

2008

Clinical Practice Guideline: Informed Consent to Donate Embryos for Research Purposes

Roxanne Mykitiuk

Osgoode Hall Law School of York University, rmykitiuk@osgoode.yorku.ca

Erin Nelson

Jeff Nisker

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Recommended Citation

Mykitiuk, Roxanne, Erin Nelson, and Jeff Nisker. "(SOGC) Clinical Practice Guideline: Informed Consent to Donate Embryos for Research Purposes." *Journal of Obstetrics and Gynaecology Canada* 30.9 (2008): 824-829.

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Informed Consent to Donate Embryos for Research Purposes

This guideline has been prepared by the Ethics Committee and reviewed and approved by the Executive and Council of the Society of Obstetricians and Gynaecologists of Canada.

PRINCIPAL AUTHORS

Erin Nelson, BSc, LLB, LLM, Edmonton AB
Roxanne Mykitiuk, BA, LLB, LLM, Toronto ON
Jeff Nisker, MD, PhD, London ON

SOGC ETHICS COMMITTEE

Jeff Nisker (Chair), MD, PhD, London ON
Jan Christilaw, MD, Vancouver BC
Julie Anne Corey, RM, Elora ON
Maureen Heaman, RN, PhD, Winnipeg MB
Abby Lippman, PhD, Montreal QC
Roxanne Mykitiuk, BA, LLB, LLM, Toronto ON
Erin Nelson, BSc, LLB, LLM, Edmonton AB
Sanda Rodgers, BA, LLB, LLM, Ottawa ON
Jodi Shapiro, MD, Toronto ON
Susan Sherwin, PhD, Halifax NS
Disclosure statements have been received from all members of the committee.

Abstract

Objective: To develop guidance for clinicians participating in the informed choice process with respect to the donation of human embryos for research purposes.

Recommendations

1. As indicated in the Canadian Institutes of Health Research Guidelines and the *Assisted Human Reproduction Act*, specific consent from both the gamete and embryo providers is required before embryos can be used for research purposes. The gamete donors may be different individuals than the embryo providers when donated gametes are used to create embryos.
2. The consent process should inform potential donors of the possible types of (and for final consent, the specific) research project(s) for which the embryos will be used; the risks involved in

donating embryos to research, such as not having these embryos available for their reproductive purposes; the fact that the woman/couple will not benefit personally from donating embryos to research; the potential for commercial gain by others; the possibility that they will be contacted in future about the disposition of the embryos; the fact that confidentiality cannot be absolutely guaranteed.

3. Designation of cryopreserved embryos no longer be required for reproductive purposes to be donated to research, donated to another couple, or discarded should be discussed prior to gamete retrieval and made at the time of cryopreservation, with the understanding that in the future, final consent will be requested. The final decision as to the donation of cryopreserved embryos research should not be made until after the woman/ couple decide they no longer require the embryos for their reproductive purposes. The decision to end cryopreservation should be made separately from the decision regarding disposition of the embryos. The woman/couple will have to be re-contacted regarding the final disposition of their embryos.
4. As a result of lack of scientific data regarding the predictability of microscopic characterization of embryos and potential for pregnancy, it is recommended that all women/couples be offered the opportunity to cryopreserve all embryos not transferred during the treatment cycle and be informed that a failure to cryopreserve all embryos may increase the chance of having to undergo an additional in vitro fertilization cycle to achieve reproductive goals.
5. Research participants should be informed that they may withdraw their consent at any time before the embryos are thawed for research purposes, or, in the case of stem cell research, before a stem cell line is created.
6. Potential donors should be informed that their medical care will not be affected by their decision regarding embryo donation.

J Obstet Gynaecol Can 2008;30(9):824–829

INTRODUCTION

This SOGC clinical practice guideline is established to assist clinicians in understanding and complying with the laws, guidelines, and obligations of best medical practice regarding the donation of embryos to research. While this policy statement and the accompanying recommendations are directed primarily at clinicians, they should guide all parties involved in research using donated human embryos.

