

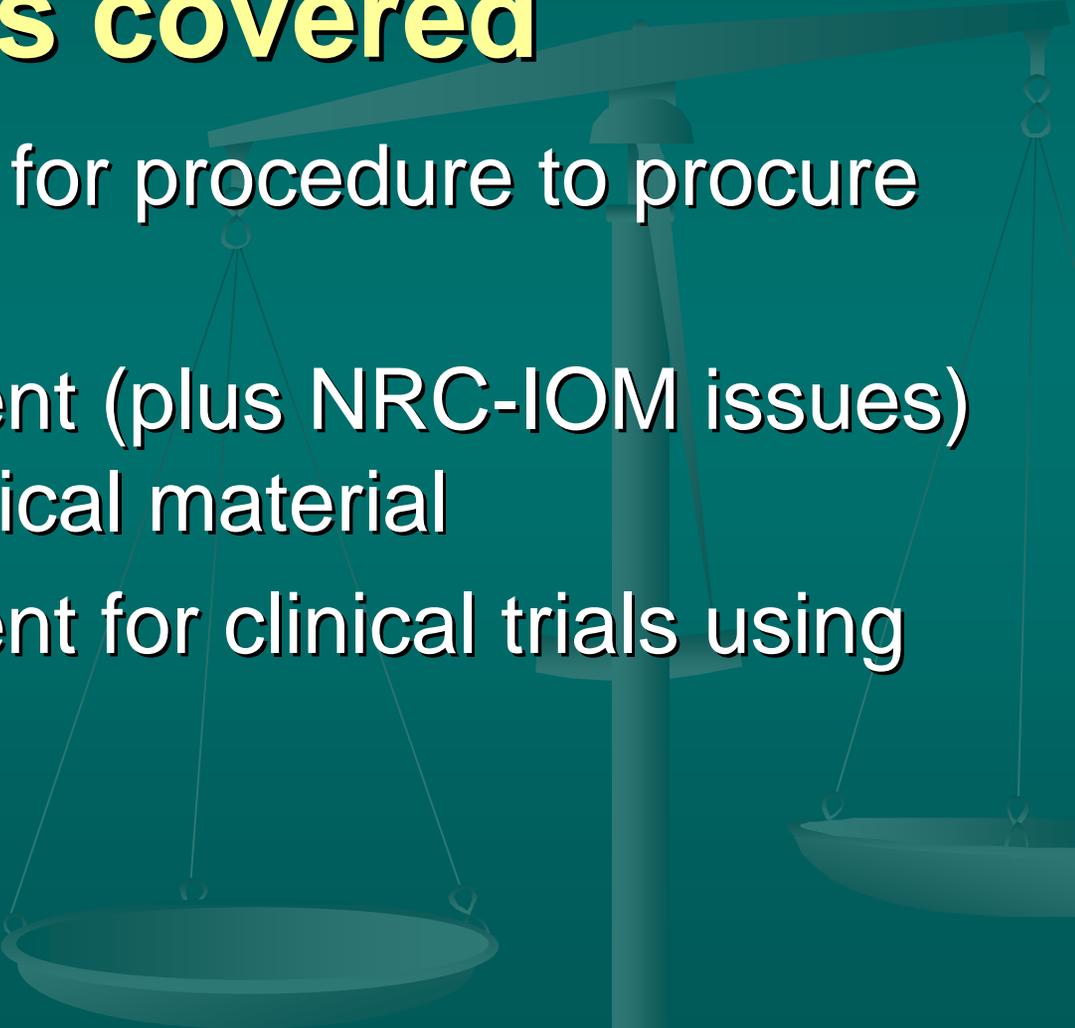
Stem cell guidelines: Next steps

David Magnus, PhD

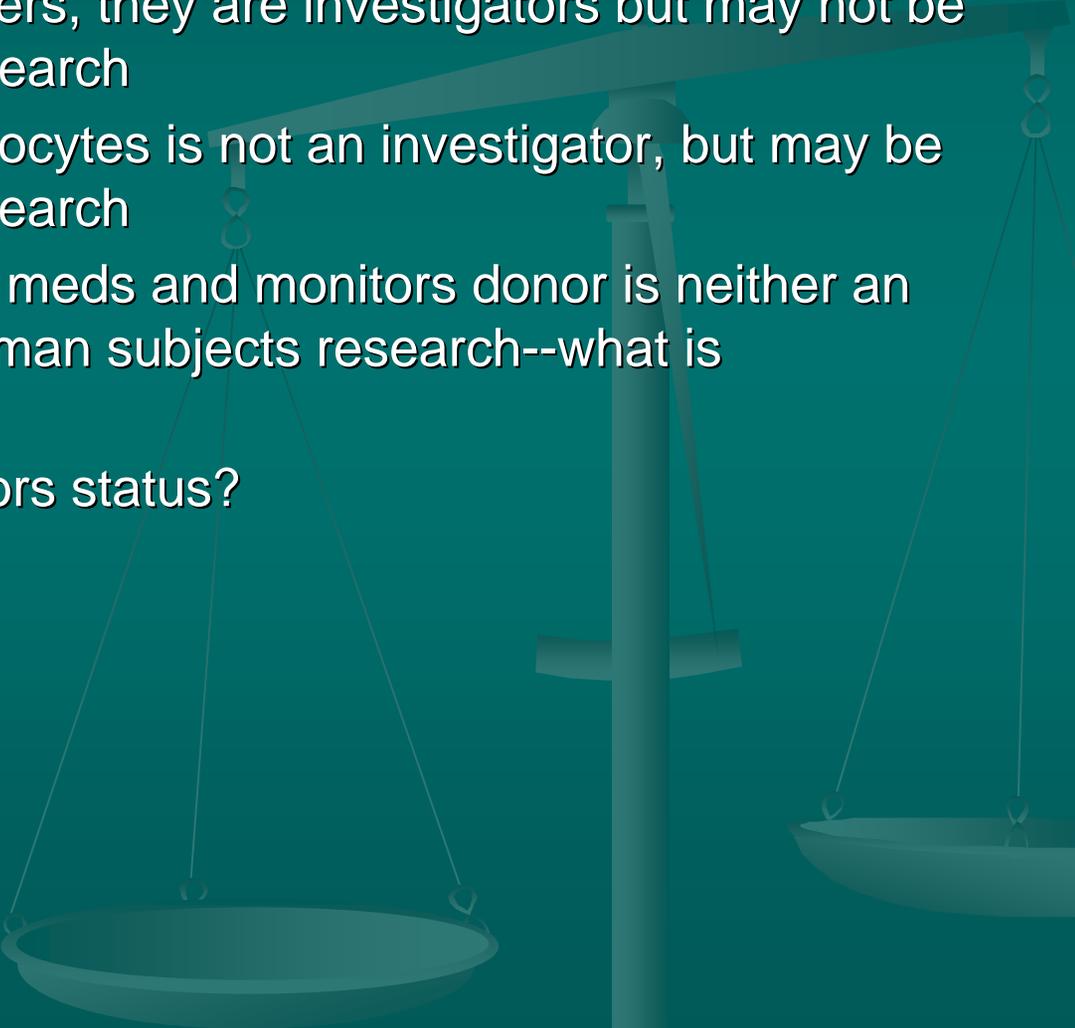
Director

Stanford University Center for
Biomedical Ethics

Donation of excess IVF oocytes, embryos- How are risks covered

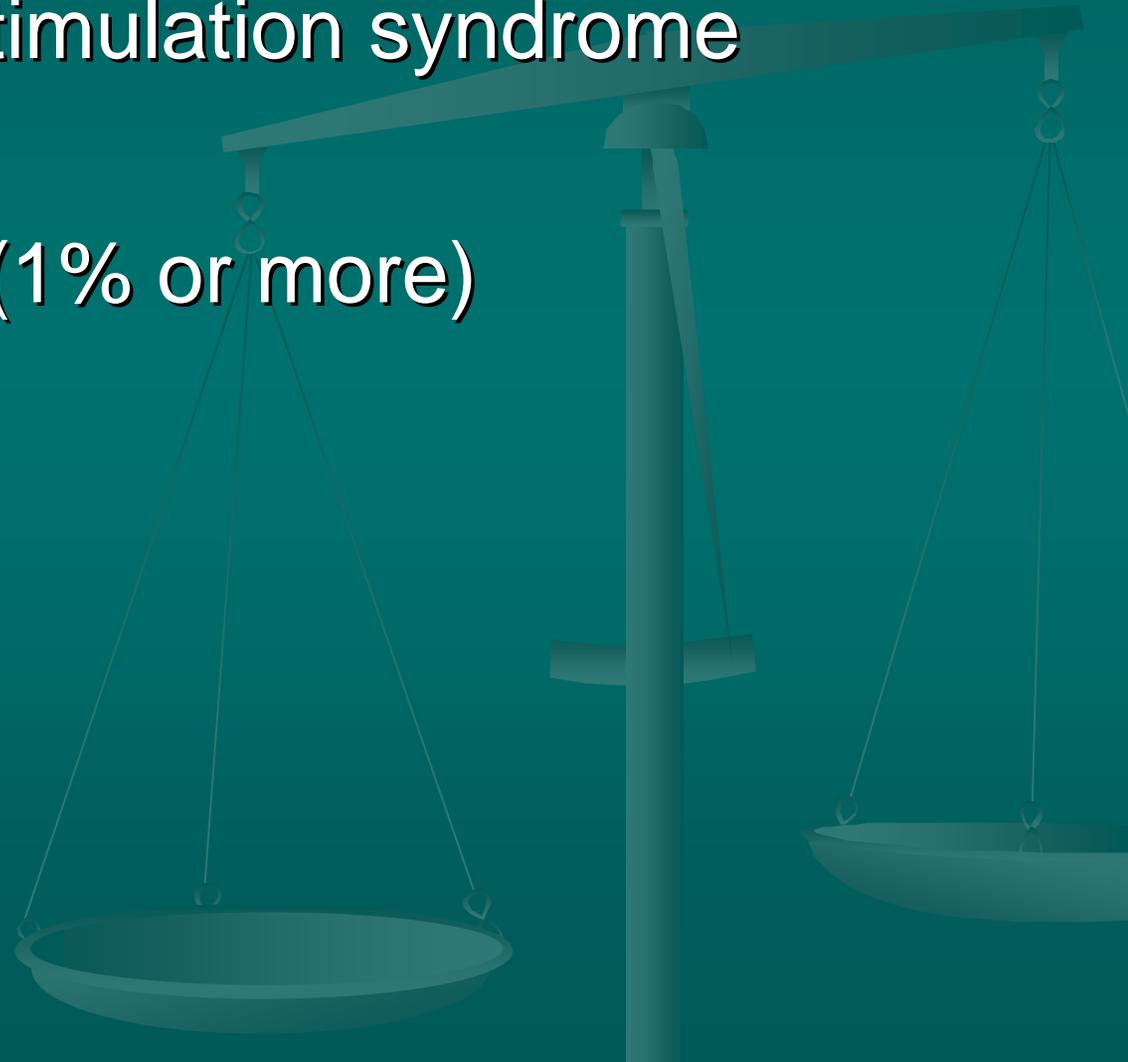
- Clinical consent for procedure to procure oocytes
 - Research consent (plus NRC-IOM issues) for use of biological material
 - Research consent for clinical trials using material
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Non-medical oocyte donors

