.C., 1985, c. F-27), provided that it fulfills the following conditions:

(1) a research procedure is submitted by the researcher in charge and is approved by the board of directors of the institution after consultation with the council of physicians, dentists and pharmacists, where applicable, and by the multidisciplinary ethics committee formed by the board of directors;

(2) an agreement is entered into by the manufacturer, the researcher and the institution which shall ensure, in particular,

(a) that all direct costs are paid by the manufacturer;

(b) that the manufacturer makes an additional contribution representing 20% of the total direct research costs;

(c) that the manufacturer makes a contribution representing the value of the indirect research costs, such as expenses related to administrative services, maintenance, security and running the facilities, which are provided by the institution;

(d) that the manufacturer makes a contribution representing 10% of the total direct research costs where the calculation of the costs referred to in paragraph (c) cannot be established;

(3) the agreement provides that the manufacturer shall bear the cost of the medicine during the entirety of the period fixed by the research procedure and it provides that the manufacturer shall also bear the cost of the medicine even after that period has ended, until the notice of compliance has been issued by the Minister of Health and Welfare pursuant to the Food and Drugs Act, if the person benefits from the medicine and if the medicine cannot be withdrawn from the person and replaced by another medicine or treatment.
An Act respecting health services and social services

19. The record of a user is confidential and no person may have access to it except with the authorization of the user or the person qualified to give authorization on his behalf, on the order of a court, or where this Act provides that an institution may be required to release information contained in the record.

However, a professional may examine a user's record for purposes of study, teaching or research, with the authorization of the director of professional services or, if there is no such director, with the authorization of the executive director granted in accordance with the criteria established in section 125 of the Act respecting Access to documents held by public bodies and the Protection of personal information (R.S.Q., chapter A-2.1).
ACT RESPECTING HEALTH SERVICES AND SOCIAL SERVICES

"19.1. Consent to a request for access to a user's record for study, teaching or research purposes must be in writing; in addition, it must be free and enlightening and given for specific purposes. Otherwise, it is without effect.

The consent is valid only for the time required for the attainment of the purposes for which it was granted or, in the case of a research project approved by an ethics committee, for the period determined, where that is the case, by the ethics committee.

"19.2. Notwithstanding section 19, the director of professional services of an institution or, failing such a director, the executive director may authorize a professional to examine the record of a user for study, teaching or research purposes without the user’s consent.

Before granting such authorization, the director must, however, ascertain that the criteria determined under section 125 of the Act respecting Access to documents held by public bodies and the Protection of personal information (chapter A-2.1) are satisfied. If the director is of the opinion that the professional’s project is not in compliance with generally accepted standards of ethics or scientific integrity, the director may refuse to grant the authorization.

The authorization may be granted for a limited period and may be subject to conditions. It may be revoked at any time if the director has reason to believe that the authorized professional is violating the confidentiality of the information obtained or is not complying with the conditions imposed or with generally accepted standards of ethics and scientific integrity."
Personal information file. **125.** The Commission may, on a written request, grant a person or an agency the authorization to receive communication of nominative information contained in a personal information file, for study, research or statistics purposes, without the consent of the persons concerned, if it is of the opinion

(1) that the intended use is not frivolous and the ends contemplated cannot be achieved unless the information is communicated in nominative form;

(2) that the nominative information will be used in a manner that will ensure its confidentiality.

**Confidentiality.**

The authorization is granted for such period and on such conditions as may be fixed by the Commission. It may be revoked before the expiry of the period granted if the Commission has reason to believe that the authorized person or body does not respect the confidentiality of the information disclosed or the other conditions. 1982, c. 30, s. 125.
Plan d'action ministériel en 

ÉTHIQUE 
DE LA RECHERCHE 
ET EN INTEGRITÉ 
SCIENTIFIQUE 

Juin 1998
La préparation du présent plan d'action a nécessité la collaboration active de plusieurs personnes :

Recherche et rédaction : André Jean, Marie-Christine Lamarche (responsables), Yves Garépy
Coordination et soutien : Sylvie Dillard, Pierre Joubert, Pierre Montambault, Roger Faquet
Traitement de texte : Nicole Charest

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Téléphone : (418) 643-3388
1 800 707-3380 (sans frais)
Télécopieur : (418) 644-4574

Le genre masculin utilisé dans ce document désigne aussi bien les femmes que les hommes.

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MESSAGE DU MINISTRE

La recherche est un facteur de progrès. Au-delà de la quête de connaissances propre à la nature humaine, les découvertes qu’elle a permis ont grandement contribué à l’amélioration de la santé et du bien-être de la population. Cependant, aussi profitables que puissent être ces retombées, elles ne suffisent pas à elles seules à justifier toute forme de recherche.

Depuis plusieurs années, tant au Québec que sur le plan international, cette idée a contribué à mettre en place les fondations d’une éthique de la recherche et à déterminer les conditions d’exercice des activités dans ce domaine. La publication du plan d’action ministériel en éthique de la recherche et en intégrité scientifique représente une étape supplémentaire dans ce processus de réflexion et de normalisation des activités de recherche.

Le Québec se dote donc d’un premier plan d’action en éthique de la recherche et en intégrité scientifique. Sa portée est universelle. Les mesures qui y sont annoncées s’adressent à tous les secteurs de la recherche, qu’elle soit biomédicale ou sociale, qu’elle porte sur des personnes, sur l’embryon humain ou sur du matériel génétique. L’approche privilégiée dans ce plan d’action repose sur la responsabilisation de l’ensemble des acteurs qui sont engagés dans le processus d’acquisition de connaissances que constitue la recherche. Organismes subventionnaires, institutions de recherche, établissements du réseau de la santé et des services sociaux, administrateurs, chercheurs, médecins, intervenants sociaux, corporations professionnelles, chacun à son niveau respectif se voit confier des responsabilités liées à un impératif incontournable, la protection des personnes dans la recherche.

Je tiens à souligner que ce plan d’action est le résultat d’une démarche qui a largement mis à contribution tout les secteurs qui gravitent autour des activités de recherche. Mes premiers remerciements vont aux membres du groupe de travail sur les mécanismes de contrôle en matière de recherche clinique au Québec. Leur rapport a servi de point de départ aux travaux qui ont suivi et demeure une référence en la matière. Je tiens aussi à souligner le travail des groupes et des personnalités qui ont participé à la consultation qui a suivi la parution du rapport du groupe d’experts. Leur contribution a fourni un éclairage considérable qui a grandement aidé à définir notre stratégie d’intervention. Finalement, mes remerciements vont particulièrement aux personnes qui acceptent à tous les jours, dans les établissements du réseau de la santé et des services sociaux du Québec, de prêter leur concours aux activités de recherche. Sans doute, aucune recherche n’est possible. Par leur participation, elles contribuent à l’amélioration des soins de santé et des services sociaux dont bénéficiera la population du Québec.

C’est précisément parce que la recherche ne peut se faire sans la contribution de ces femmes et de ces hommes qu’elle doit être impérative du souci constant de leur protection. Il faut le souligner, les mesures de protection des personnes qui participent aux activités de recherche sont aussi des mesures de protection de la recherche.

Le ministre de la Santé et des Services sociaux,
Jean Rochon
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INTRODUCTION

Depuis plus de trente ans, le ministère de la Santé et des Services sociaux se fait le promoteur, de concert avec la communauté scientifique et les universités, de l'importance de développer les activités de recherche en santé dans les lieux de pratique médicale, principalement le milieu hospitalier universitaire. Depuis une quinzaine d'années, ce mouvement s'étend du côté de la recherche sociale.

Le résultat de ce pari pris en faveur du développement de la recherche se manifeste par un système de recherche solidement implanté dans le réseau de la santé et des services sociaux.

Ce système de recherche, parvenu à maturité, témoigne du dynamisme et de la qualité des travaux des chercheurs. Il doit toutefois relever des défis importants. Le contexte d'exécution de la recherche se modifie rapidement. C'est un contexte marqué, entre autres caractéristiques, par la concurrence accrue pour l'obtention de fonds, par l'importance grandissante du financement privé, par l'exigence constante de performances scientifiques toujours à l'avant-garde et par la demande croissante d'application des résultats obtenus. Ces nouvelles conditions auxquelles la recherche est soumise influent inévitablement sur les façons de l'encadrer.

La communauté scientifique est aux prises avec une redéfinition des rapports entre les intérêts des chercheurs et les finalités de la recherche. Qu'est-ce qui doit prévaloir dans la poursuite des activités de recherche? La curiosité scientifique désintéressée, la course à la découverte primée, la quête de la notoriété ou la motivation de parvenir à résoudre un problème de santé ou un problème social? Autant de questions qui mettent au jour des enjeux aussi cruciaux que l'éthique de la recherche et l'intégrité scientifique. Cette remise en question des valeurs individuelles et des valeurs sociales liées à l'exercice de la recherche s'est cristallisée, en particulier, autour d'événements de la scène internationale et locale qui ont démontré que le rempart des valeurs et des codes pouvait être transgressé.

Reconnaître que les questions d'éthique et d'intégrité sont indissociables de la pratique quotidienne de la recherche est la marque de l'évolution des milieux de recherche qui, parvenues à maturité, voient dans la promotion de ces valeurs une garantie de qualité supplémentaire qui s'attache à leur réputation et à leurs travaux.

Les déclarations internationales qui encadrent les activités de recherche sont le fruit de cette évolution comme le sont aussi les comités d'éthique de la recherche et les comités nationaux d'éthique. Le code de Nuremberg (1947), les déclarations d'Helsinki (1964) et de Tokyo (1975), sont autant de jalons historiques qui marquent l'évolution de l'éthique de la recherche. Plus récemment (1993), l'Organisation mondiale de la santé publiait ses lignes directrices sur l'éthique et la recherche sur les sujets humains.

L’analyse de l’ensemble des lignes directrices publiées dans le monde fait ressortir, sur le plan des principes, des points de convergence qui, s’ils peuvent être exprimés ou actualisés de façons différentes, rejoignent des valeurs communes. La plus évidente est celle du consentement libre et éclairé, nécessaire à la participation d’un individu à des activités de recherche. Elle trouve son fondement dans la notion d’autonomie. En premier lieu viennent des notions comme la validité scientifique et la pertinence. Finalement, il faut qu’il existe un équilibre entre les risques courus par la personne qui prête son concours à une activité de recherche et les avantages qu’elle peut en retirer.

Par la voie du présent plan d’action, le ministère de la Santé et des Services sociaux entend donc faire de la promotion de la qualité des activités de recherche, que confère l’adhésion à des standards élevés en éthique de la recherche et en intégrité scientifique, un objectif des milieux de recherche du réseau de la santé et des services sociaux pour les prochaines années.

Le plan d’action est fondé sur la conception que l’adhésion à des normes rigoureuses en matière d’intégrité et d’éthique en recherche constitue un apport aux activités de recherche. C’est une façon de se démarquer qui indique au reste de la société que les enjeux relatifs au respect de la personne et à la fiabilité des résultats sont au cœur des préoccupations des acteurs de la recherche. Des recherches fiables faites dans le respect des personnes permettront de découvrir de nouveaux modes d’intervention sociale ou de nouveaux traitements qui pourront améliorer l’état de santé et de bien-être des Québécoises et des Québécois.

Le succès de cette démarche repose principalement sur la collaboration des principaux partenaires du Ministère, qui auront à mettre en œuvre de façon concrète les mesures contenues dans le présent plan d’action et à les respecter dans leurs activités quotidiennes. C’est donc une approche fondée sur la concertation et la responsabilisation partagée qui est proposée à l’ensemble des partenaires.

Pour les appuyer dans la mise en œuvre des différents moyens d’action, le ministère de la Santé et des Services sociaux va mettre en place un comité de suivi du plan d’action en éthique de la recherche et en intégrité scientifique. Ce groupe, composé de représentants du Ministère, du Fonds de la recherche en santé du Québec (FRSQ), du Conseil québécois de la recherche sociale (CQRS), du Collège des médecins du Québec et des associations d’établissements, aura pour principal mandat d’assurer le suivi général de l’implantation des mesures et leur évaluation, de veiller à harmoniser leur mise en place dans l’ensemble du réseau et de fournir, au besoin, le soutien nécessaire aux établissements.

Sont exposés dans les pages qui suivent le processus d’élaboration et de mise en œuvre ainsi que le cadre général, à savoir la portée, les principes d’action et les objectifs poursuivis. Sont ensuite expliqués les types de mesures qui constituent l’armature du plan d’action.
Certaines des mesures sont à mettre en place à moyen terme, d'autres requièrent une action immédiate, notamment quand il s'agit des modifications à l'article 21 du Code civil relatif à la recherche avec des personnes mineures ou majeures incaptes. Ces modifications, qui ont fait l'objet du projet de loi 412 déposé à l’Assemblée nationale, rendent le dispositif de protection de ces personnes plus efficace tout en garantissant une protection accrue de ces personnes potentiellement vulnérables. La dernière section du document porte sur ces modifications.
I. LE PROCESSUS D'ÉLABORATION ET DE MISE EN UVRE

Le présent plan d'action résulte d'une vaste démarche de consultation. Premièrement, un comité d'experts, présidé par monsieur Pierre Deschamps et formé de madame Patricia Cuenca et de monsieur Patrick Vimay, adressait au ministre de la Santé et des Services sociaux, en 1995, un rapport intitulé *L'évaluation des mécanismes de contrôle en matière de recherche clinique au Québec.*

Dans un deuxième temps, après une analyse préliminaire du rapport du comité d'experts, une consultation a été menée auprès des partenaires du réseau de la santé et des services sociaux intéressés par la question. Au total, plus de 250 interlocuteurs ont été sollicités. Cette deuxième étape s'est conclue en 1996 par la présentation au ministre de la Santé et des Services sociaux d'un document de travail intitulé *Les mécanismes de contrôle en matière de recherche clinique au Québec : bilan de la consultation et perspectives d'intervention.* Des validations additionnelles ont été obtenues par la suite auprès d'interlocuteurs ciblés. Le présent plan d'action est le résultat de l'ensemble de cette démarche.

Au terme de l'ensemble du processus, fixé à l'an 2000, le réseau de la santé et des services sociaux pourra s'appuyer sur un dispositif complet d'encadrement de la recherche. D'ici là, les acteurs du secteur de la recherche se voient confier une série de responsabilités et de tâches qui doivent être accomplies, certaines dès maintenant, pour assurer l'atteinte des objectifs.
II. LE CADRE GÉNÉRAL

Les orientations du plan d’action sont fondées sur la place primordiale que prennent les activités de recherche dans l’ensemble du réseau de la santé et des services sociaux, en particulier dans les établissements du réseau dont la recherche constitue une des missions fondamentales, soit les centres hospitaliers universitaires (CHU), les centres affiliés universitaires (CAU) et les instituts universitaires. Toutefois, ces activités de recherche doivent s’articuler autour de moyens d’action qui donnent une place centrale à l’éthique de la recherche et à l’intégrité scientifique. Ainsi, les moyens d’action proposés sont principalement basés sur la capacité d’autogestion des milieux de recherche organisés et sur la volonté de ceux-ci de continuer à accorder aux questions d’éthique de la recherche et d’intégrité scientifique toute l’attention requise.

De plus, la stratégie retenué privilégie une approche concertée qui met à contribution tous les partenaires et qui combine les divers types d’intervention, en maximisant ceux qui sont déjà disponibles et opérationnels et en renforçant ceux qui doivent l’être, notamment les interventions ayant trait à la clarification des responsabilités, à la formation, à la sensibilisation et au suivi.

A. LA PORTÉE DU PLAN D’ACTION

L’essentiel des activités de recherche du réseau est concentré dans les établissements à vocation universitaire, les CHU, les CAU et les instituts, dont la recherche est partie instigante de la mission. Cette concentration devrait se consolider au cours des prochaines années à la faveur de la transformation en cours dans le réseau et des stratégies de consolidation mises en œuvre par le FRQS et le CQRS. C’est la présence des universités, et les alliances conclues avec ces dernières, qui confèrent leur statut universitaire aux établissements du réseau. Toutefois, le présent plan d’action ne vise pas la recherche universitaire exécutée dans les campus, mais plutôt les activités se déroulant dans les établissements du réseau de la santé et des services sociaux. Là où des harmonisations sont à faire avec les pratiques en vigueur dans les universités, il reviendra aux autorités des établissements de s’en assurer.

En outre, bien que les activités de recherche soient concentrées dans les grands centres universitaires, on a tenu compte du fait que certaines activités de recherche de moindre intensité, pour lesquelles il importe tout autant de s’assurer de la conformité aux règles d’éthique et d’intégrité en vigueur, peuvent se dérouler dans des centres régionaux.

La portée du plan d’action englobe donc l’ensemble des activités de recherche qui se déroulent dans le réseau de la santé et des services sociaux. Les mesures proposées s’appliquent indistinctement à tous les établissements ou organismes du réseau de la santé et des services sociaux qui sont engagés dans des activités de recherche, peu importe leur intensité. Elles couvrent la recherche en santé et la recherche sociale, que cette recherche soit fondamentale, clinique, épidémiologique, évaluative ou autre. Elles s’appliquent également à des domaines précis de la recherche en santé, soit la recherche sur les embryons humains et la recherche en médecine génétique. Elles s’adressent à tous les intervenants en recherche, qu’ils soient chercheurs, assistants, techniciens, étudiants ou administrateurs. Enfin, des mesures complémentaires touchent de façon particulière la recherche
hors établissement, notamment la recherche en cabinet privé. Il importe de souligner que les dispositions du Code civil en matière de recherche sur les personnes mineures ou majeures inaptes prévues à l'article 219 s'appliquent à ce type de recherche et à celle qui est effectuée dans les laboratoires privés.

B. LES PRINCIPES D'ACTION

Les principes d'action suivants ont été retenus :

- la conciliation entre les impératifs de la protection des personnes avec ceux de la poursuite d'activités de recherche de haute qualité ;
- l'équilibre entre une approche principalement normative et une approche axée sur la formation et la sensibilisation ;
- l'autonomie et la responsabilité des milieux et des individus ;
- le partage des responsabilités gouvernementales ministérielles, institutionnelles et individuelles ;
- l'harmonisation des actions de l'ensemble des partenaires ;
- l'assurance que les moyens mis en place donneront des résultats et que les acteurs auront à en répondre selon leurs responsabilités respectives ;
- la transparence et l'économie de moyens.

C. LES OBJECTIFS POURSUIVIS

L'ensemble des mesures va permettre à tous les acteurs de travailler de concert à l'adoption de comportements éthiques et responsables, selon des normes et des standards reconnus. Les acteurs sont invités à se mobiliser autour de deux objectifs :

- assurer la sécurité et l'intégrité des personnes qui prennent leur concours à des activités de recherche ;
- clarifier les niveaux de responsabilité et mettre en œuvre les moyens permettant l'exercice de ces responsabilités.

Le premier défi de la mise en œuvre des mesures du plan d'action est d'amener les acteurs à adhérer davantage à un ensemble de valeurs et de comportements éthiques de haut niveau dans la réalisation d'activités de recherche, en particulier auprès de sujets humains. Le deuxième défi est de s'assurer que les acteurs nécessaires seront engagés et qu'elles produiront les effets attendus.

2. Voir la section sur les modifications à l'article 21 du Code civil.
III. LES TYPES DE MESURE

Différents types de mesures seront mises en œuvre :

Les mesures d’encadrement sous la responsabilité des établissements du réseau de la santé et des services sociaux

Le principe général mis ici en avant est que les autorités des établissements et des organismes du réseau sont responsables des activités de recherche et de la protection des personnes qui y participent, et doivent en répondre.

Les milieux de la recherche et les établissements à vocation universitaire du réseau sont dotés pour la plupart de mécanismes d’encadrement pour répondre aux impératifs de l’éthique et de l’intégrité scientifique. En ce sens, les mesures d’encadrement du plan d’action auront pour effet de compléter les efforts déjà entrepris ou d’amorcer, dans certains milieux moins structurés, la mise en place de ces mesures.

Les mesures sous la responsabilité des organismes subventionnaires de recherche

Le Fonds de la recherche en santé du Québec (FRSQ) et le Conseil québécois de la recherche sociale (CQRS) constituent le trait d’union entre le Ministère et le milieu de la recherche. Ils assument donc un rôle de chef de file en matière d’éthique de la recherche et d’intégrité scientifique. Leurs actions, notamment sur le chapitre des politiques en matière d’éthique de la recherche et d’intégrité scientifique, sont établies en complémentarité avec les stratégies du Ministère en ce domaine.

Les mesures visant à baliser les activités non encadrées sous la responsabilité des regroupements professionnels

Certaines mesures ont pour but de contribuer à mieux encadrer les activités de recherche en cabinet privé.

Les mesures sous la responsabilité du gouvernement du Québec, du ministère de la Santé et des Services sociaux et des régies régionales

A. LES MESURES D’ENCADREMENT SOUS LA RESPONSABILITÉ DES ÉTABLISSEMENTS

Les mesures d’encadrement sous la responsabilité des établissements du réseau de la santé et des services sociaux reposent sur un principe fondamental : les conseils d’administration des établissements et les organismes du réseau doivent répondre des activités de recherche qui s’y tiennent et de la protection des personnes qui y participent en vertu des pouvoirs et responsabilités qui leur sont conférés par la loi. Les conseils d’administration se voient donc investis d’une responsabilité globale relativement aux activités de recherche qui se déroulent dans leur établissement.


1. L’adoption d’un cadre réglementaire

Le cadre réglementaire, avant d’être un outil de gestion, s’inscrit dans une stratégie globale de planification et d’organisation du contexte d’exécution de la recherche. Il se trouve ainsi à remplir une double fonction. Premièrement, il précise les valeurs et les comportements qu’entend promouvoir l’organisation en rapport avec l’éthique de la recherche et l’intégrité scientifique. Deuxièmement, il contribue à sensibiliser et à responsabiliser tous les intervenants, du conseil d’administration aux chercheurs, à leurs rôles et obligations respectifs.

En ce qui concerne l’éthique de la recherche et l’intégrité scientifique, les normes préconisées doivent être en conformité avec les grands cadres normatifs en vigueur sur le plan international en matière d’éthique de la recherche et d’intégrité scientifique, cadres auxquels adhèrent les trois grands organismes de subvention de référence au Canada, soit le Conseil de la recherche médicale du Canada, le Conseil de la recherche en sciences humaines du Canada et le Conseil de la recherche en science et génie du Canada. Ces trois organismes sont d’ailleurs engagés dans la dernière étape d’un processus de révision et d’harmonisation de leurs normes, dont tiennent aussi compte les organismes subventionnaires québécois pour exercer leurs responsabilités en cette matière. Ce cadre devrait être disponible au mois de juin 1998.

Par l’entremise du comité de suivi du plan d’action, le ministère de la Santé et des Services sociaux, en concertation avec ses partenaires, fournira aux établissements qui pourraient le juger nécessaire certains outils, tels les normes sur les comités d’éthique de la recherche ou des guides d’implantation pour certaines mesures comme le cadre réglementaire, qui sont présentées dans le document. De plus, les membres du groupe de suivi pourront, le cas échéant, conseiller les établissements qui en feraient la demande.
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 gestionnement 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.

2. Un triple examen des projets de recherche

Au même titre que pour la prestation de soins et les autres services de l’établissement, c’est au conseil d’administration qu’il revient de veiller à ce que les activités de recherche se déroulent dans un climat et un milieu assurant leur qualité. Cela signifie que l’établissement doit pouvoir garantir la qualité scientifique des recherches, le respect des personnes et l’utilisation correcte des ressources affectées aux activités de recherche.

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.

MESURES | ÉCHÉANCE
---|---
1) | dec. 1999
2) | En continu
3. La transparence du processus

Les impératifs liés à la protection des personnes et à l'encadrement de la recherche ne peuvent être respectés que dans la mesure où les activités de recherche se déroulent de façon transparente. Les mesures qui suivent permettront d'assurer la visibilité des activités de recherche et d'identifier, dans le respect de la confidentialité, les personnes qui y prêtent leur concours afin de les retracer, le cas échéant. À cette fin, les établissements du réseau de la santé et des services sociaux où se déroulent des activités de recherche doivent appliquer les mesures suivantes :

<table>
<thead>
<tr>
<th>MESURES</th>
<th>ÉCHEANCE</th>
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<tbody>
<tr>
<td>3) Instaurer la déclaration obligatoire, de la part des chercheurs, de toutes les activités de recherche qu'ils accomplissent et les soumettre aux normes scientifiques, financières et éthiques en vigueur.</td>
<td>déc. 1998</td>
</tr>
<tr>
<td>4) Negocier le privilège de l'exercice de la recherche au moment du renouvellement des privilèges d'exercice dans l'établissement.</td>
<td>déc. 1999</td>
</tr>
<tr>
<td>5) Constituer un registre des projets de recherche</td>
<td>En continu</td>
</tr>
<tr>
<td>6) Faire enquête sur les cas de manquement à l'éthique et les cas d'inconduite scientifique.</td>
<td>En continu</td>
</tr>
<tr>
<td>7) Appliquer la politique de la circulaire ministérielle du 31 mars 1995 intitulée « Contribution de l'entreprise privée dans le cadre des activités contractées de recherche » (annexe 2).</td>
<td>En continu</td>
</tr>
<tr>
<td>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.</td>
<td>En continu</td>
</tr>
</tbody>
</table>

4. La protection des personnes

La personne qui accepte de prêter son concours à des activités de recherche doit pouvoir jouir des mêmes droits qu'un usager recevant des soins de santé ou des services sociaux. À cette fin, les établissements du réseau de la santé et des services sociaux où se déroulent des activités de recherche doivent appliquer les mesures suivantes :
5. Les comités d'éthique de la recherche

Les comités d'éthique de la recherche constituent la pierre angulaire du présent plan d'action. Ils ont la responsabilité d'évaluer la conformité des projets de recherche aux règles éthiques, d'en assurer le suivi éthique et de veiller à la protection des personnes. Ils doivent être les promoteurs actifs des principes et des règles d'éthique de la recherche. Par ailleurs, les autorités des établissements doivent doter les comités d'éthique de conditions propices à l'exécution de leur mandat en leur fournissant le soutien matériel et financier nécessaire.

Au Québec, le premier comité d'éthique de la recherche a été mis en place en 1967. En 1990, 56 comités d'éthique exerçaient des fonctions d'éthique de la recherche au sein du réseau de la santé et des services sociaux. Sur ce nombre, une trentaine sont désignés par le ministre de la Santé et des Services sociaux pour l'application de l'article 21 du Code civil du Québec.

Il importe de distinguer les comités d'éthique de la recherche des comités d'éthique clinique dont les fonctions sont l'analyse de cas cliniques soulevant des problèmes éthiques particuliers (acharnement thérapeutique, allocation des ressources...), l'élaboration de lignes directrices, l'information et la formation à l'éthique du personnel hospitalier. Certains établissements du réseau de la santé et des services sociaux se sont dotés de ces deux types de structure.

De plus, pour l'application de l'article 21 du Code civil, il existe un comité d'éthique de la recherche central qui veille à l'examen des projets de recherche avec des personnes mineures ou majeures inaptes se déroulant dans les établissements n'ayant pas de comité d'éthique de la recherche désigné par le ministre de la Santé et des Services sociaux ou se déroulant hors des établissements du réseau de la santé et des services sociaux.

Les mesures qui suivent visent à faire en sorte que les comités d'éthique travaillent dans des conditions optimales d'objectivité et jouissent de l'appui des autorités. Là où des complémentarités existent avec des instances hors établissement, comme les universités, les décisions quant au rattachement et au fonctionnement des comités d'éthique des établissements du réseau pourront se prendre de manière

3. Les données qui suivent sont tirées de l'enquête sur les comités d'éthique au Québec qui s'est déroulée en 1990. Les données dont nous disposons sur les caractéristiques générales des comités d'éthique de la recherche sont encore valides.
concerne avec les universités. Cependant, les arrangements convenus devront refléter la responsabilité ultime des autorités des établissements du réseau à l’endroit des comités d’éthique sous leur patronage.

**MESURES** | **ÉCHÉANCE**  
--- | ---  
12) Les comités d’administration verront à ce que les comités d’éthique de la recherche leur soient rattachés. | déc. 1994  
13) Les conseils d’administration verront à nommer les membres des comités d’éthique. | déc. 1998  
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. | En contin  
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. | déc. 1998  
16) Les comités d’éthique de la recherche doivent faire annuellement rapport au conseil d’administration des responsabilités qui leur ont été confiées. | En contin

6. **Les médicaments d’expérimentation**

Dans le plan d’action, la question du contrôle des médicaments d’expérimentation est indissociable de la protection des personnes prétant leur concours à des activités de recherche. L’utilisation de médicaments de recherche peut comporter des risques qui, en raison même de la nature expérimentale de la substance, ne sont pas entièrement connus. Ces médicaments doivent donc, au minimum, profiter des mesures de contrôle applicables aux autres médicaments d’ordonnance. À cette fin, les établissements du réseau de la santé et des services sociaux où se déroulent des activités de recherche doivent appliquer les mesures suivantes :

**MESURES** | **ÉCHÉANCE**  
--- | ---  
16) 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 1) de la Loi sur les services de santé et les services sociaux. | En contin  
17) 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 cotenus est en cours au Ministère. | En contin

De plus, si ces médicaments sont utilisés ou prescrits dans le cadre d’un projet de recherche avec des personnes mineures ou majeures inaptes, les dispositions de l’article 21 du Code civil...
s’appliquent, quel que soit le lieu où s’effectue cette recherche : établissement, cabinet de médecin ou laboratoire privé.

