2016, Vol. 81 pp.1633 and allowed 60-days for public comment. No public comments were received. The purpose of this notice is to allow an additional 30 days for public comment. The National Cancer Institute (NCI), National Institutes of Health (NIH), may not conduct or sponsor, and the respondent is not required to respond to, an information collection that has been extended, revised, or implemented on or after October 1, 1995, unless it displays a currently valid OMB control number.

Direct Comments to OMB: Written comments and/or suggestions regarding the item(s) contained in this notice, especially regarding the estimated public burden and associated response time, should be directed to the: Office of Management and Budget, Office of Regulatory Affairs, *OIRA_submission@omb.eop.gov* or by fax to 202–395–6974, Attention: NIH Desk Officer.

Comment Due Date: Comments regarding this information collection are best assured of having their full effect if received within 30 days of the date of this publication.

FOR FURTHER INFORMATION CONTACT: To obtain a copy of the data collection plans and instruments, or request more information on the proposed project, contact: Anthony Kerlavage, NCI CBIIT, Program Manager, 9609 Medical Center Drive, Room 1W–436, Rockville, MD 20850 or call non-toll-free number 240–276–5190 or email your request, including your address to: *anthony.kerlavage@nih.gov.* Formal requests for additional plans and instruments must be requested in writing.

Proposed Collection: Cancer Genomics Cloud Pilots Survey, 0925–NEW, National Cancer Institute (NCI), National Institutes of Health (NIH).

Need and Use of Information Collection Need and Use of Information Collection: The Center for Biomedical Informatics and Information Technology (CBIIT), in collaboration with the Center for Cancer Genomics at the National Cancer Instititues (NCI) in the National Institutes of Health (NIH), is coordinating a program to develop three Cancer Genomics Cloud Pilots to help meet the research community's needs to access and analyze high quality, large-scale cancer genomic data and associated clinical information. The goal of this effort is to develop an innovative, cost-effective model for computational analysis of biological data and provide broader yet secure access to genomic data that NCI generates. Cloud computing will be a valuable tool to support studies related to the mechanisms of cancer. This capability will be equally valuable to other NCI scientific areas, including clinical trials and other types of patient-focused research. In order to understand the utility and value of the tools being developed, the NCI has developed a survey instrument to capture feedback from the cancer research community. The information collected as part of this survey process will be used exclusively by the NCI to determine future funding of cloud technology projects.

OMB approval is requested for 3 years. There are no costs to respondents other than their time. The total estimated annualized burden hours are 375.

ESTIMATED ANNUALIZED BURDEN HOURS

Form name	Type of respondent	Number of respondents	Number of responses per respondent	Average burden per response (in hours)	Total annual burden hour
Cloud Pilot Survey	Principal Investigator	1500	1	15/60	375
Totals		1500	1500		375

Dated: March 14, 2016.

Karla Bailey,

Project Clearance Liaison, National Cancer Institute, NIH.

[FR Doc. 2016–06332 Filed 3–21–16; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Cancer Institute, Notice of Meeting

Pursuant to section 10(a) of the Federal Advisory Committee Act, as amended (5 U.S.C. App.), notice is hereby given of the meeting of the President's Cancer Panel.

The meeting will be open to the public, with attendance limited to space available. Individuals who plan to attend and need special assistance, such as sign language interpretation or other reasonable accommodations, should notify the Contact Person listed below in advance of the meeting.

Name of Committee: President's Cancer Panel.

Date: June 10, 2016.

Time: 9:00 a.m. to 4:00 p.m.

Agenda: Examining the Cancer Drug Cost and Access Landscape.

Place: New York Hilton Midtown, 1335 Avenue of the Americas, New York, NY 10019.

Contact Person: Abby B. Sandler, Ph.D., Executive Secretary, President's Cancer Panel, Special Assistant to the Director, NCI Center for Cancer Research, 9000 Rockville Pike, Building 31, Room B2B37, MSC 2590, Bethesda, MD 20892–8349, 301–451–9399, *sandlera@mail.nih.gov*.

Information is also available on the Institute's/Center's home page: *http://deainfo.nci.nih.gov/advisory/pcp/index.htm,* where an agenda and any additional information for the meeting will be posted when available.