- If untraceable to researchers, they are investigators but may not be doing human subjects research
 - Physician who procures oocytes is not an investigator, but may be doing human subjects research
 - Physician who prescribes meds and monitors donor is neither an investigator, nor doing human subjects research--what is relationship to donor?
 - Problem--what is the donors status?
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Oocyte Procurement Risks

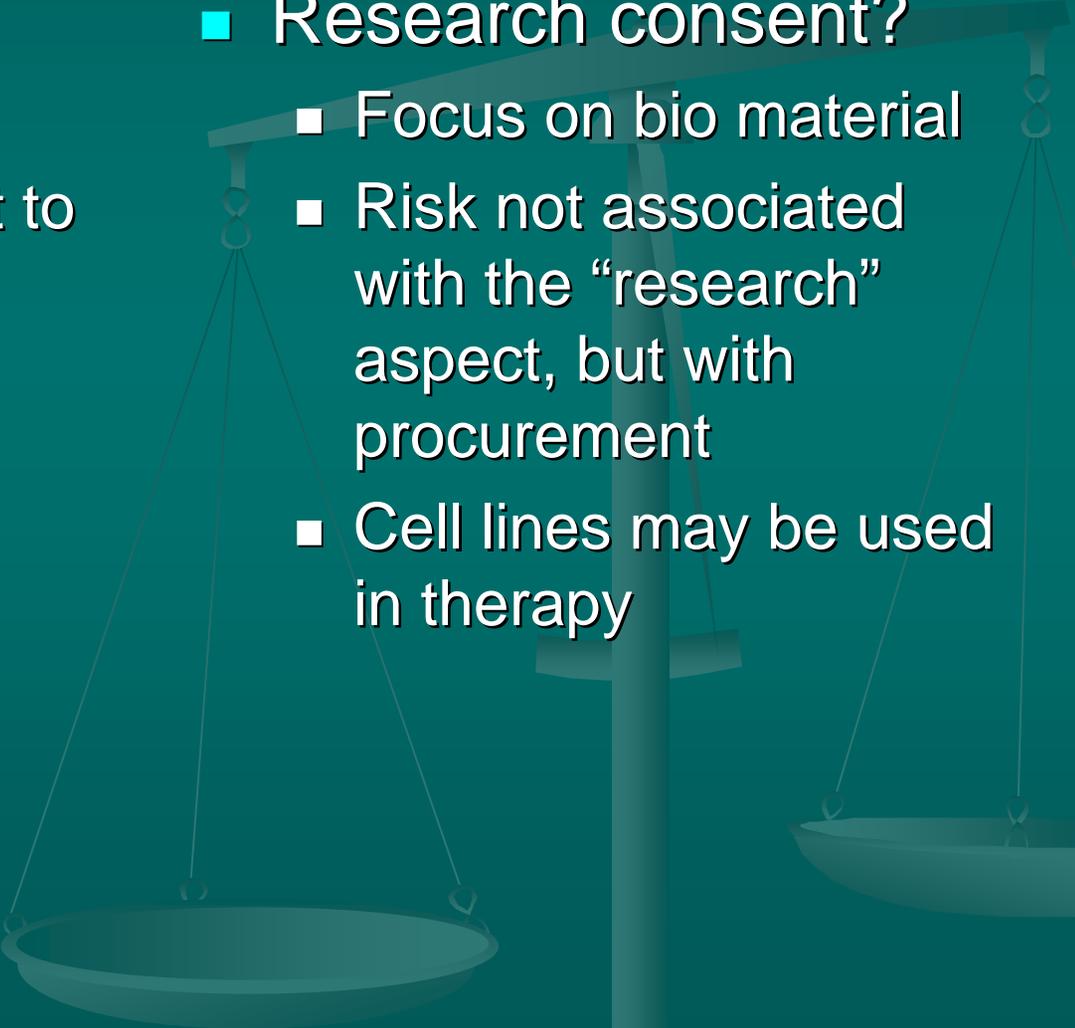
- Ovarian hyperstimulation syndrome
- Ovarian torsion
- Hospitalization (1% or more)
- Renal failure
- Infertility
- Death