B. **LES MESURES SOUS LA RESPONSABILITÉ DES ORGANISMES SUBVENTIONNAIRES DE RECHERCHE**

Les rôles et les responsabilités qui sont confiés au Fonds de la recherche en santé du Québec (FRSQ) et au Conseil québécois de la recherche sociale (CQRS) en matière de suivi sont en accord avec les stratégies globales du FRSQ et du CQRS à l’égard de l’éthique de la recherche et de l’intégrité scientifique.

Le FRSQ et le CQRS agissent comme intermédiaires entre le Ministère et la communauté scientifique. Déjà, l’obtention de fonds de ces organismes est conditionnelle à l’approbation des projets proposés par un comité d’éthique de la recherche. Le présent plan d’action conduit à un renforcement de leurs responsabilités pour ce qui est des questions d’éthique de la recherche et d’intégrité scientifique, et plus particulièrement de l’adhésion des chercheurs et des milieux de recherche aux règles de l’éthique et de l’intégrité scientifique. Ils auront à cet égard le devoir de demeurer vigilants et de proposer des moyens éducatifs pour promouvoir l’adhésion aux règles. L’exercice d’élaboration et d’adoption de standards auquel se livrent actuellement ces deux organismes va d’ailleurs dans cette direction.

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<th>MESURES</th>
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<tr>
<td>19) Veiller à l’application et à l’harmonisation des plans d’action en matière d’éthique de la recherche dont se sont dotés les deux organismes subventionnaires relevant du secteur de la santé et des services sociaux, ainsi qu’à leur conformité avec les normes éthiques en vigueur. Prévoir notamment des mécanismes statutaires visant une meilleure adhésion de la communauté scientifique à l’éthique de la recherche et à l’intégrité scientifique.</td>
<td>En continu</td>
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<tr>
<td>20) Examinant les aspects liés au respect de l’éthique de la recherche et de l’intégrité scientifique dans le processus d’évaluation des projets et des équipes des centres et instituts relevant de leur secteur respectif.</td>
<td>En continu</td>
</tr>
<tr>
<td>21) S’assurer que les enquêtes sur des centres d’excellence scientifique et de management à l’éthique dans les établissements utilisant leurs fonds soient menées à leur satisfaction.</td>
<td>En continu</td>
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<tr>
<td>22) Promouvoir activement la formation en éthique de la recherche et en intégrité scientifique dans la communauté scientifique.</td>
<td>En continu</td>
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<tr>
<td>23) Rendre compte dans leur rapport annuel des actions prises pour mettre en place les mesures qui tombent sous leur responsabilité.</td>
<td>En continu</td>
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C. LES MESURES VISANT À BALISER LES ACTIVITÉS NON ENCADRÉES SOUS LA RESPONSABILITÉ DES REGROUPEMENTS PROFESSIONNELS

Les mesures qui suivent ont pour but de contribuer à mieux encadrer les activités de recherche en cabinet ou en laboratoire privés. Ce sont principalement ces activités de recherche qui échappent aux mécanismes d'évaluation et de contrôle courants. Le ministre de la Santé et des Services sociaux saurait donc les ordres professionnels en cause afin qu'ils poursuivraient ou amorcent des démarches en cette matière.

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<th>MESURES</th>
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<tr>
<td>24) Le ministre de la Santé et des Services sociaux va requérir un avis du Conseil médical du Québec portant sur la problématique de la recherche non encadrée hors établissement, notamment la recherche en cabinet privé, et sur les moyens à mettre en place pour assurer la protection des personnes, la qualité de la recherche et la conformité aux règles de l'éthique et de l'intégrité scientifique.</td>
<td>juin 1998</td>
</tr>
<tr>
<td>25) Le Collège des médecins devra poursuivre sa démarche visant à étendre ses pouvoirs d'inspection professionnelle à la pratique de la recherche par ses membres et, en particulier, à mettre en place des mécanismes d'inspection dans le cas de la pratique de la recherche en cabinet privé.</td>
<td>En continu</td>
</tr>
<tr>
<td>26) Les ordres professionnels en cause, notamment les ordres regroupant les pharmaciens, les infirmières, les dentistes, les psychologues et les travailleurs sociaux, dont les membres sont susceptibles d'exercer des activités de recherche, doivent étendre leurs pouvoirs d'inspection professionnelle à la pratique de la recherche par leurs membres.</td>
<td>déc. 1999</td>
</tr>
<tr>
<td>27) L'Ordre des pharmaciens et le Collège des médecins doivent ajouter un addendum portant sur les médicaments d'expérimentation à leur publication commune intitulée <em>Ordonnances de médicaments Modalités d'émission et d'extinction pour la confidentialité hors établissement.</em></td>
<td>déc. 1999</td>
</tr>
<tr>
<td>28) Rendre compte de leurs activités en matière d'éthique de la recherche et d'intégrité scientifique dans leur rapport annuel.</td>
<td>En continu</td>
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</table>
D. LES MESURES SOUS LA RESPONSABILITÉ DU GOUVERNEMENT DU QUÉBEC, DU MINISTÈRE DE LA SANTÉ ET DES SERVICES SOCIAUX ET DES RÉGIES RÉGIONALES

Les mesures sous la responsabilité du gouvernement, du ministère de la Santé et des Services sociaux et des régies régionales couvrent les aspects suivants :

- premièrement, le suivi et l’évaluation du plan d’action ainsi que l’implantation par l’entremise des régies régionales, d’un mécanisme permettant d’apporter les ajustements ou, le cas échéant, les correctifs nécessaires au sein des établissements;

- deuxièmement, les modifications à l’article 21 du Code civil du Québec;

Le ministère de la Santé et des Services sociaux est particulièrement concerné par deux aspects de ce dernier point. Il s’agit de la désignation des comités d’éthique de la recherche par le ministre selon des conditions qu’il détermine, et de la définition du concept de soins innovateurs.

1. Le suivi et l’évaluation du plan d’action

a) Les responsabilités du ministère de la Santé et des Services sociaux

La Loi sur les services de santé et les services sociaux du Québec confie au Ministère un mandat explicite quant à la coordination de la recherche dans le réseau socio-sanitaire. Ce mandat confère au Ministère le rôle d’instance centrale. Dans le présent plan d’action, le rôle du Ministère se précise par des responsabilités relatives au suivi général et à l’évaluation de l’ensemble du système dans le secteur de la recherche. La responsabilité de la mise en application quotidienne des principes et des orientations revient aux autorités des établissements et des organismes en cause, qui doivent en rendre compte dans leur rapport annuel.

Pour assurer le suivi et l’évaluation des mesures mises en avant dans le plan d’action, le ministère de la Santé et des Services sociaux assumera les responsabilités qui suivent :
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<td>29) Créer un comité ministériel de suivi composé de représentants du Ministère, du FRSQ, du CQRS, du Collège des médecins et des associations des établissements. Le mandat de ce comité sera d’assurer le suivi général de l’implantation des mesures du plan d’action et leur évaluation, de veiller à harmoniser leur mise en place et de fournir, au besoin, le soutien nécessaire aux établissements.</td>
<td>juin 1998</td>
</tr>
<tr>
<td>30) Procéder à la mise à jour périodique de l’enquête sur les comités d’éthique auprès des établissements.</td>
<td>juin 1998</td>
</tr>
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<td>31) Par ailleurs, afin de combler une lacune importante et pour souligner son engagement en ce qui a trait à l’éthique de la recherche et à l’intégrité scientifique, le Ministère va se doter d’un code d’éthique à l’intention des gestionnaires et des utilisateurs de ses programmes de recherche.</td>
<td>sept. 1999</td>
</tr>
<tr>
<td>32) Faire état dans son rapport annuel du suivi des mesures du plan d’action.</td>
<td>En continuer</td>
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b) La participation des régies régionales

Bien que la recherche demeure une responsabilité centrale dont l’encadrement global est sous la responsabilité du Ministère, il n’en reste pas moins que les régies régionales ont un rôle important à jouer, ne serait-ce que parce que ces activités se déroulent au sein d’établissements qui relèvent de leur juridiction.

Les régies régionales seront informées par le ministère de la Santé et des Services sociaux de la mise en place du plan d’action. Périodiquement, elles recevront des évaluations relatives au suivi de l’implantation des mesures.

La collaboration des régies régionales sera sollicitée pour aider à la mise en place des ajustements ou des correctifs jugés nécessaires après évaluation.

c) Les modifications à l’article 21 du Code civil

L’article 21 du Code civil vise la protection de personnes mineures ou majeures inaptes qui pourraient être sollicitées pour participer à des recherches. Sa portée est large puisque toute recherche demandant la contribution de ces personnes est visée, qu’elle se déroule dans un établissement du réseau de la santé et des services sociaux, dans le cabinet d’un médecin ou dans le laboratoire d’une compagnie pharmaceutique. Cet article confie au ministre de la Santé et des Services sociaux la responsabilité d’approver, sur recommandation des comités d’éthique désignés à cette fin, les projets de recherche visant ces personnes. Il précise également des modalités de consentement substitué très précises.
Depuis sa mise en vigueur en janvier 1994, de nombreux intervenants, dont les membres du comité d'experts sur les mécanismes de contrôle en matière de recherche clinique au Québec, ont souligné les difficultés d'application. La principale critique adressée à son endroit se résume au fait que l'affirmation de principe de la protection des personnes vulnérables, affirmation qui fait l'unanimité par ailleurs, ne se traduit pas par des mécanismes d'application aussi efficaces que le texte le laisse entendre. De plus, les modalités de consentement prévues, en particulier pour les adultes inaptes, empêchent à l'heure actuelle le déroulement de toute une catégorie de recherches, notamment en urgence Đây.

C'est dans ce contexte que le ministre de la Justice, en concertation avec le ministre de la Santé et des Services sociaux, a déposé en décembre 1997 à l'Assemblée nationale l'avant-projet de loi modifiant le Code civil en matière de recherche médicale. Ces modifications visent notamment les modalités de consentement substitué et le processus d'approbation. En février 1998, la Commission parlementaire des institutions a procédé à l'examen de cet avant-projet de loi. Par la suite, le projet de loi 432 a été déposé à l'Assemblée nationale.

Actuellement, l'article 21 du Code civil se lit comme suit :

Un mineur ou un majeur inapte ne peut être soumis à une expérimentation qu'en l'absence de risque sérieux pour sa santé et d'opposition de sa part si il comprend la nature et les conséquences de l'acte; le consentement du titulaire de l'autorité parentale ou du manutentionnaire, tuteur ou curateur est nécessaire.

L'expérimentation qui ne vise qu'une personne ne peut avoir lieu que si l'on veut s'attendre à un bénéfice pour la santé de la personne qui y est soumise et l'autorisation du tribunal est nécessaire.

Lorsqu'elle vise un groupe de personnes mineures ou majeures inaptes, l'expérimentation doit être effectuée dans le cadre d'un projet de recherche approuvé par le ministre de la Santé et des Services sociaux, sur avis d'un comité d'éthique du centre hospitalier Assigné par le ministre ou d'un comité d'éthique créé par lui à cette fin; il faut de plus qu'on puisse s'attendre à un bénéfice pour la santé des personnes présentant les mêmes caractéristiques d'âge, de maladie ou de handicap que les personnes soumises à l'expérimentation.

Ne constituent pas une expérimentation les soins que le comité d'éthique du centre hospitalier concerné considère comme innovateurs qui sont requis par l'état de santé de la personne qui y soumet.

Dans le projet de loi, l'article 21 est modifié par le texte suivant :

21. Un mineur ou un majeur inapte ne peut être soumis à une expérimentation qui comporte un risque sérieux pour sa santé ou à laquelle il s'oppose alors qu'il en comprend la nature et les conséquences.

Il ne peut, en outre, être soumis à une expérimentation qu'à la condition que celle-ci laisse espérer, si elle ne vise que lui, un bienfait pour sa santé ou, si elle vise un
groupe; des résultats qui seraient bénéfiques aux personnes possédant les mêmes caractéristiques d'âge, de maladie ou de handicap que les membres du groupe. Une telle expérimentation doit s'incrire dans un projet de recherche approuvé et suivi par un comité d'éthique. Les comités d'éthique complets sont institués par le ministre de la Santé et des Services sociaux ou désignés par lui parmi les comités d'éthique de la recherche existants; le ministre en définit la composition et les conditions de fonctionnement.

Le consentement à l'expérimentation est donné, pour le mineur, par le titulaire de l'autorité parentale ou le tuteur, et, pour le majeur insaup, par le mandataire, le tuteur ou le curateur. Lorsqu'il s'agit de soumettre un majeur devenu subitement insaup à une expérimentation qui, dans la mesure où elle doit être effectuée rapidement après l'apparition de l'état qui la justifie, ne permet pas de lui attribuer un représentant en temps utile, le consentement est donné par la personne habilitée à conséderer, en l'absence de représentant légal, aux soins reçus par le majeur; il appartiendra au comité d'éthique compétent de déterminer, lors de l'examen d'un projet de recherche, si l'expérimentation remplit une telle condition.

Ne constituent pas des expérimentations les interventions qui, selon le comité d'éthique, sont des soins innovateurs reçus par l'état de santé qui y est soumise.

Les responsabilités des comités d'éthique de la recherche désignés par le ministre sont donc accrues puisque ceux-ci seront chargés de l'approbation finale des projets de recherche.

En contrepartie, le ministre de la Santé et des Services sociaux devra fournir des garanties sur le fonctionnement des comités d'éthique. Il les fournira, d'une part, par la désignation ministérielle de ces comités et, d'autre part, par l'édiction de normes régissant leur fonctionnement.

Il aura de plus la responsabilité de s'assurer que les établissements mettent à la disposition des comités d'éthique de la recherche les moyens techniques et le soutien financier nécessaires notamment au fonctionnement et à la formation, afin que le travail des comités d'éthique désignés se fasse de façon claire et responsable.

2. Les conditions d'exercice des comités d'éthique de la recherche désignés par le ministre de la Santé et des Services sociaux

Les normes qui ont été énoncées dans la présente section s'inscrivent dans le cadre général du plan d'action présenté dans les sections qui précèdent. Les mesures décrites précédemment s'appliquent donc aussi aux établissements où siègent des comités d'éthique désignés en vertu de l'article 21 du Code civil du Québec. C'est le cas, notamment, de la déclaration obligatoire des activités de recherche, de la mise en place d'un registre des projets de recherche en cours dans l'établissement ou de l'élaboration d'un cadre réglementaire régissant les activités de recherche.

4. Les règles qui suivent s'inspirent du travail des trois conseils canadiens de recherche qui procèdent actuellement à la mise à jour de leurs normes en ce qui a trait aux comités d'éthique. Ce document de référence en cours de validation devrait recevoir la sanction finale des conseils au mois de juin.
Les normes qui suivent visent à apporter une sanction ministérielle à ce qui, dans la plupart des cas, a déjà été mis en place dans les établissements du réseau de la santé et des services sociaux du Québec, en accord avec les déclarations et cadres réglementaires en vigueur sur le plan international.

Ces normes s’appliquent de façon obligatoire aux comités désignés par le ministre. Dans la mesure où elles représentent des limites incontournables quant il s’agit de la protection des personnes, elles devraient avoir un effet d’entraînement sur tous les autres comités d’éthique de la recherche au Québec.

Au moment de l’adoption du projet de loi 432 modifiant le Code civil, une période de transition de six mois est prévue pour permettre aux établissements de faire les ajustements nécessaires à leur comité d’éthique de la recherche. Au terme de ce délai, les établissements déposeront devant le ministre de la Santé et des Services sociaux une demande de désignation. Plusieurs des comités d’éthique existant actuellement leurs activités verront leur désignation reconfirmée à cette occasion. D’autres comités d’éthique de la recherche pourraient aussi être désignés, selon le besoin et selon la conformité de la candidature soumise.

a) Les normes de fonctionnement

1° Le mandat du comité d’éthique

Les comités d’éthique de la recherche désignés par le ministre de la Santé et des Services sociaux, aux fins de l’application de l’article 21 du Code civil du Québec, ont pour mandat d’approver les projets de recherche effectués auprès de personnes mineures ou majeures inaptes et d’assortir cette approbation, le cas échéant, de conditions à observer.

2° La composition du comité d’éthique

Les comités d’éthique de la recherche désignés par le ministre de la Santé et des Services sociaux aux fins de l’application de l’article 21 du Code civil du Québec doivent comprendre au moins cinq membres possédant les compétences suivantes :

- deux membres ayant une vaste connaissance des méthodes ou des domaines de recherche couverts par le comité ;
- une personne spécialisée en éthique ;
- une personne spécialisée en droit 5 ;
- au moins une personne non affiliée à l’établissement, mais provenant des groupes utilisant les services de l’établissement 6.

5. Cette personne ne peut être le conseiller juridique de l’établissement.
6. Cette personne pourrait être le Curateur public ou son représentant.
Il est évident que cette composition représente un minimum et que, dans la majorité des cas, la composition du comité d'éthique de la recherche sera plus étendue. Mais, dans tous les cas, il faut respecter la nature des représentations exigées par le ministre.

Les comités d'éthique peuvent avoir recours à des experts externes quand ils estiment ne pas disposer des compétences nécessaires à l'examen d'un projet particulier.

3° La durée du mandat des membres
La durée du mandat des membres est laissée à la discrétion de l'administration locale. Un processus de renouvellement graduel, permettant une continuité dans le fonctionnement, doit être mis en place.

4° Le rattachement administratif
Les comités d'éthique de la recherche désignés par le ministre de la Santé et des Services sociaux aux fins de l'application de l'article 21 du Code civil du Québec doivent être rattachés au conseil d'administration de l'établissement.

5° La nomination des membres
La nomination des membres des comités d'éthique de la recherche désignés par le ministre de la Santé et des Services sociaux aux fins de l'application de l'article 21 du Code civil du Québec doit être faite par le conseil d'administration de l'établissement.

6° Le mode de désignation
La demande de désignation se fait par une lettre du président du conseil d'administration de l'établissement au ministre de la Santé et des Services sociaux. Cette lettre doit être accompagnée d'un dossier qui permettra de statuer sur la demande. À la suite de l'examen du dossier, le ministre de la Santé et des Services sociaux communiquera sa décision par lettre au président du conseil d'administration de l'établissement.

7° Les responsabilités des conseils d'administration à l'endroit des comités d'éthique
Outre la nomination et la révocation des membres, les conseils d'administration ont la responsabilité de fournir aux comités d'éthique de la recherche désignés par le ministre de la Santé et des Services sociaux, aux fins de l'application de l'article 21 du Code civil du Québec, les moyens nécessaires à l'accomplissement de leur mandat en ce qui a trait au soutien administratif et, financier et à la formation.

8° L'examen éthique
Au cours de l'examen éthique des projets de recherche, les comités d'éthique doivent au minimum :
s’assurer en premier lieu de la validité scientifique et de la pertinence de l’étude ainsi que de la compétence des chercheurs;

déterminer s’il y a équilibre entre les risques et les avantages pour la personne et chercher, lorsque le cas s’y prête, les retombées éventuelles d’un tel projet sur la santé des personnes présentant les mêmes caractéristiques - âge, maladie ou handicap - que les personnes soumises à l’expérience;

examiner le mode de sélection des personnes et évaluer les modalités de consentement à la recherche;

porter une attention particulière à la confidentialité.

Les membres du comité d’éthique peuvent, lorsqu’ils le jugent nécessaire, convoquer les responsables du projet de recherche.

9°  Le suivi

Au moment de l’examen de chacun des projets de recherche, le comité d’éthique de la recherche devra convenir avec le chercheur d’un mécanisme de suivi qui pourra varier selon le type de projet. Il pourra s’agir, par exemple, d’un rapport périodique des chercheurs ou de la vérification des formulaires de consentement ou de tout autre moyen que le comité jugera pertinent.

10° Les conflits d’intérêt

Tout membre d’un comité d’éthique de la recherche désigné par le ministre de la Santé et des Services sociaux pour les fins de l’application de l’article 21 du Code civil du Québec qui est associé à un projet de recherche examiné par ce comité doit en avertir ses collègues et se retirer pour la durée de l’examen et des délibérations. Il peut cependant être entendu à titre de chercheur. De plus, le comité d’éthique de la recherche et les membres qui le composent ne doivent avoir aucun lien de dépendance avec les bailleurs de fonds des projets de recherche qu’ils examinent, particulièrement quand le financement d’un projet de recherche provient du secteur privé.

11°  Le mécanisme d’approbation pour les institutions ne disposant pas de comité d’éthique de la recherche désigné

Pour l’ensemble des chercheurs dont l’institution ne dispose pas d’un comité d’éthique de la recherche désigné par le ministre de la Santé et des Services sociaux pour les fins de l’application de l’article 21 du Code civil du Québec, le ministre maintient le comité d’éthique de la recherche central déjà en place auprès du FRSQ et lui fixe certaines conditions d’exercice :

- Les membres de ce comité sont nommés par le ministre de la Santé et des Services sociaux.
• Les normes qui s’appliquent aux comités locaux s’appliquent au comité central d’éthique de la recherche.

• Le FRSQ assure au comité le soutien nécessaire à un fonctionnement satisfaisant de son infrastructure.

b) L’obligation de rendre des comptes

Votre s’assurer de la mise en place des mesures, pour en mesurer le suivi, en évaluer l’impact et recommander l’application des correctifs nécessaires, des mécanismes de reddition de compte annuel ainsi qu’une procédure de révocation sont mis en œuvre.

12° La reddition du compte

Les conseils d’administration des établissements et des organismes du réseau de la santé et des services sociaux verront à mettre en vigueur l’obligation pour les comités d’éthique de la recherche désignés par le ministre de la Santé et des Services sociaux aux fins de l’application de l’article 21 du Code civil du Québec de faire un rapport annuel au ministre de la Santé et des Services sociaux.

Ce rapport doit comprendre au moins les éléments suivants :

• la liste des membres et leurs compétences;

• le nombre de réunions que le comité a tenues durant l’année;

• la liste des projets qui lui ont été soumis avec, pour chaque projet, le nom du chercheur, l’origine du financement, un résumé du projet et la décision du comité;

• les activités de suivi que le comité a exercées;

• tout autre élément que le comité juge pertinent de faire connaître au ministre.

Tout changement à la composition du comité doit faire l’objet d’un avis au ministre de la Santé et des Services sociaux.

13° Les visites de contrôle

Le ministre peut désigner une personne ou un groupe de personnes pour effectuer en tout temps des visites de contrôle auprès des comités d’éthique de la recherche désignés pour les fins de l’application de l’article 21. Les personnes désignées par le ministre sont soumises au devoir de réserve et de confidentialité.

14° La révocation
Le ministre peut révoquer un comité d'éthique de la recherche qu'il avait désigné si ce comité ne se conforme pas aux normes de fonctionnement qu'il détermine. Cette révocation ne peut toutefois survenir qu'après une rencontre entre les responsables ministériels de l'application de ces règles et le comité d'éthique visé, sauf si le comité d'éthique refuse cette rencontre.

Cette révocation doit faire l'objet d'un avis motivé.

3. Une disposition particulière : les soins innovateurs

Le troisième paragraphe de l'article 21 du Code civil du Québec se lit comme suit : « Ni constituent pas une expérimentation les soins que le comité d'éthique considère comme des soins innovateurs qui sont requis par l'état de santé de la personne qui s'y soumet. » Cette disposition implique qu'en pareil cas, c'est l'article 15 du Code civil, relatif au consentement aux soins pour les personnes mineures ou majeure inaptes, qui s'applique. Ce qui signifie que le mandataire, le tuteur ou le curateur peuvent consentir aux soins pour ces personnes. Si la personne majeure n'est pas ainsi représentée, le consentement est donné par son conjoint ou, à défaut de conjoint, par un proche-parent ou par une personne qui démontre un intérêt particulier pour la personne.

Pendant la période de consultation de la Commission parlementaire chargée d'examiner l'avant-projet de loi modifiant le Code civil en matière de recherche biomédicale, plusieurs organismes ont mentionné la difficulté qu'ils avaient d'arriver à une définition entièrement satisfaisante du concept de soins innovateurs. Ce concept est important puisque définir une activité comme s'il s'agissait de soins innovateurs plutôt que d'une activité de recherche soustrait par la suite celle-ci au mécanisme d'examen éthique, alors que c'est le comité d'éthique de la recherche qui détermine ce statut.

La définition proposée par le Conseil d'évaluation des technologies de la santé en 1991, à l'occasion d'un rapport sur les transplantations d'organes au Québec, a toutefois permis d'atténuer, dans des domaines similaires, un consensus important tout en conservant la flexibilité nécessaire pour s'adapter au développement de la recherche.

Montrant le caractère comparatif de ce concept par rapport à d'autres, le Conseil faisait le parallèle entre les trois notions suivantes :

Acceptée : Une procédure dont l'efficacité clinique, les indications et les protocoles sont bien établis, sera désignée comme acceptée.

Expérimentale : Par contre, une procédure dont l'efficacité clinique n'a pas encore été reconnue, est désignée comme expérimentale. Nous ne savons pas si elle produit les bénéfices escomptés. Donc, on ne s'attend pas à ce qu'une telle procédure soit acceptée par les services de santé, sauf dans un protocole de recherche.

**Innovatrice**: Il reste des procédures qui ont dépassé l'étape expérimentale. Leur efficacité a été établie mais va le manque d'expérience, les modalités d'application et même les indications exactes pour ces interventions sont à préciser. On appelle une telle technologie innovatrice. Afin d'augmenter le niveau de connaissance, il est important de recueillir toute expérience future des applications de cette technologie de façon systématique et de communiquer ces expériences au monde médical. Pour cette raison ces activités ne doivent se poursuivre que dans une institution universitaire autorisée où les ressources requises sont disponibles.

Afin de guider les comités d'éthique de la recherche et de les doter de balises communes s'agissant de la notion de soins innovateurs, le ministère de la Santé et des Services sociaux du Québec confie au FRQS, au CQRS, au Collège des médecins du Québec ainsi qu'au CETS le mandat de préciser d'avantage le concept de soins innovateurs dans le cadre de l'application de l'article 21 du Code civil.
CONCLUSION

La publication du plan d'action ministériel en éthique de la recherche et en intégrité scientifique représente une première au Québec. Cependant, elle est loin de clore la démarche entreprise en cette matière. L'implantation des mesures et leur évaluation visent aussi à faire en sorte que, de façon continue, l'ensemble des acteurs qui sont impliqués dans l'univers de la recherche soient investis d'une responsabilité claire à l'égard de la protection des personnes, sans laquelle il ne peut y avoir de recherche éthiquement acceptable.

Au-delà de ce constat, le ministère de la Santé et des Services sociaux entreprend, par la diffusion de ce plan d'action et la mise en place du comité de suivi, l'implantation des mesures annoncées. Toutefois, sur certains points, la réflexion doit se poursuivre. C'est particulièrement le cas pour ce qui est de la place de plus en plus grande qu'occupe le financement privé dans la recherche. Sur ce point, le plan d'action apporte certains éléments de réponse par l'entremise de la déclaration obligatoire des activités de recherche et du rôle des corporations professionnelles. Il est cependant nécessaire de pousser un cran plus loin la réflexion du Ministère et de ses partenaires.

Par ailleurs, il importera aussi de bien mesurer l'adéquation des mesures proposées avec la recherche sociale. Sur ce plan, il faudra vérifier si l'implantation d'un modèle largement inspiré de la recherche biomédicale constitue une transposition heureuse.
ANNEXE 1

Articles 116 et 117 de la Loi sur les services de santé et des services sociaux du Québec
Article 116

Un établissement ne peut fournir que des médicaments qui apparaissent sur la liste dressée à cette fin par le ministre. Cette liste ne comprend que des médicaments qui ont reçu un avis de conformité du gouvernement fédéral pour des indications approuvées. Elle est mise à jour périodiquement après consultation du Conseil consultatif de pharmacologie institué par l’article 39 de la Loi sur l’assurance-maladie. La Régie de l’assurance-maladie du Québec doit publier cette liste et chacune de ses mises à jour. Elles entrent en vigueur à la date de publication à la Gazette officielle du Québec, ou à toute date ultérieure qui y est fixée, d’un avis du Ministère indiquant que la liste est dressée ou qu’elle est mise à jour ou que cette liste ou cette mise à jour a été publiée par la régie.

Un établissement où est institué un conseil des médecins, dentistes et pharmaciens peut en outre fournir, pour des motifs de nécessité médicale particulière, d’autres médicaments que ceux apparaissant sur la liste visée au premier alinéa et qui ont reçu l’avis de conformité du gouvernement fédéral. Dans ce cas, le médecin ou le dentiste qui désire utiliser ou prescrire ces médicaments doit demander l’opinion du conseil des médecins, dentistes et pharmaciens. Lorsque cette opinion est favorable, elle doit être transmise au Conseil consultatif de pharmacologie.

Un établissement où est institué un conseil des médecins, dentistes et pharmaciens peut également fournir pour un traitement d’exception d’autres médicaments que ceux apparaissant sur la liste visée au premier alinéa et qui n’ont pas obtenu l’avis de conformité du gouvernement fédéral ou des médicaments apparaissant ou non à cette liste lorsqu’ils sont utilisés pour des indications reconnues mais non approuvées. Dans ces cas, le médecin ou le dentiste qui désire utiliser ou prescrire ces médicaments doit obtenir l’autorisation écrite du conseil des médecins, dentistes et pharmaciens.

