

## Health Research Ethics

### The FRSQ reassures Quebecers: Québec keeps close watch

**Montreal, January 23, 2003 — In the wake of widespread media coverage of the alleged births of cloned human babies, the Fonds de la recherche en santé du Québec (FRSQ) sees a need to reassure Quebecers. "Quebec has established tight monitoring systems to keep close watch over health research and prevent all unreasonable initiatives," FRSQ president and executive director Dr. Michel A. Bureau announces.**

The strict ethical and regulatory supervision currently practised in Québec and the exemplary conduct of the private sector to date make it difficult, if not impossible, to pursue human cloning research in Québec at this time.

Cloning for reproductive or therapeutic purposes requires sophisticated facilities, high-tech resources and cutting-edge expertise which are not that easy to come by. In Québec, teaching hospitals and their affiliated research centres, as well as a handful of private firms, are the only ones with such facilities at their disposal. This explains why those institutions and private laboratories require close monitoring, Dr. Bureau points out.

His health research funding organization is a pioneer and leader in this regard. Back in 1998, Québec's minister of health and social services at the time, Dr. Jean Rochon, instructed the FRSQ to see that no public funds went into human cloning projects. The departmental plan for research ethics and scientific integrity (Plan ministériel en éthique de la recherche et en intégrité scientifique) tasked the FRSQ with setting research standards and overseeing the quality of scientific investigation.

That same year, the FRSQ established a quality assurance system complete with standards and audit mechanisms. Working with the boards of teaching hospitals and their affiliated research centres, it devised a regulatory framework of good research practices which sets exacting guidelines for public-sector research. The FRSQ's grants to research centres are contingent on compliance with its regulatory framework and standards.

To preserve the highest standards for science, research management and ethics, all FRSQ-funded research centres and their host institutions are subject to periodic audit. During those quality inspections, the FRSQ checks that the institutional ethics committees are running smoothly and that the regulatory framework is fully operational, not merely hypothetical.

The ban on human cloning comes under criminal law, a federal purview. Federal Bill C-13 also targets prohibition of such projects.

Until consensus on these fundamental ethical issues takes shape in Québec and across Canada, the FRSQ is encouraging broad societal debate and urging Québec research scientists, institutions and social groups to join in. A word to the wise: we must ensure that this necessary time of discussion does not lead to deregulation that opens the door for all imaginable research initiatives.

The attached backgrounders give the FRSQ's position on human cloning and stem cell research. They also describe the panoply of mechanisms established by the FRSQ to protect the public interest in matters of health research ethics.

#### About the FRSQ



The Fonds de la recherche en santé du Québec (FRSQ), which reports to Québec's minister of finance, economy and research, is tasked with supporting health research and thus fostering wellness within the Québec population. Its terms of reference call for the promotion and financial support of research, the spread of knowledge and research training. It is further mandated to foster partnerships necessary for developing the Québec network of research and innovation and the international dissemination of research. The FRSQ has a staff of 25 and manages an annual budget upwards of \$85 million.

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**For information and interviews:**

Michelle Dubuc, M.Sc.  
Communications Director  
(514) 873-2114, ext. 235  
[mdubuc@frsq.gouv.qc.ca](mailto:mdubuc@frsq.gouv.qc.ca)  
[www.frsq.gouv.qc.ca](http://www.frsq.gouv.qc.ca)

## **BACKGROUNDER**

### **THE ACCOUNTABILITY OF RESEARCHERS AND INSTITUTIONS**

Regardless of how many laws and regulations are written, research could veer off course if the researchers themselves are not sensitive to basic ethical issues. In that case, research could run foul of regulatory mechanisms.

The universities and hospital-based research centres tasked with training scientific investigators include training in research ethics in their programs.

Research granting organizations, such as the FRSQ, are preparing to require ethics training as a prerequisite for research funding.

Although there is still much to be done, we can confidently point to the exemplary conduct of Québec researchers. To take an example, even without cloning legislation, they have refrained from rushing into this field but are instead waiting for rules and guidelines.

Further evidence of this sense of accountability is the regulatory framework and its periodic update.