SCNT from donor eggs

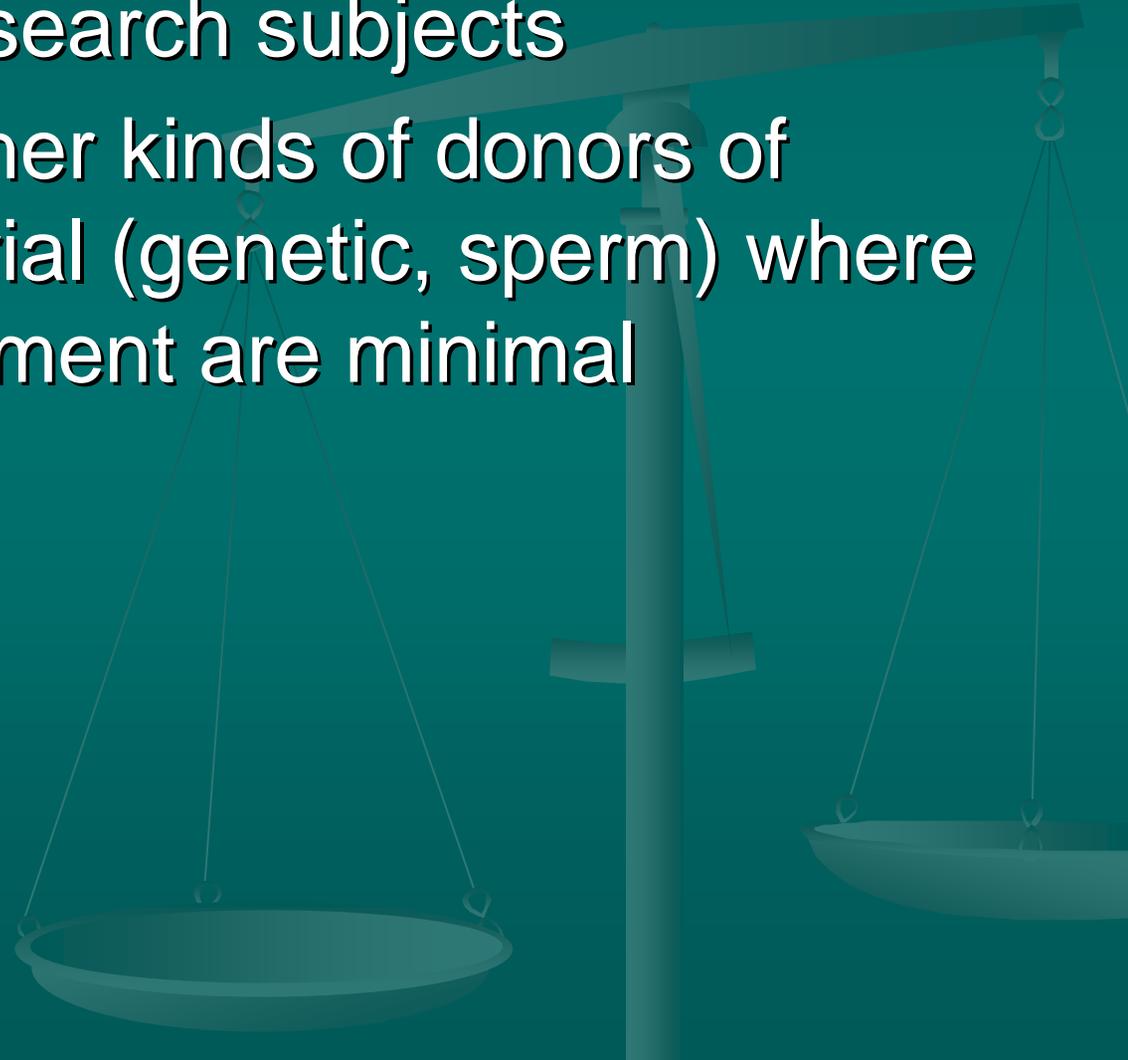
- Some evidence that results will be better if donation from very young donors
- Ovarian Hyperstimulation Syndrome more likely in younger donors
- In South Korea, of first 100 donors, 16 developed OHS and 2 had very serious medical complications--all held that they were not adequately informed of the risks

Non-medical oocyte donation

- Clinical consent?
 - Donor is not a pt
 - Risk but no benefit to donor
 - Research consent?
 - Focus on bio material
 - Risk not associated with the “research” aspect, but with procurement
 - Cell lines may be used in therapy
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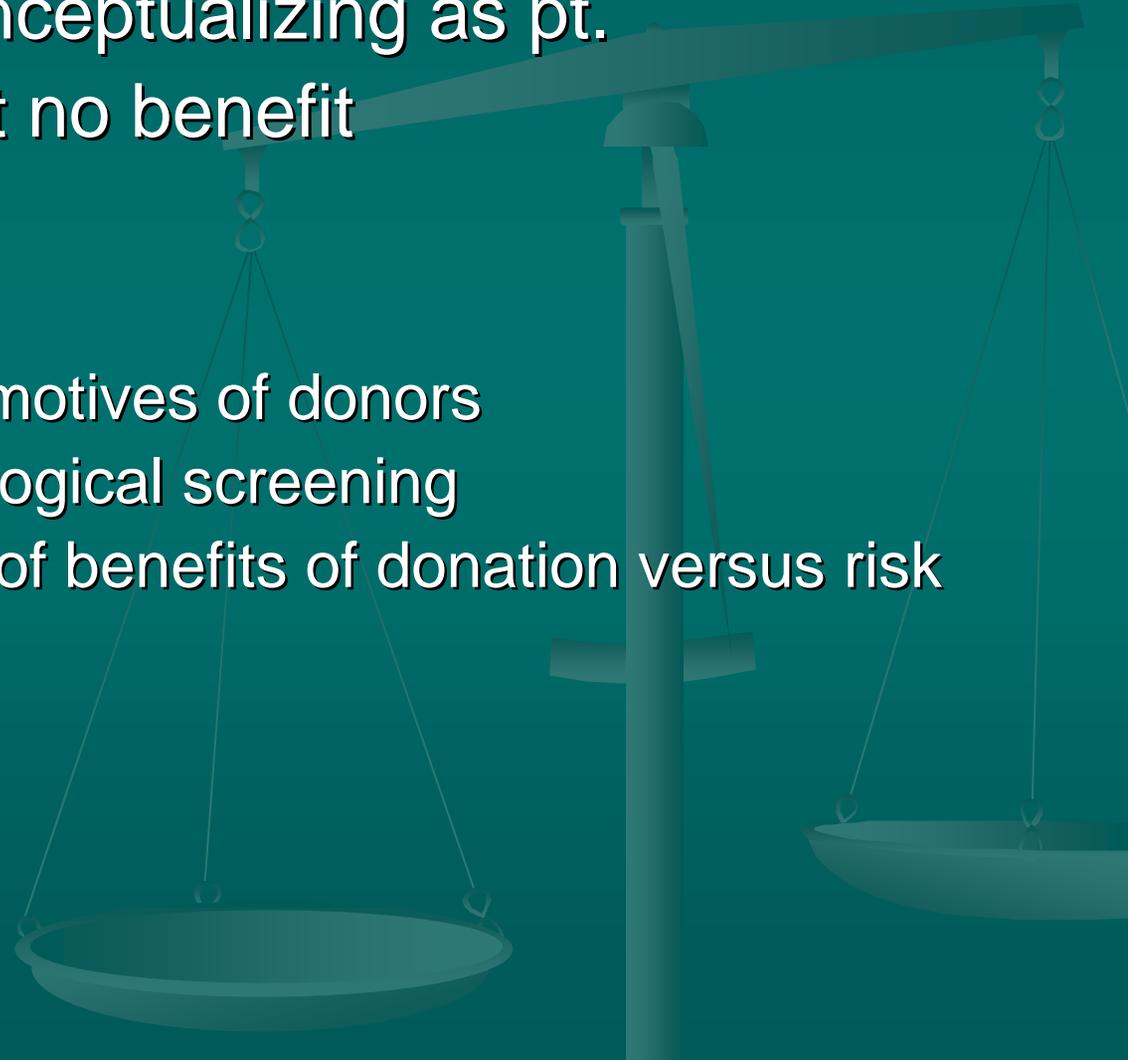
New Category--Research Donors

- Distinct from research subjects
- Distinct from other kinds of donors of biological material (genetic, sperm) where risks of procurement are minimal