En cas d’urgence, un médecin ou un dentiste peut utiliser ou prescrire un médicament visé au deuxième ou au troisième alinéa avant d’avoir obtenu l’avis ou l’autorisation écrite du conseil des médecins, dentistes et pharmaciens. Il doit cependant, le plus tôt possible obtenir l’opinion ou l’autorisation requise et motiver à la fois l’urgence d’utiliser ou de prescrire le médicament et sa décision de l’utiliser ou de le prescrire.

Article 117

Un établissement qui exploite un centre hospitalier désigné centre hospitalier universitaire ou institut universitaire ou qui gère un centre de recherche ou un institut de recherche reconnu par le Fonds de la recherche en santé du Québec ou qui exploite un centre désigné comme centre affilié universitaire et qui, selon son contrat d’affiliation, participe à des activités de recherche clinique et fondamentale peut fournir des médicaments dans les conditions et circonstances prévues par règlement.
ANNEXE 2

Circulaire sur la contribution de l’entreprise privée dans le cadre d’activités contractuelles de recherche
CETTE CIRCULAIRE REMPLACE CELLE DU 1ER OCTOBRE 1993 (1993-084) 
MÊME CORIFICATION

OBJET
Cette circulaire présente une révision de la politique ministérielle mise en vigueur le 1er avril 1992 concernant les contrats de recherche avec l'entreprise privée. Elle entre en vigueur le 1er avril 1995.
Cette politique s'applique maintenant non seulement aux centres hospitaliers et aux centres et instituts de recherche formant une corporation distincte mais aussi à tout établissement de santé et de services sociaux.
Cette politique vise tous les contrats de recherche scientifique et de recherche clinique avec l'entreprise privée exécutés en tout ou en partie dans un établissement, un centre ou un institut de recherche autonome et effectués par un ou des chercheurs ou un ou des cliniciens.
Les subventions de recherche et les montages financiers ne sont pas visés par cette circulaire.

MODALITÉS

A) Coûts de recherche
Tous les coûts découlant d'un contrat de recherche doivent être prévus au contrat et estimés sur la base des coûts anticipés des biens et services requis. Le contrat peut cependant contenir une clause d'ajustement des prix, s'il y a lieu. Une énumération des différents coûts directs découlant d'un contrat de recherche est effectuée au chapitre 1 du Manuel de gestion financière.
B) **Contribution additionnelle**

Une contribution additionnelle de 20%, calculée sur l'ensemble des frais de recherche identifiés au contrat, doit être ajoutée au coût total du contrat.

Les sommes recueillies sont partagées en deux:

- 18% servent à couvrir les frais de fonctionnement et d'infrastructure du centre de recherche ou d'autres activités de recherche non contractuelles, en fonction des priorités établies par le directeur scientifique ou le responsable de la recherche.
- 2% servent à couvrir les frais d'administration générale.

C) **Approbation**

Tous les contrats de recherche doivent être approuvés par une instance appropriée au sein de l'établissement, du centre ou de l'institut de recherche.

Ces contrats doivent être signés conjointement par le directeur général de l'établissement, ou son représentant, et par le directeur scientifique, ou le responsable de la recherche de l'établissement, de l'institut ou du centre de recherche concerné et toutes autres personnes désignées par les parties.

D) **Comptabilisation et reddition de comptes**

Toutes les règles relatives à la comptabilisation des activités de recherche, à l'identification des frais de recherche et les règles relatives à la reddition des comptes, se retrouvent au Manuel du gestion financière (Vol. 1, Chap. 01 et 04).

SUIVI

Le Service cité en référence est disponible pour tout renseignement additionnel.

Le sous-ministre,

André TRUDEAU
1.4.7 Recherche

1.4.7.1 Frais de recherche

a) Frais directs

Pour les fins du calcul de la contribution additionnelle prévue à la circulaire 05.01.41.13 les frais suivants, sans être nécessairement exhaustifs, sont considérés comme frais directs de recherche:

- tous les honoraires et les salaires (incluant les chercheurs-boursiers), avantages sociaux et autres charges sociales pour réaliser et pour administrer le projet de recherche, à l'exception des bourses accordées à des étudiants et des honoraires professionnels payés directement aux chercheurs principaux et versés par une entreprise contractante;

- les frais de déplacement et de séjour des chercheurs et de l'équipe de recherche;

- les fournitures générales, de bureau, de laboratoires ou d'animalerie;

- les médicaments, sauf ceux fournis gratuitement par une compagnie pharmaceutique pour la réalisation du projet;

- les frais d'acquisition d'équipements, sauf dans le cas des équipements fournis gracieusement par l'entreprise contractante;

- les frais de location, d'entretien, de réparation et d'utilisation des équipements;

- les frais d'examens de laboratoires, de radiologie ou d'autres;

- les frais relatifs à l'informatique, l'audiovisuel, la documentation, les communications et la publicité;

- les frais d'hospitalisation (par dîner), les frais de chirurgie et de médecine d'un jour et les frais ambulatoires engendrés par le projet de recherches.
- la compensation accordée aux patients pour participer au projet de recherche ainsi que les frais de déplacement et de séjour des patients à l'extérieur de l'hôpital;
- autres frais directs.

L'imputation des frais directs de recherche aux sous-centres d'activités 0106 "Entreprises privées" peut s'effectuer sur la base de l'avancement des travaux ou à partir des coûts réels encourus.

b) Contribution additionnelle

La contribution additionnelle prévue à la circulaire mentionnée au point a) est comptabilisée à l'intérieur des revenus du sous-centre d'activités 0106 "Recherche (non réparti) à titre de revenus d'autres sources", à l'exclusion du 26 prévu pour l'administration générale qui est comptabilisée à l'intérieur des revenus du sous-centre d'activités 0106 "Entreprises privées".

c) Frais directs de recherche et d'administration générale encourus à l'intérieur de différents centres d'activités principales.

Ces frais doivent être imputés aux sous-centres d'activités de recherche concernés à titre d'achats de services ou autres charges directes et comptabilisés aux centres d'activités principales concernés à titre de vente de services ou recouvrement (voir 1.1.3 du chapitre 3).

d) Revenus reportés

Le résultat annuel des opérations de recherche peut se solder par un surplus, compté principalement de la politique sur la contribution additionnelle de l'entreprise privée dans le cadre d'activités contractuelles de recherche.

Dans un tel cas, les établissements effectuant de la recherche sur une base régulière sont autorisés à éliminer ce surplus en ayant recours aux principes des revenus reportés. Ces revenus reportés peuvent servir uniquement pour des fins de recherche incluant l'acquisition d'équipement de recherche.

Mise en vigueur le: 95-04-01
Révisé le: 01 01 14
APPENDIX G
THE NUREMBERG CODE

1. The voluntary consent of the human subject is absolutely essential.

This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved to enable him to make an understanding and enlightened decision. This latter element requires that before the acceptance of any affirmative decision by the experimental subject there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonably to be expected; and the effects upon his health or person which may possibly come from his participation in the experiment.

The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs or engages in the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity.

2. The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature.

3. The experiment should be so designed and based on the results of animal experimentation and a knowledge of the natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment.

4. The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.

5. No experiment should be conducted where there is an a priori reason to believe that death or disabling injury will occur; except, perhaps, in those experiments where the experimental physicians also serve as subjects.

6. The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.

7. Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death.

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8. The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment.

9. During the course of the experiment the human subject should be at liberty to bring the experiment to an end if he has reached the physical or mental state where continuation of the experiment seemed to him to be impossible.

10. During the course of the experiment the scientist in charge must be prepared to terminate the experiment at any stage, if he has probably [sic] cause to believe, in the exercise of the good faith, superior skill and careful judgment required of him that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.
APPENDIX H
WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI

Ethical Principles for Medical Research Involving Human Subjects

A. INTRODUCTION

1. The World Medical Association has developed the Declaration of Helsinki as a statement of ethical principles to provide guidance to physicians and other participants in medical research involving human subjects. Medical research involving human subjects includes research on identifiable human material or identifiable data.

2. It is the duty of the physician to promote and safeguard the health of the people. The physician's knowledge and conscience are dedicated to the fulfillment of this duty.

3. The Declaration of Geneva of the World Medical Association binds the physician with the words, "The health of my patient will be my first consideration," and the International Code of Medical Ethics declares that, "A physician shall act only in the patient's interest when providing medical care which might have the effect of weakening the physical and mental condition of the patient."

4. Medical progress is based on research which ultimately must rest in part on experimentation involving human subjects.

5. In medical research on human subjects, considerations related to the well-being of the human subject should take precedence over the interests of science and society.

6. The primary purpose of medical research involving human subjects is to improve prophylactic, diagnostic and therapeutic procedures and the understanding of the etiology and pathogenesis of disease. Even the best proven prophylactic, diagnostic, and therapeutic methods must continuously be challenged through research for their effectiveness, efficiency, accessibility and quality.
7. In current medical practice and in medical research, most prophylactic, diagnostic and therapeutic procedures involve risks and burdens.

8. Medical research is subject to ethical standards that promote respect for all human beings and protect their health and rights. Some research populations are vulnerable and need special protection. The particular needs of the economically and medically disadvantaged must be recognized. Special attention is also required for those who cannot give or refuse consent for themselves, for those who may be subject to giving consent under duress, for those who will not benefit personally from the research and for those for whom the research is combined with care.

9. Research Investigators should be aware of the ethical, legal and regulatory requirements for research on human subjects in their own countries as well as applicable international requirements. No national ethical, legal or regulatory requirement should be allowed to reduce or eliminate any of the protections for human subjects set forth in this Declaration.

B. BASIC PRINCIPLES FOR ALL MEDICAL RESEARCH

10. It is the duty of the physician in medical research to protect the life, health, privacy, and dignity of the human subject.

11. Medical research involving human subjects must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and on adequate laboratory and, where appropriate, animal experimentation.

12. Appropriate caution must be exercised in the conduct of research which may affect the environment, and the welfare of animals used for research must be respected.

13. The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol. This protocol should be submitted for consideration, comment, guidance, and where appropriate, approval to a specially appointed ethical review committee, which must be independent of the investigator, the sponsor or any other kind of undue influence. This independent committee should be in conformity with the laws and regulations of the country in which the research experiment is performed. The committee has the right to monitor ongoing trials. The researcher has the obligation to provide monitoring information to the committee, especially any serious adverse events. The researcher should also submit to the committee, for review, information regarding funding, sponsors, institutional affiliations, other potential conflicts of interest and incentives for subjects.

14. The research protocol should always contain a statement of the ethical considerations involved and should indicate that there is compliance with the principles enunciated in this Declaration.

The Declaration of Helsinki (Document 17.C) is an official policy document of the World Medical Association, the global representative body for physicians. It was first adopted in 1964 (Helsinki, Finland) and revised in 1975 (Tokyo, Japan), 1983 (Venice, Italy), 1990 (Hong Kong), 1996 (Moscow-West, South Africa) and 2000 (Edinburgh, Scotland). A note of clarification on Paragraph 29 added by the WMA General Assembly, Washington 2002.
15. Medical research involving human subjects should be conducted only by scientifically qualified persons and under the supervision of a clinically competent medical person. The responsibility for the human subject must always rest with a medically qualified person and never rest on the subject of the research, even though the subject has given consent.

16. Every medical research project involving human subjects should be preceded by careful assessment of predictable risks and burdens in comparison with foreseeable benefits to the subject or to others. This does not preclude the participation of healthy volunteers in medical research. The design of all studies should be publicly available.

17. Physicians should abstain from engaging in research projects involving human subjects unless they are confident that the risks involved have been adequately assessed and can be satisfactorily managed. Physicians should cease any investigation if the risks are found to outweigh the potential benefits or if there is conclusive proof of positive and beneficial results.

18. Medical research involving human subjects should only be conducted if the importance of the objective outweighs the inherent risks and burdens to the subject. This is especially important when the human subjects are healthy volunteers.

19. Medical research is only justified if there is a reasonable likelihood that the populations in which the research is carried out stand to benefit from the results of the research.

20. The subjects must be volunteers and informed participants in the research project.

21. The right of research subjects to safeguard their integrity must always be respected. Every precaution should be taken to respect the privacy of the subject, the confidentiality of the patient's information and to minimize the impact of the study on the subject's physical and mental integrity and on the personality of the subject.

22. In any research on human beings, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail. The subjects should be informed of the right to abstain from participation in the study or to withdraw consent to participate at any time without reprisal. After ensuring that the subject has understood the information, the physician should then obtain the subject's freely-given informed consent, preferably in writing. If the consent cannot be obtained in writing, the non-written consent must be formally documented and witnessed.

23. When obtaining informed consent for the research project the physician should be particularly cautious if the subject is in a dependent relationship with the physician or may consent under duress. In that case the informed consent should be obtained by a well-informed physician who is not engaged in the investigation and who is completely independent of this relationship.

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24. For a research subject who is legally incompetent, physically or mentally incapable of giving consent or is a legally incompetent minor, the investigator must obtain informed consent from the legally authorized representative in accordance with applicable law. These groups should not be included in research unless the research is necessary to promote the health of the population represented and this research cannot instead be performed on legally competent persons.

25. When a subject deemed legally incompetent, such as a minor child, is able to give assent to decisions about participation in research, the investigator must obtain that assent in addition to the consent of the legally authorized representative.

26. Research on individuals from whom it is not possible to obtain consent, including proxy or advance consent, should be done only if the physical/mental condition that prevents obtaining informed consent is a necessary characteristic of the research population. The specific reasons for involving research subjects with a condition that renders them unable to give informed consent should be stated in the experimental protocol for consideration and approval of the review committee. The protocol should state that consent to remain in the research should be obtained as soon as possible from the individual or a legally authorized surrogate.

27. Both authors and publishers have ethical obligations. In publication of the results of research, the investigators are obliged to preserve the accuracy of the results. Negative as well as positive results should be published or otherwise publicly available. Sources of funding, institutional affiliations and any possible conflicts of interest should be declared in the publication. Reports of experimentation not in accordance with the principles laid down in this Declaration should not be accepted for publication.

C. ADDITIONAL PRINCIPLES FOR MEDICAL RESEARCH COMBINED WITH MEDICAL CARE

28. The physician may combine medical research with medical care, only to the extent that the research is justified by its potential prophylactic, diagnostic or therapeutic value. When medical research is combined with medical care, additional standards apply to protect the patients who are research subjects.

29. The benefits, risks, burdens and effectiveness of a new method should be tested against those of the best current prophylactic, diagnostic, and therapeutic methods. This does not exclude the use of placebo, or no treatment, in studies where no proven prophylactic, diagnostic or therapeutic method exists. (See footnote *)

30. At the conclusion of the study, every patient entered into the study should be assured of access to the best proven prophylactic, diagnostic and therapeutic methods identified by the study.

31. The physician should fully inform the patient which aspects of the care are related to the research. The refusal of a patient to participate in a study must never interfere with the patient-physician relationship.

The Declaration of Helsinki (Document 17.3) is an official policy document of the World Medical Association, the global representative body for physicians. It was first adopted in 1964 (Helsinki, Finland) and revised in 1975 (Tokyo, Japan), 1983 (Venice, Italy), 1990 (Hong Kong), 1996 (Summed-Weier, South Africa) and 2000 (Edinburgh, Scotland). Note of clarification on Paragraph 29 added by the WMA General Assembly, Washington 2002.
32. In the treatment of a patient, where proven prophylactic, diagnostic and therapeutic methods do not exist or have been ineffective, the physician, with informed consent from the patient, must be free to use unproven or new prophylactic, diagnostic and therapeutic measures, if in the physician’s judgement it offers hope of saving life, re-establishing health or alleviating suffering. Where possible, these measures should be made the object of research, designed to evaluate their safety and efficacy. In all cases, new information should be recorded and, where appropriate, published. The other relevant guidelines of this Declaration should be followed.

*FOOTNOTE:

Note of Clarification on Paragraph 29 of the WMA Declaration of Helsinki

The WMA hereby reaffirms its position that extreme care must be taken in making use of a placebo-controlled trial and that in general this methodology should only be used in the absence of existing proven therapy. However, a placebo-controlled trial may be ethically acceptable, even if proven therapy is available, under the following circumstances:

- Where for compelling and scientifically sound methodological reasons its use is necessary to determine the efficacy or safety of a prophylactic, diagnostic or therapeutic method; or

- Where a prophylactic, diagnostic or therapeutic method is being investigated for a minor condition and the patients who receive placebo will not be subject to any additional risk of serious or irreversible harm.

All other provisions of the Declaration of Helsinki must be adhered to, especially the need for appropriate ethical and scientific review.

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6.10.2002

The Declaration of Helsinki (Document 17.C) is an official policy document of the World Medical Association, the global representative body for physicians. It was first adopted in 1964 (Helsinki, Finland) and revised in 1975 (Tokyo, Japan), 1983 (Venice, Italy), 1989 (Hong Kong), 1996 (Oslo/Osterøy, South Africa) and 2000 (Edinburgh, Scotland). Note of clarification on Paragraph 29 added by the WMA General Assembly, Washington 2002.
APPENDIX I
The Belmont Report

Ethical Principles and Guidelines for the Protection of Human Subjects of Research

The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research

April 18, 1979
The Belmont Report attempts to summarize the basic ethical principles identified by the Commission in the course of its deliberations. It is the outgrowth of an intensive four-day period of discussions that were held in February 1976 at the Smithsonin Institution’s Belmont Conference Center supplemented by the monthly deliberations of the Commission that were held over a period of nearly four years. It is a statement of basic ethical principles and guidelines that should assist in resolving the ethical problems that surround the conduct of research with human subjects. By publishing the Report in the Federal Register, and providing reprints upon request, the Secretary intends that it may be made readily available to scientists, members of institutional review boards, and Federal employers. The two-volume Appendix, containing the lengthy reports of experts and specialists who assisted the Commission in fulfilling this part of its charge, is available as DHEW Publication No. (OS) 78–0013 and No. (OS) 78–0014, for sale by the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402.

Unlike most other reports of the Commission, the Belmont Report does not make specific recommendations for administrative action by the Secretary of Health, Education, and Welfare. Rather, the Commission recommended that the Belmont Report be adopted in its entirety, as a statement of the Department’s policy. The Department requests public comment on this recommendation.

National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research

Members of the Commission

Kenneth John Ryan, N.D., Chairman, Chief of Staff, Boston Hospita1 for Women
Joseph V. Brady, Ph.D., Professor of Behavioral Biology, Johns Hopkins University
Robert E. Cooke, M.D., President, Medical College of Pennsylvania
Dorothy M. Height, President, National Council of Negro Women, Inc.
Albert R. Jonsen, Ph.D., Associate Professor of Bioethics, University of California at San Francisco
Patricia King, J.D., Associate Professor of Law, Georgetown University Law Center
Karen Leland, Ph.D., Associate Professor of Christian Ethics, Pacific School of Religion

*David W. Louisell, J.D., Professor of Law, University of California at Berkeley

Donald W. Selz, M.D., Professor and Chairman, Department of Internal Medicine, University of Texas at Dallas
Eliot Stelz, Ph.D., Provost of the University and Professor of Physiological Psychology, University of Pennsylvania


*Deceased.

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Ethical Principles and Guidelines for Research Involving Human Subjects

Scientific research has produced substantial social benefits. It has also posed some troubling ethical questions. Public attention was drawn to these questions by reports about abuse of human subjects in biomedical experiments, especially during the Second World War. During the Nuremberg War Crime Trials, the Nuremberg code was drafted as a set of standards for judging physicians and scientists who had conducted biomedical experiments on concentration camp prisoners. This code became the prototype of many later codes intended to assure that research involving human subjects would be carried out in an ethical manner.

The codes consist of rules, some general, others specific, that guide the investigators or the reviewers of research in their work. Such rules often are inadequate to cover complex situations; at times they come into conflict, and they are frequently difficult to interpret or apply. Broader ethical principles will provide a basis on which specific rules may be formulated, criticized, and interpreted.

Three principles, or general prescriptive judgments, that govern the conduct of research involving human subjects are identified in this statement. Other principles may also be relevant.

These three are comprehensive, however, and are stated at a level of generalization that should assist scientists, subjects, reviewers and interested citizens to understand the ethical issues inherent in research involving human subjects. These principles

1Since 1945, various codes for the better and more responsible conduct of human experimentation in medical research have been adopted by different organizations. The best known of these codes are the Nuremberg Code of 1947, the Helsinki Declaration of 1964 (revised in 1975), and the "70 Guidelines" (codified into Federal Regulations in 1974) issued by the U.S. Department of Health, Education, and Welfare Codes for the conduct of social and behavioral research have also been adopted, one best known being that of the American Psychological Association, published in 1973.

cannot always be applied so as to resolve beyond dispute particular ethical problems. The objective is to provide an analytical framework that will guide the resolution of ethical problems arising from research involving human subjects.

This statement consists of a distinction between research and practice, a discussion of the three basic ethical principles, and remarks about the application of these principles.

A. Boundaries Between Practice and Research

It is important to distinguish between biomedical and behavioral research, on the one hand, and the practice of accepted therapy on the other, in order to know what activities ought to undergo review for the protection of human subjects of research. The distinction between research and practice is blurred partly because both often occur together (as in research designed to evaluate a therapy) and partly because notable departures from standard practice are often called "experimental" when the term "experimental" and "research" are not carefully defined.

For the most part, the term "practice" refers to interventions that are designed solely to enhance the well-being of an individual patient or client and that have a reasonable expectation of success. The purpose of medical or behavioral practice is

Although practice usually involves interventions designed solely to enhance the well-being of a particular individual, interventions are sometimes applied to one individual for the enhancement of the well-being of another (e.g., blood donation, skin grafts, organ transplants) or an intervention may have the dual purpose of enhancing the well-being of a particular individual and, at the same time, providing some benefit to others (e.g., vaccination, which protects both the person who is vaccinated and society generally). The fact that some forms of practice have elements other than immediate benefit to the individual receiving an intervention, however, should not cloud the general distinction between research and practice. Even when a procedure applied in practice may benefit some other person, it remains an intervention designed to enhance the well-being of a particular individual or group of individuals; thus, it is practice and need not be reviewed as research.

to provide diagnosis, preventive treatment or therapy to particular individuals. By contrast, the term "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). Research is usually described in a formal protocol that sets forth an objective and a set of procedures designed to reach that objective.

When a clinician deviates in a significant way from standard or accepted practices, the 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. Thus, it is the responsibility of medical practice committees, for example, to insist that a major innovation be incorporated into a formal research project.

Research and practice may be carried on together when research is designed to evaluate the safety and efficacy of a therapy. This need not cause any confusion regarding whether or not the activity requires review; the general rule is that if there is any element of research in an activity, that activity should undergo review for the protection of human subjects.

B. Basic Ethical Principles

The expression "basic ethical principles" refers to those general judgments that serve as a basic justification for the many particular ethical prescriptions and evaluations of

1Because the problems related to social experimentation may differ substantially from those of biomedical and behavioral research, the Commission specifically declines to make any policy determination regarding such research at this time. Rather, the Commission believes that the problem ought to be addressed by one of its successor bodies.\n
human actions. Three basic principles, among those generally accepted in our cultural tradition, are particularly relevant to the ethics of research involving human subjects: the principles of respect for persons, beneficence and justice.

1. Respect for Persons.—Respect for persons incorporates at least two ethical convictions: first, that individuals should be treated as autonomous agents and, second, that persons with diminished autonomy are entitled to protection. The principle of respect for persons thus divides into two separate moral requirements: the requirement to acknowledge autonomy and the requirement to protect those with diminished autonomy.

As autonomous person is an individual capable of deliberating about personal goals and of acting under the direction of such deliberation. To respect autonomy is to give weight to autonomous persons' considered opinions and choices while refraining from obstructing their actions unless they are clearly detrimental to others. To show lack of respect for an autonomous agent is to repudiate that person's considered judgments, to deny him or her the freedom to act on those considered judgments, or to withhold information necessary to make a considered judgment, when there are no compelling reasons to do so.

However, not every human being is capable of self-determination. The capacity for self-determination matures during an individual's life, and some individuals lose this capacity wholly or in part because of illness, mental disability, or circumstances that severely restrict liberty. Respect for the immature and the incapacitated may require protecting them as they mature or while they are incapacitated.

Some persons are in need of extensive protection, even to the point of excluding them from activities which may harm them; other persons require little protection beyond making sure they undertake activities freely and with awareness of possible adverse consequences.

The extent of protection afforded should depend upon the risk of harm and the likelihood of benefit. The judgment that any individual lacks autonomy should be periodically re-evaluated and will vary in different situations.

In most cases of research involving human subjects, respect for persons demands that subjects enter into the research voluntarily and with adequate information. In some instances, however, application of the principle is not obvious. The involvement of prisoners as subjects of research provides an instructive example. On the one hand, it would seem that the principle of respect for persons requires that prisoners not be deprived of the opportunity to volunteer for research. On the other hand, under prison conditions they may be subtly coerced or subtly influenced to engage in research activities for which they would not otherwise volunteer. Respect for persons would then dictate that prisoners be protected. Whether to allow prisoners to "volunteer" or to "protect" them presents a dilemma. Respecting persons, in most hard cases, is often a matter of balancing competing claims urged by the principle of respect itself.

2. Beneficence.—Persons are treated in an ethical manner not only by respecting their decisions and protecting them from harm, but also by taking actions to secure their well-being. Such treatment falls under the principle of beneficence. The term "beneficence" is often understood to cover acts of kindness or charity that go beyond strict obligation. In this document, beneficence is understood in a narrower sense, as an obligation.

Two general rules have been formulated as complementary expressions of beneficial actions in this sense: (1) do no harm and (2) maximize possible benefits and minimize possible harm.

The Hippocratic maxim "do no harm" has long been a fundamental principle of medical ethics. Claude Bernard extended it to the realm of research, saying that one should not forgive one person regardless of the benefits that might come to others. However, even avoiding harm requires learning what is harmful; and, in the process of obtaining this information, persons may be exposed to risk of harm. Further, the Hippocratic Oath requires physicians to benefit their patients "according to their best judgment." Learning what will in fact benefit may require exposing persons to risk. The problem posed by these imperatives is to decide when it is justifiable to seek certain benefits despite the risks involved, and when the benefits should be foregone because of the risks.

The obligations of beneficence affect both individual investigators and society; as large, because they extend both to particular research projects and to the entire enterprise of research. In the case of particular projects, investigators and members of their institutions are obliged to give forethought to the maximization of benefits and the reduction of risk that might occur from the research investigation. In the case of scientific research in general, members of the larger society are obliged to recognize the longer term benefits and risks that may result from the improvement of knowledge and from the development of novel medical, psycho-therapeutic, and social procedures.

The principle of beneficence often occupies a well-defined justifying role in many areas of research involving human subjects. An example is found in research involving children. Effective ways of treating childhood diseases and fostering healthy development are benefits that serve to justify research involving children, even when individual research subjects are not direct beneficiaries. Research also makes it possible to avoid the harm that may result from the application of previously accepted routine practices that turn out to be dangerous. But the role of the principle of beneficence is not always so unambiguous. A difficult ethical problem remains, for example, about research that poses...
ents more than minimal risk without immediate prospect of direct benefit to the children involved. Some have argued that such research is inadmissible, while others have pointed out that this constitutes a betrayal of trust in which benefits may come into conflict and force difficult choices.

3. Justice. Who ought to receive the benefits of research and bear its burdens? This is a question of justice, in the sense of “fairness in distribution” or “what is deserved.” An injustice occurs when some benefit to which a person is entitled is denied without good reason or when some burden is imposed undeservedly. Another way of conceiving the principle of justice is that equals ought to be treated equally. However, this statement requires explanation. Who is equal and who is unequal? What considerations justify departure from equal distribution? Almost all commentators agree that distinctions based on experience, age, deprivation, competence, merit and position are not criterion in determining the distribution of benefits and burdens in research. For example, the selection of research subjects need not be scrutinized in order to determine whether some classes (e.g., welfare patients, particular racial and ethnic minorities, or persons confined to institutions) are being systematically selected simply because of their easy availability, their compromised position, or their manipulability, rather than for reasons directly related to the problem being studied. Finally, whenever research supported by public funds leads to the development of therapeutic devices and procedures, justice demands both that these not provide advantages only to those who can afford them and that such research not falsely involve persons from groups unlikely to be among the beneficiaries of subsequent applications of the research.

Questions of justice have long been associated with social practices such as punishment, taxation and political representation. Until recently these questions have not generally been associated with scientific research. However, they are forefronted even in the earliest reflections on the ethics of research involving human subjects. For example, during the 19th and early 20th centuries the burden of serving as research subjects fell largely upon poor ward patients, while the benefits of improved medical care flowed primarily to private patients. Subsequently, the exploitation of unwilling prisoners as research subjects in Nazi concentration camps was condemned as a particularly flagrant injustice. In this country, in the 1940s, the Tuskegee syphilis study used disadvantaged, rural black men to study the unwieldy course of a disease that led to beyond the confine to that population. These subjects were deprived of demonstrate effective treatment in order not to disrupt the project, long after such treatment became generally available.

