COUNCIL ON GOVERNMENTAL RELATIONS

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Office of Science Policy
National Institutes of Health
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Subject: NIH Request for Public Comments on the Proposed Action Under the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines)

To Whom this May Concern:

The Council on Governmental Relations (COGR) is an association of 190 research universities and their affiliated academic medical centers and research institutes. COGR concerns itself with the influence of federal regulations, policies, and practices on the performance of research conducted at its member institutions. We and our members appreciate the opportunity to comment on the *Proposed Action Under the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines).*

We support the interest of the NIH to maximize the benefits of the NIH Recombinant DNA Advisory Committee **(**RAC**)** review process by maintaining the NIH protocol submission and safety reporting requirements, but restricting individual gene transfer protocol review to exceptional cases that meet specific criteria.

We have no objections to the proposed amendment to the NIH Guidelines that describe the criteria and process for RAC review, although we acknowledge that the Institutional Biosafety Committees or Institutional Review Board(s) will have new responsibilities for determining whether a human gene transfer protocol submitted for approval would significantly benefit from RAC review, and that projects submitted for RAC review fit one or more of the following criteria:

a. The protocol uses a new vector, genetic material, or delivery methodology that represents a first-in-human experience, thus presenting an unknown risk.
b. The protocol relies on preclinical safety data that were obtained using a new preclinical model system of unknown and unconfirmed value.
c. The proposed vector, gene construct, or method of delivery is associated with possible toxicities that are not widely known and that may render it difficult for oversight bodies to evaluate the protocol rigorously.

One of the potential complications we foresee, however, is differing interpretation of the proposed criteria, above, by local oversight bodies in the case of clinical trial sites being added after completion of the NIH protocol registration process.

There are also several areas in the amended language that would benefit from clarification. One example included below involves an apparent inconsistency between two of the amended sections regarding when the enrollment of subjects can begin:

> Section IV-B-1-f, states at (iii) "no research participant shall be enrolled (see definition of enrollment in Section I-E-7) in a human gene transfer experiment until the NIH protocol registration process has been completed (see Appendix M-I-B, Selection of Individual Protocols for Public RAC Review and Discussion), Institutional Biosafety Committee approval has been obtained, Institutional Review Board approval has been obtained, and all applicable regulatory authorizations have been obtained. Institutional Biosafety Committee approval must be obtained from the clinical trial site."
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> Appendix M-1-B, states, "If no oversight body would significantly benefit from public RAC review and discussion, then the Principal Investigator shall submit all of the documentation required to register the submission (see Appendix M-I-A) to the NIH Office of Science Policy at any time but shall occur not less than three working days prior to the anticipated date of enrollment of the first subject …. Enrollment may proceed upon acknowledgement that the submission is registered."

We note that except for the section on Long-Term Follow-Up, all of Appendix M-III on Informed Consent is being removed. It would be useful to clarify whether there remain any special expectations for the informed consent document and process in human gene transfer clinical trials.

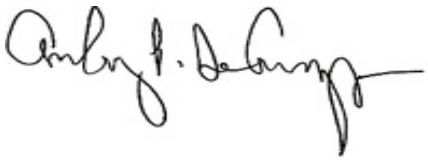
One suggestion we have for future proposed changes to NIH Guidelines is for NIH to provide a redlined version of the old guidelines reflecting the proposed changes. This would make it easier to review the changes.

We appreciate the proposed streamlining of the NIH submission requirements for protocols, outlined at Appendix M-I-A, by reducing the documents required and eliminating Appendices M-II, III, IV, and V in favor of condensed questions on the nature of the gene transfer product.

We hope that OBA will provide guidance on this new process, similar to the instructions and diagrams that were provided for the Dual Use Research of Concern policy.

Thank you for the opportunity to provide comments. If you have any questions, please contact COGR staff member Lisa Nichols at lnichols@cogr.edu.

Sincerely,



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