## BACKGROUND

### REGULATORY AND MONITORING MECHANISMS IN QUÉBEC (PUBLIC-SECTOR RESEARCH)

#### 1. Regulatory framework for good research practices (GRP)

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##### *– For FRSQ research centres affiliated with Québec's teaching hospitals*

In seeking the highest standards of ethics and scientific integrity for health research in Québec, the FRSQ proposed in 2001 a standard regulatory framework for university health institutions that host FRSQ-funded research centres and for the Clinical Research Institute of Montreal (an FRSQ research centre reporting to the ministère des Finances, de l'Économie et de la Recherche, MFER) (department of finance, economics and research).

In 2001-2002, that regulatory framework (good research practice plans), which rigorously governs research practices, was implemented in the 19 centres. The boards of directors of the host institutions take responsibility for ethics management in Québec in keeping with a flexible external audit procedure carried out by the FRSQ.

The FRSQ is very pleased with the quality of those GRP plans, which are the only ones of their kind in Canada.

##### *– For FRSQ research centres affiliated with Québec's non-teaching hospitals*

Since March 2002, the FRSQ has sat on a task force established by the Association des hôpitaux du Québec (AHQ) to help provide a proper regulatory framework for non-teaching hospitals that host research involving human subjects.

##### *– For FRSQ research groups on Québec university campuses*

In 2000, the Québec government broadened the FRSQ's mission to include health research carried out on university campuses. Although the universities have their own ethics framework mechanisms, the FRSQ is holding talks with its university partners with a view to supporting good ethical practices within the campus-based research groups that it funds.

## 2. Ethics committees

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All health research within Québec's public institutions requires the approval of an ethics committee. For years now, health institutions engaged in research involving human subjects (e.g. hospitals, CLSCs and youth centres) have therefore had a **research ethics committee** (REC).

The RECs report not to researchers or research centres, but to the institutional boards of directors. They are highly responsible committees headed by experts in the field: ethicists, legal scholars, judges and other specialized professionals.

The RECs of institutions hosting an FRSQ-funded research centre must adhere to the regulatory framework and standards established by the FRSQ. The FRSQ funds only REC-approved projects.

In 1994, the FRSQ instituted its **Advisory Committee on Research Ethics and Scientific Integrity**, which reports to its board of directors. This committee draws up policies and opinions on various matters submitted for its consideration.

Also in 1994, the ministère de la Santé et des Services sociaux, MSSS (department of health and social services) established the **Central Ethics Committee** (CEC), which reports to the department and is under FRSQ administrative management. The CEC is responsible for enforcing article 21 of the Québec Civil Code and thus for safeguarding the dignity, safety, well being and rights of incompetent minor and adult research subjects. It sees that research projects involving those subjects adhere to the ethical rules before authorizing the start-up or pursuit of such projects. It also follows up approved projects. The CEC is empowered to approve, amend, suspend or reject any proposal or research project within its purview. ([www.frsq.gouv.qc.ca/ethique/default.htm](http://www.frsq.gouv.qc.ca/ethique/default.htm))

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### **3. Research centre audits (visits)**

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The FRSQ, together with the MSSS, is visiting the 19 **FRSQ-funded research centres** and their host **institutions** to audit implementation of GRP regulatory frameworks. It has visited ten institutions thus far and will complete that work by fall 2003. In July 2002, it submitted its initial report to the two departments concerned (MSSS and the ministère de la Recherche, de la Science et de la Technologie, MRST). (The FRSQ now reports to the ministère des Finances, de l'Économie et de la Recherche, MFER.) That report describes compliance with the regulatory framework for research, including research ethics, within the audited institutions and includes recommendations for their attention.

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#### **4. Codes of ethics for health professionals**

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The codes of ethics for professional orders represent another important protection.

Because many research projects require access to human tissues, ova and stem cells, investigators frequently call on doctors, as well as nurses and other health professionals.

The Collège des médecins du Québec (college of physicians) set the tone when, subsequent to discussion with the FRSQ, it added an entire panoply of measures to its code of ethics (amendment dated November 7, 2002 - Section III, Consent, articles 28-31). Those measures require physicians to apply the ethics mechanisms to their professional activities, including research.

It is again reassuring to see that even if Québec professionals were not governed by hospital rules, they could not engage in cloning activities anywhere in Québec. Any doctor contemplating cloning research, for example, would need the approval of a research ethics committee, which would certainly reject the project.