Against this historical background, it can be seen how conceptions of justice are relevant to research involving human subjects. For example, the selection of research subjects need not be scrutinized in order to determine whether the classes (e.g., welfare patients, particular racial and ethnic minorities, or persons confined to institutions) are being systematically selected simply because of their easy availability, their compromised position, or their manipulability, rather than for reasons directly related to the problem being studied. Finally, whenever research supported by public funds leads to the development of therapeutic devices and procedures, justice demands that these not provide advantages only to those who can afford them and that such research not falsely involve persons from groups unlikely to be among the beneficiaries of subsequent applications of the research.

C. Applications

Applications of the general principles to the conduct of research leads to consideration of the following requirements: informed consent, risk/benefit assessment, and the selection of subjects of research.

1. Informed Consent.—Respect for persons requires that subjects, to the degree that they are capable, be given the opportunity to choose what shall or shall not happen to them. This opportunity is provided when adequate standards for informed consent are satisfactorily met. While the importance of informed consent is unquestioned, controversy prevails over the nature and possibility of an informed consent. Nonetheless, there is widespread agreement that the consent process can be analyzed as containing three elements: information, comprehension and voluntariness.

Information. Most codes of research establish specific items for disclosure intended to assure that subjects are given sufficient information. These items generally include: the research procedure, their purposes, risks and anticipated benefits, alternative procedures (where therapy is involved), and a statement offering the subject the opportunity to ask questions and to withdraw at any time from the research. Additional items have been proposed, including whether subjects are selected, the person responsible for the research, etc.

However, a simple listing of items does not answer the question of what the standard should be for judging how much and what sort of information should be provided. One standard frequently invoked in medical practice, namely the information commonly provided by practitioners in the field or in the locality, is inadequate since research takes place precisely when a common understanding does not exist. Another standard, currently popular in malpractice law, requires the practitioner to reveal the information that reasonable persons would wish to know in order to make a decision regarding their care. This, too, seems unsatisfactory since the research subject, being in essence a volunteer, may wish to know considerably more about risks gratuitously undertaken than do patients who deliver themselves into the hands of a clinician for needed care. It may be that a standard of “the reasonable volunteer” should be proposed: the
extent and nature of information should be such that persons, knowing that the procedure is neither necessary for their care nor perhaps fully understood, can decide whether they wish to participate in the furthering of knowledge. Even when some direct benefit to them is anticipated, the subjects should understand clearly the range of risk and the voluntary nature of participation.

A special problem of consent arises where informing subjects of some pertinent aspect of the research is likely to impair the validity of the research. In many cases, it is sufficient to indicate to subjects that they are being invited to participate in research of which some features will not be revealed until the research is concluded. In all cases of research involving incomplete disclosure, such research is justified only if it is clear that (1) incomplete disclosure is truly necessary to accomplish the goals of the research, (2) there are no undisclosed risks to subjects that are more than minimal, and (3) there is an adequate plan for debriefing subjects, when appropriate, and for dissemination of research results to them. Information about risks should never be withheld for the purpose of eliciting the cooperation of subjects, and truthful answers should always be given to direct questions about the research. Care should be taken to distinguish cases in which disclosure would destroy or invalidate the research from cases in which disclosure would simply invite the investigator.

Comprehension. The manner and context in which information is conveyed is as important as the information itself. For example, presenting information in a disorganized and rapid fashion, allowing too little time for consideration or curtailing opportunities for questioning, all may seriously affect a subject's ability to make an informed choice. Because the subject's ability to understand is a function of intelligence, rationality, maturity and language, it is necessary to adapt the presentation of the information to the subject's capacities. Investigators are responsible for ascertaining that the subject has comprehended the information. While there is always an obligation to ascertain that the information about risk to subjects is complete and adequately comprehended, when the risks are more serious, that obligation increases. On occasion, it may be suitable to give some oral or written tests of comprehension.

Special provision may need to be made when comprehension is severely limited—for example, by conditions of immaturity or mental disability. Each class of subjects that one might consider as incompetent (e.g., infants and young children, mentally disabled persons, the terminally ill and the elderly) should be considered on its own terms. Even for these persons, however, respect requires giving them the opportunity to choose to the extent they are able, whether or not to participate in research. The objections of these subjects to involvement should be honored, unless the research entails providing them a therapy unavailable elsewhere. Respect for persons also requires seeking the permission of other parties in order to protect the subjects from harm. Such persons are thus respected both by acknowledging their own wishes and by the use of third parties to protect them from harm.

The third parties chosen should be those who are most likely to understand the incompetent subject's situation and to act in that person's best interest. The person authorized to act on behalf of the subject should be given an opportunity to observe the research as it proceeds in order to be able to withdraw the subject from the research, if such action appears in the subject's best interest.

Voluntariness. An agreement to participate in research constitutes a valid consent only if voluntarily given. This element of informed consent requires conditions free of coercion and undue influence. Coercion occurs when an overt threat of harm is instrumentally presented by one person to another in order to obtain compliance. Undue influence, by contrast, occurs through an offer of an excessive, unwarranted, inappropriate or improper reward or other overture in order to obtain compliance. Also, inducements that would ordinarily be acceptable may become undue influences if the subject is especially vulnerable. Unjustifiable pressures usually occur when persons in positions of authority or commanding influence—especially where possible sanctions are involved—urge a course of action for a subject. A continuum of such influencing factors exists, however, and it is impossible to state precisely where justifiable persuasion ends and undue influence begins. But undue influence would include actions such as manipulating a person's choice through the controlling influence of a close relative and threatening to withdraw health services to which an individual would otherwise be entitled.

2. Assessment of Risks and Benefits. The assessment of risks and benefits requires a careful array of relevant data, including, in some cases, alternative ways of obtaining the benefits sought in the research. Thus, the assessment presents both an opportunity and a responsibility to gather systematic and comprehensive information about proposed research. For the investigator, it is a means to examine whether the proposed research is properly designed. For a review committee, it is a method for determining whether the risks that will be presented to subjects are justified. For prospective subjects, the assessment will assist the determination whether or not to participate.

The Nature and Scope of Risks and Benefits. The requirement that research be justified on the basis of a favorable risk/benefit assessment bears a close relation to the principle of beneficence, just as the moral requirement that informed consent be obtained is derived primarily from the principle of respect for persons.
The term "risk" refers to a possibility that may occur. However, when expressions such as "small risk" or "high risk" are used, they usually refer (often ambiguously) both to the chance (probability) of experiencing a harm and the severity (magnitude) of the envisioned harm. The term "benefit" is used in the research context to refer to something of positive value related to health or welfare. Unlike "risk," "benefit" is not a term that expresses probabilities. Risk is properly contrasted to probability of benefits, and benefit are properly contrasted with harms rather than risks of harm. Accordingly, so-called risk/benefit assessments are concerned with the probabilities and magnitudes of possible harms and anticipated benefits. Many kinds of possible harms and benefits need to be taken into account. There are, for example, risks of psychological harm, physical harm, legal harm, social harm and economic harm and the corresponding benefits. While the most likely harms to research subjects are those of psychological or physical pain or injury, other possible kinds should not be overlooked. Risks and benefits of research may affect the individual subjects, the families of the individual subjects, and society at large (or special groups of subjects in society). Previous codes and Federal regulations have required that risks to subjects be outweighed by the sum of both the anticipated benefit to the subject, if any, and the anticipated benefit to society in the form of knowledge to be gained from the research. In balancing these different elements, the risks and benefits affecting the immediate research subject will normally carry special weight. On the other hand, interests other than those of the subject may on some occasions be sufficient by themselves to justify the risks involved in the research, so long as the subjects' rights have been protected. Beneficence thus requires that we proceed against risk of harm to subjects and also that we be concerned about the loss of the substantial benefits that might be gained from research.

The Systematic Assessment of Risks and Benefits. It is commonly said that benefits and risks must be "balanced" and shown to be "in a favorable ratio." The metaphorical character of these terms draws attention to the difficulty of making precise judgments. Only on rare occasions will quantitative techniques be available for the scrutiny of research protocols. However, the idea of systematic, nonarbitrary analysis of risks and benefits should be emulated insofar as possible. This ideal requires those making decisions about the justifiability of research to be thorough in the accumulation and assessment of information about all aspects of the research, and to consider alternatives systematically. This procedure renders the assessment of research more rigorous and precise, while making communication between review board members and investigators less subject to misunderstanding, misinterpretation and conflict of judgments. Thus, there should first be a determination of the validity of the presuppositions of the research; then the nature, probability and magnitude of risk should be distinguished with as much clarity as possible. The method of ascertaining risks should be explicit, especially where there is no alternative to the use of such vague categories as small or slight risk. It should also be determined whether an investigator's estimate of the probability of harm or benefits are reasonable, as judged by known facts or other available studies.

Finally, assessment of the justifiability of research should reflect at least the following considerations:

(i) Brutal or inhumane treatment of human subjects is never morally justified. (ii) Risks should be reduced to those necessary to achieve the research objective. It should be determined whether it is in fact necessary to use human subjects at all. Risk can perhaps never be entirely eliminated, but it can often be reduced by careful attention to alternative procedures. (iii) When research involves significant risk of serious impairment, review committees should be extraordinarily insistent on the justification of the risk (looking usually to the likelihood of benefit to the subject—or, in some rare cases, to the manifest voluntariness of the participation). (iv) When vulnerable populations are involved in research, the appropriateness of involving them should be demonstrated. A number of variables go into such judgments, including the nature and degree of risk, the condition of the particular population involved, and the nature and level of the anticipated benefits. (v) Relevant risks and benefits must be thoroughly arrayed in documents and procedures used in the informed consent process. 3. Selection of Subjects.—Just as the principle of respect for persons finds expression in the requirements for consent, and the principle of beneficence in risk/benefit assessment, the principle of justice gives rise to moral requirements that there be fair procedures and outcomes in the selection of research subjects. Justice is relevant to the selection of subjects of research at two levels: the social and the individual. Individual justice in the selection of subjects would require that research involve ethical fairness: that they should not offer potentially beneficial research only to some patients who are in their favor or select only "undesirable" persons for risky research. Social justice requires that distinction be drawn between classes of subjects that ought, and ought not, to participate in any particular kind of research, based on the ability of members of that class to bear burdens and on the appropriateness of placing further burdens on already burdened persons. Thus, it can be considered a matter of social justice that there is an order of preference in the selection of classes of subjects (e.g., adults before children) and that some classes of potential subjects (e.g., the institutionalized mentally infirm or prisoners, may be involved as research subjects, if at all, only on certain conditions.)
Injustice may appear in the selection of subjects, even if individual subjects are selected fairly by investigators and treated fairly in the course of research. Thus injustice arises from social, racial, sexual and cultural biases institutionalized in society. Thus, even if individual researchers are treating their research subjects fairly, and even if IRBs are taking care to assure that subjects are selected fairly within a particular institution, unjust social patterns may nevertheless appear in the overall distribution of the burdens and benefits of research. Although individual institutions or investigators may not be able to resolve a problem that is pervasive in their social setting, they can consider distributive justice in selecting research subjects.

Some populations, especially institutionalized ones, are already burdened in many ways by their infirmities and environments. When research is proposed that involves risks and does not include a therapeutic component, other less burdened classes of persons should be called upon first to accept those risks of research, except where the research is directly related to the specific conditions of the class involved. Also, even though public funds for research may often flow in the same direction as public funds for health care, it seems unfair that populations dependent on public health care constitute a pool of preferred research subjects if more advantaged populations are likely to be the recipients of the benefits.

One special instance of injustice results from the involvement of vulnerable subjects. Certain groups, such as racial minorities, the economically disadvantaged, the very sick, and the institutionalized may continually be sought as research subjects, owing to their ready availability in settings where research is conducted. Given their dependent status and their frequently compromised capacity for free consent, they should be protected against the danger of being involved in research solely for administrative convenience, or because they are easy to manipulate as a result of their illness or socioeconomic condition.
APPENDIX J
PROTECTION OF HUMAN SUBJECTS

TITLE 45
CODE OF FEDERAL REGULATIONS
PART 46

REVISED JUNE 18, 1991
THE PUBLIC HEALTH SERVICE ACT
AS AMENDED BY THE HEALTH RESEARCH EXTENSION ACT OF 1985
PUBLIC LAW 99-158
NOVEMBER 20, 1985

"INSTITUTIONAL REVIEW BOARDS: ETHICS GUIDANCE PROGRAM

Title IV. Section 488. (a) The Secretary shall by regulation require that each entity which applies for a grant, contract, or cooperative agreement under this Act for any project or program which involves the conduct of biomedical or behavioral research involving human subjects submit to or with its application for such grant, contract, or cooperative agreement a statement satisfactory to the Secretary that it has established in accordance with regulations which the Secretary may prescribe a board (to be known as an "Institutional Review Board") to review biomedical and behavioral research involving human subjects conducted at or supported by such entity in order to protect the rights of such human subjects if such research.

(b) The Secretary shall establish a program within the Department of Health and Human Services under which requests for certification and guidance with respect to ethical issues raised in connection with biomedical and behavioral research involving human subjects are expedited to promptly and appropriately.

(c) The Secretary shall establish a program for the prompt and appropriate request to information provided to the Director of NIH regarding the existence of requests of human subjects for which funds have been withheld under this Act. The program shall include procedures for the reviewing of reports of such information from recipients of funds under this Act and taking appropriate action with respect to such violations.

TOTAL RESEARCH

Title V. Section 508. (a) The Secretary may not conduct or support any research or experimentation in the United States or in any other country, on a normal living human fetus as yet or on any human fetus at or after about the mid-trimester of pregnancy when viability has not been ascertained unless the research or experimentation:

(1) is intended for or will bring or meet the health needs of the fetus or enhance the probability of its survival to viability in order to protect the rights of human subjects for which funds have been withheld under this Act.

(2) is intended for or will bring or meet the health needs of the fetus or enhance the probability of its survival to viability in order to protect the rights of human subjects for which funds have been withheld under this Act.

(3) is intended for or will bring or meet the health needs of the fetus or enhance the probability of its survival to viability in order to protect the rights of human subjects for which funds have been withheld under this Act.

(4) is intended for or will bring or meet the health needs of the fetus or enhance the probability of its survival to viability in order to protect the rights of human subjects for which funds have been withheld under this Act.

(5) is intended for or will bring or meet the health needs of the fetus or enhance the probability of its survival to viability in order to protect the rights of human subjects for which funds have been withheld under this Act.

(6) is intended for or will bring or meet the health needs of the fetus or enhance the probability of its survival to viability in order to protect the rights of human subjects for which funds have been withheld under this Act.

(7) is intended for or will bring or meet the health needs of the fetus or enhance the probability of its survival to viability in order to protect the rights of human subjects for which funds have been withheld under this Act.

(8) is intended for or will bring or meet the health needs of the fetus or enhance the probability of its survival to viability in order to protect the rights of human subjects for which funds have been withheld under this Act.

(9) is intended for or will bring or meet the health needs of the fetus or enhance the probability of its survival to viability in order to protect the rights of human subjects for which funds have been withheld under this Act.

(10) is intended for or will bring or meet the health needs of the fetus or enhance the probability of its survival to viability in order to protect the rights of human subjects for which funds have been withheld under this Act.

(11) is intended for or will bring or meet the health needs of the fetus or enhance the probability of its survival to viability in order to protect the rights of human subjects for which funds have been withheld under this Act.

(12) is intended for or will bring or meet the health needs of the fetus or enhance the probability of its survival to viability in order to protect the rights of human subjects for which funds have been withheld under this Act.

THE CODE OF FEDERAL REGULATIONS,
TITLE 45 CFR PART 46,
IMPLEMENTS THESE AMENDMENTS
TO THE PUBLIC HEALTH SERVICE ACT

NOTE: Section 45.312(g) becomes Section 45.312(h) in Title 45 CFR, part 46 as revised on June 30, 1991.
PART 46—PROTECTION OF HUMAN SUBJECTS
Revised June 18, 1991
(Effective August 19, 1991)
PART 46—PROTECTION OF HUMAN SUBJECTS

Subpart A—Federal Policy for the Protection of Human Subjects (Basic DHHS Policy for Protection of Human Research Subjects)

Sec. 46.101 To what does this policy apply?

46.102 Definitions.

46.103 Avoidance compliance with this policy—research conducted or supported by any Federal Department or Agency.

46.104-46.106 [Reserved]

46.107 IRB membership.

46.108 IRB functions and operations.

46.109 IRB review of research.

46.110 Expedited review procedures for certain kinds of research involving no more than minimal risk, and for minor changes in approved research.

46.111 Criteria for IRB approval of research.

46.112 Review by institutional research.

46.113 Suspension or termination of IRB approval of research.

46.114 Cooperative research.

46.115 IRB records.

46.116 General requirements for informed consent.

46.117 Documentation of informed consent.

46.118 Applications and proposals lacking adequate plans for involvement of human subjects.

46.119 Research undertaken without the consent of involving human subjects.

46.120 Evaluation and disposition of applications and proposals for research to be conducted or supported by a Federal Department or Agency.

46.121 [Reserved]

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46.123 Early termination of research effort; Evaluation of applications and proposals.

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Subpart B—Additional DHHS Protection Pertaining to Research, Development, and Related Activities Involving Infants, Pregnant Women, and Human Implantable Devices

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46.203 Definitions.

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46.208 Activities directed toward fetal tissues or stems, including implantable devices, as subjects.

46.209 Activities involving the death, fetal material, or the placenta.

46.211 Modifications or waiver of specific requirements.

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46.303 Definitions.

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46.305 Additional duties of the Institutional Review Boards where prisoners are involved.

46.306 Permitted research involving prisoners.

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46.403 IRB duties.

46.404 Research not involving greater than minimal risk.

46.405 Research involving greater than minimal risk but not the prospect of direct benefit to the individual subject.

46.406 Research involving greater than minimal risk and the prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject’s disorder or condition.

46.407 Research not otherwise approachable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.

46.408 Requirements for permission by parents or guardians and for assent by children.

46.409 Waiver.

that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

(6) Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are properly shielded so that the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

(7) Research and demonstration projects which are conducted by or subject to the approval of Department or Agency heads, and which we designed to study, evaluate, or otherwise examine:

(a) Public benefit or service programs,
(b) procedures for obtaining benefits or services under those programs,
(c) possible changes in or alternatives to those programs or procedures, or
(d) possible changes in methods or levels of payment for benefits or services under those programs.

(8) Tests and food quality evaluation and consumer acceptance studies.

(9) If wholeblood or foods without additives are contained in or if a food is consumed that contains a food ingredient at or below the level found to be safe, by the Food Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

(10) Department or Agency heads retain final judgment as to whether a particular activity is covered by this policy.

(11) Department or Agency heads may require that specific research activities be classified as research activities conducted, supported, or otherwise subject to regulation by the Department or Agency, but not otherwise covered by this policy, comply with some or all of the requirements of this policy.

(12) Compliance with this policy requires compliance with pertinent Federal laws or regulations which provide additional protections for human subjects.

(13) This policy does not affect any state or local laws or regulations which may otherwise be applicable and which provide additional protections for human subjects.

(g) This policy does not affect any foreign laws or regulations which may otherwise be applicable and which provide additional protections for human subjects of research.

(h) This policy does not affect any foreign laws or regulations which may otherwise be applicable and which provide additional protections for human subjects of research.

(i) When research covered by this policy takes place in foreign countries, procedures normally followed in the foreign countries to protect human subjects may differ from those set forth in this policy. (An example is a foreign institution which complies with guidelines consistent with the World Medical Assembly Declaration (Declaration of Helsinki) 1964 issued either by sovereign states or by an organization whose function for the protection of human research subjects is internationally recognized.) In these circumstances, if the Department or Agency head determines that the procedures prescribed by the institution affect protections that are at least equivalent to those provided in this policy, the Department or Agency head may approve the substitution of the foreign procedures in lieu of the procedural requirements provided in this policy. Except when otherwise required by statute, Executive Order, or the Department or Agency head, notices of these actions to the extent they occur will be published in the Federal Register or will be otherwise published as provided in Department or Agency procedures.

(i) Unless otherwise required by law, Department or Agency heads may not require the replication of some or all of the provisions of the policy to specific research activities or classes of research activities otherwise covered by this policy. Except when otherwise required by statute or Executive Order, the Department or Agency head shall forward advance notice of these actions to the Office for Protection from Research Risks, National Institutes of Health, Department of Health and Human Services (DHHS), and shall also publish them in the Federal Register or in such other manner as provided in Department or Agency procedures. 1

1 institutions with DHHS-approved assurances in the hits slide by proviso-
§ 46.142 Definitions.
(a) Department or agency head means the head of any Federal Department or Agency or any other officer or
employee of any Department or Agency to whom authority has been delegated.
(b) Investigation means any public or
private entity or Agency (including Federal, State, and other agencies).
(c) Legally authorized representative means an individual or an entity that is authorized under
applicable law by another agency or by a duly authorized entity in order to conduct a
research project(s).
(d) Research means a systematic investigation, including research
development, testing and evaluation, designed to develop or contribute to
understandable knowledge. Activities which meet this definition constitute research for purposes of this policy,
whether or not they are conducted or supported under a program which is considered research for other
purposes. For example, some demonstration and service programs may or may not be considered research.
(e) Research project is regulation, and
similar terms are intended to encompass those research activities for
which a Federal Department or Agency has specific responsibility for
research activities, for example, investigational New Drug requirements administered by the Food and Drug Administrations. It does not
include research activities which are
regulated or conducted by a Federal Department or Agency solely as part of
the Department's or Agency's budget and review.
(3) Certain types of activities whether
research or non-research in nature for
example, Wage and Hour requirements
administered by the Department of
Labor).
(4) Human subject means a living
individual about whom an investigator (whether professional or volunteer)
conducting research obtains
(1) data through intervention or
interaction with the individual, or
(2) identifiable, private information.
(5) Human subject means a living
individual about whom an investigator (whether professional or volunteer)
conducting research obtains
(1) data through intervention or
interaction with the individual, or
(2) identifiable, private information.
(6) Determination is the process by which data are gathered
for example, questionnaires and
questionnaires of the subject or the
subject's environment that are
performed for research purposes.
(7) Private information includes information about
behavior that is in a form in which an individual can reasonably
expect that it will be kept private and which is not available
to the investigator or associated with
the investigator in order for obtaining the
information to be used or revealed, or
communicated, or disclosed to others.
(8) IRB means an Institutional
Review Board established in accord
with the requirements set forth in the
policy.
(9) IRB approval means the
determination of the IRB that the research has been reviewed and
may be conducted, at an inspection within the
requirements set forth by the IRB and
by Federal and institutional and Federal
requirements.
(10) Minimal risk means the
minimum risk to the subjects that arises
from the research procedures, and
which does not involve procedures or
invasive data collection, or procedures involving a low probability of
discomfort anticipated in the research.
(11) Certification means the official
presentation of the Department or
Agency's in accordance with the requirements of this
policy, that a research project
or activity involving human subjects has been reviewed and approved by an
IRB in accordance with an approved

§ 46.133 Assuring compliance with this
policy—research conducted or
supported by a Federal Department or
Agency.
(a) Each institution engaged in
research which is conducted or
supported by a Federal Department or
Agency shall provide written
assurances satisfactory to the
Department or Agency head that it
will comply with the requirements set
forth in this policy. In lieu of requiring
submission of an assurance, individual
Department or Agency heads shall
accept the existence of a current
assurance appropriate for the research in
question, on file with the Office for
Prevention from Research Risks,
National Institutes of Health, DHHS, and
approved for federally or
supported by that
office. When the existence of an
DHHS-approved assurance is accepted
in lieu of requiring submission of an
assurance, reports (except certification)
required by this policy to be made to
Department and Agency heads shall
also be made to the Office for
Prevention from Research Risks.
National Institutes of Health, DHHS.
(b) Department and agencies will
conduct or support research covered
by this policy only if the institution has an
assurance approved as provided in
this section, and only if the institution has notified the
Department and Agency head that the research has been
reviewed and approved by an
IRB, and that the research will be
subject to continuing review by
the IRB and by other institutional and
Federal requirements.
applicable to any research exempted or waived under §46.101 (9) or (10).

(2) Designation of one or more IRBs established in accordance with the requirements of this policy, and for which provisions are made for meeting space and sufficient staff to support the IRB's review and recordkeeping.

(3) A list of IRB members identified by name, title, and institutional affiliation, including the principal investigator or top ring member of the research team, institutional representatives, and any other people or groups of people providing substantial input to the IRB.

The governing board of the IRB and any committee performing the functions of a subcommittees, shall approve the composition and any changes to the composition of the IRB.

(b) In instances where the research is supported by Federal funds, the IRB shall, to the extent possible in consultation with the investigator, approve the review of the research by the IRB in accordance with the requirements of this section.

(c) The IRB shall ensure that the principal investigator or top ring member of the research team is named as the principal investigator or top ring member of the research team.

(d) The IRB shall ensure that the principal investigator or top ring member of the research team is named as the principal investigator or top ring member of the research team.

(e) The principal investigator or top ring member of the research team shall be named as the principal investigator or top ring member of the research team.

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member whose primary concern is in nonclinical areas.
(c) Each IRB shall include at least one member who is not otherwise affiliated with the institution and who is not part of the administrative staff of a person who is affiliated with the institution.
(d) No IRB may have a member participate in the IRB's initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB.
(e) An IRB may, in its discretion, invite individuals with competence in special areas to assist in the review of issues which require expertise beyond or in addition to that available on the IRB. These individuals may not vote with the IRB.
§ 46.108 IRB functions and operations.
In order to fulfill the requirements of this policy each IRB shall:
(a) Follow written procedures in the same detail as described in § 46.103(b)(1) and to the extent required by § 46.103(b)(2).
(b) Except when an expedited review procedure is used as described in § 46.110, review proposed research at convened meetings at which a majority of the members of the IRB are present, including at least one member whose primary concerns are in nonclinical areas. In no case for the research to be approved, it shall receive approval of a majority of those members present at the meeting.
§ 46.110 IRB review of research.
(a) An IRB shall review and, as appropriate, approve, reject, or disapprove all research activities covered by this policy.
(b) An IRB shall require that information given to subjects as part of informed consent be in accordance with § 46.116. The IRB may require that information, in addition to that specifically mentioned in § 46.116, be given to the subjects whom the IRB's judgment of the information would meaningfully add to the protection of the rights and welfare of subjects.
(c) An IRB shall require documentation of informed consent or may waive documentation in accordance with § 46.117.
(d) An IRB shall notify investigators and the institution in writing of its decision to approve or disapprove the proposed research activity, or of modifications required to secure IRB approval of the research activity. If the IRB decides to disapprove a research activity, it shall include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in person or in writing.
(e) An IRB shall conduct continuing review of research covered by this policy at intervals appropriate to the degree of risk, but not less than once per year, and shall have authority to observe or have a third party observe the consent process and the research.
(Approved by the Office of Management and Budget under Control Number 0995-0050.)
§ 46.110 Expedited review procedures for certain kinds of research involving so much more than minimal risk, and for minor changes in approved research.
(a) The Secretary, HHS, has established, and published as a Notice in the Federal Register, a list of categories of research that may be reviewed by the IRB through an expedited review procedure. The list will be amended, as appropriate, after consultation with other departments and agencies, through periodic republication by the Secretary, HHS, in the Federal Register. A copy of the list is available from the Office for Protection from Research Risks, National Institutes of Health, DHHS, Bethesda, Maryland 20892.
(b) An IRB may use the expedited review procedure to review either or both of the following:
(1) Some or all of the research appearing on the list and found by the review board(s) to involve no more than minimal risk.
(2) Minor changes in previously approved research during the period (of one year or less) for which approval is authorized.
Under an expedited review procedure, the review may be carried out by the IRB chairperson or by one or more experienced reviewers designated by the chairperson from among members of the IRB. In reviewing the research, the reviewers may exercise all of the authorities of the IRB except that the reviewers may not disapprove the research. A research activity may be disapproved only after review in accordance with the non-expedited procedures set forth in § 46.105(c).
(c) Each IRB which uses an expedited review procedure shall adopt a method for keeping all members advised of research proposals which have been approved under the procedures.
(d) The Department of Agriculture may, in its discretion, adopt a method for keeping all members advised of research proposals which have been approved under the procedures.
§ 46.115 Criteria for IRB approval of research.
(a) In order to approve research covered by this policy the IRB shall determine that all of the following requirements are satisfied:
(1) Risks to subjects are minimized by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (2) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.
(b) Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of theories or procedures that are not yet participating in the research). The IRB should not consider the possibility long-range effects of applying knowledge gained in the research to public policy (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.
(c) Selection of subjects is equitable.
In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly conscious of the special problems of research involving vulnerable populations, such as children, pregnant women, mentally disabled persons, or
economically or educationally disadvantaged persons.

(4) Informed consent will be sought from each prospective subject or the subject’s legally authorized representative, in accordance with, and to the extent required by §46.116.

(5) Informed consent will be appropriately documented, in accordance with, and to the extent required by §46.117.

(6) When appropriate, the research plan makes adequate provision for monitoring the data collected to assure the safety of subjects.

(7) When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

(8) When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

§ 46.112 Review by institution.

Research covered by this policy that has been approved by an IRB may be subject to further appropriate review and approval or disapproval by officials of the institution. However, these officials may not approve the research if it has not been approved by an IRB.