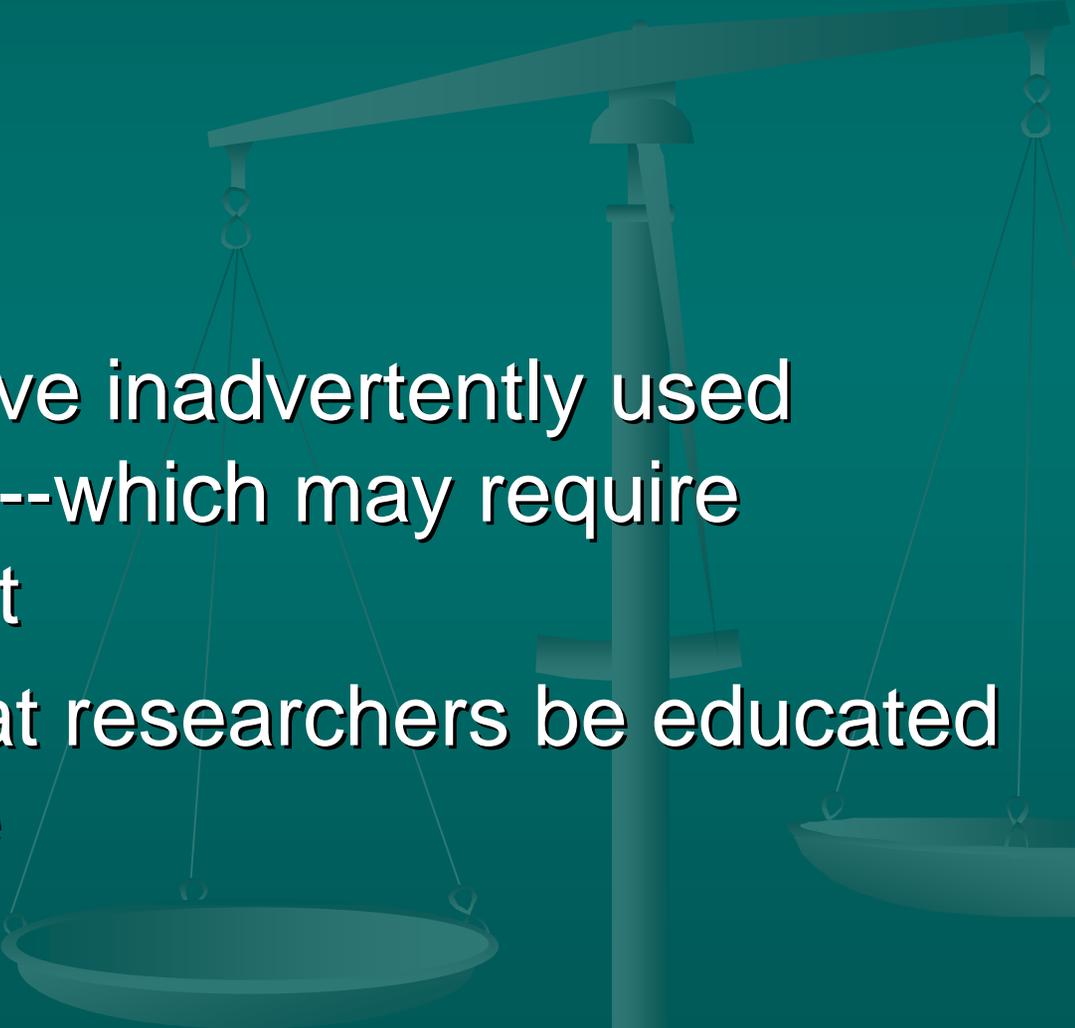


Analogy with live organ donation

- Problems with conceptualizing as pt.
- Risks to donor but no benefit
- Result:
 - Close scrutiny of motives of donors
 - Adequate psychological screening
 - Serious weighing of benefits of donation versus risk

