MRT and Human Research Ethics
MRT Trials

- Genetic modification of the early embryo or gametes used to create embryo

- Primary intent is to alter genes in later-born child, but affects descendants, too

- Complex subject monitoring
Vulnerable Populations

- Phase I research
- Impact on fetuses and children
- Uncertain direct benefit
MRT Trials

- Embryo Control and Disposition
- Lack of Regulatory Guidance on Certain MRT Research Issues
Potential Harms and Benefits

- Risks to human subjects must be minimized

- Any unavoidable risks justified by potential benefits to subjects, if any, and by value of knowledge study expected to produce
Risk Minimization & Justification

- What preclinical data needed?
- Would alternatives diminish justification for MRT research?
- What is appropriate study population?
- What monitoring needed?
Choice of Study Population

- Relative risk evaluation [e.g., phase I cancer trials]
- Uncertainty in determining which cases are at highest risk of serious mitochondrial disorders
- When there is reasonable chance child would be healthy or mildly affected, harder to justify research risks
Multi-Generational Effects

- Follow modified children throughout lives
- Monitor offspring – what tests, etc.?
- What is sufficient study length?
Series of Participants

- Prospective parents
- Modified children
- Modified adults
- Offspring
Enrollment & Retention Questions

Would sufficient number of people enroll and remain in studies to produce data needed to determine safety and efficacy?