§ 46.113 Suspension or termination of IRB approval of research.

The IRB shall have the authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB’s requirements or that has been associated with unexpected serious harm to subjects. Any suspension or termination of approval shall include a statement of the reasons for the IRB’s action and shall be reported promptly to the investigator, appropriate institutional officials, and the Department or Agency having (Approved by the Office of Management and Budget under Control Number 9999- 0001.)

§ 46.134 Cooperative research.

Cooperative research projects are those projects covered by this policy which involve more than one institution. In the conduct of cooperative research projects, each institution is responsible for safeguarding the rights and welfare of human subjects and for complying with this policy. With the approval of the Department or Agency head, an institutional representative in a cooperative project may enter into a joint review arrangement, rely upon the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort.

§ 46.115 IRB records.

(a) An institution, or when appropriate an IRB, shall prepare and maintain adequate documentation of IRB activities including the following:

(1) Copies of all research proposals reviewed, scientific evaluations, if any, that accompany the proposals, approved sample consent documents, progress reports submitted by investigators, and reports of injuries to subjects.

(2) Minutes of IRB meetings which shall be in sufficient detail to show attendance at the meetings, actions taken by the IRB, the vote on these actions including the number of members voting for, against, and abstaining, the basis for requiring changes in or disproving research, and a written summation of the discussion of countermeasures and their resolution.

(3) Records of continuing review activities.

(4) Copies of all correspondence between the IRB and the investigators.

(b) A list of IRB members in the same detail as described in § 46.103(b)(3).

(6) Written procedures for the IRB in the same detail as described in § 46.103(b)(4) and § 46.110(b)(3).

(7) Statements of significant new findings provided to subjects, as required by §46.103(b)(5).

(b) The records required by this policy shall be retained for at least 3 years, and records relating to research which is concluded shall be retained for at least 3 years after completion of the research. All records shall be accessible for inspection and copying by authorized representatives of the Department or Agency at reasonable times and in a reasonable manner.

(Approved by the Office of Management and Budget under Control Number 9999- 0001.)

§ 46.116 General requirements for informed consent.

Except as provided elsewhere in this policy, no investigator shall involve a human being as a subject in research covered by this policy unless the investigator has obtained the legally effective informed consent of the subject or the subject’s legally authorized representative. An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the representative shall be in language understandable to the subject or the representative. No informed consent, whatever oral or written, may include any compulsory language through which the subject or the representative is made to waive or appear to waive any of the subject’s legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

(b) Basic elements of informed consent. Except as provided in paragraph (e) of this section, in seeking informed consent the following information shall be provided to each subject:

(1) a statement that the study involves research; the purposes of the research and the expected duration of the subject’s participation; a description of the procedures to be followed, and identification of any reasonably foreseeable procedures which are experimental;

(2) a description of any reasonably foreseeable risks or discomforts to the subject;

(3) a description of any benefits to the subject or to others which may reasonably be expected from the research;

(4) a disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;

(5) a statement describing the extent, if any, to which confidentiality of
records identifying the subject will be maintained;
(6) for research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;
(7) an assurance of whom to contact for answers to pertinent questions about the research and research subjects’ rights, and whom to contact in the event of a research-related injury to the subject; and
(8) a statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to the individual, or otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.
(b) Additional elements of informed consent. When appropriate, one or more of the following elements of information shall be provided to each subject:
(1) a statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are reasonably foreseeable;
(2) an expectation of circumstances under which the subject may be terminated by the investigator without regard to the subject’s consent;
(3) any additional costs to the subject that may result from participation in the research;
(4) the consequences of a subject’s decision to withdraw from the research and procedures for orderly termination of participation by the subject;
(5) a statement that significant new findings are being developed during the course of the research which may relate to the subject’s well-being and continue participation will be provided to the subject; and
(6) the approximate number of subjects involved in the study.
(c) An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirement to obtain informed consent provided the IRB finds and documents that:
1. the research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine:
2. public benefits or service programs; or protocols for assessing benefits or services under federal programs; (g) possible changes in or alternatives to those programs or procedures; or (h) possible changes in methods, levels, or payment, for benefits or services under state programs; and
2. the research could not practically be carried out without the waiver or alteration.
(d) An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirements to obtain informed consent provided the IRB finds and documents that:
1. the research involves no more than minimal risk to the subjects;
2. the waiver or alteration will not adversely affect the rights and welfare of the subjects;
3. the research could not practicably be carried out without the waiver or alteration; and
4. whatever appropriate, the subjects will be provided with additional pertinent information after participation.
(e) The informed consent requirement in this policy are not intended to be more stringent than applicable Federal, State, or local laws which require additional information to be disclosed, in lieu of informed consent, to be legally effective. Nothing in this policy is intended to limit the authority of a physician to provide emergency medical care to the extent the physician is permitted to do so under applicable Federal, State, or local law.
(Approved by the Office of Management and Budget under Control Number 0990-0035.)

§46.317 Documentation of informed consent.
(a) Except as provided in paragraph (c) of this section, informed consent shall be documented by the use of a written consent form approved by the IRB and signed by the subject or the subject’s legally authorized representative. A copy shall be given to the person signed for form.
(b) Except as provided in paragraph (a) of this section, the consent form may be either of the following:
(1) A written consent document that includes the elements of informed consent required by §46.116. This form may be read to the subject or the subject’s legally authorized representative, but in any event, the investigator shall give the subject or the representative adequate opportunity to read it before he is asked to sign it.
(2) A short form written consent document stating that the elements of informed consent required by §46.116 have been presented orally to the subject or the subject’s legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Also, the IRB shall approve a written summary of what is so said to the subject or the representative. Only the short form used to be signed by the subject or the representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the representative, in case of a copy of the short form.
(c) An IRB may waive the requirement for the investigator to obtain consent from each subject or from all subjects if it finds either:
(1) That the only record linking the subject under research would be the consent document and the principal risk would be minimal, consisting of injury from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject’s wishes will govern; or
(2) That the research presents no more than minimal risk to harm to the subject and involves no procedures for which written consent is normally required outside of the research context.
In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.
§ 46.118 Applications and proposals lacking definite plans for involvement of human subjects.

Certain types of applications for grants, cooperative agreements, or contracts are submitted to departments or agencies with the knowledge that the subjects may be involved within the period of support, but definite plans would not normally be set forth in the application or proposal. These include activities such as institutional type grants when selection of specific projects in the institution's responsibility, research training grants in which the activities involving subjects remain to be selected, and projects in which human subjects' involvement will depend upon completion of immunology, price, quality studies, or certification of compounds. These applications need not be reviewed by an IRB before an award may be made. However, except for research exempted or waived under § 46.103 (b) or (e), no human subjects may be involved in any project supported by these awards until the project has been reviewed and approved by the IRB, as provided in this policy, and certification submitted, by the institution, to the Department or Agency.

§ 46.119 Research undertaken without the intent of involving human subjects.

Research that is undertaken without the intention of involving human subjects, but is later proposed to involve human subjects in the research, shall first be reviewed and approved by an IRB as provided in this policy, a certification submitted, by the institution, to the Department or Agency, and final approval given to the proposed change by the Department or Agency.

§ 46.128 Evaluation and disposition of applications and proposals for research to be conducted or supported by a Federal Department or Agency.

(a) The Department or Agency head will evaluate all applications and proposals involving human subjects submitted to the Department or Agency through such officers and employees of the Department or Agency and such experts and consultants as the Department or Agency head determines to be appropriate. This evaluation will take into consideration the risks to the subjects, the adequacy of protection against those risks, the potential benefits of the research to the subjects and others, and the importance of the knowledge gained or to be gained.

(b) On the basis of this evaluation, the Department or Agency head may approve or disapprove the application or proposal, or enter into negotiations to develop an approvable plan.

§ 46.121 [Reserved]

§ 46.122 Use of Federal funds.

Federal funds administered by a Department or Agency may not be expended for research involving human subjects unless the requirements of this policy have been satisfied.

§ 46.123 Early termination of research support; Evaluation of applications and proposals.

(a) The Department or Agency head may require that Department or Agency support for any project be terminated or suspended in the manner prescribed in applicable program requirements, when the Department or Agency head finds an investigator has materially failed to comply with the terms of this policy.

(b) In making decisions about suspending or approving applications or proposals covered by this policy the Department or Agency head may take into account, in addition to all other eligibility requirements and program criteria, factors such as whether the applicant has been subject to a suspension or penalty under paragraph (a) of this section and whether the applicant or the person or persons who would direct or have directed the scientific and technical aspects of an activity has/have, in the judgment of the Department or Agency head, materially failed in discharging responsibility for the protection of the rights and welfare of human subjects (whether or not the research was subject to Federal regulation).

§ 46.124 Conditions.

With respect to any research project or any class of research projects the Department or Agency head may impose additional conditions prior to or at the time of approval when in the judgment of the Department or Agency head additional conditions are necessary for the protection of human subjects.

Subpart B—Additional DHHS Protections Pertaining to Research, Development, and Related Activities Involving Female, Pregnant Women, and Humankind in Vitro Fertilization


§ 46.201 Applicability.

(a) The regulations in this subpart are applicable to all Department of Health and Human Services grants and contracts supporting research, development, and related activities involving (1) the fetus, (2) pregnant women, and (3) human oocytes fertilization.

(b) Nothing in this subpart shall be construed as indicating that compliance with the procedures set forth herein will in any way render inapplicable pertinent State or local laws bearing upon activities covered by this subpart.

(c) The requirements of this subpart are in addition to those imposed under the other subparts of this part.

§ 46.202 Purpose.

It is the purpose of this subpart to provide additional subparts in reviewing activities to which this subpart is applicable to ensure that they conform to appropriate ethical standards and relate to important societal needs.

§ 46.203 Definitions.

As used in this subpart:

(a) "Secretary" means the Secretary of Health and Human Services and any other officer or employee of the Department of Health and Human Services (DHHS) to whom authority has been delegated.

(b) "Pregnancy" encompasses the period of time from confirmation of...
implantation (through any of the presumptive signs of pregnancy, such as missed menstus, or by any medically acceptable pregnancy test), until expulsion or extraction of the fetus.

(c) "Fetus" means the product of conception from the time of implantation (as evidenced by any of the presumptive signs of pregnancy, such as missed menses, or a medically acceptable pregnancy test), until a determination is made, following expulsion or extraction of the fetus, that it is viable.

(d) "Viable" as it pertains to the fetus means being able, after spontaneous or induced delivery, to survive (given the benefit of available medical therapy) to the point of independently sustaining heart beat and respiration. The Secretary may from time to time, taking into account medical advances, publish in the Federal Register guidelines to assist in determining whether a fetus is viable for purposes of this subpart. If a fetus is viable after delivery, it is a premature infant.

(e) "Nonviable fetus" means a fetus ex utero which, although living, is not viable.

(f) "Dead fetus" means a fetus ex utero which excludes either heart beat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, or pulsation of the umbilical cord (if still attached).

(g) "In vitro fertilization" means any fertilization of a human egg cell which occurs outside the body of a female, either through manipulation of the human sperm and ovum or by other means.

§ 46.204 Ethical Advisory Boards.

(a) One or more Ethical Advisory Boards shall be established by the Secretary. Members of these Board(s) shall be so selected that the Board(s) will be competent to deal with medical, legal, social, ethical, and related issues and may include, for example, research scientists, physicians, psychologists, sociologists, educators, lawyers, and ethicists, as well as representatives of the general public.

(b) At the request of the Secretary, the Ethical Advisory Board shall render advice consistent with the policies and requirements of this part as to ethical issues, involving activities covered by this subpart, raised by individual applicants or proposals. In addition, upon request by the Secretary, the Board shall render advice as to causes of applications or proposals and general policies, guidelines, and procedures.

(c) A Board may establish, with the approval of the Secretary, a class of applications or proposals which: (1) must be submitted to the Board, or (2) need not be submitted to the Board.

(d) A Board may establish, with the approval of the Secretary, a class of applications or proposals which must be submitted, no application or proposal within the class may be funded by the Department or any component thereof until the application or proposal has been reviewed by the Board and the Board has rendered advice as to its acceptability from an ethical standpoint.

(e) No application or proposal involving human in vitro fertilization may be funded by the Department or any component thereof until the application or proposal has been reviewed by the Ethical Advisory Board and the Board has rendered advice as to its acceptability from an ethical standpoint.

§ 46.205 Additional duties of the Institutional Review Boards in connection with activities involving fe	entes, pregnant women, or human in vitro fertilization.

(a) In addition to the responsibilities prescribed for Institutional Review Boards under subsection (a) of this part, the applicant's or offeror's Board shall, with respect to activities covered by this subpart, carry out the following additional duties:

1. determine that all aspects of the activity meet the requirements of this subpart;

2. determine that adequate consideration has been given to the manner in which potential subjects will be selected, and adequate provision has been made by the applicant or offeror for monitoring the accrual informed consent process (e.g., through such mechanisms as appropriate participation in the Institutional Review Board or subject advocates in: (i) overseeing the actual process by which individual consents required by this subpart are secured either by

3. approving induction of each individual into the activity or verifying, perhaps through sampling, that approved procedures for induction of individuals into the activity are being followed, and (ii) monitoring the progress of the activity and intervening as necessary through such steps as visits to the activity site and continuing evaluation to determine if any unanticipated risks have arisen.

4. carry out other responsibilities as may be assigned by the Secretary.

(b) No award may be issued until the applicant or offeror has certified to the Secretary that the Institutional Review Board has made the determinations required under paragraph (a) of this section and the Secretary has approved these determinations, as provided in § 46.120 of Subpart A of this part.

(c) Applicants or offerors seeking support for activities covered by this subpart must provide for the designation of an Institutional Review Board, subject to approval by the Secretary, where no such Board has been established under Subpart A of this part.

§ 46.206 General limitations.

(a) No activity to which this subpart is applicable may be undertaken unless:

1. appropriate studies on animals and nonpregnant individuals have been conducted;

2. except where the purpose of the activity is to meet the health needs of the mother or the particular fetus, the risk to the fetus is minimal and, in all cases, the least possible risk for achieving the objectives of the activity is employed.

(b) Individuals engaged in the activity will have no part in: (1) any decisions as to the timing, method, and procedures used to terminate the pregnancy, and (2) determining the viability of the fetus at the termination of the pregnancy; and

(c) No procedural changes which may cause greater than minimal risk to the fetus or the pregnant woman will be introduced into the procedures for terminating the pregnancy solely in the interest of the activity.

(d) No inducements, monetary or otherwise, may be offered to terminate pregnancy for purposes of the activity.
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\textbf{46.307 Activities directed toward pregnant women as subjects.}

(a) No pregnant woman may be involved as a subject in any activity covered by this subpart unless: (1) the purpose of the activity is to meet the health needs of the mother and the fetus will be placed at risk only to the minimum extent necessary to meet such needs, or (2) the risk to the fetus is minimal.

(b) An activity permitted under paragraph (a) of this section may be conducted only if the mother and father are legally competent and have given their informed consent after having been fully informed according to the extent of possible impact on the fetus, except that the father's informed consent need not be secured if: (1) the purpose of the activity is to meet the health needs of the mother; (2) his identity or whereabouts cannot reasonably be ascertained; (3) he is not reasonably available; or (4) the pregnancy resulted from rape.

\section*{46.308 Activities directed toward fetuses in utero as subjects.}

(a) No fetus in utero may be involved as a subject in any activity covered by this subpart unless: (1) the purpose of the activity is to meet the health needs of the particular fetus and the fetus will be placed at risk only to the minimum extent necessary to meet such needs, or (2) the risk to the fetus is minimal and the purpose of the activity is the development of important biomedical knowledge which cannot be obtained by other means.

(b) An activity permitted under paragraph (a) of this section may be conducted only if the mother and father are legally competent and have given their informed consent, except that the father's consent need not be secured if: (1) his identity or whereabouts cannot reasonably be ascertained; (2) he is not reasonably available; or (3) the pregnancy resulted from rape.

\section*{46.309 Activities directed toward fetuses in vivo, including asviable, newborn infants, as subjects.}

(a) Until it has been ascertained whether or not a fetus ex utero is viable, a fetus ex utero may not be involved as a subject in an activity covered by this subpart unless: (1) there will be no added risk to the fetus resulting from the activity, and the purpose of the activity is the development of important biomedical knowledge which cannot be obtained by other means; or (2) the purpose of the activity is to enhance the possibility of survival of the particular fetus to the point of viability.

(b) No viable fetus may be involved as a subject in an activity covered by this subpart unless: (1) vital functions of the fetus will not be artificially maintained; (2) experimental activities which of themselves would terminate (euthanasia or resuscitation of the fetus) will not be employed, and (3) the purpose of the activity is the development of important biomedical knowledge which cannot be obtained by other means.

(c) In the event the fetus or ex utero is found to be viable, it may be included as a subject in the activity only to the extent permitted by and in accordance with the requirements of other subparts of this part.

(d) An activity permitted under paragraph (a) of this section may be conducted only if the mother and father are legally competent and have given their informed consent, except that the father's informed consent need not be secured if: (1) his identity or whereabouts cannot reasonably be ascertained; (2) he is not reasonably available; or (3) the pregnancy resulted from rape.

\section*{46.210 Activities involving the dead fetus, fetal material, or the placenta.}

Activities involving the dead fetus, macerated fetal material, or cells, tissues, or organs derived from a dead fetus shall be conducted only in accordance with any applicable State or local laws regarding such activities.

\section*{46.211 Modification or waiver of specific requirements.}

Upon the request of an applicant or sponsor (with the approval of its Institutional Review Board), the Secretary may modify or waive specific requirements of this subpart, with the approval of the Ethical Advisory Board after such opportunity for public comment as the Ethical Advisory Board considers appropriate in the particular instance. In making such decisions, the Secretary will consider whether the risks to the subject are so outweighed by the net of the benefit to the subject and the importance of the knowledge to be gained as to warrant such modification or waiver and that such benefit cannot be gained except through a modification or waiver. Any such modifications or waivers will be published as notices in the Federal Register.

\section*{Subpart C—Additional DHHS Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects}

\textbf{45.301 Applicability.}

(a) The regulations in this subpart are applicable to all biomedical and behavioral research conducted or supported by the Department of Health and Human Services involving prisoners as subjects.

(b) Nothing in this subpart shall be construed as indicating that compliance with the procedures set forth herein will authorize research involving prisoners as subjects, to the extent such research is limited or barred, by applicable State or local law.

(c) The requirements of this subpart are in addition to those imposed under the other subparts of this part.

\section*{46.302 Purpose.}

Inasmuch as prisoners may be under constraints because of their incarceration which could affect their ability to make a truly voluntary and uncoerced decision whether or not to participate as subjects in research, it is the purpose of this subpart to provide additional safeguards for the protection of prisoners involved in activities to which this subpart is applicable.

\section*{46.303 Definitions.}

As used in this subpart:

(a) "Secretary" means the Secretary of Health and Human Services and...
any other officer or employee of the Department of Health and Human Services to whom authority has been delegated.

(9) "DHHS" means the Department of Health and Human Services.

(c) "Prisoner" means any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of an order or commitment procedure which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.

(10) "Minimal risk" is the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.

§ 46.304 Composition of Institutional Review Boards where prisoners are involved.

In addition to satisfying the requirements in § 46.307 of this part, an Institutional Review Board, carrying out responsibilities under this part with respect to research covered by this part, shall also meet the following specific requirements:

(A) A majority of the Board (exclusive of prisoner members) shall have no association with the prison(s) involved, apart from their membership on the Board.

(B) At least one member of the Board shall be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity, except where a specific research project is reviewed by more than one Board only one Board need satisfy this requirement.

§ 46.305 Additional duties of the Institutional Review Board where prisoners are involved.

(a) In addition to all other responsibilities prescribed for Institutional Review Boards under this part, the Board shall review research covered by this subject and approve such research only if it finds that:

(1) the research under review represents one of the categories of research permissible under § 46.306(a)(7);

(2) any possible advantages accruing to the prisoners through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, sanitation and opportunity for exercise in the project, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited closed environment of the prison is impaired;

(3) the risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers;

(4) procedures for the selection of subjects within the prison are fair to all prisoners and inmates from arbitrary intervention by prison authorities or prisoners. Unless the principal investigator provides to the Board justification in writing for following some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project;

(5) the information is presented in a language which is understandable to the subject population;

(6) adequate assurance exists that parole boards will not take into account a prisoner's participation in the research in making decisions regarding parole; and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole;

(7) where the Board finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoner sentences, and for informing participants of this fact.

(b) The Board shall carry out each other duty as may be assigned by the Secretary.

(c) The institution shall certify to the Secretary, in such form and manner as the Secretary may require, that the duties of the Board under the section have been fulfilled.

§ 46.306 Permitted research involving prisoners.

(a) Biomedical or behavioral research conducted or supported by DHHS may involve prisoners in projects only if:

(1) the institution responsible for the conduct of the research has certified to the Secretary that its Institutional Review Board has approved the research under § 46.302 of this part; and

(2) in the judgment of the Secretary the proposed research involves no more than minimal risk and no more than inconvenience to the subjects;

(b) Study of prisoners as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;

(c) Research on conditions particularly affecting prisoners as a class (for example, values, trials and other research or hepatitis which is spread more prevalent in prison than elsewhere); and research on social and psychological problems such as addiction, drug addiction, and sexual assault provided that the study may proceed only after the Secretary has communicated with appropriate experts including experts in psychology, medicine, and ethics, as published notices, in the Federal Register, of his intent to approve such research or

(d) Research on practices, both innovative and accepted, which have the largest and reasonable probability of improving the health or well-being of the subject. In cases in which these studies require the assignment of prisoners in a manner consistent with the research approved by an IRB to control groups which may not benefit from the research, six study may proceed only after the Secretary has communicated with appropriate experts, including experts in psychology, medicine, and ethics, as published notices, in the Federal Register, of his intent to approve such research.

(e) Except as provided in paragraph (d) of this section, biomedical or behavioral research conducted or
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supported by DHHS shall not involve prisoners as subjects.

Subpart D—Additional DHHS Protections for Children Involved as Subjects in Research

Source: 45 FR 9133, Mar. 19, 1980; 46 FR 30212, June 18, 1981

§ 46.401 To what do these regulations apply?

(a) This subpart applies to all research involving children as subjects, conducted or supported by the Department of Health and Human Services.

(1) This includes research conducted by Department employees, except that each head of an Operating Division of the Department may adopt such nonstatutory, procedural modifications as may be appropriate from an administrative standpoint.

(2) It also includes research conducted or supported by the Department of Health and Human Services outside the United States, but is appropriate circumstances, the Secretary may, under paragraph (6) of § 46.101 of Subpart A, waive the applicability of some or all of the requirements of these regulations for research of this type.

(b) Exemptions as at § 46.101(b)(1) and (b)(3) through (b)(5) are applicable to this subpart. The exemption at § 46.101(b)(2) concerning educational research is also applicable to this subpart. However, the exemption at § 46.101(b)(2) for research involving surveys or interview procedures or collections of public behavior does not apply to research covered by this subpart, except for research involving observation of public behavior when the investigator does not participate in the activities being observed.

(c) The exceptions, additions, and provisions for waiver as they appear in paragraphs (a) through (b) of § 46.101 of Subpart A are applicable to this subpart.

§ 46.402 Definitions.

The definitions in § 46.102 of Subpart A are applicable to this subpart.

§ 46.403 Children.

Children are persons who have not attained the legal age for consent to treatment or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.

“Patient” means a child’s affirmative agreement to participate in research. Mere failure to object shall not be deemed to indicate agreement.

“Consent” means the agreement of parent(s) or guardian to the participation of the child’s or ward or wards in research.

“Guardians” means an individual who is authorized under applicable state or local law to consent on behalf of a child or to give medical care.

§ 46.404 IRB standards.

In addition to other responsibilities assigned to IRBs under this part, each IRB shall review research covered by this subpart and approve only research which satisfies the conditions of all applicable sections of this subpart.

§ 46.404 Research not involving greater than minimal risk.

DHHS will conduct or fund research in which the IRB finds that no greater than minimal risk to children is present, only if the IRB finds that adequate provisions are made for soliciting the consent of the children and the permission of their parents or guardians, as set forth in § 46.402.

§ 46.405 Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subject.

DHHS will conduct or fund research in which the IRB finds that more than minimal risk to children is present by an intervention or procedure that holds the prospect of direct benefit to the individual subject, provided that the IRB finds that adequate provisions are made for soliciting the consent of the children and the permission of their parents or guardians, as set forth in § 46.405.

§ 46.406 Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject’s disorder or condition.

DHHS will conduct or fund research in which the IRB finds that more than minimal risk to children is present by an intervention or procedure that does not hold out the prospect of direct benefit for the individual subject, but which is likely to contribute to the well-being of the subject only if the IRB finds that:

(a) the risk represents a minor increase over minimal risk;

(b) the intervention or procedure present experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;

(c) the intervention or procedure is likely to yield generalizable knowledge about the subjects’ disorder or condition which is of vital importance for the understanding or amelioration of the subjects’ disorder or condition; and

(d) adequate provisions are made for soliciting the consent of the children and the permission of their parents or guardians, as set forth in § 46.406.

§ 46.407 Research not otherwise approveable which presents an opportunity to alleviate a serious problem affecting the health or welfare of children.

DHHS will conduct or fund research in which the IRB does not believe measures to protect risks of harm as required by § 46.404, § 46.405, or § 46.406 apply if:

(a) the IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; and

(b) the Secretary, after consultation with a panel of experts in pertinent
disciplinary (for example, science, medicine, education, ethics, law) and the following opportunity for public review and comments has been determined either:

(1) that the research in fact satisfies the conditions of § 46.404, § 46.405, or § 46.406, as applicable, or (2) the following:

(i) the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;

(ii) the research will be conducted in accordance with sound ethical principles;

(iii) adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians, as set forth in § 46.408.

§ 46.408 Requirements for permission by parents or guardians and for assent by children.

(a) In addition to the determinations required under other applicable sections of this subpart, the IRB shall determine that adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent. In determining whether children are capable of assenting, the IRB shall take into account the age, maturity, and psychological state of the children involved. This judgment may be made for all children to be involved in research under a particular protocol, or for each child, as the IRB deems appropriate. If the IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only to the consent of the research, the assent of the children is not a necessary condition for proceeding with the research. Even where the IRB determines that the subjects are capable of assenting, the IRB may waive the assent requirement under circumstances in which consent may be waived in accord with § 46.116 of Subpart A.

(b) In addition to the determinations required under other applicable sections of this subpart, the IRB shall determine, in accordance with (a) to the extent that consent is required by § 46.116 of Subpart A, that adequate provisions are made for soliciting the permission of each child's parents or guardians. Where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient for research to be conducted under § 46.404 or § 46.405. Where research is covered by § 46.406 and § 46.407 and permission is to be obtained from parents, both parents must give their permission unless the parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

(c) In addition to the provisions for waiver contained in § 46.116 of Subpart A, if the IRB determines that a research protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the consent requirements in Subpart A of this part and paragraph (a) of this section provided an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and provided further that the waiver is not inconsistent with Federal, State, or local laws. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefits to the research subjects, and their age, maturity, status, and condition.

(d) Permission by parents or guardians shall be documented in accordance with and to the extent required by § 46.117 of Subpart A.

(e) When the IRB determines that assent is required, it shall also determine whether and how assent must be documented.

§ 46.409 Waiver.

(a) Children who are wards of the State or any other agency, institution, or entity may be included in research approved under § 46.404 or § 46.407 only if such research is:

(1) related to their status as wards; or

(2) conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

(b) If the research is approved under paragraph (a) of this section, the IRB shall require appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the ward as guardian or in loco parentis. One individual may serve as advocate for more than one child. The advocate shall be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research and who is not associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian(s).
Research activities involving no more than minimal risk and in which the only involvement of human subjects will be in one or more of the following categories (carried out through standard methods) may be reviewed by the Institutional Review Board through the expedited review procedure authorized in §46.110 of 45 CFR Part 46.

1. Collection of hair and nail clippings, in a nonsignificant manner, and permanent with respect to the individual, and permanent with respect to the individual, if patient care indicates a need for extraction.

2. Collection of excreta and external secretions including sweat, unconsented saliva, viscera removed at delivery, and amniotic fluid at the time of rupture of the membranes prior to or during labor.

3. Recording of data from subjects 15 years of age or older using noninvasive procedures commonly employed in clinical practice. This includes the use of physical sensors that are applied either to the surface of the body or at a distance and do not involve invasion of the subject or an invasion of the subject's privacy. It also includes such procedures as weighing, resting heart rate, electrocardiography, electromyography, thermography, detection of naturally occurring radioactive, diagnostic echography, and electroencephalography. It does not include exposure to electromagnetic radiation outside the visible range for example, x-rays, microwave.

4. Collection of blood samples by venipuncture, in amounts not exceeding 450 milliliters in an eight-week period and not more often than two times per week, from subjects 18 years of age or older and who are in good health and not pregnant.

5. Collection of both supra- and subgingival dental plaque and calculus, provided the procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques.

6. Voice recordings made for research purposes such as investigation of speech defects.

7. Moderate exercise by healthy volunteers.

8. The study of existing data, documents, records, pathological specimens, or diagnostic specimens.

9. Research on individual or group behavior or characteristics of individuals, such as studies of perception, cognition, genetic theory, or test development, where the investigator does not manipulate subjects' behavior and the research will not involve stress to subjects.

