



*Documentation of Informed Consent for
Assisted Reproduction:
Embryo Thawing, Embryo Biopsy
and Freezing*

Under certain circumstances, frozen embryos of any developmental stage i.e. zygotes to blastocyst may be thawed and refrozen for future use. In addition, previously biopsied and frozen embryos may be thawed, re-biopsied and refrozen for primary or secondary PGS testing. Primary PGS indicates first time- biopsy and screening embryos during a fresh IVF cycle. Secondary PGS involves thawing frozen embryos for initial biopsy and screening, or retesting embryos that have failed to produce genetic test results upon primary testing. Although live births have been reported with refreezing of previously frozen-thawed embryos, these techniques are still in the early stages of development and the potential for loss of embryos through such procedures exists.

Date Imaged _____
Clerk Initials _____

Signatures

Patient	Partner (if applicable)	Date
_____	_____	_____
_____	_____	_____
_____	_____	_____

Embryo Thawing

Embryo Biopsy

Embryo Cryopreservation

Physician/Witness _____

Embryo Thawing, re-Biopsy and/or re-freezing

Thawing of frozen zygotes and embryos is the reverse process of cryopreservation. The cryoprotective agents, used to protect embryos during the freezing process, are carefully removed from the embryos. The success of the freezing and thawing procedures depend on multiple factors including the quality of the fertilized oocytes and embryos.

Risks

There is a possibility that all to none of the zygotes or embryos cryopreserved will survive the procedures, there is no assurance that the embryos will implant and result in a pregnancy. Surviving cryopreserved embryos appear to divide as well as fresh embryos. There has been a proposed increased risk of infants having developmental defects after cryopreservation and thawing in animal studies. The human experience has not proven any increase in such defects.

I/We elect to: (please initial your choice).

	Patient	Partner (if applicable)
1) Have my cryopreserved embryos thawed	_____	_____

Embryo biopsy

- Embryo biopsy removes one or more cells from an embryo for genetic screening or diagnosis
- These cells can then be used for pre-implantation genetic screening (PGS) or diagnosis (PGD)

Patients having their embryos genetically screened (PGD/PGS) must have their embryos biopsied to obtain material for genetic analysis. Typically, embryo biopsy may be performed on day 5 or day 6, by removing

several cells from the trophectoderm of a blastocyst. Biopsies can also be performed on day 3 embryos when no more than 2 cells (blastomeres) are removed for diagnosis. For the biopsy procedure, the embryologist makes an opening in the covering of the embryo (zona pellucida), by dissolving a small hole in the shell with the use of laser. A cell or a group of cells is then removed via aspiration with a pipette. The embryo is returned to an incubator while the cell is placed in a tube and sent to a reference laboratory for analysis using same-day or next-day delivery courier. The embryo is then frozen for future use.

Risks that may be associated with embryo biopsy include damage to the embryo resulting in demise of the embryo. Artificial manipulation of the embryo may increase the rates of monozygotic (identical) twinning which are significantly more complicated pregnancies. There may be other risks not yet known. It is unknown whether biopsied embryos are less likely to implant than embryos that have not been biopsied. Risks included with transport include weather and air travel conditions, and may delay the receipt of samples, which may delay analysis and transfer.

The biopsied cells are analyzed by the reference laboratory for the presence of specific number of chromosomes or detection of specific deviations in the genetic code. If the cell is found to be free of the disorders, then it is inferred that the embryo it was derived from is also clear of the disorder. Embryos found to be unaffected are transferred to the mother or frozen for transfer in the future. Embryos that are predicted to be affected by the disease will not be transferred and will be discarded unless donated to research. If inconclusive results or no signal is obtained, or if embryos are determined to be unaffected carriers of genetic diseases, these embryos may be transferred after discussion with the patient.

Several embryos are generated during PGD to maximize the probability that at least one unaffected embryo will be found. However, it is possible that no unaffected embryos will be detected and consequently no embryos will be eligible for transfer to the uterus. Additionally, embryos may be excluded from transfer because they are not developing normally.