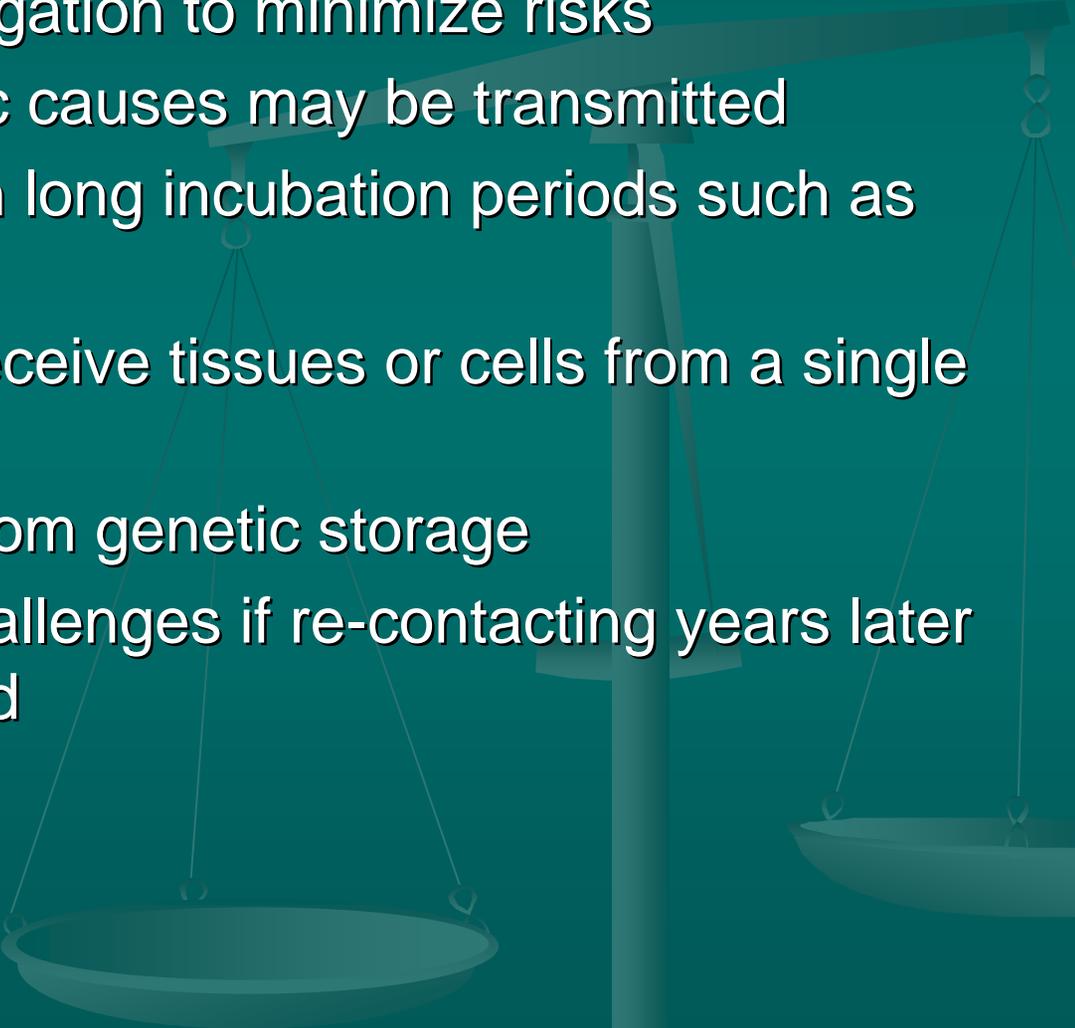


Researcher confusion in informed consent forms

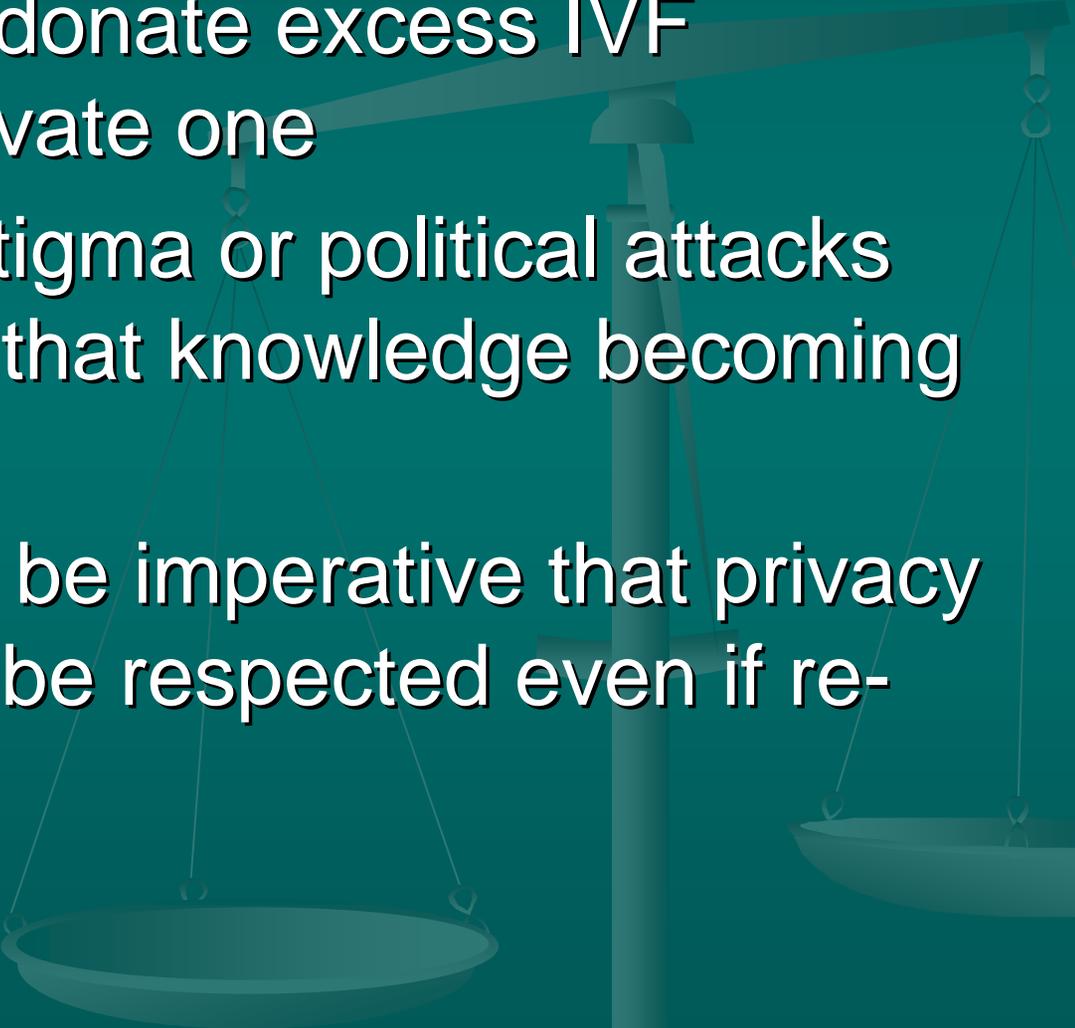
- De-identified
 - Anonymized
 - Researchers have inadvertently used wrong language--which may require different consent
 - Recommend that researchers be educated about difference
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Need to protect future Phase I subjects

Lo, et al

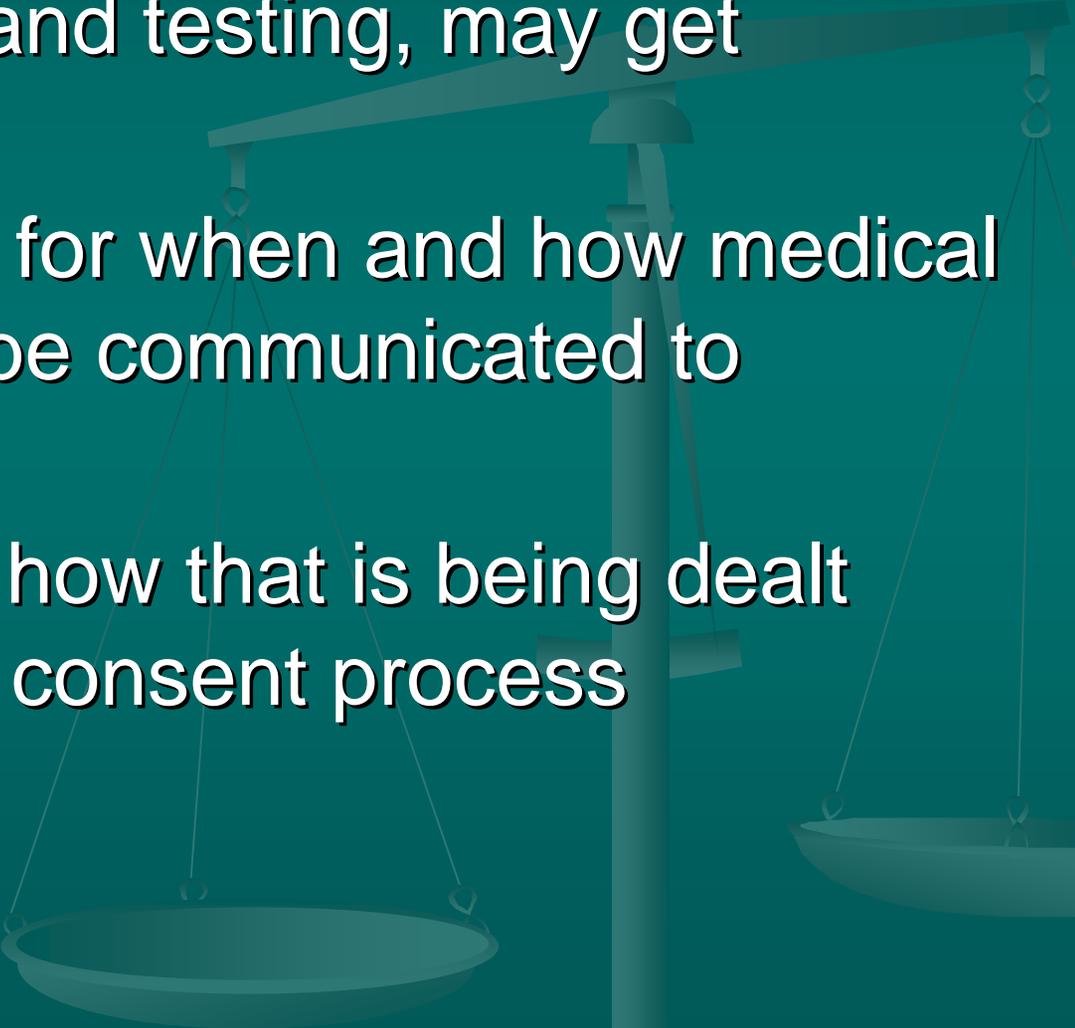
- Phase I research obligation to minimize risks
 - Diseases with genetic causes may be transmitted
 - Infectious agents with long incubation periods such as prions, viruses
 - Many patients may receive tissues or cells from a single source
 - Changes paradigm from genetic storage
 - Presents practical challenges if re-contacting years later is to become standard
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Confidentiality