Key Words: Embryo research, consent, embryo donation

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In Canada, research involving human embryos is permitted in some circumstances and is governed by the Assisted Human Reproductive Act¹ and the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans.² Guidelines specific to human pluripotent stem cell research were issued by the CIHR in 2002, and updated in 2005 and 2006.³

In Canada, embryos may be created only for reproductive purposes.¹ The only embryos available for research in Canada are those that are no longer required for reproductive purposes, when the gamete and embryo providers have given written consent to their use. Embryos may also be used for improving, or providing instruction in, assisted human reproduction procedures in some circumstances.¹

Consistent with the provisions of the AHR Act, the TCPS, and the CIHR Guidelines, this policy statement is underpinned by five fundamental considerations:

1. Safeguards must be present to ensure that embryos donated for research are no longer required for reproductive purposes.
2. A recognition that providing free and informed consent to the donation of embryos for research is a multi-staged process that involves all gamete and embryo donors.
3. A recognition of the importance of non-commercialization of reproductive materials and capacities.
4. A recognition that while all persons are affected by assisted reproductive technologies, women are more directly and significantly affected than men by their application, and the health and wellbeing of women are of paramount concern.
5. A recognition that consent to the use of embryos in research “means fully informed and freely given consent” thereby acknowledging that freedom of consent can be undermined in many ways, including by financial pressures and uncertainty about the confidentiality of decisions.

ABBREVIATIONS

AHR	Assisted Human Reproduction
CIHR	Canadian Institutes of Health Research
IVF	in vitro fertilization
TCPS	Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans

INFORMED CONSENT TO THE DONATION OF EMBRYOS FOR RESEARCH

Because each egg retrieval cycle involves significant potential harm to women, best practice requires that clinicians ensure that women not undergo avoidable egg retrieval procedures. These potential harms are related to the medications used in ovarian stimulation^{4,7} and include ovarian hyperstimulation syndrome, which can cause severe complications in about 0.05% to 5% of IVF cycles^{4,8} and, in very rare cases, can be fatal. Long-term risks of ovarian stimulation are hypothesized⁹ but remain unproven. Risks are also associated with oocyte retrieval.¹⁰ Given the health risks involved in menotropin stimulation and oocyte retrieval, all embryos that are created following ovum retrieval are to be made available for the reproductive goals of the woman/couple concerned. It is for the woman/couple to decide when their reproductive needs have been met. Therefore, after transfer of one or two fresh embryos to the woman’s uterus,¹¹ all additional embryos should generally be frozen for possible use in future cycles, depending upon the wishes of the woman or couple.¹² It is only after it is confirmed that the woman/couple will have no interest in using the embryos for future reproductive purposes that it becomes appropriate to consider use of these embryos in research projects. The informed consent process must be designed to clearly and specifically reflect both clinical and psychosocial concerns.

Who Should Give Consent?

The TCPS,² CIHR Guidelines,³ and the AHR Act¹ all require specific consent from both the gamete and embryo providers before embryos can be used for research purposes. The gamete donors may be different individuals than the embryo providers when donated gametes are used to create embryos. When embryos are created from gametes of a third party donor, it may not be possible to ascertain whether the gamete donor(s) consented to research on embryos created using their gametes. This may be the case, for example, in the context of anonymous gamete donation. Without the consent of the gamete donor(s) these embryos cannot be donated for use in research.

When Should Consent Be Obtained?

The decision to cryopreserve

The purpose of this policy statement is to provide guidance for SOGC members who may be in a position to seek informed consent to the use of embryos in research. It does not speak directly to policy and practice concerning cryopreservation of embryos. However, as this issue is intimately bound up with the question of embryo donation, and, in particular, with the donation of fresh embryos, some discussion of this is necessary.

Following IVF, women/couples will be provided with information about the number of embryos that have been produced and offered the opportunity to cryopreserve embryos that are not to be transferred in a particular IVF cycle for transfer in the future.

