Basic Research - Regulation

- Institutional Biosafety Committees
  - Focus on laboratory safety
- Institutional Review Boards
  - Focus on protection of privacy and other interests of those whose tissues or cells are being used
- NIH Recombinant DNA Advisory Committee
  - Advice on conduct of research; venue for public discussion

Somatic Therapy - Regulation

- Institutional Biosafety Committees
- Institutional Review Boards
  - Protection of subjects in clinical trials; informed consent
- Recombinant DNA Advisory Committee
  - Advice and some protocol review; venue for public discussion
- FDA
  - Control over initiating clinical trials
  - Control over approval for clinical use
  - Long term follow-up

RECOMMENDATIONS
Basic Research & Somatic Therapy

- Already managed under existing ethical norms and regulatory regimes at local, state, and federal levels
- Use existing regulatory processes to oversee basic laboratory research and somatic research and uses
- Limit clinical trials or therapies to treatment and prevention of disease or disability at this time
- Evaluate safety and efficacy in the context of risks and benefits of intended use
- Somatic genome editing; efficiency, specificity and off-target events, must be evaluated in the context of the specific intended use and method. No single standard can be defined at this time.

Heritable Genome Editing - Regulations

- Regulations covering laboratory work and human subject protections in clinical trials are applicable
- If done with embryos (as opposed to gametes), it would be prohibited in some states; at federal level there are restrictions on funding
- At this time, clinical trials are not possible in U.S. due to limitations on FDA authority
- Other countries vary, from prohibition to possible authorization under strict regulation

Heritable Editing Clinical Trials

- Caution is needed but being cautious does not mean prohibition
- Heritable genome editing research trials might be permitted, but only after:
  - much more research to meet existing risk/benefit standards,
  - under strict oversight, and
  - restricted to specific set of criteria

Criteria to Initiate Clinical Trials

- Absence of reasonable alternatives;
- Restriction to prevention of a serious disease or condition;
- Editing only genes that have been convincingly demonstrated to cause or to strongly predispose to the disease or condition;
- Converting such genes to versions that are prevalent in the population and are known to be associated with ordinary health with little or no evidence of adverse effects;
- Availability of credible pre-clinical and/or clinical data on risks and potential health benefits of the procedures;

Criteria to Initiate Clinical Trials

- ongoing, rigorous oversight during clinical trials of the effects of the procedure on the health and safety of the research participants;
- comprehensive plans for long-term, multigenerational follow-up;
- maximum transparency consistent with patient privacy;
- continued reassessment of both health and societal benefits and risks, with broad on-going participation and input by the public; and
- reliable oversight mechanisms to prevent extension to uses other than preventing a serious disease or condition

Public Engagement

> It is essential that **transparent** and **inclusive** public policy debates precede any consideration of whether to authorize clinical trials for indications that go beyond treatment or prevention of disease or disability.

- For laboratory research and gene therapy, there are existing mechanisms that provide opportunities for public engagement
- For somatic cell editing, public policy debates should precede any clinical trial use beyond treatment or prevention of disease and disability.
- For heritable editing, public input should precede any clinical trial

Key Messages of Report

- Genome editing in the context of basic research and somatic gene therapy is valuable and adequately regulated
- Somatic therapy should be used only for treatment and prevention of disease and disability; it should not be tried for enhancement at this time; public engagement and input is needed
- Heritable genome editing needs more research before it might be ready to be tried; also, public input and engagement needed
- When tried, heritable genome editing must be approached cautiously: used only for treating or preventing severe diseases (no enhancement), and according to strict criteria with stringent oversight