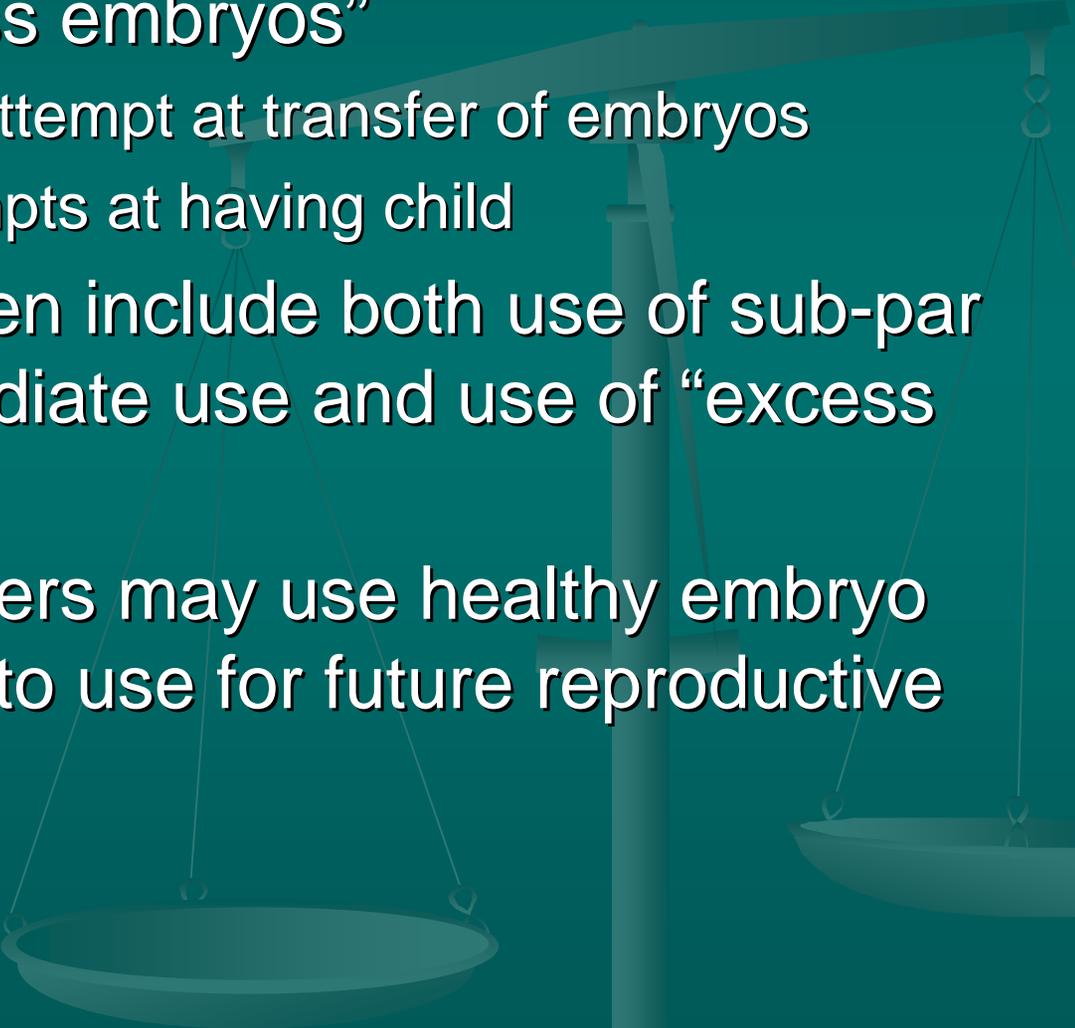


- The decision to donate excess IVF embryos is a private one
- Concerns that stigma or political attacks may result from that knowledge becoming public
- Therefore, it will be imperative that privacy rights of donors be respected even if re-contacting

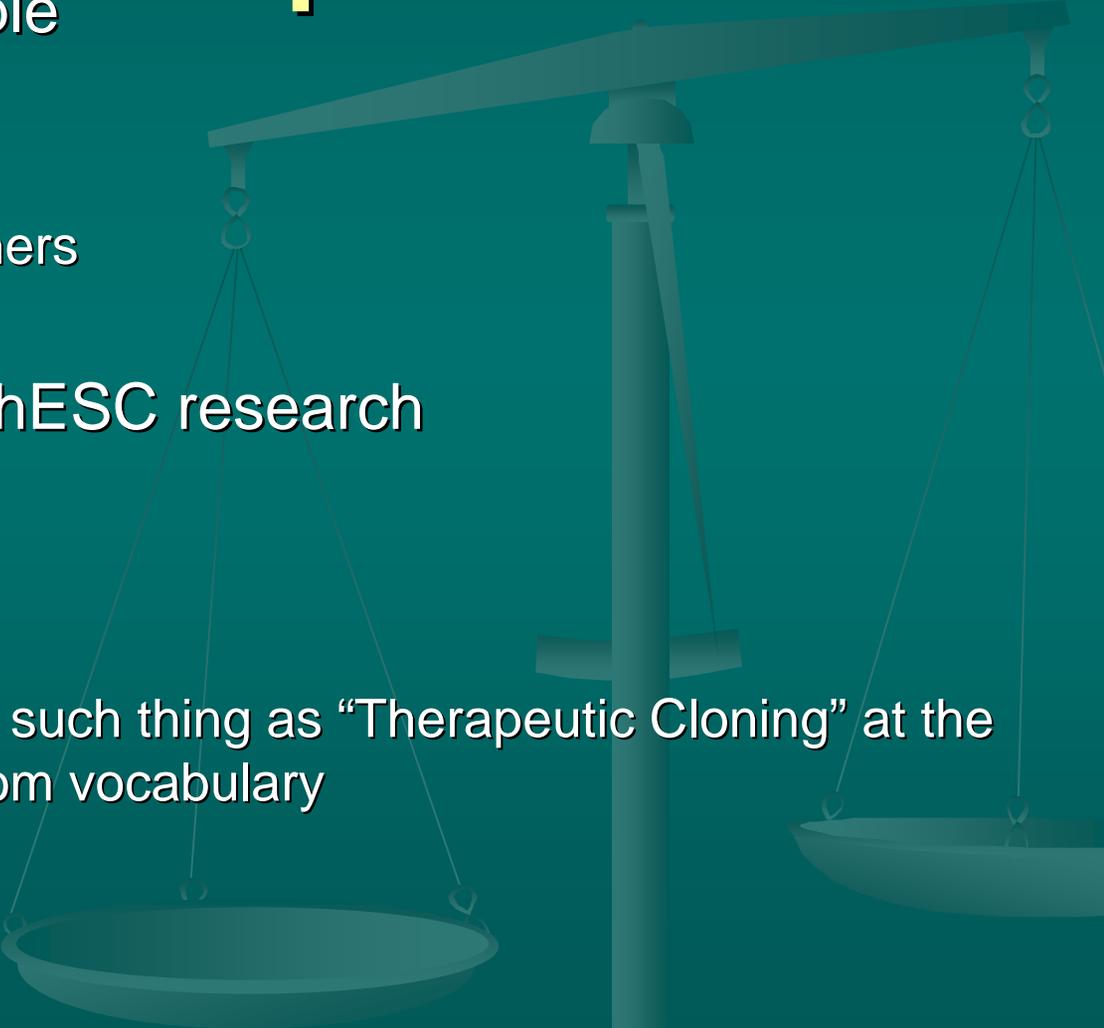
Incidental findings

- If re-contacting and testing, may get results
 - Need standards for when and how medical information will be communicated to donors
 - Need to include how that is being dealt with in informed consent process
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Consent Language Problems

- Meaning of “excess embryos”
 - Excess from this attempt at transfer of embryos
 - Excess from attempts at having child
 - Consent forms often include both use of sub-par embryos for immediate use and use of “excess embryos”
 - Risk that researchers may use healthy embryo that couple wants to use for future reproductive attempts
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Consent Language Problems- -the Therapeutic Misconception