The decision of the Collège des médecins, inspired by the FRSQ's leadership, is snowballing as other health professionals (pharmacists, dentists, nurses and other groups) follow suit.

## **CODE OF ETHICS FOR ORDERS OF HEALTH PROFESSIONALS**

Selected provisions of the code of professional ethics for professionals involved in academic, contract or sponsored research.

(text adapted from the Code of Ethics of the Collège des médecins, R.S.Q., c. C-26, s. 87; 2001)

With respect to research subjects or their legal representatives, professionals must ensure

- that each subject is informed of the research project's objectives and its advantages, risks or disadvantages for the subject, the advantages provided by the usual care, if applicable, as well as the fact, as the case may be, that the professionals will derive a material gain from enrolling or keeping the subject in the research projects;
- that voluntary and informed written consent, which can be withdrawn at any time, is obtained from each subject prior to participation in the research project or when there is any significant change in the research protocol.

Before undertaking research on humans, professionals must obtain approval of the project by a research ethics committee that observes existing standards, particularly in its composition and procedures. They must also ensure that all those collaborating with them in the research project are informed of the professionals' ethical obligations.

Professionals who undertake or participate in research on human beings must comply with the scientific principles and ethical standards generally recognized and justified by the nature and purpose of their research.

Professionals must refuse to collaborate in any research activity where the risks to the health of subjects, healthy or ill, appear disproportionate to the potential advantages they may derive from such or the advantages they may derive from the usual care, if any.

Professionals who undertake or participate in a research project must state their interests and disclose any real, apparent or potential conflicts of interest to the research ethics committee.

In research-related matters, professionals must not be party to any agreement or accept or grant any compensation that would call their professional independence into question.

Remuneration or compensation of professionals for the time and professional expertise they devote to research must be reasonable and known to the ethics committee.

Professionals who obtain royalties or are part of an enterprise which is within their power to control and which manufactures or markets products of benefit to health must so inform the persons to whom they prescribe them and the circles in which they promote them.

Professionals must not knowingly conceal the negative findings of research projects in which they have taken part.

Professionals must express the appropriate caution when informing the public of a new diagnostic, investigative or treatment procedure which has not been sufficiently tested.

## **BACKGROUNDER**

### **PRIVATE RESEARCH AND PRIVATE ETHICS COMMITTEES**

Private laboratories in Québec are careful to subscribe to the codes of professional conduct and the research ethics enacted in Québec and all of Canada. They are most at risk, for any breach of ethics would arouse public distrust and entail the loss of funding and possibly their closing.

In light of this, they readily call on private ethics committees to validate their projects.

Even without regulations, the few Québec firms that have the technical capability to research reproductive or therapeutic cloning are refraining from such activities as long as federal and provincial regulations have not marked out the territory.

Québec is home to private ethics committees that deal generally with pharmacological research and therapeutic testing. According to our information, none of that research involves cloning.

We regard private ethics committees as an efficient approach, but it would be good to have them certified or accredited by an independent body to ensure their independence and effectiveness.

## BACKGROUND

### THREE KEY SETS OF GUIDELINES

Three key documents provide guidance and guidelines for the FRSQ and Québec's researchers.

Naturally, the FRSQ also subscribes to the principles set out in the Nuremberg Code (1946) and the Declaration of Helsinki (updated in 2000).

#### 1. Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (1998 - Medical Research Council of Canada (MRC), Natural Sciences and Engineering Research Council (NSERC) and Canadian Institutes of Health Research (CIHR))

In 1998, Canada's three research councils developed a policy of research ethics for scientific investigations involving human subjects. That policy is set out in the Tri-Policy Statement: Ethical Conduct for Research Involving Humans.

The FRSQ scientific community helped write these Canadian guidelines, and the FRSQ acknowledges the general principles contained in the policy statement.

However, this policy allows human embryo research without dealing with research on human pluripotent stem cells (cells with the potential to develop into different organs). In February 2002, the Canadian Institutes of Health Research (CIHR) developed guidelines to fill that gap (see CIHR Guidelines).

The Tri-Council Statement sets out the following ethical principles:

- the research must have the potential to provide health benefits for Canadians;
- consent must be free, informed and voluntarily given after disclosure of all relevant information;
- review and mandatory follow-up of research projects by an REC;
- respect for privacy and confidentiality;
- no direct or indirect payment, or any other financial incentive, for tissues collected for purposes of stem cell research.