10. Research on drugs or devices for which an investigational new drug exemption or an investigational device exemption is not required.

Source: 45 FR 6392, January 26, 1981.
[Code of Federal Regulations]
[Title 21, Volume 1, Parts 1 to 99]
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TITLE 21—FOOD AND DRUGS

CHAPTER I—FOOD AND DRUG ADMINISTRATION,
DEPARTMENT OF HEALTH AND HUMAN SERVICES

PART 56—INSTITUTIONAL REVIEW BOARDS—Table of Contents

Subpart A—General Provisions

Sec. 56.101 Scope.

(a) This part contains the general standards for the composition, operation, and responsibility of an Institutional Review Board (IRB) that reviews clinical investigations regulated by the Food and Drug Administration under sections 305(i), 307(d), and 520(g) of the act, as well as clinical investigations that support applications for research or marketing permits for products regulated by the Food and Drug Administration, including food and color additives, drugs for human use, medical devices for human use, biological products for human use, and electronic products. Compliance with this part is intended to protect the rights and welfare of human subjects involved in such investigations.

(b) References in this part to regulatory sections of the Code of Federal Regulations are to chapter I of title 21, unless otherwise noted.

Subpart A—General Provisions

Sec. 56.102 Definitions.

As used in this part:


(b) Application for research or marketing permit includes:

(1) A color additive petition, described in part 71.

(2) Data and information regarding a substance submitted as part of the procedures for establishing that a substance is generally recognized as safe for a use which results or may reasonably be expected to result,
directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food, described in Sec. 170.35.

(3) A food additive petition, described in part 171.

(4) Data and information regarding a food additive submitted as part of the procedures regarding food additives permitted to be used on an interim basis pending additional study, described in Sec. 180.1.

(5) Data and information regarding a substance submitted as part of the procedures for establishing a tolerance for unavoidable contaminants in food and food-packaging materials, described in section 409 of the act.

(6) An investigational new drug application, described in part 312 of this chapter.

(7) A new drug application, described in part 314.

(8) Data and information regarding the bioavailability or bioequivalence of drugs for human use submitted as part of the procedures for issuing, amending, or repealing a bioequivalence requirement, described in part 320.

(9) Data and information regarding an over-the-counter drug for human use submitted as part of the procedures for classifying such drugs as generally recognized as safe and effective and not misbranded, described in part 330.

(10) Data and information regarding an antibiotic drug submitted as part of the procedures for issuing, amending, or repealing regulations for such drugs, described in Sec. 314A330 of this chapter.

(11) An application for a biological product license, described in part 681.

(12) Data and information regarding a biological product submitted as part of the procedures for determining that licensed biological products are safe and effective and not misbranded, as described in part 601.

(13) An application for an investigational Device Exemption, described in parts 812 and 813.

(14) Data and information regarding a medical device for human use submitted as part of the procedures for classifying such devices, described in part 869.

(15) Data and information regarding a medical device for human use submitted as part of the procedures for establishing, amending, or repealing a standard for such device, described in part 861.

(16) An application for premarket approval of a medical device for human use, described in section 515 of the act.

(17) A product development protocol for a medical device for human use, described in section 515 of the act.

(18) Data and information regarding an electronic product submitted as part of the procedures for establishing, amending, or repealing a standard for such products, described in section 358 of the Public Health Service Act.

(19) Data and information regarding an electronic product submitted
as part of the procedures for obtaining a variance from any electronic product performance standard, as described in Sec. 1010.4.

20. Data and information regarding an electronic product submitted as part of the procedures for granting, amending, or extending an exemption from a radiation safety performance standard, as described in Sec. 1010.5.

21. Data and information regarding an electronic product submitted as part of the procedures for obtaining an exemption from notification of a radiation safety defect or failure of compliance with a radiation safety performance standard, described in subpart D of part 1003.

(c) Clinical investigation means any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section 505(i), 507(c), or 520(g) of the act, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not include experiments that must meet the provisions of part 58, regarding nonclinical laboratory studies. The terms research, clinical research, clinical study, study, and clinical investigation are deemed to be synonymous for purposes of this part.

(d) Emergency use means the use of a test article on a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval.

(e) Human subject means an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient.

(f) Institution means any public or private entity or agency (including Federal, State, and other agencies). The term facility as used in section 520(g) of the act is deemed to be synonymous with the term institution for purposes of this part.

(g) Institutional Review Board (IRB) means any board, committee, or other group formally designated by an institution to review, to approve the initiation of, and to conduct periodic review of, biomedical research involving human subjects. The primary purpose of such review is to assure the protection of the rights and welfare of the human subjects. The term has the same meaning as the phrase institutional review committee as used in section 580(g) of the act.

(h) Investigator means an individual who actually conducts a clinical investigation (i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject) or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team.

(i) Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of
themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

(i) Sponsor means a person or other entity that initiates a clinical investigation, but that does not actually conduct the investigation, i.e., the test article is administered or dispensed to, or used involving, a subject under the immediate direction of another individual. A person other than an individual (e.g., a corporation or agency) that uses one or more of its own employees to conduct an investigation that it has initiated is considered to be a sponsor (not a sponsor-investigator), and the employees are considered to be investigators.

(ii) Sponsor-investigator means an individual who both initiates and actually conducts, alone or with others, a clinical investigation, i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject. The term does not include any person other than an individual, e.g., it does not include a corporation or agency. The obligations of a sponsor-investigator under this part include both those of a sponsor and those of an investigator.

(iii) Test article means any drug for human use, biological product for human use, medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the act or under sections 351 or 354-361I of the Public Health Service Act.

(a) IRB approval means the determination of the IRB that the clinical investigation has been reviewed and may be conducted at an institution within the constraints set forth by the IRB and by other institutional and Federal requirements.


Subpart A—General Provisions

Sec. 56.183 Circumstances in which IRB review is required.

(a) Except as provided in Secs. 56.104 and 56.105, any clinical investigation which must meet the requirements for prior submission (as required in parts 312, 812, and 813) to the Food and Drug Administration shall not be initiated unless that investigation has been reviewed and approved by, and remains subject to continuing review by, an IRB meeting the requirements of this part.

(c) Except as provided in Secs. 56.104 and 56.105, the Food and Drug Administration may decide not to consider in support of an application for a research or marketing permit any data or information that has been derived from a clinical investigation that has not been approved by, and that was not subject to initial and continuing review by, an IRB meeting the requirements of this part. The determination that a clinical
investigation may not be considered in support of an application for a research or marketing permit does not, however, relieve the applicant for such a permit of any obligation under any other applicable regulations to submit the results of the investigation to the Food and Drug Administration.
(c) Compliance with these regulations will in no way render inapplicable pertinent Federal, State, or local laws or regulations. [46 FR 8975, Jan. 27, 1981; 46 FR 14340, Feb. 27, 1981]

Sec. 56.104 Exceptions from IRB requirement.

The following categories of clinical investigations are exempt from the requirements of this part for IRB review:
(a) Any investigation which commenced before July 27, 1981 and was subject to requirements for IRB review under FDA regulations before that date, provided that the investigation remains subject to review of an IRB which meets the FDA requirements as effect before July 27, 1981.
(b) Any investigation commenced before July 27, 1981 and was not otherwise subject to requirements for IRB review under Food and Drug Administration regulations before that date.
(c) Emergency use of a test article, provided that such emergency use is reported to the IRB within 5 working days. Any subsequent use of the test article at the institution is subject to IRB review.
(d) Taste and food quality evaluations and consumer acceptance studies, if wholesome foods without additives are consumed or if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural, chemical, or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture. [46 FR 8975, Jan. 27, 1981, as amended at 56 FR 28028, June 18, 1991]

Sec. 56.105 Waiver of IRB requirement.

On the application of a sponsor or sponsor-investigator, the Food and Drug Administration may waive any of the requirements contained in these regulations, including the requirements for IRB review, for specific research activities or for classes of research activities, otherwise covered by these regulations.
Subpart B—Organization and Personnel

Sec. 56.107 IRB membership

(a) Each IRB shall have at least five members, with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution. The IRB shall be sufficiently qualified through the experience and expertise of its members, and the diversity of the members, including consideration of race, gender, cultural backgrounds, and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. In addition to possessing the professional competence necessary to review the specific research activities, the IRB shall be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards or professional conduct and practice. The IRB shall therefore include persons knowledgeable in these areas. If an IRB regularly reviews research that involves a vulnerable category of subjects, such as children, prisoners, pregnant women, or handicapped or mentally disabled persons, consideration shall be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with those subjects.

(b) Every nondiscriminatory effort will be made to ensure that no IRB consists entirely of men or entirely of women, including the institution’s consideration of qualified persons of both sexes, so long as no selection is made to the IRB on the basis of gender. No IRB may consist entirely of members of one profession.

(c) Each IRB shall include at least one member whose primary concerns are in the scientific area and at least one member whose primary concerns are in nonscientific areas.

(d) Each IRB shall include at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution.

(e) No IRB may have a member participate in the IRB’s initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB.

(f) No IRB may, in its discretion, invite individuals with competence in special areas to assist in the review of complex issues which require expertise beyond or in addition to that available on the IRB. These individuals may not vote with the IRB.

Subpart C—IRB Functions and Operations

Sec. 56.108 IRB functions and operations.

In order to fulfill the requirements of these regulations, each IRB shall:

(a) Follow written procedures: (1) For conducting its initial and continuing review of research and for reporting its findings and actions to the investigator and the institution; (2) for determining which projects require review more often than annually and which projects need verification from sources other than the investigator that no material changes have occurred since previous IRB review; (3) for ensuring prompt reporting to the IRB of changes in research activity and (4) for ensuring that changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except where necessary to eliminate apparent immediate hazards to the human subjects.

(b) Follow written procedure for ensuring prompt reporting to the IRB, appropriate institutional officials, and the Food and Drug Administration of: (1) Any unanticipated problems involving risks to human subjects or others; (2) any instance of serious or continuing noncompliance with these regulations or the requirements or determinations of the IRB; or (3) any suggestion or termination of IRB approval.

(c) Except when an expedited review procedure is used (see Sec. 56.110), review proposed research at convened meetings at which a majority of the members of the IRB are present, including at least one member whose primary concerns are in nonscientific areas. In order for the research to be approved, it shall receive the approval of a majority of those members present at the meeting.

(Information collection requirements in this section were approved by the Office of Management and Budget (OMB) and assigned OMB control number 0910-0130)

[46 FR 8975, Jan. 27, 1981, as amended at 56 FR 24028, June 18, 1991]

Sec. 56.109 IRB review of research.

(a) An IRB shall review and have authority to approve, require modifications in, to secure approval, or disapprove all research activities covered by these regulations.

(b) An IRB shall require that information given to subjects as part of informed consent is in accordance with Sec. 50.25. The IRB may require that information, in addition to that specifically mentioned in Sec. 50.25, be given to the subjects when in the IRB’s judgment the information would meaningfully add to the protection of the rights and
welfare of subjects.

(c) An IRB shall require documentation of informed consent in accordance with Sec. 50.27 of this chapter, except as follows:

(1) The IRB may, for some or all subjects, waive the requirement that the subject, or the subject's legally authorized representative, sign a written consent form if it finds that the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside the research context; or

(2) The IRB may, for some or all subjects, find that the requirements in Sec. 50.24 of this chapter for an exception from informed consent for emergency research are met.

(d) In cases where the documentation requirement is waived under paragraph (c)(1) of this section, the IRB may require the investigator to provide subjects with a written statement regarding the research.

(e) An IRB shall notify investigators and the institution in writing of its decision to approve or disapprove the proposed research activity, or of modifications required to secure IRB approval of the research activity. If the IRB decides to disapprove a research activity, it shall include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in person or in writing. For investigations involving an exception to informed consent under Sec. 50.24 of this chapter, an IRB shall promptly notify in writing the investigator and the sponsor of the research when an IRB determines that it cannot approve the research because it does not meet the criteria in the exception provided under Sec. 50.24(d) of this chapter or because of other relevant ethical concerns. The written notification shall include a statement of the reasons for the IRB's determination.

(f) An IRB shall conduct continuing review of research covered by these regulations at intervals appropriate to the degree of risk, but not less than once per year, and shall have authority to observe or have a third party observe the consent process and the research.

(g) An IRB shall provide in writing to the sponsor of research involving an exception to informed consent under Sec. 50.24 of this chapter a copy of information that has been publicly disclosed under Sec. 50.24(a)(7)(ii) and (a)(7)(iii) of this chapter. The IRB shall provide this information to the sponsor promptly so that the sponsor is aware that such disclosure has occurred. Upon receipt, the sponsor shall provide copies of the information disclosed to FDA.


Sec. 56.110 Expedited review procedures; for certain kinds of research involving no more than minimal risk, and for minor changes in approved research.

(a) The Food and Drug Administration has established, and published
in the Federal Register, a list of categories of research that may be
reviewed by the IRB through an expedited review procedure. The list will
be amended, as appropriate, through periodic republication in the
Federal Register.

(5) An IRB may use the expedited review procedure to review either
or both of the following: (1) Some or all of the research appearing on
the list and found by the reviewer(s) to involve no more than minimal
risk, (2) minor changes in previously approved research during the
period (of 1 year or less) for which approval is authorized. Under an
expedited review procedure, the review may be carried out by the IRB
chairperson or by one or more experienced reviewers designated by the
IRB chairperson from among the members of the IRB. In reviewing the
research, the reviewers may exercise all of the authorities of the IRB
except that the reviewers may not disapprove the research. A research
activity may be disapproved only after review in accordance with the
nonexpedited review procedure set forth in Sec. 56.108(c).

(c) Each IRB which uses an expedited review procedure shall adopt a
method for keeping all members advised of research proposals which have
been approved under the procedure.

(d) The Food and Drug Administration may restrict, suspend, or
terminate an institution's or IRB's use of the expedited review
procedure when necessary to protect the rights or welfare of subjects.
[46 FR 8975, Jan. 27, 1981, as amended at 56 FR 28029, June 18, 1991]

Sec. 56.111 Criteria for IRB approval of research.

(a) In order to approve research covered by these regulations, the
IRB shall determine that all of the following requirements are satisfied:

(1) Risks to subjects are minimized; (ii) by using procedures which
are consistent with sound research design and which do not unnecessarily
expose subjects to risk, and (ii) whenever appropriate, by using
procedures already being performed on the subjects for diagnostic or
treatment purposes.

(2) Risks to subjects are reasonable in relation to anticipated
benefits, if any, to subjects, and the importance of the knowledge that
may be expected to result. In evaluating risks and benefits, the IRB
should consider only those risks and benefits that may result from the
research (as distinguished from risks and benefits of therapies that
subjects would receive even if not participating in the research). The
IRB should not consider possible long-range effects of applying
knowledge gained in the research (for example, the possible effects of the
research on public policy) in assessing research risks that fall
within the purview of its responsibility.

(3) Selection of subjects is equitable. In making this assessment
the IRB should take into account the purposes of the research and the
setting in which the research will be conducted and should be
particularly cognizant of the special problems of research involving
vulnerable populations, such as children, prisoners, pregnant women, handicapped, or mentally disabled persons, or economically or educationally disadvantaged persons.

(4) Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with and to the extent required by part 50.

(5) Informed consent will be appropriately documented, in accordance with and to the extent required by Sec. 50.27.

(6) Where appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

(7) Where appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

(b) When some or all of the subjects, such as children, prisoners, pregnant women, handicapped, or mentally disabled persons, or economically or educationally disadvantaged persons, are likely to be vulnerable to coercion or undue influence additional safeguards have been included in the study to protect the rights and welfare of these subjects.

[46 FR 8975, Jan. 27, 1981, as amended at 56 FR 28029, June 18, 1991]

Sec. 56.112 Review by institution.

Research covered by these regulations that has been approved by an IRB may be subject to further appropriate review and approval or disapproval by officials of the institution. However, those officials may not approve the research if it has not been approved by an IRB.

Sec. 56.113 Suspension or termination of IRB approval of research.

An IRB shall have authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB’s requirements or that has been associated with unexpected serious harm to subjects. Any suspension or termination of approval shall include a statement of the reasons for the IRB’s action and shall be reported promptly to the investigator, appropriate institutional officials, and the Food and Drug Administration.

Sec. 56.114 Cooperative research.

In complying with these regulations, institutions involved in multi-institutional studies may use joint review, reliance upon the review of another qualified IRB, or similar arrangements aimed at avoidance of duplication of effort.
Subpart D—Records and Reports

Sec. 56.115 IRB records.

(a) An institution, at where appropriate an IRB, shall prepare and maintain adequate documentation of IRB activities, including the following:

(1) Copies of all research proposals reviewed, scientific evaluations, if any, that accompany the proposals, approved sample consent documents, progress reports submitted by investigators, and reports of injuries to subjects.

(2) Minutes of IRB meetings which shall be in sufficient detail to show attendance at the meetings; actions taken by the IRB; the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution.

(3) Records of continuing review activities.

(4) Copies of all correspondence between the IRB and the investigators.

(5) A list of IRB members identified by name; earned degrees; representative capacity; indications of experience such as board certifications, licenses, etc., sufficient to describe each member's chief anticipated contributions to IRB deliberations; and any employment or other relationship between each member and the institution; for example: full-time employee, part-time employee, a member of governing panel or board, stockholder, paid or unpaid consultant.

(6) Written procedures for the IRB as required by Sec. 56.108 (a) and (b).

(7) Statements of significant new findings provided to subjects, as required by Sec. 50.25.

(b) The records required by this regulation shall be retained for at least 3 years after completion of the research, and the records shall be accessible for inspection and copying by authorized representatives of the Food and Drug Administration at reasonable times and in a reasonable manner.

(c) The Food and Drug Administration may refuse to consider a clinical investigation in support of an application for a research or marketing permit if the institution or the IRB that reviewed the investigation refuses to allow an inspection under this section.

(Information collection requirements in this section were approved by the Office of Management and Budget (OMB) and assigned OMB control number 0910-0130)

46 FR 8975, Jan. 27, 1981, as amended at 56 FR 28029, June 18, 1991)
Subpart E—Administrative Actions for Noncompliance

Sec. 56.120 Lesse administrative actions.

(a) If apparent noncompliance with these regulations in the operation of an IRB is observed by an FDA investigator during an inspection, the inspector will present an oral or written summary of observations to an appropriate representative of the IRB. The Food and Drug Administration may subsequently send a letter describing the noncompliance to the IRB and to the parent institution. The agency will require that the IRB or the parent institution respond to this letter within a time period specified by FDA and describe the corrective actions that will be taken by the IRB, the institution, or both to achieve compliance with these regulations.

(b) On the basis of the IRB's or the institution's response, FDA may schedule a reinspection to confirm the adequacy of corrective actions. In addition, until the IRB or the parent institution takes appropriate corrective action, the agency may:

(1) Withhold approval of new studies subject to the requirements of this part that are conducted at the institution or reviewed by the IRB;
(2) Direct that no new subjects be added to ongoing studies subject to this part;
(3) Terminate ongoing studies subject to this part when doing so would not endanger the subjects; or
(4) When the apparent noncompliance creates a significant threat to the rights and welfare of human subjects, notify relevant State and Federal regulatory agencies and other parties with a direct interest in the agency's action of the deficiencies in the operation of the IRB.

(c) The parent institution is presumed to be responsible for the operation of an IRB, and the Food and Drug Administration will ordinarily direct any administrative action under this subpart against the institution. However, depending on the evidence of responsibility for deficiencies, determined during the investigation, the Food and Drug Administration may require its administrative actions to the IRB or to a component of the parent institution determined to be responsible for forestal designation of the IRB.

Sec. 56.121 Disqualification of an IRB or an institution.

(a) Whenever the IRB or the institution has failed to take adequate steps to correct the noncompliance stated in the letter sent by the agency under Sec. 56.120(a), and the Commissioner of Food and Drugs determines that this noncompliance may justify the disqualification of the IRB or of the parent institution, the Commissioner will institute proceedings in accordance with the requirements for a regulatory hearing set forth in part 16.

(b) The Commissioner may disqualify an IRB or the parent institution if the Commissioner determines that:

(1) The IRB has refused or repeatedly failed to comply with any of
the regulations set forth in this part, and

(2) The noncompliance adversely affects the rights or welfare of the human subjects in a clinical investigation.

(c) If the Commissioner determines that disqualification is appropriate, the Commissioner will issue an order that explains the basis for the determination and that prescribes any actions to be taken with regard to ongoing clinical research conducted under the review of the IRB. The Food and Drug Administration will send notice of the disqualification to the IRB and the parent institution. Other parties with a direct interest, such as sponsors and clinical investigators, may also be sent a notice of the disqualification. In addition, the agency may elect to publish a notice of its action in the Federal Register.

(d) The Food and Drug Administration will not approve an application for a research permit for a clinical investigation that is to be under the review of a disqualified IRB or that is to be conducted at a disqualified institution, and it may refuse to consider in support of a marketing permit the data from a clinical investigation that was reviewed by a disqualified IRB or conducted at a disqualified institution, unless the IRB or the parent institution is reinstated as provided in Sec. 56.123.

Sec. 56.122 Public disclosure of information regarding revocation.

A determination that the Food and Drug Administration has disqualified an institution and the administrative record regarding that determination are disclosable to the public under part 20.

Sec. 56.123 Reinstatement of an IRB or an institution.

An IRB or an institution may be reinstated if the Commissioner determines, upon an evaluation of a written submission from the IRB or institution that explains the corrective action that the institution or IRB plans to take, that the IRB or institution has provided adequate assurance that it will operate in compliance with the standards set forth in this part. Notification of reinstatement shall be provided to all persons notified under Sec. 56.121(c).

Sec. 56.124 Actions alternative or additional to disqualification.

Disqualification of an IRB or of an institution is independent of, and neither in lieu of nor a precondition to, other proceedings or actions authorized by the Act. The Food and Drug Administration may, at any time, through the Department of Justice institute any appropriate judicial proceedings (civil or criminal) and any other appropriate regulatory action, in addition to or in lieu of, and before, at the time of, or after, disqualification. The agency may also refer pertinent matters to another Federal, State, or local government agency for any action that that agency determines to be appropriate.
TITLE 21—FOOD AND DRUGS

PART 50—PROTECTION OF HUMAN SUBJECTS—Table of Contents

Subpart A—General Provisions

Sec. 50.1 Scope.

(a) This part applies to all clinical investigations regulated by the Food and Drug Administration under sections 505(i) and 520(a) of the Federal Food, Drug, and Cosmetic Act, as well as clinical investigations that support applications for research or marketing permits for products regulated by the Food and Drug Administration, including food and color additives, drugs for human use, medical devices for human use, biological products for human use, and electronic products. Additional specific obligations and commitments of, and standards of conduct for, persons who sponsor or monitor clinical investigations involving particular test articles may also be found in other parts (e.g., parts 312 and 812). Compliance with these parts is intended to protect the rights and safety of subjects involved in investigations filed with the Food and Drug Administration pursuant to sections 406, 409, 502, 503, 505, 510, 513-516, 518-520, 721, and 801 of the Federal Food, Drug, and Cosmetic Act and sections 351 and 354-360F of the Public Health Service Act.

(b) References in this part to regulatory sections of the Code of Federal Regulations are to chapter I of title 21, unless otherwise noted.


Effective Date Note: At 64 FR 399, Jan. 5, 1999, Sec. 50.2 was amended by removing "" from the first sentence of paragraph (a), and by removing "" from the last sentence of paragraph (a), effective May 20, 1999.
Sec. 59.3 Definitions.

As used in this part:
(a) Act means the Federal Food, Drug, and Cosmetic Act, as amended
(secs. 201—902, 52 Stat. 1040 et seq.; as amended (21 U.S.C. 321—392)).
(b) Application for research or marketing permit includes:
(1) A color additive petition, described in part 71.
(2) A food additive petition, described in parts 171 and 571.
(3) Data and information about a substance submitted as part of the
procedures for establishing that the substance is generally recognized
as safe for use that results or may reasonably be expected to result,
directly or indirectly, in its becoming a component or otherwise
affecting the characteristics of any food, described in Secs. 170.30 and
570.30.
(4) Data and information about a food additive submitted as part of the
procedures for food additives permitted to be used on an interim
basis pending additional study, described in Sec. 180.1.
(5) Data and information about a substance submitted as part of the
procedures for establishing a tolerance for unavoidable contaminants in
food and food-packaging materials, described in section 406 of the act.
(6) An investigational new drug application, described in part 312
of this chapter.
(7) A new drug application, described in part 314.
(8) Data and information about the bioavailability or bioequivalence
of drugs for human use submitted as part of the procedures for issuing,
amending, or repealing a bioequivalence requirement, described in part
320.
(9) Data and information about an over-the-counter drug for human
use submitted as part of the procedures for classifying these drugs as
generally recognized as safe and effective and not misbranded, described
in part 330.
(10) Data and information about a prescription drug for human use
submitted as part of the procedures for classifying these drugs as
generally recognized as safe and effective and not misbranded, described
in this chapter.
(11) Data and information about an antibiotic drug submitted as part
of the procedures for issuing, amending, or repealing regulations for
these drugs, described in Sec. 314.300 of this chapter.
(12) An application for a biological product license, described in
part 601.
(13) Data and information about a biological product submitted as
part of the procedures for determining that licensed biological products
are safe and effective and not misbranded, described in part 601.
(14) Data and information about an in vitro diagnostic product
submitted as part of the procedures for establishing, amending, or
repealing a standard for these products, described in part 809.
(15) An Application for an Investigational Device Exemption,
described in part 512.
(16) Data and information about a medical device submitted as part of the procedures for classifying these devices, described in section 513.
(17) Data and information about a medical device submitted as part of the procedures for establishing, amending, or repealing a standard for these devices, described in section 514.
(18) An application for premarket approval of a medical device, described in section 515.
(19) A product development protocol for a medical device, described in section 515.
(20) Data and information about an electronic product submitted as part of the procedures for establishing, amending, or repealing a standard for these products, described in section 358 of the Public Health Service Act.
(21) Data and information about an electronic product submitted as part of the procedures for obtaining a variance from any electronic product performance standard, as described in Sec. 1010.4.
(22) Data and information about an electronic product submitted as part of the procedures for granting, amending, or extending an exemption from a radiation safety performance standard, as described in Sec. 1010.5.
(c) Clinical investigation means any experiment that involves a test article and one or more human subjects and that either is subject to requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the act, or is not subject to requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not include experiments that are subject to the provisions of part 58 of this chapter, regarding nonclinical laboratory studies.
(d) Investigator means an individual who actually conducts a clinical investigation, i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject, or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team.
(e) Sponsor means a person who initiates a clinical investigation, but who does not actually conduct the investigation, i.e., the test article is administered or dispensed to or used involving, a subject under the immediate direction of another individual. A person other than an individual (e.g., corporation or agency) that uses one or more of its own employees to conduct a clinical investigation it has initiated is considered to be a sponsor (not a sponsor-investigator), and the employees are considered to be investigators.
(f) Sponsor-investigator means an individual who both initiates and
actually conducts, alone or with others, a clinical investigation, i.e.,
under whose immediate direction the test article is administered or
dispensed to, or used involving, a subject. The term does not include
any person other than an individual, e.g., corporation or agency.
(g) Human subject means an individual who is or becomes a
participant in research, either as a recipient of the test article or as
a control. A subject may be either a healthy human or a patient.
(h) Institution means any public or private entity or agency
(including Federal, State, and other agencies). The word facility as
used in section 520(g) of the act is deemed to be synonymous with
the term institution for purposes of this part.
(i) Institutional review board (IRB) means any board, committee, or
other group formally designated by an institution to review biomedical
research involving humans as subjects, to approve the initiation of and
conduct periodic review of such research. The term has the same meaning as
the phrase institutional review committee as used in section 520(g) of the
act.
(j) Test article means any drug (including a biological product for
human use), medical device for human use, human food additive, color
additive, electronic product, or any other article subject to regulation
under the act or under sections 351 and 354-360F of the Public Health
Service Act (42 U.S.C. 262 and 263b-263n).
(k) Minimal risk means that the probability and magnitude of harm or
discomfort anticipated in the research are not greater in and of
themselves than those ordinarily encountered in daily life or during the
performance of routine physical or psychological examinations or tests.
(l) Legally authorized representative means an individual or
judicial or other body authorized under applicable law to consent on
behalf of a prospective subject to the subject's participation in the
procedure(s) involved in the research.
(m) Family member means any one of the following legally competent
persons: Spouse; parents; children (including adopted children);
brothers, sisters, and spouses of brothers and sisters; and any
individual related by blood or affinity whose close association with the
subject is the equivalent of a family relationship.

2, 1996; 62 FR 39440, July 23, 1997; 64 FR 399, Jan. 5, 1999]

Effective Date Note: At 64 FR 399, Jan. 5, 1999, Sec. 50.3 was
amended by removing and reserving paragraph (b)(11), and by removing ",
507(d)," from paragraph (c), effective May 20, 1999.

4
Subpart B—Informed Consent of Human Subjects

Sec. 50.20 General requirements for informed consent.

Source: 46 FR 8951, Jan. 27, 1981, unless otherwise noted.

Except as provided in Secs. 50.23 and 50.24, no investigator may involve a human being as a subject in research covered by these regulations unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the representative shall be in language understandable to the subject or the representative. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence.