- Gene Therapy example
 - Lots of hype
 - Desperate patients
 - Enthusiastic Researchers
 - Misleading Language
 - Similar situation with hESC research
 - Hype
 - Desperation
 - Enthusiasm
 - Language--there is no such thing as “Therapeutic Cloning” at the present time--ban it from vocabulary
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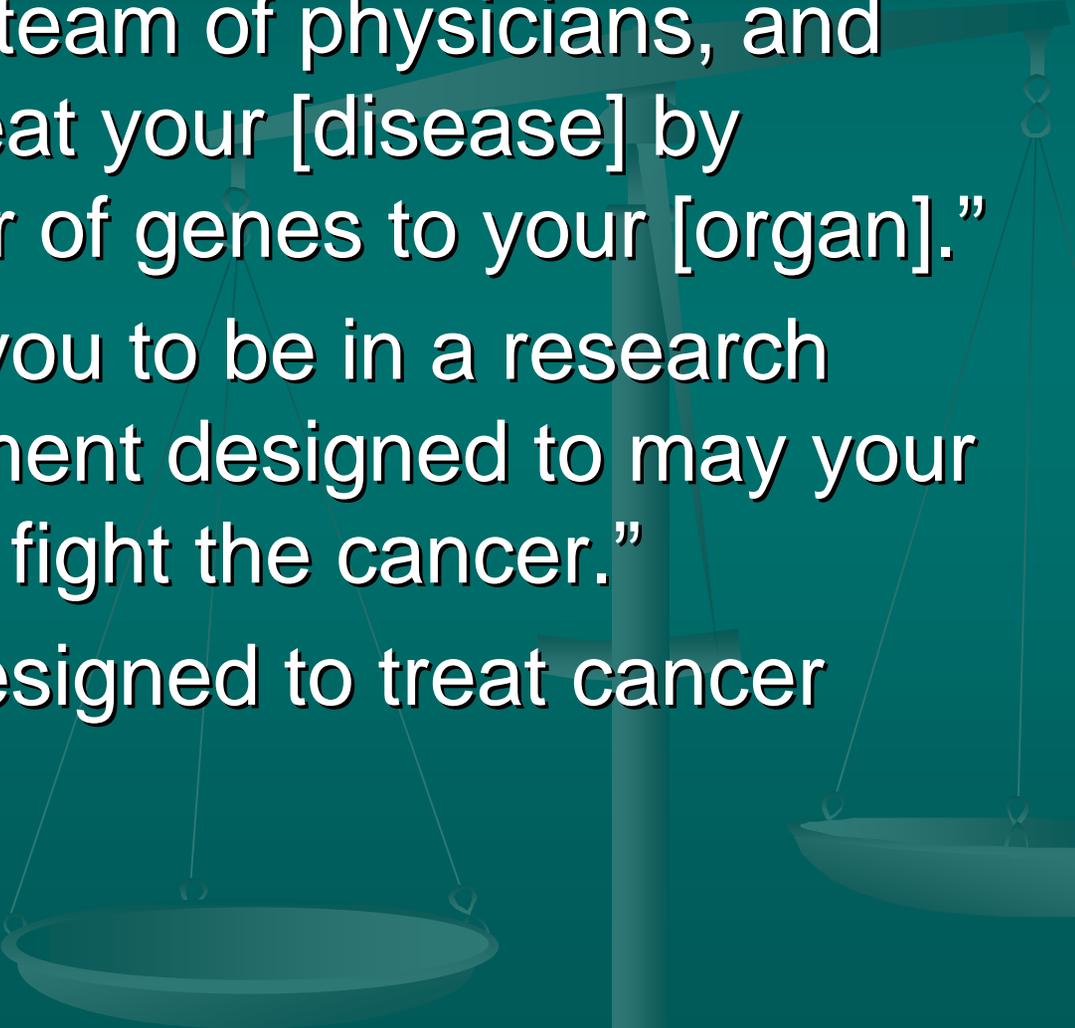
hESC clinical trials

- Therapeutic misconception again
- Choice of patient populations for initial clinical trials

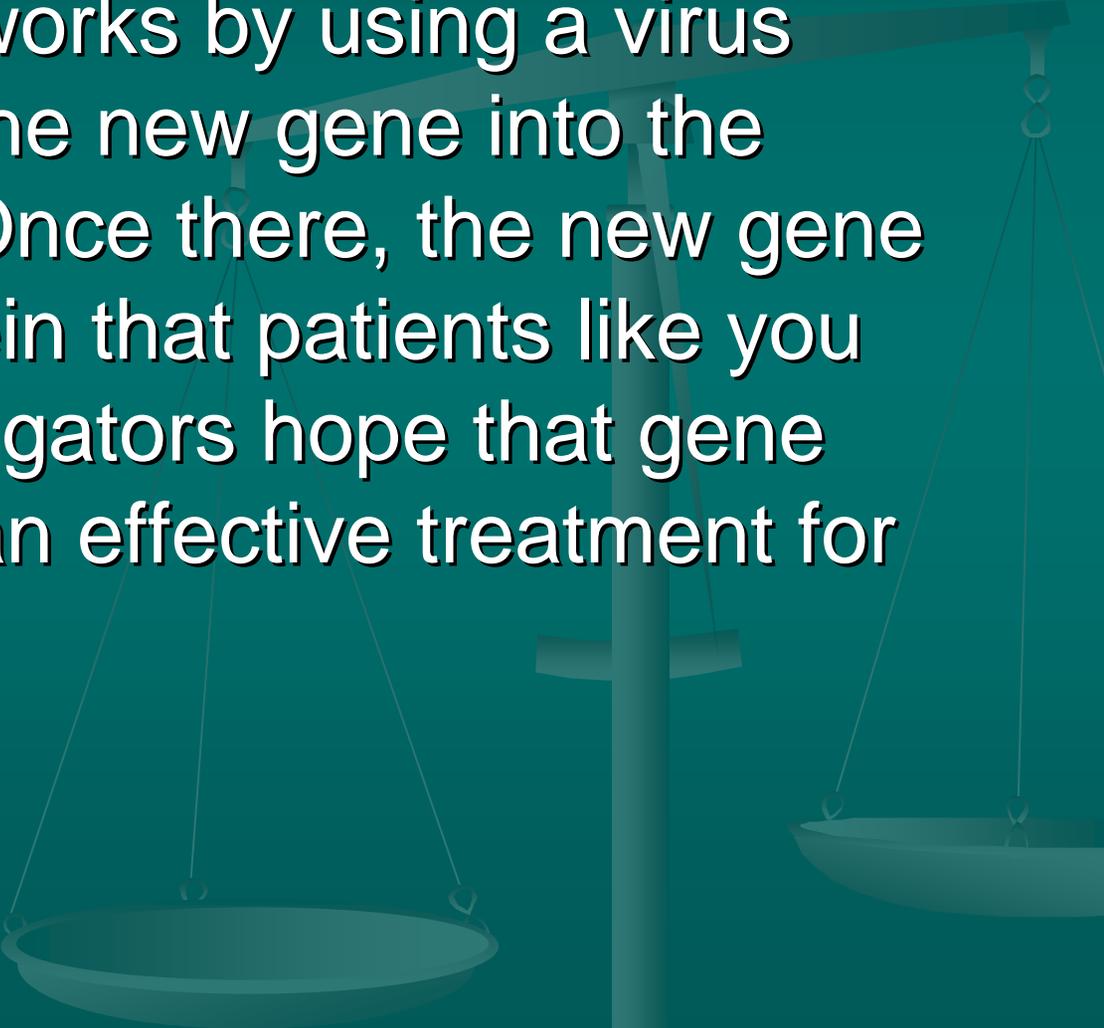


Example language

Kimmelman and
Lennestadt

- “In this study, a team of physicians, and scientists will treat your [disease] by delivery of a pair of genes to your [organ].”
 - “We would like you to be in a research study of a treatment designed to may your immune system fight the cancer.”
 - “This study is designed to treat cancer patients with...”
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Example Language King, et al

- “Gene therapy works by using a virus vector to carry the new gene into the patient’s cells. Once there, the new gene makes the protein that patients like you lack. The investigators hope that gene therapy will be an effective treatment for your disease.”
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Example Language King et. al.