## 2. Human Pluripotent Stem Cell Research: Guidelines for CIHR-Funded Research (2002, Health Research Institutes of Canada - CIHR)

In February 2002, the CIHR clarified the Tri-Council Policy Statement, particularly as regards human embryo research, in a document titled Human Pluripotent Stem Cell Research: Guidelines for CIHR-Funded Research.

The FRSQ, together with its researchers, helped prepare this document. Its Advisory Committee on Research Ethics and Scientific Integrity shared in the consultations staged by the CIHR and submitted recommendations. The FRSQ developed a position and decided in March 2002 to espouse these guidelines.

The FRSQ recommended that the RECs (research ethics committees within health institutions) adopt these guidelines to evaluate research projects involving human pluripotent stem cells and added a few recommendations regarding the application of those rules.

The Guidelines identify the types of research eligible or ineligible for CIHR funding. They provide the scientific community and research ethics committees with useful information about the requirements for consent, privacy and confidentiality. They make provision for creating a national registry of human embryonic stem cell lines generated in Canada.

In sum, the FRSQ and the CIHR agree to fund studies on cells from human embryos under certain conditions. The FRSQ favours research using **adult**, **umbilical** or **placental** tissue cells.

### 3. Standards of research ethics and scientific integrity (2001, FRSQ)

In 2001, the FRSQ produced an important reference tool titled *Les Standards en éthique de la recherche et en intégrité scientifique* (standards of research ethics and scientific integrity). These standards are intended chiefly but not solely for researchers and members of the ethics committees within Québec's public health institutions. ([www.frsq.gouv.qc.ca/ethique/standards/page\\_accueil.htm](http://www.frsq.gouv.qc.ca/ethique/standards/page_accueil.htm))

Québec has its own Civil Code distinct from the Canadian counterpart. This made it critically important to give Québec investigators standards governing protection of the dignity, well-being and rights of research subjects, especially when it comes to competent adults. Article 21 of the Civil Code already protects incompetent minors and adults.

These FRSQ standards harmonize the rules set out in numerous documents that researchers used to consult, and they also underline matters specific to Québec.

This tool stipulates that every research project requiring the involvement of human subjects must be approved and monitored by a research ethics committee (REC) established by the host health institution.

The FRSQ agrees to fund only those research centres, institutes and other organizations whose boards of directors have espoused a regulatory framework consistent with the standards set out in this reference document.

This tool defines *ethics* as the discipline proposing a set of rules of conduct conducive to human well being and respect in the area of scientific health research. *Integrity* is a characteristic of individuals who uphold honesty. The concept of integrity applied to scientific research embraces intellectual probity, the conscientious use of investigative resources and abstention from situations entailing conflict of interest.

This tool for researchers and other members of the scientific community was presented at the first research ethics committee workshop, staged in 2002 by the MSSS, and at the 2002 training day of the National Council on Ethics in Human Research (NCEHR).

The standards contained in this document will undergo periodic review to account for evolving societal issues involving ethics and research.

Beyond the legal and administrative norms provided for researchers and institutions, the FRSQ promotes the shaping of an attitude that prioritizes respect for human beings. It would like these standards to serve not only as rules, but also as guidelines useful for educational purposes.

## BACKGROUND

### THE FRSQ'S POSITIONS ON HUMAN CLONING AND STEM CELL RESEARCH

#### **Human cloning (reproductive and therapeutic)**

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In 1998, the then minister of health and social services, Dr. Jean Rochon, asked the FRSQ to see that no public funds went into funding human cloning. Consequently, the FRSQ does not award grants for studies in this area. Given the strict ethical and regulatory framework now in effect in Québec and the private sector's exemplary conduct thus far, it is difficult – if not impossible – to conduct human cloning research in Québec at this time.

More specifically, it is ethically unacceptable to

- produce genetic modifications involving germ cells or human embryos;
- create or seek to create hybrid species through such methods as the combination of human and animal gametes or the transfer of germ or somatic cell nuclei between cells taken from human beings and other species;
- create human embryos solely for research purposes;
- conduct research entailing human cloning by any means whatever, including the transfer of somatic cell nuclei, the forming of animal-human hybrid species or embryo transfer between humans and other species.