At present, preimplantation analysis detects about 95% of affected embryos. This means that misdiagnoses can occur, although they are uncommon. The preimplantation genetic diagnosis that we perform for you will only provide information concerning the specific disorder or mutation(s) that we are made aware of via medical notes. Additional genetic disease mutations that might exist in an embryo will not be tested unless specifically requested by the patient and/or care provider and agreed in writing with the reference laboratory.

	Patient	Partner (if applicable)
1) Have my embryos biopsied	_____	_____
a) to have any disease-diagnosed embryos donated to research	Patient	Partner (if applicable)
	_____	_____
b) to have any disease-diagnosed embryos discarded	Patient	Partner (if applicable)
	_____	_____

Freezing (or “cryopreservation”) of embryos is a common procedure. Since multiple eggs (oocytes) are often produced during ovarian stimulation, on occasion there are more embryos available than are considered

appropriate for transfer to the uterus. These embryos, if viable, can be frozen for future use. This saves the expense and inconvenience of stimulation to obtain additional eggs in the future. Furthermore, the availability of cryopreservation permits patients to transfer fewer embryos during a fresh cycle, reducing the risk of high-order multiple gestations (triplets or greater). Other possible reasons for cryopreservation of embryos include freezing all embryos in the initial cycle to prevent severe ovarian hyperstimulation syndrome (OHSS), or if a couple were concerned that their future fertility potential might be reduced due to necessary medical treatment (e.g., cancer therapy or surgery). The pregnancy success rates for cryopreserved embryos transferred into the human uterus can vary from practice to practice. Overall pregnancy rates at the national level with frozen embryos are lower than with fresh embryos. This, at least in part, results from the routine selection of the best-looking embryos for fresh transfer, reserving the 'second-best' for freezing. There is some evidence that pregnancy rates are similar when there is no such selection.

- **Freezing of viable embryos not transferred after egg retrieval provides additional chances for pregnancy.**
- **Frozen embryos do not always survive the process of freezing and thawing.**
- **Freezing of eggs before fertilization is currently much less successful than freezing of fertilized eggs (embryos).**
- **Ethical and legal dilemmas can arise when couples separate or divorce; disposition agreements are essential.**
- **It is the responsibility of each couple with frozen embryos to remain in contact with the clinic on an annual basis.**

Indications:

- To reduce the risks of multiple gestation
- To preserve fertility potential in the face of certain necessary medical procedures
- To increase the chance of having one or more pregnancies from a single cycle of ovarian stimulation
- To minimize the medical risk and cost to the patient by decreasing the number of stimulated cycles and egg retrievals
- To temporarily delay pregnancy and the risks of OHSS occurs by freezing all embryos, when this risk is high.

Risks of embryo cryopreservation: There are several techniques for embryo cryopreservation, and research is ongoing. Traditional methods include “slow,” graduated freezing in a computerized setting, and “rapid” freezing methods, called “vitrification.” Current techniques deliver a high percentage of viable embryos thawed after cryopreservation, but there can be no certainty that embryos will thaw normally or will be viable enough to divide and eventually implant in the uterus. Cryopreservation techniques could theoretically be injurious to the embryo. Additionally, mechanical or equipment failure could occur during cryopreservation, storage, or thawing, which may compromise embryo viability. Extensive animal data (through several generations), and limited human data, do not indicate any likelihood that children born of embryos that have been cryopreserved and thawed will experience greater risk of abnormalities than those born of fresh embryos. However, until very large numbers of children have been born following freezing and thawing of embryos, it is not possible to be certain that the rate of abnormalities is no different from the normal rate.

Specimen cryopreserved, storage, disposition

This informed consent relates to the medical procedure(s) you are undertaking with regard to assisted reproduction. To the extent Clinic or the University of Michigan stores any of your specimens, that service is outside the context of this consent and all terms and conditions related thereto are contained in the Clinic's Cryopreservation Specimens Storage Agreement (CSSA). The Clinic will not store your specimens unless, and until, you execute a CSSA.

I have discussed all of this information with my treating team and people that I trust such as my spouse, partner, my religious advisor, etc. and have agreed to the procedures listed above with full knowledge and understanding of these procedures, their risks and possible benefits, my actions and their possible consequences.

Signature: _____ Date: _____

References:

General IVF overviews available on the internet

<http://www.sart.org/>

<http://www.cdc.gov/art/>

<http://www.resolve.org/site/PageServer>