(Catalogue of Federal Domestic Assistance Program Nos. 93.392, Cancer Construction; 93.393, Cancer Cause and Prevention Research; 93.394, Cancer Detection and Diagnosis Research; 93.395, Cancer Treatment Research; 93.396, Cancer Biology Research; 93.397, Cancer Centers Support; 93.398, Cancer Research Manpower; 93.399, Cancer Control, National Institutes of Health, HHS)

Dated: March 16, 2016.

Melanie Gray,

Program Analyst, Office of Federal Advisory Committee Policy.

[FR Doc. 2016–06335 Filed 3–21–16; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Final Action Under the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines)

AGENCY: National Institutes of Health (NIH), HHS.

ACTION: Notice of changes to the *NIH Guidelines.*

SUMMARY: This notice sets forth final changes to the *National Institutes of Health Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines)* to incorporate the recommendations of the Institute of Medicine (IOM) regarding human gene transfer protocols, as initially outlined by the NIH Office of Science Policy (OSP) in a **Federal Register** notice issued on October 16, 2015 (80 FR 62543). Following the solicitation of public comment on its original proposal, the NIH is amending the *NIH Guidelines* in the following areas: (A) The criteria for selecting protocols for in-depth review and public discussion by the NIH Recombinant DNA Advisory Committee (RAC), (B) the process by which human gene transfer protocols are reviewed and registered with the NIH, and (C) the streamlining of the NIH protocol submission requirements under Appendix M–I–A of the *NIH Guidelines.* In a continuing effort to harmonize with the Food and Drug Administration (FDA) regulations, a change is being made to the reporting requirement for additional clinical trial sites allowing for a delay of 30 days to submit appropriate documentation.

The changes set forth in this notice do not affect the responsibility of the Principal Investigator to submit documentation to his or her local oversight bodies and to the NIH, nor do they affect the requirement to submit appropriate documentation to the NIH when new clinical trial sites are registered. The changes also do not affect the responsibility of a Principal Investigator (or a delegated clinical trial sponsor) to submit appropriate and timely follow up information to the NIH as outlined in the *NIH Guidelines* (*e.g.,* protocol amendments, serious adverse events, annual reports with cumulative safety data).

DATES: Changes outlined in this notice will be effective April 27, 2016, to coincide with the RAC review cycle and to allow institutions and investigators to establish processes for implementing the new review procedures.

FOR FURTHER INFORMATION CONTACT: If you have questions, or require additional background information about these changes, please contact the NIH by email at *SciencePolicy@od.nih.gov*, by telephone at 301–496–9838, by fax at 301–496–9839, or by mail to the Office of Science Policy, National Institutes of Health, 6705 Rockledge Drive, Suite 750, Bethesda, Maryland 20892–7985.

SUPPLEMENTARY INFORMATION: The NIH Office of the Director requested that the IOM review whether gene transfer research raises issues of concern that warrant the current level of RAC oversight of individual clinical trials involving gene transfer techniques. The IOM noted that the RAC has served a valuable role, but concluded that the current level of oversight over individual clinical trials is no longer justifiable. In an effort to maximize the benefits of the RAC review process, the IOM recommended that the NIH maintain its protocol submission and safety reporting requirements, but restrict individual gene transfer protocol reviews to exceptional cases that meet specified criteria (full recommendations are listed in the IOM report *Oversight and Review of Clinical Gene Transfer Protocols: Assessing the Role of the Recombinant DNA Advisory Committee* (*http://www.iom.edu/Reports/2013/Oversight-and-Review-of-Clinical-Gene-Transfer-Protocols.aspx*)).

After careful consideration of the IOM's recommendations and public consultation, the NIH is amending the *NIH Guidelines* in the following areas:

A. *Criteria and process for selecting protocols for RAC review.* The following criteria (subsequently referred to as the NIH RAC review criteria) are being implemented for initiating RAC review of individual human gene transfer protocols (criteria listed in both items 1 and 2 must be met):

1. An oversight body (an Institutional Biosafety Committee (IBC) or an Institutional Review Board (IRB)) determines that a human gene transfer protocol submitted to it for approval would significantly benefit from RAC review; and

2. One or more of the criteria below are satisfied:

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.