[46 FR 8951, Jan. 27, 1981, as amended at 64 FR 10942, Mar. 8, 1999]

Sec. 50.23 Exception from general requirements.

(a) The obtaining of informed consent shall be deemed feasible unless, before use of the test article (except as provided in paragraph (b) of this section), both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the following:

(1) The human subject is confronted by a life-threatening situation necessitating the use of the test article.

(2) Informed consent cannot be obtained from the subject because of an inability to communicate with, or obtain legally effective consent from, the subject.

(3) Time is not sufficient to obtain consent from the subject's legal representative.

(4) There is available no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the subject.

(b) If immediate use of the test article is, in the investigator's opinion, required to preserve the life of the subject, and time is not sufficient to obtain the independent determination required in paragraph (a) of this section in advance of using the test article, the determinations of the clinical investigator shall be made and, within 5 working days after the
use of the article, be reviewed and evaluated in writing by a physician who is not participating in the clinical investigation.

(c) The documentation required in paragraph (a) or (b) of this section shall be submitted to the IRRS within 5 working days after the use of the test article.

(d)(1) The Commissioner may also determine that obtaining informed consent is not feasible when the Assistant Secretary of Defense (Health Affairs) requests such a determination in connection with the use of an investigational drug (including a biological product) in a specific protocol under an investigational new drug application (IND) sponsored by the Department of Defense (DOD). DOD's request for a determination that obtaining informed consent from military personnel is not feasible must be limited to a specific military operation involving combat or the immediate threat of combat. The request must also include a written justification supporting the conclusions of the physician(s) responsible for the medical care of the military personnel involved and the investigator(s) identified in the IND that a military combat exigency exists because of special military combat (actual or threatened) circumstances in which, in order to facilitate the accomplishment of the military mission, preservation of the health of the individual and the safety of other personnel require that a particular treatment be provided to a specified group of military personnel, without regard to what might be any individual's personal preference for no treatment or for some alternative treatment. The written request must also include a statement that a duly constituted institutional review board has reviewed and approved the use of the investigational drug without informed consent. The Commissioner may find that informed consent is not feasible only when withholding treatment would be contrary to the best interests of military personnel and there is no available satisfactory alternative therapy.

(2) In reaching a determination under paragraph (d)(1) of this section that obtaining informed consent is not feasible and withholding treatment would be contrary to the best interests of military personnel, the Commissioner will review the request submitted under paragraph (d)(1) of this section and take into account all pertinent factors, including, but not limited to:

(i) The extent and strength of the evidence of the safety and effectiveness of the investigational drug for the intended use;

(ii) The context in which the drug will be administered, e.g., whether it is intended for use in a battlefield or hospital setting or whether it will be self-administered or will be administered by a health professional;

(iii) The nature of the disease or condition for which the preventive or therapeutic treatment is intended; and

(iv) The nature of the information to be provided to the recipient of the drug concerning the potential benefits and risks of taking or not taking the drug.

(3) The Commissioner may request a recommendation from appropriate
expert before reaching a determination on a request submitted under paragraph (d)(1) of this section.

(4) A determination by the Commissioner that obtaining informed consent is not feasible and withholding treatment would be contrary to the best interests of military personnel will expire at the end of 1 year, unless renewed at DOD's request, or when DOD informs the Commissioner that the specific military operation creating the need for the use of the investigational drug has ended, whichever is earlier. The Commissioner may also revoke this determination based on changed circumstances.


Effective Date Note: At 64 FR 399, Jan. 5, 1999, in Sec. 50.23, paragraph (d)(1) was amended by removing the phrase "(including an antibiotic or biological product)" and adding in its place the phrase "(including a biological product)" effective May 20, 1999.

Sec. 50.24 Exception from informed consent requirements for emergency research.

(a) The IRB responsible for the review, approval, and continuing review of the clinical investigation described in this section may approve that investigation without requiring that informed consent of all research subjects be obtained if the IRB (with the concurrence of a licensed physician who is a member of or consultant to the IRB and who is not otherwise participating in the clinical investigation) finds and documents each of the following:

1. The human subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.

2. Obtaining informed consent is not feasible because:

(i) The subjects will not be able to give their informed consent as a result of their medical condition;

(ii) The intervention under investigation must be administered before consent from the subjects' legally authorized representatives is feasible; and

(iii) There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.

3. Participation in the research holds out the prospect of direct benefit to the subjects because:

(i) Subjects are facing a life-threatening situation that necessitates intervention;
(ii) Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects; and

(iii) Risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.

(4) The clinical investigation could not practically be carried out without the waiver.

(5) The proposed investigational plan defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a legally authorized representative for each subject within that window of time and, if feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent. The investigator will summarize efforts made to contact legally authorized representatives and make this information available to the IRB at the time of continuing review.

(6) The IRB has reviewed and approved informed consent procedures and an informed consent document consistent with Sec. 50.25. These procedures and the informed consent document are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is feasible. The IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a subject's participation in the clinical investigation consistent with paragraph (e)(7)(v) of this section.

(7) Additional protections of the rights and welfare of the subjects will be provided, including, at least:

(i) Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn;

(ii) Public disclosure to the communities in which the clinical investigation will be conducted and from which the subjects will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits;

(iii) Public disclosure of sufficient information following completion of the clinical investigation to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results;

(iv) Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation; and

(v) If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the investigator has committed, if feasible, to attempting to contact within the
therapeutic window the subject's family member who is not a legally authorized representative, and asking whether he or she objects to the subject's participation in the clinical investigation. The investigator will summarize effects made to contact family members and make this information available to the IRB at the time of continuing review.

(b) The IRB is responsible for ensuring that procedures are in place to inform, as the earliest feasible opportunity, each subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, of the subject's inclusion in the clinical investigation, the details of the investigation and other information contained in the informed consent document. The IRB shall also ensure that there is a procedure to inform the subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, that he or she may discontinue the subject's participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. If a legally authorized representative or family member is told about the clinical investigation and the subject's condition improves, the subject is also to be informed as soon as feasible. If a subject is entered into a clinical investigation with waived consent and the subject dies before a legally authorized representative or family member can be contacted, information about the clinical investigation is to be provided to the subject's legally authorized representative or family member, if feasible.

(c) The IRB determinations required by paragraph (a) of this section and the documentation required by paragraph (c) of this section are to be retained by the IRB for at least 3 years after completion of the clinical investigation, and the records shall be accessible for inspection and copying by FDA in accordance with Sec. 56.115(b) of this chapter.

(d) Protocols involving an exception to the informed consent requirement under this section must be performed under a separate investigational new drug application (IND) or investigational device exemption (IDE) that clearly identifies such protocols as protocols that may include subjects who are unable to consent. The submission of those protocols to a separate IND/IDE is required even if an IND for the same drug product or an IDE for the same device already exists. Applications for investigations under this section may not be submitted as amendments under Secs. 312.30 or 812.35 of this chapter.

(e) If an IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception provided under paragraph (a) of this section or because of other relevant ethical concerns, the IRB must document its findings and provide these findings promptly in writing to the clinical investigator and to the sponsor of the clinical investigation. The sponsor of the clinical investigation must promptly disclose this information to FDA and to the sponsor's clinical investigators who are participating or are
asked to participate in this or a substantially equivalent clinical investigation of the sponsor, and to other IRBs that have been, or are, asked to review this or a substantially equivalent investigation by that sponsor.

Sec. 50.25 Elements of informed consent.

(a) Basic elements of informed consent. In seeking informed consent, the following information shall be provided to each subject:

(1) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental.

(2) A description of any reasonably foreseeable risks or discomforts to the subject.

(3) A description of any benefits to the subject or to others which may reasonably be expected from the research.

(4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.

(5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained and that notes the possibility that the Food and Drug Administration may inspect the records.

(6) For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.

(7) An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject.

(8) A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

(b) Additional elements of informed consent. When appropriate, one or more of the following elements of information shall also be provided to each subject:

(1) A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable.

(2) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.

(3) Any additional costs to the subject that may result from participation in the research.

(4) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the
subject.

(5) A statement that significant new findings developed during the course of the research which may relate to the subject’s willingness to continue participation will be provided to the subject.

(6) The approximate number of subjects involved in the study.

(c) The informed consent requirements in these regulations are not intended to preempt any applicable Federal, State, or local laws which require additional information to be disclosed for informed consent to be legally effective.

(d) Nothing in these regulations is intended to limit the authority of a physician to provide emergency medical care to the extent the physician is permitted to do so under applicable Federal, State, or local law.

Sec. 50.27 Documentation of informed consent.

(a) Except as provided in Sec. 50.109(c), informed consent shall be documented by the use of a written consent form approved by the IRB and signed and dated by the subject or the subject’s legally authorized representative at the time of consent. A copy shall be given to the person signing the form.

(b) Except as provided in Sec. 50.109(c), the consent form may be either of the following:

(1) A written consent document that embodies the elements of informed consent required by Sec. 50.25. This form may be read to the subject or the subject’s legally authorized representative, but, in any event, the investigator shall give either the subject or the representative adequate opportunity to read it before it is signed.

(2) A short form written consent document stating that the elements of informed consent required by Sec. 50.25 have been presented orally to the subject or the subject’s legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Also, the IRB shall approve a written summary of what is to be said to the subject or the representative. Only the short form itself is to be signed by the subject or the representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining the consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the representative in addition to a copy of the short form.

B. FOOD AND DRUG ADMINISTRATION REGULATIONS AND POLICIES

i. INTRODUCTION

The Food and Drug Administration (FDA) regulates but does not, for the most part, support or conduct research. Its regulatory mandate, therefore, differs substantially from other DHHS agencies and other departments and agencies that conduct and support a significant amount of research. While the structural and functional requirements for IRBs in FDA regulations are identical to DHHS regulations, the substantive provisions differ in several significant respects. IRBs should note that where a protocol is subject to review under both FDA and DHHS human subjects regulations, both sets of regulations apply, and the requirements of both sets of regulations must be met. This situation may arise, for example, with Treatment Investigational New Drug Exemptions (see discussion of Treatment INDs, below) or when applying the provisions on waiver of documentation of informed consent, in cases where both the FDA and DHHS have jurisdiction over the research.

FDA regulations pertaining to human subjects research are codified at 21 CFR 50 [Protection of Human Subjects (containing the informed consent requirements)] and 21 CFR 56 [Institutional Review Board].

In addition to the information provided in this Section, see the various FDA Information Sheets and guidelines (e.g., IRB Information Sheets, Clinical Investigator Information Sheets, Guidance for the Monitoring of Clinical Investigations, and Compliance Program Guidance Manual: Chapter 48, Bioresearch Monitoring - Human Drugs, Institutional Review Board). For further information on FDA human subjects research regulations, contact:

Mr. Richard M. Klein
Office of Health Affairs (HFY-20)
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857
(301) 443-1382

ii. COMPARING FDA AND DHHS HUMAN SUBJECTS REGULATIONS

The DHHS regulations (45 CFR 46) apply to research involving human subjects conducted by DHHS or supported in whole or in part by DHHS. The FDA regulations (21 CFR 50 and 56) apply to all research involving products regulated by the FDA, including research and marketing permits for drugs, biological products, or medical devices for human use, food and color additives, or electronic products.

Federal funds do not need to be involved. When research involving products regulated by the FDA is funded by DHHS, both DHHS and FDA regulations apply. This Section describes significant differences between FDA and DHHS regulations, including departures from the new Federal Policy.
COMPARISON OF REGULATIONS

IRB Regulations

§312.120 (FDA)
§46.101(b) (DHHS)

The FDA regulations provide criteria for accepting foreign clinical studies not conducted under an Investigational New Drug Application (IND). The DHHS regulations allow a department or agency head to determine that if procedures prescribed by a foreign institution afford protections at least equivalent to DHHS regulations, the department or agency head may approve the substitution of foreign procedures. [See also 21 CFR 812.1.]

§56.102 (FDA)
§46.102 (DHHS)

FDA definitions are included for terms specific to the type of research covered by the FDA regulations (test article, application for research or marketing permit, clinical investigation). A definition for emergency use is provided. The definition of "IRB approval," added as a result of the Federal Policy, substitutes the term "clinical investigation" for the term "research" used in the Federal Policy [§56.102(m)]. FDA also adopted the Federal Policy’s new wording for the definition of "minimal risk" ("the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests") [§56.102(i)].

§46.103 (DHHS)

DHHS requires that institutions provide an Assurance of Compliance with human subjects regulations, which is negotiated with CFRR. FDA does not require Assurances of Compliance, but does require that IRBs have written policies and procedures.

§56.104 (FDA)

Unlike DHHS, FDA exemptions from prospective IRB review the "emergency use" of a test article in specific situations. FDA added the Federal Policy’s new "taste testing" exemption at §56.104(d).

§56.105 (FDA)

FDA provides for sponsors and sponsor-investigators to request a waiver of IRB review requirements (not informed consent requirements). DHHS regulations do not have a similar provision.
DHHS requires prompt reporting of unanticipated problems to the Secretary. FDA does not specify that a similar report be made by the IRB to the FDA Commissioner, but that the IRB have and follow written procedures to ensure that such reporting is done by the sponsor and clinical investigator.

Unlike DHHS, FDA does not provide that an IRB may waive the requirement for signed consent when the principal risk is a breach of confidentiality because FDA does not regulate studies that would fall into that category of research. (Both regulations allow for IRB waiver of documentation of informed consent in instances of minimal risk.)

FDA does not include research on behavior or characteristics of groups or individuals such as studies of perception, cognition, game theory, or test development (DHHS activity #9) in its list of research activities that may be reviewed through expedited review procedures, because those types of studies are not regulated by FDA.

FDA regulations do not discuss administrative matters dealing with grants and contracts because they are irrelevant to the scope of the Agency's regulation. (Both regulations make allowances for review of multi-institutional studies.)

DHHS, but not FDA, requires the IRB or institution to report changes in membership. FDA has neither an assurance mechanism nor files of IRB membership; there is therefore no reason for FDA to be informed about changes in membership.

FDA may refuse to consider a study in support of a research or marketing permit if the IRB or the institution refuses to allow FDA to inspect IRB records. DHHS has no such provision because it does not issue research or marketing permits.
§§56.120-124 (FDA)

FDA regulations provide sanctions for noncompliance with regulations. There is no parallel DHHS regulation, other than §46.123, which permits early termination of research support and evaluation of applications and proposals in light of prior noncompliance.

Informed Consent Regulations

§50.3(c)

FDA adopted the Federal Policy's new wording for the definition of "minimal risk" ("the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests") (§§6.102(f)).

§50.23 (FDA)

FDA, but not DHHS, provides explicit guidance for an exemption from the informed consent requirements in emergency situations. The provision is based on a statutory requirement in the Medical Device Amendments of 1976, and may be used in investigations involving drugs, devices, and other FDA-regulated products in situations described in §50.23.

§46.116(c) and (d) (DHHS)

DHHS provides for waiving or altering elements of informed consent under certain conditions. FDA has no such provision because the types of studies that would qualify for waiver or alteration are either not regulated by FDA or are covered by the emergency treatment provisions of §50.23.

§50.25(a)(5) (FDA)
§46.116(a)(5) (DHHS)

FDA explicitly requires that subjects be informed that FDA may inspect the records of the study because FDA may occasionally examine a subject's medical records as they pertain to the study. While DHHS has the right to inspect records of studies it funds, it does not impose the same informed consent requirement because of the infrequency with which the Department actually inspects subject records.
APPENDIX K
An Act respecting
Access to documents
held by public bodies
and the Protection of
personal information

R.S.Q., chapter A-2.1

Updated to 15 January 1991
Last amendment: 1 January 1991

Québec
AN ACT RESPECTING ACCESS TO DOCUMENTS HELD BY PUBLIC BODIES AND THE PROTECTION OF PERSONAL INFORMATION

CHAPTER I
APPLICATION AND INTERPRETATION

Documents.  1. This Act applies to documents kept by a public body in the exercise of its duties, whether it keeps them itself or through the agency of a third party.

Documents.  This Act applies whether the documents are recorded in writing or print, on sound tape or film, in computerized form, or otherwise.

1982, c. 30, s. 1.

Exception.  2. This Act does not apply to:
   (1) acts and registers of civil status;
   (2) the documents registered in a registry office or the registers, lists, indexes or any other books kept there;
   (3) the central register of matrimonial regimes or the notices registered therein;
   (4) private archives referred to in section 27 of the Archives Act (chapter A-21.1).

1982, c. 30, s. 2; 1983, c. 38, s. 54.

Adoption.  2.1. Access to documents contained in a file respecting the adoption of a person held by a public body and the protection of the personal information contained in such a file are governed by the Civil Code of Québec and other legislation respecting adoption.

Application.  In respect of the personal information contained in such a file, this Act applies only to allow the Commission to exercise the duty contemplated in paragraph 5 of section 123 and the powers contemplated in subparagraph 2 of the first paragraph of section 127 and in section 128.1.

1987, c. 68, s. 2.

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municipality, as well as any body otherwise under municipal authority.
(2) an urban or regional community, an intermunicipal board, an
intermunicipal transit corporation, an intermunicipal board of
transport, the Kativik Regional Government and any other body
whose board of directors is composed in the majority of elected
municipal officers, except a private body.
1982, c. 30, s. 5; 1984, c. 42, s. 137; 1985, c. 32, s. 159; 1990, c. 57, s. 2.

School bodies. 6. School bodies include regional school boards, the Conseil
Scolaire de l’Estrie, the Conseil scolaire de la Vallée-du-Sud and the Conseil
de l’Estrie-de-la-Saguenay. The Act respecting the Conseil scolaire de l’Estrie
is the subject of an international agreement within the meaning of the
Act respecting the Ministère des Affaires internationales (chapter
M-21.1), general and vocational colleges, the Université du Québec
and its branches, research institutes and schools of higher education.
They also include institutions declared to be of public interest or
recognized for purposes of grants under the Act respecting private
education (chapter E-9) and institutions of higher education more
than one-half of whose operating expenses are paid out of the
appropriations entered in the budget estimates tabled in the National
Assembly.
1982, c. 30, s. 6; 1982, c. 62, s. 143; 1988, c. 84, s. 541; 1989, c. 17, s. 1.

Health and social services establishments. 7. Health services and social services establishments include the
public establishments referred to in sections 10 and 11 of the Act
respecting health services and social services (chapter S-5), the
private establishments referred to in the said Act which operate with
sums of money taken out of the consolidated revenue fund, the
regional health services and social services councils established pursuant to the said Act, and the Corporation d’Hébergement du
Quebec.
1982, c. 30, s. 7; 1990, c. 57, s. 3.

Person in charge. 8. The person exercising the highest authority in a public body shall
perform the duties conferred by this Act on the person in charge of
access to documents or of protection of personal information.
Delegation. However, that person may designate a member of the public body
or of its board of directors, as the case may be, or a member of its
management staff as the person in charge, and delegate all or part of
his duties to him.
Notice. The delegation must be made in writing, and given public notice by
the delegator.
1982, c. 30, s. 7; 1987, c. 58, s. 3.
(2) have a serious adverse effect on the economic interests of the public body or group of persons under its jurisdiction.

1982, c. 30, s. 21.

Industrial secret. **22.** A public body may refuse to release an industrial secret that it owns.

It may also refuse to release other industrial, financial, commercial, scientific or technical information that it owns if its disclosure would likely hamper negotiations in view of a contract, or result in losses for the body or in considerable profit for another person.

A public body established for industrial, commercial or financial management purposes may also refuse to release such information if its disclosure would likely substantially reduce its competitive margin.

1982, c. 30, s. 22.

Third person. **23.** No public body may release industrial secrets of a third person or confidential industrial, financial, commercial, scientific, technical or union information supplied by a third person and ordinarily treated by a third person as confidential, without his consent.

1982, c. 30, s. 23.

Third person. **24.** No public body may release information supplied by a third person if its disclosure would likely hamper negotiations in view of a contract, result in losses for the third person or in considerable profit for another person or substantially reduce the third person’s competitive margin, without his consent.

1982, c. 30, s. 24.

Prior notice. **25.** A public body, before releasing industrial, financial, commercial, scientific, technical or union information supplied by a third person, must give him notice, in accordance with section 49, of the release to enable him to submit his observations unless the information was supplied in carrying out an Act requiring that the information be accessible to the applicant, or unless the third person has waived the notice by consenting to the release of the information or otherwise.

1982, c. 30, s. 25.

Health hazard. **26.** No public body may refuse to release information referred to in sections 22, 23 and 24 if the information reveals or confirms the existence of an immediate hazard to the health or safety of persons or...
CHAPTER III
PROTECTION OF PERSONAL INFORMATION

DIVISION I
CONFIDENTIALITY OF NOMINATIVE INFORMATION

Confidentiality. 53. Nominative information is confidential, except in the following cases:
(1) where its disclosure is authorized by the person concerned by the information; in the case of a minor, the authorization may also be given by the person having parental authority;
(2) where it relates to information obtained in the performance of an adjudicative function by a public body performing quasi-judicial functions; the information remains confidential, however, if the body obtained it when holding a sitting incamera or if the information is contemplated by an order not to disclose, publish or distribute.
1982, c. 30, s. 53; 1985, c. 30, s. 3; 1989, c. 54, s. 150; 1990, c. 57, s. 11.

Identifying information. 54. In any document, information concerning a natural person which allows the person to be identified is nominative information.
1982, c. 30, s. 54.

Exception. 55. Personal information which, by law, is public is not nominative information.
1982, c. 30, s. 55.

Name of a natural person. 56. The name of a natural person is not nominative information, except where it appears in conjunction with other information concerning him, or where the mere mention of his name would disclose nominative information concerning him.
1982, c. 30, s. 56.

Public information. 57. The following is public information:
(1) the name, title, duties, classification, salary, address and telephone number at work of a member, the board of directors or the management personnel of a public body and those of the deputy minister, the assistant deputy ministers and the management personnel of a government department;
(2) the name, title, duties, address and telephone number at work and classification, including the salary scale attached to the classification, of a member of the personnel of a public body;
74.15. (Repealed).

1990, c. 57, s. 19.

Declaration. 76. The establishment of a file must be the subject of a declaration to the Commission.

Content. The declaration must contain the following indications:

(1) the title of the file, the kind of information it contains, the use to which the information is to be put and the method by which the file is maintained;
(2) the source of the information entered in the file;
(3) the categories of persons concerned in the information entered in the file;
(4) the categories of persons who have access to the file in carrying on their duties;
(5) the security measures taken within the public body to ensure the confidentiality of the nominative information and its use according to the purposes for which it was collected;
(6) the title, address and telephone number of the person in charge of protection of personal information;
(7) the modalities of access to the file of the person concerned;
(8) any other indication prescribed by government regulation.

Rules. The declaration must be made in accordance with the rules established by the Commission.

1982, c. 50, s. 76; 1990, c. 57, t. 20.

Change. 77. Every public body must notify the Commission of every change that renders the declaration provided for in section 76 inaccurate or incomplete.

1982, c. 30, s. 77.

Natural person. 78. Sections 64 to 77 do not apply to the processing of nominative information collected and used as a working tool by a natural person, to the extent that the information is not disclosed to any person other than the person concerned or to a body other than that to which he belongs, and that it is used judiciously.

Research. The same rule applies to the processing of nominative information collected by a natural person and which is used by him for scientific research purposes.

Public body. The public body is subject to the said sections from the time the person contemplated in the first or second paragraph discloses to the public body nominative information that he has collected or which was obtained through processing.

1982, c. 30, s. 78.

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A-3.1 / 21 (42)
Fee. However, the applicant may be charged a fee not greater than the cost for transcribing, reproducing and sending the information. The amount and modalities of payment of the fee are prescribed by government regulation, which may prescribe the cases where a person may be exempt from payment of a fee.

Estimate. A public body which intends to charge a fee under this section shall, before transcribing, reproducing or sending a document, inform the applicant of the approximate amount that will be charged to him.

1982, c. 30, s. 85; 1987, c. 68, s. 8.

§ 2. — Restrictions to the right of access

Refusal. 86. A public body may refuse to release or confirm the existence of nominative information to the person concerned if the information is filed in a confidential file.

1982, c. 30, s. 86.

Refusal. 86.1. A public body may refuse to release to a person nominative information concerning him where such information is contained in an opinion or recommendation given by one of its members or a member of its personnel, or a member of another public body or a member of its personnel, in the performance of his duties, or given at the request of the body by a consultant or adviser on a matter within his competence and where the body has not rendered its final decision on the matter which is the subject of the opinion or recommendation.

1990, c. 57, s. 23.

Refusal. 87. Except in the case provided for in section 86.1, a public body may refuse to release or to confirm the existence of nominative information to the person concerned, to such extent as its release would disclose information whose release may or must be denied pursuant to Division II of Chapter II.

1982, c. 30, s. 87; 1990, c. 57, s. 24.

Retention of information. 87.1. A health services or social services establishment, the Commission de la santé et de la sécurité du travail, the Société de l'assurance automobile du Québec or the Régie des rentes du Québec may refuse for the moment to release, to a recipient, nominative information which concerns him where, in the opinion of his attending physician, serious harm to the person's health would likely result.
Release. In such a case, the public body, on the recommendation of the attending physician, shall determine when the information may be released and inform the person concerned.
1987, c. 68, s. 9; 1990, c. 19, s. 11.

Release. 88. Except in the case provided for in paragraph 4 of section 59, a public body must refuse to release nominative information to the person concerned if its release would likely disclose nominative information concerning another natural person or the existence of such information, unless the latter person gives written consent.
1982, c. 30, s. 83.

Release. 88.1. A public body must refuse to release nominative information to the heir or successor of the person to whom the information relates unless the information pertains directly to his interests or rights as an heir or successor.
1986, c. 95, s. 5.

§3. — Right of correction

Request. 89. Every person who receives confirmation of the existence of nominative information concerning him on a file may request that the file be corrected if the information is inaccurate, incomplete or equivocal, or if the collection, release or keeping of the information is not authorized by law.
1982, c. 30, s. 89.

Release. 89.1. A public body must refuse to accept a request for correction of nominative information filed by the heir or successor of the person to whom the information relates, unless the correction pertains directly to his interests or rights as an heir or successor.
1986, c. 95, s. 6.

Continuation. 90. If a request for correction is contested, the public body must prove that the file does not need to be corrected, unless it obtained the information in question from the person concerned or with his consent.
1982, c. 30, s. 90.
Principal Investigator: ___________________ Department/Institution: ________________________

Tel: ___________________ Fax: ___________________ E-mail: ___________________

Mailing Address: ________________________________________________________________

IRB Review Number: ___________________ Study Number (if applicable): ___________________

Title of Research Proposal: _______________________________________________________

__________________________________________________________

STUDY DESCRIPTION (PLEASE INDICATE ALL THAT APPLY)

Is the research: Biomedical? ☐ Behavioural? ☐ Other? ☐ ☐

Interventional? ☐ Observational? ☐

Is the research: Clinical? ☐ Phase I, II, III or IV?: ☐ Epidemiological? ☐ Other? ☐ ☐

Does the study involve: Randomization? ☐ Control Group? ☐ Placebo Control? ☐

Study scope is: International ☐ National ☐ Quebec multi-centre ☐ McGill based ☐

Projected McGill Hospital participation (if applicable): JGH: ☐ MUHC/MCH: ☐ MUHC/Mt. Chest Ins.: ☐

MUHC/IMGH: ☐ MUHC/MNH-MINI: ☐ MUHC/RH: ☐ SMH: ☐ Douglas: ☐ Other: ☐

STUDY POPULATION (PLEASE INDICATE YES, NO, N/A OR EXPLAIN)

Number of subjects to be enrolled at above sites: ______

Will subjects be recruited from the general population?: Yes ☐ No ☐

Will the study population require hospitalisation for study purposes?: Yes ☐ No ☐

Will the study involve recruiting minor subjects?: Yes ☐ No ☐

Are the study subjects members of a specialized group (incompetent patients, prisoners or otherwise legally restricted)? Yes ☐ No ☐

Will the research require written informed consent?: Yes ☐ No ☐

Will the research require specimen collection for other than routine tests?: Yes ☐ No ☐

If yes, a separate consent is required. Has this been provided?: Yes ☐ No ☐

Does the consent form follow the required IRB guidelines (www.medicine.mcgill.ca/research/irb/forms.htm) for format and
content? Yes ☐ No ☐

Has the consent form been approved by the local Principal Investigator? Yes ☐ No ☐

Will the research require a Self-administered questionnaire?: ☐ Interviewer questionnaire?: ☐

Will the research require recruitment advertisement?: ☐ If so, please provide a copy.

Will the research involve subject compensation?: ☐ If so, how much?___________

STUDY SUPPORT (PLEASE INDICATE YES, NO, N/A OR EXPLAIN)

Has financial support been granted? Yes ☐ No ☐ Requested / Pending Yes ☐ No ☐

Please identify financial support: Granting Agency: ________________ Industrial Sponsor: ________________

Cooperative Group: ________________ Other ____________________ Non-Funded: ☐

Do you intend to proceed with the study even if funding is not received? Yes ☐ No ☐

Has the research study received regulatory approval from? TPD: ☐ FDA: ☐ MSSS: ☐

Has the research study been submitted to ethics review elsewhere? Yes ☐ No ☐

If yes, where and what was the outcome?: ________________

Has the research study been peer reviewed? Yes ☐ By whom______________________________ No ☐

Is monitoring required? Yes ☐ No ☐ If yes, how will it be done? Industrial Sponsor: ☐ Cooperative Group: ☐

Other (please provide details)______________________________

Will study be audited? Yes ☐ No ☐ If yes, by whom ____________________

In cases where the use of hospital facilities is required, has approval been obtained from the appropriate departments? Yes ☐ No ☐

Has a summary (required, expressed in lay terms, been provided? Yes ☐ No ☐ This must include specific details on recruitment process.

