Informed consent and the use of gametes and embryos for research: a committee opinion

The Ethics Committee of the American Society for Reproductive Medicine

American Society for Reproductive Medicine, Birmingham, Alabama

The ethical conduct of human gamete and embryo research depends upon conscientious application of principles of informed consent developed in the context of clinical research. This document explores these principles, which entail, for example, that investigations occur under Institutional Review Board oversight. This document also discusses the complexities in obtaining informed consent from the persons whose gametes or embryos are being used in research but were originally intended for reproductive purposes. This statement replaces the document of the same name last published in 2004 (Fertil Steril 2004;82:S251–252). (Fertil Steril® 2014;101:332–5. ©2014 by American Society for Reproductive Medicine.)

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KEY POINTS

- Many constituencies, including scientific, medical, political, and religious organizations, have debated the ethical acceptability of research involving human gametes and embryos. While broad unanimity of opinion has yet to emerge, and likely never will be achieved, this committee joins other national committees and commissions in deeming such research ethically permissible.
- Institutional review board (IRB) approval and appropriate informed consent are necessary before research is performed on any gamete or embryo.
- Research donors (those who donate gametes or embryos specifically for research) should be provided the specific categories of research and disposition of their gametes or embryos before collection (gametes) or creation (embryos) for research and research activities are initiated. As with other research, the informed consent process should address the specific goals, objectives, and procedures of the project.
- In this document "reproductive donors" are individuals whose gametes or embryos are primarily intended for reproduction. Third-party reproductive donors should be informed when research disposition is one potential option for gametes or embryos not utilized for reproductive purposes. Third-party donors' authorization or refusal of authorization should be documented in their written agreement of whether or not gametes or embryos may be used in research.
- In vitro fertilization (IVF) clinics should confirm that research investigators have obtained appropriate IRB approval before participating in or donating gametes or embryos to research activities. They should coordinate with research centers in obtaining appropriate informed consent and maintaining appropriate records pertaining to research on and disposition of all gametes and embryos.
- Donors must be informed that research using donated gametes or embryos may have commercial value and that the act of donation does not confer a right to such commercial value.
- Similar medical screening and counseling standards should be outlined for male research donors as for female research donors.
- Donors of gametes or embryos for research or reproduction should be advised that if genomic sequencing is performed, information about their genetic information might be published, thereby creating the potential that genetic information about them or their close relatives may be linked to their identities or the identities of their relatives.
- This Committee recognizes that human embryonic stem cell (hESC) research carries additional moral

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issues and refers members to the Ethics Committee Report "Donating spare embryos for stem cell research" (1).

Many constituencies, including members of the scientific, medical, political, and religious communities, have debated the ethical permissibility of research involving human gametes or embryos. While broad unanimity of opinion has not yet emerged, national commissions and other national groups have affirmed the ethical permissibility of such research; research findings have been published in their respective reports (1–5). In view of the level of interest in human embryo and gamete research, this Committee advises that the investigator bear the burden of demonstrating that the proposed studies merit using human gametes or embryos, that there is no adequate alternative research methodology, that the study is likely to yield important scientific or clinical data, that the number of gametes or embryos will be the minimum required for adequate study design, and that risks to donors will be minimized.

This Committee emphasizes that a critical component of ethical research includes the investigator's obligation to obtain IRB approval for the research project and informed consent from every prospective study participant prior to any research use of his/her donated cells, embryos, or tissues.

In the field of assisted reproduction, the following cells and tissues might be studied: oocytes, spermatozoa, nonviable or abnormal embryos, abnormally fertilized embryos that will not be transferred to the uterus, normal fresh or frozen embryos donated by IVF patients who no longer wish to use the embryos for reproductive purposes, ovarian tissue, testicular tissue, or gametes obtained to generate research embryos but never intended to be transferred. Sensitive ethical and policy issues arise when research involves the destruction of existing viable embryos or the generation of embryos for research that involves their ultimate destruction. This committee recommends informed consent for use in research should be obtained from each cell or tissue donor before any research activities are carried out on any of these cells or tissues. IRB approval is required for all such research.

For the sake of clarity, we use the term "research donors" when referring to individuals who participate in research that involves donation of gametes or embryos directly to research and the term "reproductive donors" when referring to individuals who participate in research that involves donation of gametes or embryos initially intended for reproductive use (6). "Third-party donors" are individuals who donate gametes or embryos to another individual or couple specifically for reproductive purposes.

Informed consent protects donors and investigators and promotes clarity about the investigator's research plans. Precise statements about intended benefits and methods also address misconceptions patients and members of the public may have about embryo research. The informed consent process for research should make it clear when gametes will not be used for fertility treatment but will not be used only for research.

Reproductive donors (including third-party donors) must be assured that nonparticipation in research will not adversely affect their status in the fertility program.

Donors should be provided with information that addresses the goals and benefits of the research, and investigators should specifically address ethical concerns about embryo or gamete research. Donors should be apprised that the cells or tissues they donate might yield a commercial value. They must also be informed that the cells might be destroyed in the process of research or if not utilized. The IVF facility and research investigators should disclose all conflicts of interests to the donors, including but not limited to financial conflicts of interest.