The chair of an oversight body or an authorized oversight body representative may submit a request for RAC review by sending the request to the NIH as part of the submission materials provided by the Principal Investigator. Requests for RAC review must originate from oversight bodies involved in the initial site(s) review. This request must include the rationale for why the protocol satisfies both items 1 and 2 of the NIH RAC review criteria. The NIH will review the request and notify the requestor of a decision within 10 working days.

1. If the NIH determines that the criteria listed in both 1 and 2 above are satisfied, the NIH Director will convene the RAC.

2. If the NIH receives a request for RAC review of a protocol that the NIH determines does not meet both of these criteria, the NIH will:

a. Inform the requestor that RAC review is not warranted, and

b. indicate that information regarding human gene transfer trials is available in the Genetic Modification Clinical Research Information System (GeMCRIS®), which may be found at *https://www.gemcris.od.nih.gov*.

3. Even if the protocol does not meet the proposed criteria listed in both items 1 and 2 above, the NIH Director, in consultation (if necessary) with appropriate regulatory authorities (*e.g.,* the Office for Human Research Protections, the Food and Drug Administration), can select protocols for review that may present significant scientific, societal, or ethical concerns.

B. *Process by which human gene transfer protocols are registered with the NIH.* All human gene transfer protocols subject to Section III–C of the *NIH Guidelines* will continue to be registered with the NIH. However, the following changes are being implemented:

1. The Principal Investigator will continue to be responsible for submitting documentation regarding a proposed human gene transfer protocol to his or her local oversight bodies. The Principal Investigator will also continue to be responsible for submitting documentation as outlined in Appendix M–I–A to the NIH. As part of the submission to the NIH, documentation shall also include written assessments originating from all oversight bodies involved in the review at an initial site(s) as to whether or not RAC review is warranted.

2. Completion of the protocol registration process:

a. If no oversight body involved in the review at an initial site(s) requests public RAC review, the IBC(s) may proceed with its approval process upon receipt of documentation from the NIH indicating that the initial protocol registration process is complete. This documentation will be provided by the NIH to the Principal Investigator within 10 working days.

b. If one or more oversight bodies involved in the review at an initial site(s) requests public RAC review and

the NIH agrees that the submission has met the above criteria in (A), the protocol will undergo RAC review and public discussion. The IBC(s) may not approve a protocol until the RAC has completed its review. The IBC(s) may proceed with the approval process upon receipt of a letter from the NIH summarizing the RAC's comments and recommendations (if any) regarding the protocol. Unless the NIH determines that there are exceptional circumstances, the NIH will send notification to the Principal Investigator within 10 working days after the completion of the RAC meeting at which the experiment was reviewed. Receipt of this letter concludes the protocol registration process.

C. *Streamlining the submission requirements for protocol registration.* Section III–C–1 and Appendix M of the *NIH Guidelines* specify the requirements for protocol submission, RAC review, and reporting requirements for human gene transfer experiments. In an effort to streamline the protocol submission process, the NIH is reducing the submission requirements as outlined in Appendix M–I–A. Specifically, only a subset of the information listed under the current Appendices M–II through M–V will be required mainly for oversight bodies to determine RAC review eligibility and to support GeMCRIS®, which facilitates safety data reporting and enables public access to information about human gene transfer protocols registered with the NIH.

The changes to the RAC review process, outlined above, will require amendment of multiple portions of the *NIH Guidelines* (see section below on ''Amendments to the *NIH Guidelines''*).

Overview of Comments Received in Response to the October 16, 2015 Notice

In response to its October 16, 2015, **Federal Register** notice, the NIH received 11 letters of comment from academic institutions, private companies, and trade organizations representing the biosafety and biomedical research communities. The majority of letters endorsed the proposed changes to the review process; however commenters suggested that some revisions would be helpful to clarify the proposal. All comments, regardless of position, were reviewed and considered by the NIH. These comments, along with the NIH responses, are summarized below:

Submission requirements for human gene transfer protocols. Several comments focused on the appropriate amount of documentation needed for the registration of human gene transfer protocols, especially in light of other federal reporting requirements. In its report, the IOM recognized the value of ongoing registration of all protocols, the dissemination of that information on these protocols through GeMCRIS, the ongoing reporting and analysis of safety data, and their public discussion at scientific workshops and symposia for the benefit of this field. Thus, to continue the NIH's role in fostering a public discussion of human gene transfer research, no further changes to the material required under Appendix M–I–A are being made.