Please provide evidence of right to publish.

(Attach information from the protocol or the contract – the contract takes precedence.)

Is there a potential of conflict of interest? (please refer to the University policy at http://www.mcgill.ca/researchoffice/policies/sponsored/policies/proprietary/) Yes ☐ No ☐ If yes, please give full details on a separate sheet.

______________________________ Date ____________________

Signature of Dept Head ____________________ Signature of Investigator ____________________

Date of submission to IRB ____________
McGill Faculty of Medicine
Institutional Review Board
-Continuing Review-

Principal Investigator: ___________________________  Department/institution: ___________________________

IRB Review Number: ___________________________  Study Number (if any): ___________________________  Review Interval: ___________________________

Title of Research Study: ___________________________

Date of initial IRB approval: ___________________________  Date of previous continuing review (if applicable): ___________________________

INTERIM REPORT (PLEASE CHECK OR SPECIFY)

Current Status of Study:
Active Study: ___________________________  On Hold: ___________________________  Closed to Enrolment: ___________________________
Interim Analysis: ___________________________  Final Analysis: ___________________________  Study Not Activated*: ___________________________

*If the study has not become active at McGill, please provide correspondence to explain; enclosed.

McGill hospital(s) where study is being conducted and has received approval of local Research Ethics Board(s) (if applicable):

JGH: ☐  MUHC/MCH: ☐  MUHC/MGH: ☐  MUHC/MNH-MNI: ☐
MUHC/CRH: ☐  SMH: ☐  Douglas: ☐  Other: ☐  ___________________________

McGill hospital(s) where study has not received approval of local Research Ethics Board(s) (if applicable): ___________________________

If study sponsorship or financial support has changed, please provide correspondence to explain; enclosed:

Number of subjects to be enrolled by the McGill PI: __ __  Number of subjects enrolled by the McGill PI to date: __ __

Number of subjects enrolled by the McGill PI since last review: __ __

Have any of these subjects withdrawn from the study?: __ __

Has the study been revised since the last review?: __ __  Have the study revisions been approved by the IRB?: __ __

Has the consent form been revised since the last review?: __ __  Date of the current consent form: ___________________________

Are there new data since the last review that could influence a subject's willingness to provide continuing consent?: __ __

Have there been any serious adverse experiences (SAEs)?: ___________________________

Have all serious adverse experiences (SAEs) and safety reports relevant to the study been reported to the IRB?: ___________________________

SIGNATURES:

Principal Investigator: ___________________________  Date: ___________________________

IRB Chair: ___________________________  Date: ___________________________
Principal Investigator: 

Department/Institution: 

IRB Review Number: 

Protocol Title: 

Brief description of the protocol: 

Brief description of the results of the protocol: 

- Have any articles been published using the results? Y ☐ N ☐
  * If yes, please submit a copy of the publication(s) to the IRB/REB.

- Total number of subjects entered: 

- Any adverse reactions? Y ☐ N ☐
  If yes, how many? 
  Were these reported to the IRB/REB? Y ☐ N ☐
  * If no, please submit all adverse reactions to the IRB/REB at this time.

Please check one or more reasons that may apply for protocol termination and if necessary, explain:

☐ protocol reached accrual goals
☐ protocol never received funding
☐ principal investigator left the institution; no one is continuing study
☐ not enough subjects for project to be completed
☐ protocol closed due to adverse reaction(s)
☐ investigator lost interest in the study
☐ other

I certify that as of the date below, subjects are no longer being studied or followed on the above protocol and therefore, this protocol should be officially terminated by the IRB.

Signature of Investigator: 

Date: 

I have reviewed the above termination report: 

Chair, IRB 

Date: 

IMPROVING MCGILL'S CONSENT FORMS

PURPOSE OF A CONSENT FORM

➤ To give a layperson a fair idea of what participating in the study might mean for the potential subject, how her/his life might be changed.

➤ To provide the Investigator with the opportunity to clarify her or his reasons for inviting patient participation. (The investigator should assist with an oral explanation).

➤ To provide a clear account of legal and administrative issues.

LANGUAGE

➤ Investigators should be encouraged to use plain English whenever possible.

➤ When technical terms are used, they should be defined at first use. It is helpful to have draft versions of consent forms read over by a layperson for comprehensibility before the form is sent to the committee.

➤ Finally, investigators should check consent forms carefully for grammar and spelling.

SPECIFIC COMMENTS ON SECTIONS OF THE CONSENT FORM

Title

➤ The form should provide the title of the study, the principal investigator, the institution in which the study is being conducted, and, if the study is funded by private industry, the name of the company.

➤ Pharmaceutical sponsorship is frequently acknowledged but in a somewhat disguised form, e.g., “Sheffield Clinical Research Unit”. Preferable would be the statement, “The pharmaceutical company sponsoring this study is...”
Introduction

➢ State clearly what disease is being studied and why the subject is being approached.

➢ Explain, as appropriate, how the condition is usually treated and why this particular study is being done.

➢ If the study involves adding a particular experimental treatment to standard therapy, e.g., testing whether the addition of radiation therapy to standard chemotherapy is of benefit, the introduction should explain the following:
  - how the disease is usually treated
  - what procedures are involved in standard treatment
  - what the risks and benefits of standard treatment are
  - why the study is adding an experimental treatment on top of standard treatment (e.g., "despite the observed efficacy of chemotherapy, many patients experience local recurrences post-treatment")

➢ Subjects should be given some information on the testing experience with the new treatment date, including the number of patients treated and the response rate observed.

➢ The last sentence of the introduction should clearly and honestly state the purpose of the study. If the study is looking at the benefit of adding a treatment to standard therapy, this should be reflected in the statement of purpose (e.g., "The purpose of this study is to see if the risks of adding radiation therapy to standard treatment are outweighed by the benefits"). Investigators should be careful to ensure that statement of purpose is accurate. If the purpose of the trial (and this means the primary outcome of the study) is to measure toxicity or cost-effectiveness, this must be clearly stated.

➢ In phase I trials, the consent needs to be cohort specific, i.e., the subject needs to be informed what dose level she/he is being entered in and, in more general terms, about the relationship between dose and benefits/side effects.

Study Procedures

➢ Since procedures relating to standard therapy, if applicable, will have been explained above, the study procedures section should clearly describe the therapeutic and non-therapeutic experimental procedures involved in the study. There must be a clear indication of which procedures are being done for therapeutic reasons and which are non-therapeutic, that is, done to answer the research questions rather than treat the patient.
In most cases, it will be clearest to provide subjects with a chronological account of the procedures involved. It is important for the procedures to be sufficiently explained so that a layperson can have some idea of what is involved. How much time will each treatment take?

Non-therapeutic procedures (including additional blood draws, x-rays, and questionnaires) should be set out in a separate paragraph. The form should clearly state how many of these procedures are involved and why they are being done.

If the study places restrictions on other treatments that the patient may receive (concomitant treatments such as steroids, antiemetics, and growth factors), these restrictions must be clearly stated and justified.

Benefits and Risks

The anticipated benefits of study participation should be stated in an even-handed manner; both excessive pessimism and undue optimism are to be avoided. For example, if the hoped-for benefit is a reduction in the probability of a local recurrence, this should be plainly stated. If there are no benefits for the individual participant, hoped-for benefits to others afflicted with the disease may be pointed out.

The law requires that risks to research subjects be fully disclosed. The risks in the consent form should mirror the risks disclosed in the protocol.

When a study involves a component of standard therapy, the risks of that therapy ought to have been disclosed in the introduction. The risks section should focus on the incremental risks associated with study participation. In the example of a study looking at adding radiation therapy to standard chemotherapy, the risks associated with radiation therapy ought to be detailed here plus the risks association with combining two therapies (i.e., the risk of additive toxicity).

A “drop in blood counts” does not constitute a fully disclosed risk; what this means for the patient must be explained.

It is helpful to divide risks quantitatively, e.g.,

- rare risks (less than 2%)
- uncommon risks (2-10%)
- frequent risks (11-30%)
- expected risks (31%+)

If there is little experience with a new treatment or a new combination of treatments, it is important to state this and that unexpected side-effects may be seen.
- Side-effects that may not be reversible must be clearly identified as such.

- Subjects should be warned to look out for early symptoms and signs of serious or life threatening side effects (e.g. mouth sores or fever in the context of chemotherapy) and be told to immediately report these to the investigator.

Withdrawal from Study

- If applicable, the conditions under which a subject may be withdrawn from a study ought to be clearly laid out.

Alternative Treatments

- It is rare indeed for a consent form to provide an adequate explanation of alternative treatments. A statement that "your doctor will explain other treatments available" is unacceptable; so, too, a statement of the form, "other treatments for your disease include surgery, chemotherapy and radiation therapy", is never sufficient. Patients should be clearly told what the standard treatment or treatments for their condition is. It would be helpful to provide some idea of what the basic difference between these treatments are.

- If the patient has advanced cancer, the option of supportive care, including details on comfort control measures, must be detailed.

Cost / Insurance

- If there are any costs to the research participants, these should be clearly outlined.

- Some studies, particularly those funded by drug companies, have no-fault insurance coverage. If the study has such a policy, it should be briefly explained. If no such policy exists, the section should be left out.

Compensation

- Details regarding compensation should not be listed under study benefits. Subjects should be informed of the amount of compensation and how this has been calculated. Subjects who withdraw early may not be penalized for doing so and must receive compensation proportionate to their time in the study.

Subject Rights

- Detail the rights of research subjects, including

  - the right to ask questions at any time
  - the fact that study participation is voluntary
- the fact that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled
- the right to discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

Confidentiality

- Subjects should be told who will have access to their medical information, including Therapeutic Products Directorate (TPD) or the Food and Drug Administration (FDA).
- Steps taken to protect the confidentiality of the subjects' medical information should be briefly described.

Contact

- The subject should be told who to contact regarding their rights (e.g., patient representative).
- The subjects should be told who to contact in the event of an adverse event (e.g., the study investigator).

Signature

- The final portion of the form should include a statement to the effect of "The study has been explained to me and my questions have been answered to my satisfaction. I agree to participate in this study."
- The phrase "I understand" is to be avoided.
- Subjects should be told that they will be given a copy of the form.
- The signature should be witnessed by someone not directly associated with the study who has witnessed the consent negotiation.
McGill University, Faculty of Medicine
Adopted Guidelines for

Consent Form
Genetic Research and DNA Banking
By Geneviève Cardinal, Mylène Deschênes, Bartha Maria Knoppers
and Kathleen Cranley Glaz

Title: ____________________________

Principal researcher responsible for the project: (Name and function)
Collaboration: (Names and functions)

Institution: ____________________________

Project sponsored by: ____________________________

1. RESEARCH PROJECT DESCRIPTION

1.1 Justification:
- Purpose of the research
- Simplification of relevant terms

DNA: Molecule containing all the transmissible genetic information, which controls
the activities of the body cells. DNA provides the instructions for determining the
hereditary characteristics of a person such as eye colour or blood type.

1.2 Description of the research project: specify goals, contribution to the advancement
of human knowledge and welfare in a particular domain.

1.3 Request for participation

We are asking for your participation in this research project.

*We wish to thank Marie Hirtle, Claude Laberge, Thomas Hudson, Denise Ayard, Martin Letendre et Dominic
Grégoire who contributed to the analysis of the issues discussed in this text.
2. PROGRESSION OF THE RESEARCH PROJECT

2.1 Procedures (description of the procedures, number and duration)

2.2 Duration of the research project

2.3 Scope of the research project (local or multicentre: name of the responsible organizations)

Several research centres (options: worldwide, in Canada, in Quebec, in Montreal) are participating in this research project coordinated by _____ (institution or organization).

OR

This research will take place at ______ (name of the institution).

2.4 Access to your medical record

The research team will consult your medical record to obtain information, which is pertinent to the research project.

2.5 Combination with other information

Your name will be forwarded to _____ (a demographic or genealogical data bank or tumour registry, for example) so that additional research can be performed (nature of the research: genealogical, demographic…). We will combine this information with the results of our work in order to ______ (explanation).

3. STORAGE AND SAFEKEEPING OF DNA SAMPLES

3.1 Identification of the sample

<table>
<thead>
<tr>
<th>Coded</th>
<th>Anonymized</th>
</tr>
</thead>
<tbody>
<tr>
<td>We will protect the confidentiality of the samples by assigning them a specific code. Your DNA sample will not be specifically identified but a code will link you to the sample. Decoding can only be performed by the principal researcher or an individual authorized by the latter.</td>
<td>We will protect the confidentiality of the samples by rendering them anonymous; in other words, after the sample is taken, all identifiers, which would allow you to be retraced, will be deleted. The researcher may decide to include specific information with the sample (such as your age, your gender, or certain clinical, pathological or demographic data, etc.); this information, however, would not allow you to be identified or retraced.</td>
</tr>
</tbody>
</table>

↓ ▼
### 3.2 Length of storage

<table>
<thead>
<tr>
<th>CODED</th>
<th>ANONYMIZED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Samples of your DNA will be kept at (institute, research institute/centre or bank) for a period to be determined by (researcher or person(s) responsible for the bank). All the samples will be destroyed at the end of (length of time).</td>
<td>Samples of your DNA will be kept in the form of immortalized cell lines, hence for an indefinite period at (institute, research centre or the bank).</td>
</tr>
</tbody>
</table>

### 3.3 Other research

<table>
<thead>
<tr>
<th>CODED</th>
<th>ANONYMIZED</th>
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</thead>
<tbody>
<tr>
<td>Your sample will be used only for the purposes of this research project.</td>
<td>Your sample, once anonymised, may be used in other human genetic research on (disease X or related diseases) approved by the research ethics board. Such research may necessitate the releasing of samples to other researchers, including those outside of this institution.</td>
</tr>
<tr>
<td>A new consent will be necessary for the use of your coded DNA sample in other research. May we recontact you in the future for other research? Yes No</td>
<td></td>
</tr>
<tr>
<td>OR</td>
<td>OR</td>
</tr>
<tr>
<td>At the end of the research project, instead of destroying your sample, could we anonymize it so that it can be used for additional research on (disease X or related diseases) approved by the research ethics board? This research could involve the sending of samples to other researchers, including those outside of this institution. However, you would no longer be identifiable. Yes No</td>
<td></td>
</tr>
<tr>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>At the end of the research project, your sample will be anonymized for</td>
<td></td>
</tr>
</tbody>
</table>
4. BENEFITS

You will receive no personal benefit from your participation in this research project. We hope, however, that the results obtained will permit us to further our knowledge in the area of _______ by _______ (in what way?) _______ and eventually, benefit society as a whole.

OR

The information gathered might be useful for you and your family’s health. We also hope that the results will permit us to further our knowledge in the area of _______ by _______ (in what way?) _______ and eventually, benefit society as a whole.

5. RISKS

5.1 Physical Risks

Although the taking of the blood sample causes no serious problems for most people, it can cause some bleeding, bruising, malaise, dizziness, infection and/or discomfort at the injection site.

OR

Since this research is being performed with samples that have already been taken, you will not be exposed to any physical risk associated with the taking of a DNA sample.

5.2 Socio-economic Risks

One of the risks associated with this research project relates to the disclosure of the results or the disclosure of your participation to third parties. Mere participation in genetic research projects could compromise or diminish your chances and the chances of your family of obtaining insurance (life insurance, disability, mortgage, or health) or certain types of employment.

AND

In cases of specific population studies:

In consideration of the fact that the research project relates to _______ (specify: a social group, an ethnic group, a sub-population, a visible minority), it is possible that the release of the general results may cause you to be associated with this gene even if you are not a carrier. You may be identified as a person at risk by virtue of your membership in this group.
6. CONFIDENTIALITY

6.1 Safety/security of the data

<table>
<thead>
<tr>
<th>CODED</th>
<th>ANONYMIZED</th>
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</thead>
</table>
| All of the information obtained about you and the results of the research will be treated confidentially. This information will be (coded, encrypted, kept under lock and key). The study file will be kept at ______ under the Responsibility of ______ and also in the Electronic files of ______. Your participation and the results of the research will (will not) appear in your medical record.
| All of the information obtained about you and the results of the research will be treated confidentially. This information will be anonymized. Your participation and the results of the research will not appear in your medical record, as it is impossible to identify you. The results of this study may be published or communicated in other ways, but it will be impossible to identify you. |
| The results of this study may be published or communicated in other ways, but it will be impossible to identify you. | |

6.2 Third-party Access to Results

<table>
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<tr>
<th>CODED</th>
<th>ANONYMIZED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unless you have provided specific authorization or where the law permits or a court order has been obtained, your personal results will not be made available to third parties such as employers, governmental organizations, insurance companies or educational institutions. This also applies to your spouse, other members of your family and your physician.</td>
<td>As all the information in this research project is rendered anonymous, your personal results cannot be made available to third parties such as employers, governmental organisations, insurance companies or educational institutions. This also applies to your spouse, other members of your family and your physician.</td>
</tr>
<tr>
<td>However, for the purposes of ensuring the proper management of the research, it is possible that a member of an ethics committee, a Health Canada representative or (list the designated institutions) may consult your research data as well as your medical record.</td>
<td></td>
</tr>
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</table>

7. COMMUNICATION OF RESULTS
<table>
<thead>
<tr>
<th>CODED</th>
<th>8. GENETIC COUNSELLING SERVICES</th>
</tr>
</thead>
<tbody>
<tr>
<td>You can communicate with the research team to obtain information on the general progress or the results of the research project. Project updates will be ______ (specify: sent by mail, posted on our website...), ______ (specify: once a year, at the end of the project...). However, we will not communicate any individual results to you.</td>
<td>At any time, you may meet with a genetic counsellor.</td>
</tr>
<tr>
<td>ANONYMIZED</td>
<td>9. COMMERCIALIZATION/RENUCIATION</td>
</tr>
<tr>
<td>Since your data has been anonymized, it is therefore impossible to communicate personal results. Nevertheless, you can communicate with the research team to obtain information on the status of the work or the general results of the research project. Project updates will be ______ (specify: sent by mail, posted on our website...), ______ (specify: once a year, at the end of the project...).</td>
<td></td>
</tr>
</tbody>
</table>

In the case where there are scientifically validated results with possible impact for your health and preventive measures or treatment are available, would you like to be informed through a physician? Yes or No

The communication of this type of information carries risks for you and your family, such as anxiety, discrimination (employment, insurance), and has implications for reproductive decisions.

AND/OR in the case of a family study:

The results of the analysis may uncover non-paternity but this will not be communicated to you.
The analysis of your DNA sample may contribute to the creation of commercial products from which you will receive no financial benefit.
10. CONFLICT OF INTEREST

The principal researcher and/or the institution is/are paid by the _____ company, which is sponsoring this project.

AND/OR

The principal researcher and/or the institution has/have a financial interest in the _____ company which is sponsoring this project.

11. RECRUITMENT OF OTHER FAMILY MEMBERS

Over the course of the study, it is possible that we may ask you or a person you will designate, to contact other members of your family to offer them the opportunity to participate in the study. The researchers and their medical team cannot personally contact your family members for recruitment purposes.

12. FREEDOM OF PARTICIPATION AND PERIOD OF REFLECTION

<table>
<thead>
<tr>
<th>CODED</th>
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<tbody>
<tr>
<td>Your participation is completely free and voluntary. The quality of medical services available to you will not be affected by your decision. You may take the time necessary to reflect on your decision and discuss your participation in the project with persons close to you before giving us your answer.</td>
<td></td>
</tr>
<tr>
<td>AND</td>
<td>AND</td>
</tr>
<tr>
<td>You are free to withdraw from the study at any time. If you withdraw, your DNA sample will be recounted and destroyed.</td>
<td>As your DNA sample will be anonymized, it will be impossible to recount and destroy it.</td>
</tr>
</tbody>
</table>

13. COMPENSATION FOR EXPENSES INCURRED AND FOR INCONVENIENCE

If you incur expenses by reason of your participation (for example: parking, travel, child-care, meals) you will be reimbursed upon presentation of receipts.

OR

You will receive a lump sum of _____ as compensation for expenses and inconvenience suffered.
OR

Expenses incurred by reason of your participation will not be reimbursed.

14. CIVIL LIABILITY

If you suffer any injury as a result of your participation in this project, you retain all legal recourses against the research collaborators.

15. RESOURCE PERSONS

Members of the research team

If you would like additional information regarding the progression of the research project or would like to communicate any change of address to us, you can contact ______ (name, designation/position and availability) at the following phone number:______

Ombudsman, ethics committee or authorized person

If you would like to discuss your participation with an individual not directly involved in the project, we invite you to contact _____ (name, designation/position and availability) at the following phone number:______

16. FINAL WORD : UNDERSTANDING, FREEDOM, QUESTIONS

____ (Name)____ explained the nature and the progression of the research project. I have familiarized myself with the consent form and have received a copy. I have had the opportunity to ask questions that have been answered. Upon reflection, I agree to participate in this research project.

17. SIGNATURE, NAME, DATE

Name: ___________ Surname: ___________
Address: ___________ Tel. (home): ___________
Tel. (work): ___________

I will inform the principal researcher of any change of address.

Signature of participant: ___________ Date: ___________
18. VERBAL TRANSLATION

I was present during the meeting between the research team member and the participant. I translated, for the participant, the consent form and all information conveyed/presented regarding the research project.

Name: __________________ Signature: __________________ Date: __________

19. AGREEMENT OF THE RESEARCHER

The research project, as well as the conditions of participation, were described to the participant. A member of the research team answered any questions and explained that participation was free and voluntary.

Name: __________________ Signature of the researcher: __________________ Date: __________

20. ETHICS COMMITTEE APPROVAL

The research project was approved by the research ethics committee of (institution), on (date).
Modern health research involving genetics, DNA and the use of databanks increases concerns about maintaining the confidentiality of subjects and the protection of their privacy. In December 2000, the Research Ethics Committee of the Faculty of Medicine adopted Guidelines for a consent document for Genetic Research and DNA Banking (Cardinal, Deschênes, Knoppers, Glass) and in June 2003 extended these principles to apply to both tissue and data banking. The “Guidelines 2003” considered individual research projects as well as the establishment of larger, more widely used, data/tissue banks. This current document outlines the principles for the management of multi-user “databanks”.

The following procedural guidelines fulfill the minimal requirements to establish, maintain and access data and/or tissue banks. They are meant to be consistent with the “CIHR Best Practices for Protecting Privacy in Health Research” (2005). McGill affiliated hospitals may already have procedures in place or plan to develop procedures in the future, that provide details specific to their needs.

These guidelines apply to all new and existing data repositories and tissue banks to be used for human subjects’ research. A databank includes any systematic collection of data or tissues and can include personal and medical data, genetic data, proteomic data, and biological material (cells, tissues, organs, blood, saliva and other substances). While all data or tissues collected or used for research involving human subjects potentially constitute a databank, these guidelines are intended primarily for management of those banks and repositories that serve the needs of multiple research projects and/or multiple research groups.

1. Management

The holder of the bank refers to the individuals, groups, and institutions that created the bank. The institution is responsible to ensure that the databank has appropriate administration. The administrator (individual or institution) of the data and/or tissue bank is responsible for its operation according to this policy, and includes privacy, confidentiality and appropriate access by users.

Researchers have access to the bank as limited by the nature of the consent given by subjects. As governed by this policy, researchers are responsible to the Research Ethics Board (REB), to the Institution and to the Administrator with whom they will sign an agreement establishing, for example, the type of access (eg user or user/contributor), as well as ensuring confidentiality and clarifying any potential intellectual property rights. Researchers, institutions and sponsors can acquire intellectual property rights over inventions derived from the use of the databank.

The creation and/or use of databanks must be reviewed by a McGill Approved Research Ethics Board (see Appendix II, Policy on the Ethical Conduct of Research Involving Human Subjects, for a list of these REBs)
2. Collection of data and/or tissue and recruitment of subjects

As part of a research project
An REB with authority in the McGill jurisdiction is to review and approve the creation and use of the data and/or tissue bank before collection begins. Unless specifically provided for in the consent document, data and tissue collected are not to be used for purposes other than for those initially requested. Only the data and tissue directly pertaining to the study are to be collected and stored. Data and tissue are to be collected legally and in good faith.

Data and/or tissue are to be collected with the subjects’ consent and the adopted consent guidelines for Genetic Research and DNA Banking are to be consulted when drafting the consent document. These guidelines also contain information that provides for:

- Informing the subject of the use and lifetime of the bank;
- Identifying information and its potential traceability;
- Length of storage and disposition of data/tissue;
- Requesting whether or not the subject may be contacted again for further research;
- What happens to data and/or tissues at the end of the project (i.e. coded data/tissue destroyed or rendered anonymous so that all identifiers which would allow the subject to be retraced are deleted);
- The possibility or not for the subject to withdraw consent and an explanation of what happens to the stored data and/or tissue once consent has been withdrawn;
- Describing the potential benefits or lack of benefits for the subjects;
- Describing the possible risks for the subjects;
- Disclosing incidental findings that could affect the well-being of the subjects or their relatives, particularly while the research findings are linkable with the subjects’ identity;
- Describing confidentiality, and how it will be maintained (e.g. who has keycode to data and/or tissue; where the data will be stored; and type of security measures taken);
- Restricting access to researchers or research teams involved in the study and conditional to approval by the administrator;
- Keeping data confidential within the limits of the law or within the limits set by the consent of the subject;
- The potential uses for the data or tissues including potential development of intellectual property and commercial uses.

As part of a retrospective review
- DPS approval is obtained in the case of medical charts/records (LSSS); or
- Subjects’ consent to collect health information and REB approval were obtained.

Secondary (research) use of nominal, coded or anonymized data and/or tissue already collected
- REB approval is required for secondary use of existing research data and/or tissue;
- In the case of data and/or tissue collected in the course of patient care, written consent for the proposed research use must have been or must be obtained from the prospective subjects or their legal representatives;
- In the case of data and/or tissue collected in the course of a research project, the consent document must have anticipated the proposed use of the data and/or tissue for research.

Secondary (research) use of tissue and/or data collected anonymously
- The anonymous collection of tissue and/or data must have been authorized by the subject;
- REB review and approval is required.
3. Storage and safekeeping of data and/or tissue

**Identification of the data and/or tissue:**
The data and/or tissue can either be:

- **Nominative** - Containing elements that allow for subject’s identification, either by name, or by identifiers, or can reasonably be deducted from a combination of identifiers. Secondary code lists cannot be created;
- **Coded** - The confidentiality of the data and/or tissue will be protected by assigning them a specific code. A code will link the subject to the sample. Decoding can only be performed by the principal researcher or an individual authorized by the former; or
- **Anonymized** - The confidentiality of the data and/or tissue will be protected by rendering them anonymous; in other words, after the sample is taken, all identifiers which would allow the subject to be retraced will be deleted. The researcher may decide to include specific information with the sample (such as age, sex, or certain clinical, pathological or demographic data, etc.); this information, however, must not allow the subject to be identified or retraced;
- **Anonymous/non-nominative** – Data and/or tissue is originally collected without identifiers.

**Security of data and/or tissue bank**

- A list of all internal users (members of the research team) and all external users (persons or organizations) is to be kept and the criteria for accessing the data are to be defined. This is to be overseen by the Administrator.
- Security mechanisms that prevent non-authorized persons from accessing data or tissue are to be implemented (i.e. coding, double-coding, encryption, anonymization, lock and key, etc.)

**Length of storage**

- Coded data and/or tissue are to be kept for a defined period of time as outlined in the consent document (usually for a period of 25 years), after which they will be destroyed, or anonymized. Coded or linked data and/or tissue cannot be kept indefinitely.
- Anonymized data and/or tissue can be kept for an indefinite period of time, provided that subjects’ consent and REB authorization for doing so were obtained at the time of collection;
- Anonymous data and/or tissue can be kept for an indefinite period of time.

4. Access to and use of data and/or tissue

- Any use of data and/or tissue for research is to be approved by an REB.
- Use of data and/or tissue is limited to the purposes originally requested, unless otherwise indicated in the consent document (e.g. The consent document discloses the possible future secondary use of data and/or tissue for other purposes).
- Access is restricted to researchers or research teams approved by the administrator as consistent with the original purpose of the databank.

**Secondary use of data**

- Secondary use of data and/or tissue is to be approved by an REB.
Third party access

- If the personal data is coded, it is not to be made available to third parties such as employers, governmental organizations, insurance companies or educational institutions. However, for research monitoring and regulatory purposes, members of REBs, government officials, or other legally authorized parties may consult the data.
- If the personal information is rendered anonymous (i.e. stripped of all identifiers), third party access to the data and/or tissue is generally acceptable in accordance with the provisions of this policy and may be obtained through REB approval.

5. Commercialization

- The consent document must indicate that intellectual property might derive from the use of the bank with potential commercialization of results by researchers and institutions;
- Agreement as how to share any intellectual property rights must be part of the agreement signed by users;

March 2007