Decisions about the disposition of embryos that are not immediately transferred following IVF are made at a time when women/couples are uncertain about reproductive outcomes and when they are uncertain about whether those embryos that have not been transferred will be required in the future for reproductive purposes.

While some take the view that it is possible to determine the likelihood that any specific embryo will go on to create a pregnancy, or will survive the freeze/thaw process, there is no scientific consensus on this point.^{12–14} A decision not to cryopreserve all remaining embryos can be an informed decision only when women/couples are told that there is no consensus about how to determine which embryos are suitable for cryopreservation, and that different clinics have different views about whether any specific embryo is suitable for cryopreservation.^{12–13} Because of this lack of consensus, it is recommended that all women/couples be offered the opportunity to cryopreserve all remaining embryos, and that clinicians ensure they understand that a failure to cryopreserve all embryos may increase the chance of having to undergo an additional IVF cycle in order to achieve reproductive goals.

Cryopreserved embryo donation

In Canada, the only embryos that can be used for research are those no longer required for the reproductive needs of the women/couples for whom they were created through IVF¹; therefore, women/couples should not be asked to donate embryos to research until they have decided they no longer require their embryos for reproductive purposes. However, the AHR Act¹ and CIHR Guidelines³ indicate that the informed consent process for donating embryos no longer required for reproductive purposes to research should begin prior to gamete retrieval. The options for disposition of any embryos that are no longer required for reproductive purposes are to donate the embryos to another party for reproductive use, to donate them to research, or to discard them. This initial stage of the informed consent process registers the preliminary intention of the woman/couple who are informed at that time that they will be contacted again to make a final decision about the disposition and use of their embryos.

After completing their families through IVF or abandoning infertility treatment, women/couples will need to confirm their original disposition intention before it can be acted upon. At this stage, it is imperative to ensure that the two decisions—to end embryo storage and to determine

disposition of embryos—are made separately, because potential donors may now have come to different views about donating their excess embryos for use in research. Further, regarding donation to research, the particular project should be identified prior to consent being given. Potential donors must, therefore, be asked again whether they wish to donate their embryos to research when the embryos are being sought for use in a particular research project.

Fresh embryo donation

The donation of fresh, rather than cryopreserved, embryos gives rise to unique issues and concerns, and poses challenges for the process of informed consent. First, in the case of fresh embryos, donors will not have the ability to reconsider their initial decision about donation at some distance from the clinical encounter and in circumstances in which they are informed about the reproductive outcomes of a specific IVF treatment cycle. It is important that potential donors understand that once the embryos have been donated and used in research, there is no possibility of re-thinking the decision not to cryopreserve the embryos in question. Second, the time frame in which a decision about fresh embryo donation needs to be made is significantly abbreviated and might not provide potential donors with the time they need to make a thoughtful decision about donation that reflects their own needs and interests. Third, potential donors might feel pressured to agree to donate embryos or might worry that refusing consent will lead to their ongoing IVF treatment being compromised, even though the clinicians do not purposefully give this impression.^{12,15,16} Based on these concerns, clinicians should not ask their patients to consider donating fresh embryos to research unless and until the woman/couple have decided that they do not wish to cryopreserve their embryos.

Information to Provide to Potential Donors

Cryopreserved embryo donation

In order for consent to donate embryos for research to be considered informed, the following must be provided:

- **Project information:** Potential embryo donors should be informed about the specific research project in which their embryos will be used. They should be given a description of the purpose of the proposed project, including the title of the project, the names of the principal investigator(s) and the participating institutions, and the sources of funding. Potential donors should also be informed that there may be other possible future research uses that are unknown at the time.
- **Information about voluntary choice:** Potential donors must be informed that their decision is voluntary and

that, should they choose not to participate their choice will be respected. In addition, potential donors must be informed that they may withdraw their consent to participate even after they have signed the consent form. It must be made clear in the consent form what steps must be taken to withdraw consent. Potential donors must be informed that if they decide not to participate, or if they initially consent but later decide to withdraw from participation, their medical care will not be affected in any way.

