BRMAC Meeting #32, May 9, 2002
DRAFT QUESTIONS FOR COMMITTEE DISCUSSION'

Meeting Goals

The principal goals of this BRMAC discussion are:

- To determine whether there are data supporting both the safety of and rationale for ooplasm transfer sufficient to justify the risks of clinical trials with this technique in humans and
- To determine what additional data are needed prior to initiation of clinical trials if sufficient data are not presently available.

Safety Issues

1. Please discuss nonclinical (animal) data assessing the risks of the procedure to offspring and mother. Please consider the following:

   Risks to the offspring

   - Might the procedure damage or alter the oocyte? Concerns include the following:
     1. mechanical damage to oocyte cytoarchitecture,
     2. inadvertent transfer of chromosomes, chromosome fragments, or other cellular constituents,
     3. enhanced survival of abnormal embryos, increasing the likelihood of children born with significant birth defects,
     4. risks associated with heteroplasmy

   Risks to the mother:

   - Might risks to the mother be different than those incurred with established ART procedures? For example, the possibility exists that ooplasm transfer might enhance survival of abnormal embryos sufficiently late in gestation to incur additional medical risks to the mother (e.g. late term abortion).
   - Are there risks to the mother's future fertility or ability to engage in subsequent ART procedures?

2. Please discuss what clinical data are available to assess the risks to the mother and offspring.

3. Are these data sufficient to determine that ooplasm transfer does not present an unreasonable and significant risk to offspring and mother, and to support further clinical investigations?

4. What further nonclinical experimentation would be useful to provide additional safety data to assess the risks to the offspring and mother in further human investigations? If further nonclinical experimentation is considered appropriate:

    - What model(s)?
    - How many generations?
    - How large will studies need to be to generate meaningful conclusions?

Rationale for ooplasm transfer as a means of fertility enhancement

5. What defect(s) in the oocyte is (are) being addressed by ooplasm transfer? Please discuss relevant data.

6. Do existing clinical data from humans support a rationale for the procedure?

Clinical Issues

7. Please discuss the critical design elements that should be incorporated into future clinical trials to demonstrate the safety and efficacy of ooplasm transfer as therapy for a subset of infertile women.

    - What are appropriate suitability criteria for patient selection for ooplasmic transfer?

    - What issues are critical to appropriate informed consent? In particular, how will risks to the offspring be considered?

    - Given that ooplasm transfer causes genetic alteration of the germline, what follow-up of human offspring is appropriate?

    - What controls are appropriate?

Cellular Product Issues

- What are appropriate suitability criteria for ooplasm donors?

- What are appropriate acceptance criteria for oocytes used for ooplasm donation? (e.g., frozen vs. fresh vs oocytes with multiple pronuclei?)

- How is successful ooplasm transfer demonstrated before implantation?

- What procedures should be used to confirm that transfer of undesired cellular components has not occurred?

- How are the conception products evaluated prior to transfer to the recipient (mother)? Are there characteristics that are reliably associated with desirable or undesirable outcomes?