

Human Gene Transfer Protocols and Institutional Biosafety Committees: Proposed Exemption for Low Biosafety Risk Protocols

Jacqueline Corrigan-Curay, J.D., M.D.

December 14, 2011



Overview

- **Role of Institutional Biosafety Committees (IBCs) in review of human gene transfer (HGT) trials**
- **Feedback from some investigators**
- **Potential proposal for exemption of certain gene transfer trials from IBC review**
- **Next steps for IBC exemption proposal**
- **OBA proposal regarding selection of protocols for in-depth public review**

Role of IBC Review in HGT Trials

- **Identify and manage biosafety issues raised by gene transfer agents**
 - Horizontal or vertical transmission risk
 - Safe handling and administration
 - Ensure that the informed consent incorporates information regarding risks that arise from the biological nature of the agent
 - Examine the preclinical animal data that supports the safety of the vector
 - Identify new biosafety issues through analysis of adverse event reports
 - For protocols that undergo in-depth public review by the NIH Recombinant DNA Advisory Committee (RAC), ensure that the RAC recommendations are considered

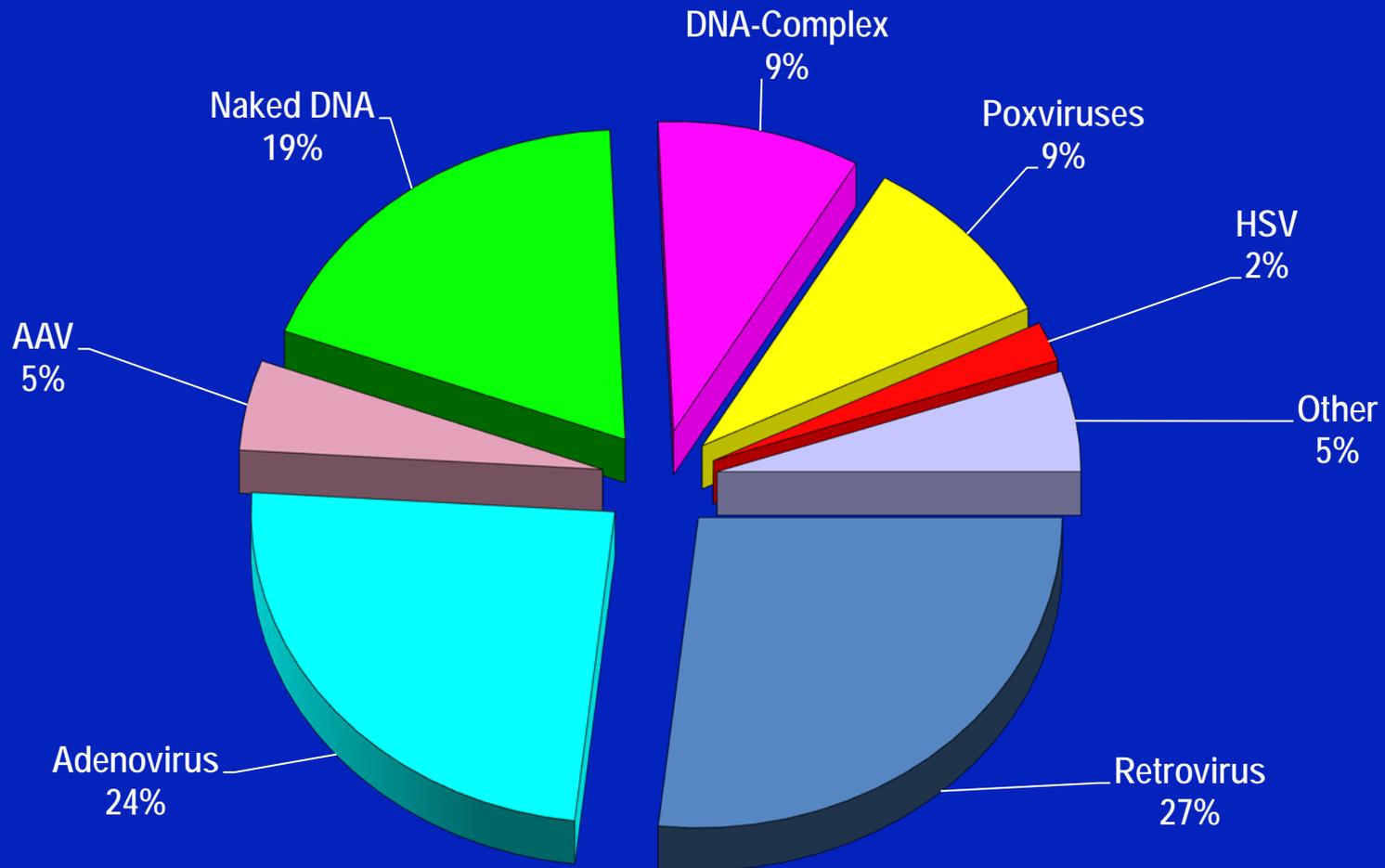
Feedback from Some Investigators Regarding IBC Review of Multisite Trials