- Information about what will be done with donated embryos: Potential donors must be informed about what will be done with and to the embryos donated to research (and with any cell lines, tissue, etc. extracted or derived from the embryo). If embryos will be destroyed in the research process, this must be explained to potential donors. Potential donors must also be informed that embryos used in research will not be transferred to a woman's uterus, nor will they be used to create a pregnancy.
- Risks and benefits of participation in research: Potential donors must be informed of all of the risks of embryo donation including the following. They must be told that donating embryos prior to the completion of their reproductive goals will reduce the number of embryos available for reproductive purposes and that, should they later decide that they wish to undertake another attempt at conception, women who have donated embryos for use in research may have to undergo another egg retrieval cycle, with all of the risks that this entails. Potential donors must also be informed about the possible psychological implications of embryo donation.
- Protection of donor's privacy: Potential donors must be informed about how their personal information will be protected in the context of the study, as well as about any risks to their privacy. In particular, as genetic information about the donor may be obtained, potential donors should be told about the risks of inadvertent disclosure of such information.
- Disclosure of researcher's financial incentives: All the potential benefits to the researcher and the clinicians involved in the patient's care must be disclosed to the potential donor. This disclosure must include the possible financial or commercial benefit that may be derived from the use of the embryo or cells derived from it, and an explanation that research subjects will not benefit from commercialization of the products of the research.
- Information about stem cell research: The CIHR Guidelines stipulate that those donating embryos to stem cell research must, in addition to the information

usually conveyed to research participants, also be given, at a minimum, the following information: (1) that the cell lines will be anonymized; (2) that subjects are free not to participate, and that they may withdraw their consent at any time prior to the creation of an anonymized cell line; (3) that the research could result in the production of a stem cell line that could be maintained for many years, distributed to other parts of the world, and used for various research purposes; and (4) that subjects will not benefit personally from the cell lines created, that subjects will not have dispositional authority over the cell line(s), and that they will not benefit from any commercialization of the stem cell line(s).

The above-noted information is necessary but not sufficient for donors' consent to be fully informed. The CIHR Guidelines clearly assume that potential donors will be informed about the risks and benefits of participation in stem cell research, but it is important to specify in detail what potential donors should be told in the context of the informed consent process. Potential donors should also be informed that stem cell research results in the destruction of the embryo and that stem cell lines might exist indefinitely (not just for many years, as outlined in the CIHR Guidelines). Potential donors should also be made aware of whether true anonymization of stem cell lines is possible. For example, if stem cell lines are to be used clinically, it will probably be necessary to re-contact donors to determine their current health status. Thus, cell lines intended for clinical use cannot be made truly anonymous, and this has implications for the confidentiality of donor health and genetic information.

Fresh embryo donation

In addition to being given the information required for donation of cryopreserved embryos set out above, potential donors of fresh embryos must be informed that a decision to donate fresh embryos may result in the potential physical, emotional, and financial harm of further medical and surgical procedures should a woman/couple later decide that they require additional embryos for reproductive purposes. Although considerations are similar when a final decision is made about cryopreserved embryo donation, decisions about fresh embryos must be made within hours or two days at most, whereas for cryopreserved embryos, the final decision can be made after as many years as it takes to come to this decision. Further, in the case of fresh embryos, potential donors must make a decision about donation without knowing the reproductive outcome of the current IVF cycle.

Who Should Obtain Consent?

Cryopreserved embryo donation

The CIHR Guidelines state that “[m]embers of the health team treating and/or counselling the client should not be the persons to obtain consent from the embryo provider at the time of re-consent,” nor should physicians who are part of the stem cell research team.³ The concerns are physician conflict of interest and that patients might feel they should agree to donate embryos to research because their physician, whom they trust, is raising the possibility with them.^{4,10,12,17,18} This rule has recently been challenged by Caulfield et al.,¹⁹ on the basis that physicians obtaining consent for donation of embryos for stem cell research is not different from physicians obtaining consent for other areas of research participation.