The ban on human cloning comes under criminal law, a federal purview. Federal Bill C-13 also targets prohibition of such projects.

#### **Human stem cells (therapeutic research)**

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In Québec, scientists are allowed for therapeutic reasons to conduct research on human pluripotent embryonic stem cells (cells with the potential to develop into different organs). Where possible, however, the FRSQ favours research using **adult, umbilical or placental** tissue cells.

The FRSQ has developed a position in this regard and subscribes overall to the Guidelines of the Canadian Institutes of Health Research (CIHR). (See CIHR Guidelines)

Like the CIHR, the FRSQ does not fund research projects

- meant to create human embryos conceived solely to isolate stem cell lines or other pluripotent cell lines;
- concerned with the nuclear transfer of somatic cells into human oocytes in order to design embryonic stem cell lines or other human pluripotent cell lines (e.g. cloning);
- concerned with the directed donation of stem cell lines or other pluripotent cell lines to given individuals, except if autologous donations are involved;

or during which:

- SE cells, GE cells or other pluripotent cells, whether human or non-human, are combined with a human embryo or transplanted into a human foetus;
- SE cells, GE cells or other human pluripotent cells are combined with non-human embryos or transplanted into a non-human foetus.

## BACKGROUND

## REFERENCES ON ETHICS

### FRSQ publications

- *Les Standards en éthique de la recherche et en intégrité scientifique* (first edition, 2001) (standards for research ethics and scientific integrity).
- *Cadre réglementaire des Bonnes pratiques de la recherche dans les établissements universitaires de santé du Québec* (regulatory framework for good research practices in university health institutions in Québec) (includes implementation, audit mechanism and implementation follow-up).

Documents on human stem cell research

- *Research on Human Pluripotent Stem Cells* (recommendations and guidelines for research funded by the Canadian Institutes of Health Research, CIHR).
- *Réponse du Comité consultatif d'éthique de la recherche et d'intégrité scientifique du FRSQ aux sept recommandations préliminaires des IRSC* (response of the FRSQ advisory committee on research ethics and scientific Integrity to the CIHR's seven preliminary recommendations).
- *Recherche sur les cellules pluripotentes embryonnaires humaines* (human pluripotent embryonic cell research) (resolution of FRSQ Board of Directors - 26/03/2002).

### MSSS Publications

- *Plan d'action ministériel en éthique de la recherche et en intégrité scientifique* (1998) (departmental action plan on research ethics and scientific integrity)

The MSSS action plan pursues two objectives, i.e. the protection of human subjects and proper division of responsibilities. It deals with four kinds of measures:

- a) framework measures under the responsibility of the institutions comprising the health and social services network;
- b) measures under the responsibility of funding organizations;
- c) measures aimed at setting out guidelines for activities not covered by framework measures but under the responsibility of professional groups;
- d) measures under the responsibility of the Québec government, the MSSS and the regional boards.

The institutions within the health and social services network are given clear responsibilities for research conducted within their walls. The last section of the action plan sets out standards for the research ethic committees that the minister of health and social services designates to enforce article 21 of the Civil Code.

- *Rapport d'enquête concernant les activités des comités d'éthique de la recherche au Québec*, 1999 (report on the activities of Québec's research ethics committees).
- *Répertoire des comités d'éthique du réseau québécois de la santé et des services sociaux*, 2001 (directory of research ethics committees of the Québec health and social services network).

#### **Publications of the Central Ethics Committee (MSSS)**

- *Les règles de fonctionnement du Comité central d'éthique* (operating rules of the Central Ethics Committee).

#### **Other references**

- Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (1998), Medical Research Council of Canada (MRC), Natural Sciences and Engineering Research Council (NSERC) and Canadian Institutes of Health Research (CIHR).
- *Conditions d'exercice des comités d'éthique de la recherche désignés ou institués* (operating conditions for designated or instituted research ethics committees), Notice published in the *Gazette Officielle du Québec*, No. 35 (29/08/1998).
- *Évaluation des mécanismes de contrôle en matière de recherche clinique au Québec* (evaluation of control mechanisms for clinical investigation in Québec), Deschamps report submitted to MSSS in 1995.
- Good Clinical Practice: Consolidated Guideline (Health Canada, 1997).
- Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects, World Medical Association (WMA), 1964 document successively updated until 2000.
- The Nuremberg Code (1946).