- A number of gene transfer clinical trials are conducted utilizing vectors for which there is considerable clinical experience and biosafety risks are well characterized**
- Multiple individual IBC reviews of low risk trials may add little benefit to protect public health and such reviews can be costly, e.g. setting up new IBCs, delays in initiating important research**
- A mechanism to streamline review of low biosafety risk trials is needed to facilitate research, especially for multisite trials**

Proposal to Exempt Certain Low Risk Trials from IBC Review

- **Multisite Phase II or III studies will not require IBC review if:**
 - The vector is a plasmid or a specified non-integrating vector derived from a RG2-virus
 - There is a previous safety study (e.g. Phase I study) that tested the proposed dose for the Phase II or III study.
 - In the prior safety study there were no unexpected toxicities related to the investigational agent using the same delivery method at the dose proposed.
 - The concomitant interventions are comparable to the previous Phase I safety study or Phase II.
 - The study populations are comparable.

Gene Transfer Trials By Delivery System



Proposal to Exempt Certain Low Risk Trial from IBC Review

- **Further specification of the following criteria will be developed by the RAC Working Group:**
 - Which non-integrating RG-2 viral vectors are low biosafety risk?
 - Unexpected toxicities
 - Will this be primarily based on the absence of a dose limited toxicity with the propose dose[s] to be tested in the Phase II or Phase III study?
 - Comparable concomitant interventions
 - Comparable study populations
 - Immune status? Age? Geographic/infectious disease background?

Proposal to Exempt Trials, Cont...

- A trial that meets all the above criteria can be exempt from IBC review under the *NIH Guidelines* although the IBC has the discretion to review the trial in accordance with institutional policy.
- The protocol must still register with OBA in accordance with the requirements of Appendix M and the PI is responsible for all reporting requirements under Appendix M.
- Reporting to the IBC would not be required under the *NIH Guidelines* but institutions can establish their own reporting requirements in accordance with institutional policy.

Next Steps

- **The RAC Working Group will continue to refine proposal**
- **A final proposal will be presented to the RAC in March 2011**
- **The RAC recommendations will be considered by NIH**
- **If accepted, a proposal will be published in the Federal Register for public comment**

Streamlining the RAC Review Process

- **OBA proposes the following change to the initial review process:**
 - Currently approximately 15-20 percent of protocols are selected for in-depth public review
 - Protocols are selected by OBA if at least three members of the Committee recommend public review because of novel scientific, clinical or ethical issues
 - OBA proposes that it will only accept a recommendation for review if it is made by at least 20 percent of RAC members
 - This may lead to approximately 10 percent less protocols selected for public review
 - If the RAC concurs, this change can be implemented immediately.

Questions/Comments