The most important clinical discussion occurs when embryo cryopreservation is considered, and this discussion must include a physician intimately involved in the care of the woman/couple. When a woman/couple indicate to the clinical team that they no longer require their cryopreserved embryos for reproductive purposes, the team should determine whether the woman/couple indicated an interest in donating embryos to research at the time of embryo cryopreservation. If this is the case, a representative of the clinical team who has not been a part of the patient’s care may contact the woman/couple to inquire whether they are still interested in donating embryos no longer required for reproductive purposes to research.¹¹ If the woman/couple indicate that they are still interested in donating embryos to research, they should be informed that they will be sent a package with the details of the specific research study and will be provided with the information they need to provide free and informed consent for that research study.

Fresh embryo donation

Separating the clinicians providing patient care from the free and informed consent process is more problematic for fresh embryo donation, as the decision not to cryopreserve all embryos is made following consultation between the physician responsible and the patient(s). However, once the decision not to cryopreserve embryos is made, and the irrevocable nature of this decision has been fully explained to the patient(s), the patient’s name can be given to a clinical team member who has not participated in, and will not in the future participate in, the patient’s care in order to approach the patient about the opportunity to donate their fresh embryo(s) to a research project.

Withdrawing Consent

The CIHR Guidelines and AHR Act provide that embryo donors may withdraw their consent at any time prior to the thawing of frozen embryos or, in the case of stem cell research, the creation of a stem cell line.

SUMMARY

These guidelines are primarily concerned with safeguarding the health, well-being, and autonomy of women and couples. Decisions about donation of embryos to research should be made in accordance with national guidelines^{2,3} and laws¹ that inform the ethical conduct of research involving human embryos. Safeguards must be present to ensure that embryos donated for research are no longer required for reproductive purposes. Obtaining free and informed consent to the donation of embryos for research is a multi-staged process. While all persons are affected by assisted reproductive technologies, women are more directly and significantly affected than men by their application, and the health and well-being of women are of paramount concern (AHR Act, Section 2).¹

Recommendations

1. As indicated in the Canadian Institutes of Health Research Guidelines and the Assisted Human Reproduction Act, specific consent from both the gamete and embryo providers is required before embryos can be used for research purposes. The gamete donors may be different individuals than the embryo providers when donated gametes are used to create embryos.
2. The consent process should inform potential donors of the possible types of (and for final consent, the specific) research project(s) for which the embryos will be used; the risks involved in donating embryos to research, such as not having these embryos available for their reproductive purposes; the fact that the woman/couple will not benefit personally from donating embryos to research; the potential for commercial gain by others; the possibility that they will be contacted in future about the disposition of the embryos; the fact that confidentiality cannot be absolutely guaranteed.
3. Designation of cryopreserved embryos no longer be required for reproductive purposes to be donated to research, donated to another couple, or discarded should be discussed prior to gamete retrieval and made at the time of cryopreservation, with the understanding that in the future, final consent will be requested. The final decision as to the donation of cryopreserved embryos research should not be made until after the woman/couple decide they no longer require the embryos for their reproductive purposes. The decision to end cryopreservation should be made separately from the decision regarding disposition of the embryos. The woman/couple will have to be re-contacted regarding the final disposition of their embryos.
4. As a result of lack of scientific data regarding the predictability of microscopic characterization of embryos and

potential for pregnancy,^{12,20} it is recommended that all women/couples be offered the opportunity to cryopreserve all embryos not transferred during the treatment cycle and be informed that a failure to cryopreserve all embryos may increase the chance of having to undergo an additional in vitro fertilization cycle to achieve reproductive goals.

5. Research participants should be informed that they may withdraw their consent at any time before the embryos are thawed for research purposes, or, in the case of stem cell research, before a stem cell line is created.

6. Potential donors should be informed that their medical care will not be affected by their decision regarding embryo donation.

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