Clinicians and researchers should acknowledge that prospective research or reproductive donors might change their minds and decide not to donate their gametes or embryos for research purposes. Prospective donors should be informed about the circumstances, procedures, and limitations that will govern the withdrawal of consent. To ensure appropriate informed consent, IVF clinics and researchers should ensure that vulnerable groups and donors are not exploited (3). Additionally, similar medical screening and counseling standards should be outlined for male research donors as for female research donors (7).

The informed consent process should be led by a clinician competent to explain the nature of the research, its benefits and risks, and to authoritatively answer potential participants' questions. The person or persons on the research team who will have the authority to obtain informed consent should be approved by the IRB. An explanation of the research purpose, when known, is important because prospective donors may be willing to donate for some purposes, such as studies designed to improve success rates in assisted reproduction, but not for others. Investigators should obtain reapproval by the IRB if significant changes are made in the purpose or nature of the research; they may need to engage in a re-consent process with the research donors after a review of the changes. Presence of an impartial third-party witness or ombudsperson is encouraged when appropriate. Donations of gametes or embryos to repositories may allow for more categorical or generic consents such as infertility, embryology, or human health research (8). Creation of human embryonic stem cell lines generally requires more detailed consents (9, 10).

Reproductive donors should provide consent for specific research studies in a manner similar to that of research donors. Although certain training or laboratory quality control activities involving use of gametes or embryos, including abnormal ones, may not meet federal or local criteria for research, consent for such uses might still be appropriate from reproductive donors. It is understood by this Committee that third-party reproductive donors generally have relinquished all the dispositional authority to their oocytes, sperm, and/or embryos that have been created. To be transparent about this matter, consent should be obtained prior to reproductive donation to allow excess gametes or embryos to be used for research purposes (11, 12).

The Committee recognizes that the burden of obtaining clinical informed consent from research donors for the clinical processes involved in the procurement of gametes/embryos rests with the IVF team but that the research team bears the burden for the actual research consent (2). For

reproductive donors who are having their gametes or embryos used for research simultaneously or at a later date, the informed consent must be appropriately obtained. The Committee refers readers to the 2009 National Institutes of Health (NIH) guidelines (2). The NIH guidelines explain that the gamete or embryo is the subject of research, not the donor(s). We recommend that IRB approval and informed consent be obtained for gamete or embryo research following these guidelines.

Frozen embryos and gametes preserved in the course of fertility treatment may present unique challenges prior to use for research purposes. Consent given during the course of the infertility treatment may not reflect the sentiment of the patient, couple, individual, or reproductive donor at the time of the proposed study. Obtaining consent from a reproductive donor to use his/her frozen embryos or gametes for research is best done after fertility treatment is complete. The person who is best able to obtain consent from a prospective donor is one who is knowledgeable about the research processes but has no vested interest in the procedure(s).

It is understood by this Committee that third-party reproductive donors generally have relinquished all rights to their oocytes, sperm, and/or embryos. Most third-party reproductive donors will be focused on the collection and "reproductive" consequences of their donation; informed consent for these third-party reproductive donors is always demanding. Ethically, this Committee feels it is important to assure that third-party reproductive donors understand that the disposition of their gametes or embryos includes both reproduction and potential uses in research.

Regarding the benefits and risks, prospective donors who donate unused gametes or embryos for research should be informed that the benefit will take the form of laboratory quality control, training, and/or advancement of knowledge, and that they may not directly benefit from the study. Prospective donors should be aware that any discoveries from use of gametes or embryos such as the presence of a genetic mutation might or might not be conveyed to them, depending on then-current practice standards for reporting such mutations to patients. Reproductive donors should be advised of the risk that they later might regret not having saved the embryos or gametes for their own use or for donation to other couples or individuals.

The informed consent process and informed consent forms for donors should receive prior approval from the IRB or equivalent oversight committee and include the information deemed appropriate by the Society for Assisted Reproductive Technologies (SART) and ASRM. With research donors, consent to study gametes intended for research should be sought before the collection of a semen sample, oocyte recovery, or tissue sampling, giving potential donors time to consider consent forms and other material. Completed consent forms should be stored in a confidential file that is kept along with the relevant medical records by the appropriate facility. Records should be kept safely according to IRB protocol with arrangements made for transfer of documents should a clinic, clinician, investigator, or research facility cease to exist.

A genome or extended DNA sequence in a public database could be linked to the identity of a gamete or embryo donor, or even a donor's close relatives. Donors of gametes or embryos for fertility purposes and research should be informed of this risk. This risk can be substantially reduced by depositing genome sequences in secure databases. The accuracy of future technology may link the published genetic information to the identity of the donor(s) or that of his or her close relatives (13).

In summary, a carefully specified procedure for obtaining informed consent is vital for the ethical implementation of studies involving human gametes and embryos. All research activities must be performed with strict attention to ethical standards including respect for autonomy and confidentiality. Informed consent and active IRB involvement are important features in the ethical conduct of human research.

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The following members of the ASRM Ethics Committee participated in the development of this document. All Committee members disclosed commercial and financial relationships with manufacturers or distributors of goods or services used to treat patients. Members of the Committee who were found to have conflicts of interest based on the relationships disclosed did not participate in the discussion or development of this document.

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