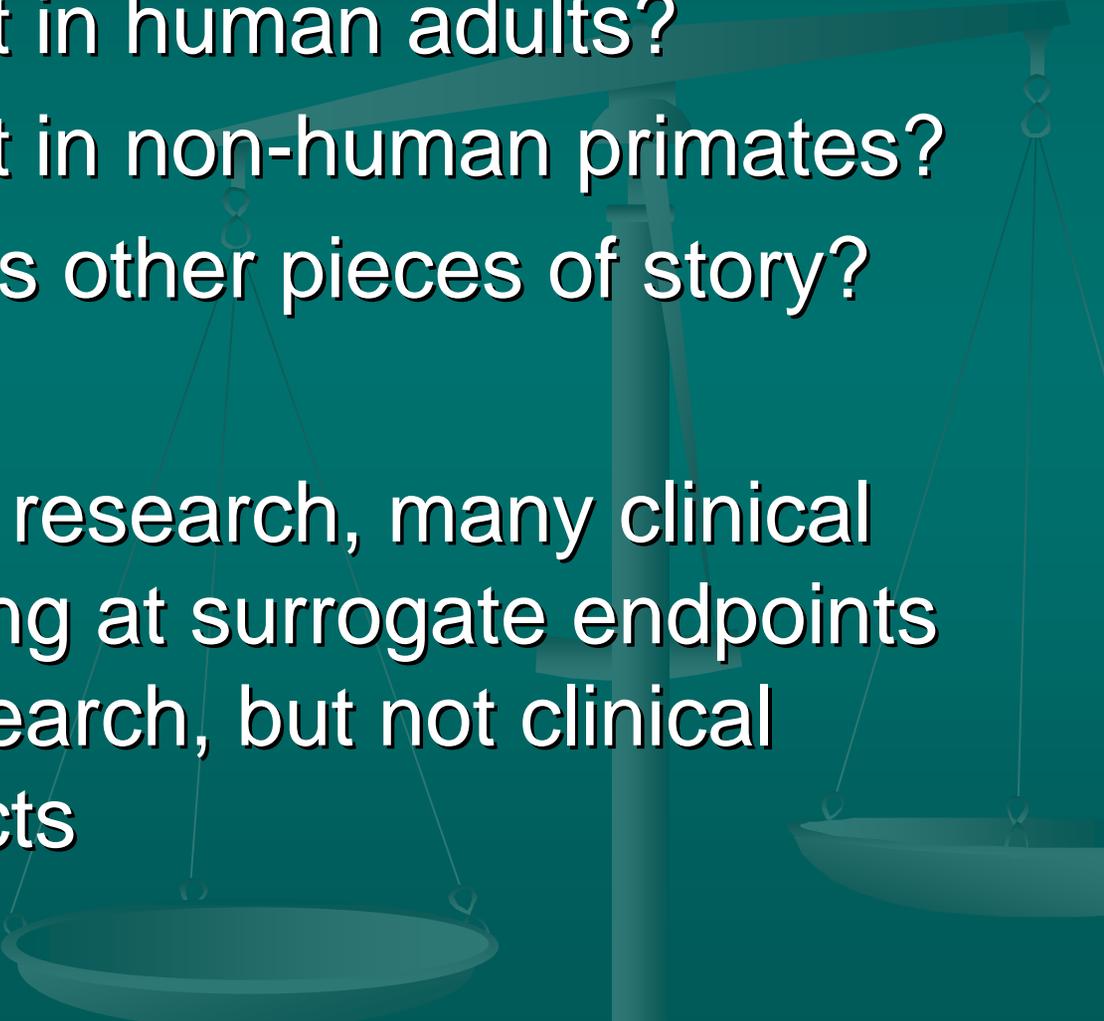
- “The hope is that we can improve your symptoms and prolong your life with this treatment...The purpose of this study is to determine whether this procedure is safe and to evaluate the effect of this treatment on your disease.” from Purpose
- From Benefits section: “It is not possible to predict whether or not any personal benefit will result.”

Should hESC trials be done on children?

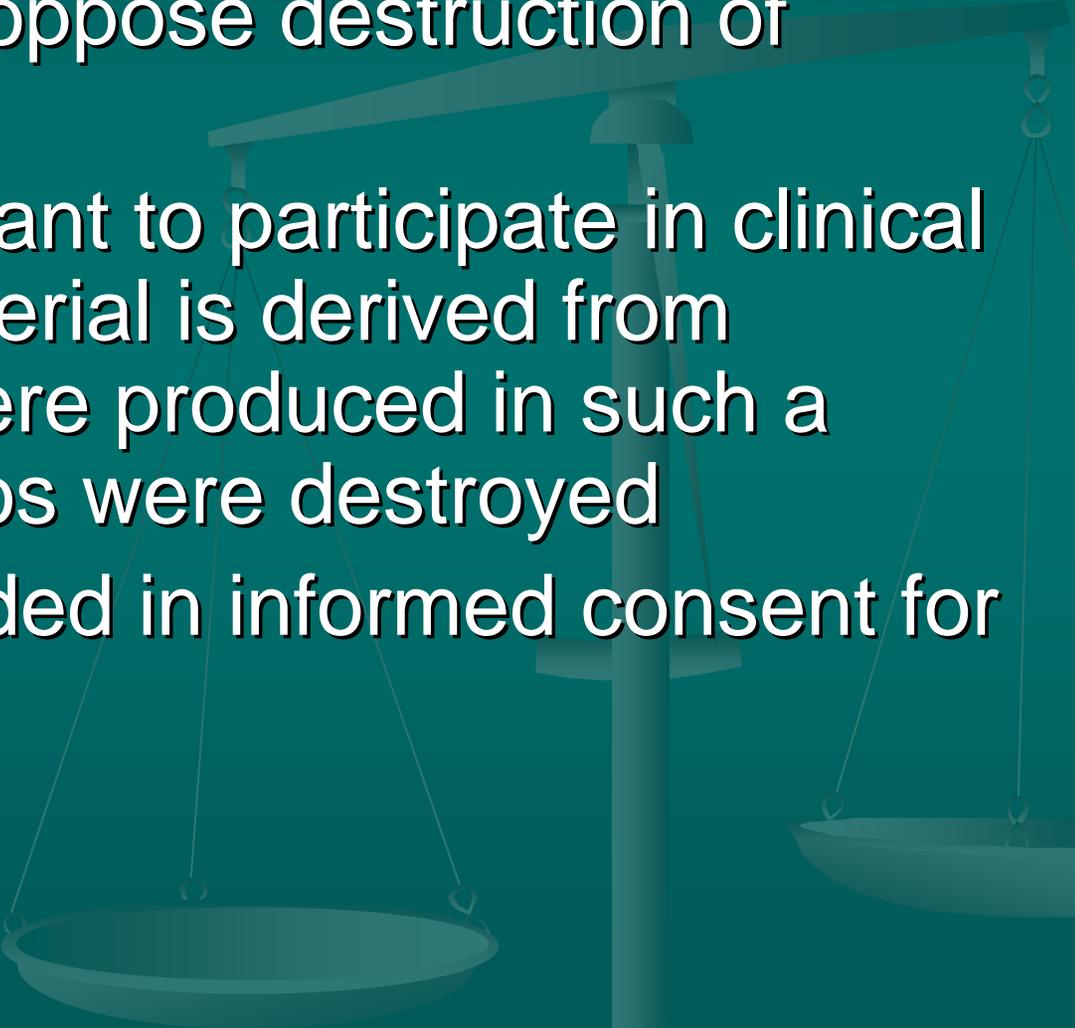
- Minimal risk (46.404 or 50.51 for FDA)
- Minor increase over minimal risk, but yields knowledge about the subject's condition (46.406 or 50.53)
- Clearly greater than minimal risk, but offers prospect of direct benefit to subject (46.405 or 50.52))
- 46.407 or 50.54--if opportunity to understand or help treat diseases that affect children, HHS (FDA for parallel) can create committee with law, medicine, ethics represented to approve trial

When is there a prospect of direct benefit?

- Proof of concept in human adults?
 - Proof of concept in non-human primates?
 - Mouse data, plus other pieces of story?

 - In gene transfer research, many clinical trials really aiming at surrogate endpoints of benefit to research, but not clinical benefit to subjects
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Consent in clinical trials

- Because some oppose destruction of embryos
 - They may not want to participate in clinical trials where material is derived from products that were produced in such a way that embryos were destroyed
 - Should be included in informed consent for clinical trials
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Summary

- Recognize research donor category
 - Clarify meaning of de-identify vs anonymize
 - Advise on need to recontact
 - Advise on confidentiality
 - Avoid accidental destruction of embryos stored for future use
 - Avoid use of term “therapeutic cloning”
 - Avoid therapeutic misconception in consent
 - Advise on requirements for clinical trials
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