Criteria by which human gene transfer protocols will be selected. Some entities raised concerns about the difficulty in applying the IOM criteria to human gene transfer protocols, specifically in terms of defining ''novelty.'' Given the evolving field of human gene transfer research, it is important that the RAC review criteria maintain a degree of flexibility. Thus, the NIH intends to implement the IOM criteria as outlined in its report. Of relevance, the IOM did elaborate that ''[n]ovelty indicates an untested area of science, one that brings an additional layer of uncertainty as compared to research in areas of greater experience and one for which institutional review bodies typically do not have the requisite expertise.'' This may include a novel approach, application of a new technology, or a new route of administration of a gene transfer product to target a disease.

Process by which human gene transfer protocols will be selected. Several comments requested clarification regarding the process by which a RAC public discussion would occur, whether entities other than oversight bodies (*e.g.* investigational new drug sponsors or Principal Investigators) could request review, or in the case of trials being conducted at more than one site, whether a clinical trial site added after completion of the protocol registration process for the initial site(s) could request RAC review. The ability to request RAC review lies initially and solely within the purview of the local oversight bodies (*i.e.,* IBC and IRB), although the NIH Director in consultation (as needed) with the appropriate regulatory authorities may also require it. Since both the expertise that these oversight bodies (IBCs and IRBs) have regarding the review of human gene transfer trials and their rationale for requesting public review are potentially very different, a recommendation for public review from either oversight body will be sufficient to trigger a determination from the NIH as to whether the IOM criteria are met. To clarify the process for requesting RAC review, the *NIH Guidelines* will be amended to specify that a request for RAC review must be made by oversight bodies involved in the review at an initial site(s) registering the protocol with the NIH.

RAC expertise and review. Several comments discussed the value of RAC review in terms of scientific expertise, and expressed concerns about removing this resource for local oversight bodies. The NIH recognizes the value of the RAC and intends to continue to support its review of those protocols that would benefit from additional expertise and public discussion. Historically, only a fraction of all protocols registered with the NIH are publicly reviewed and it is expected that oversight bodies will continue to review and approve protocols in the same manner they always have. In cases where an oversight body feels additional expertise is needed, it is encouraged to augment its membership with *ad hoc* experts.

Proprietary confidential information. Comments were raised regarding the confidentiality of information submitted to the NIH, especially in cases where the submitter considers the information to be confidential or proprietary. The *NIH Guidelines* state that documents submitted to the NIH should not contain information considered ''confidential'' and that the amended *NIH Guidelines* will further indicate that an entire document such as a clinical protocol cannot be classified as ''confidential'' in its entirety. Should a submitter choose to provide information that is considered to be trade secret, confidential commercial, or financial in nature, it is incumbent on the submitter to identify clearly these specific portions, outlining how the release of this information would cause financial or competitive harm. All records submitted to the NIH, including human gene transfer clinical trial information, are subject to the Freedom of Information Act (FOIA—5 U.S.C. 552) and the Department of Health and Human Services FOIA regulations (45 CFR part 5). Details about the FOIA and the regulations can be found on the NIH Web site at this address: *http://www.nih.gov/institutes-nih/nih-office-director/office-communications-public-liaison/freedom-information-act-office.*

Amendments to the NIH Guidelines

Throughout the document the following global changes will be made: (i) The NIH OSP will replace the NIH OBA, (ii) the term ''RAC review'' will be replaced with the term ''NIH protocol registration process'' as appropriate; (iii) the title for Appendix M–I–B will be changed; and (iv) the requirement for a CV/biosketch of key personnel will be

deleted (except for the requirements under the membership provisions of IBCs, Section IV–B–2–a).

Section I–E will be amended to include the following new definitions:

I–E–11. An ''oversight body'' is an institutional entity (an Institutional Biosafety Committee or an Institutional Review Board) that must review and approve a human gene transfer trial.

I–E–12. A ''regulatory authority'' in the context of human gene transfer research is a federal entity that by statute has oversight over research involving human subjects.

Section III–C–1 will be amended as follows:

Section III–C–1. Experiments Involving the Deliberate Transfer of Recombinant or Synthetic Nucleic Acid Molecules, or DNA or RNA Derived from Recombinant or Synthetic Nucleic Acid Molecules, into One or More Human Research Participants Human gene transfer is the deliberate transfer into human research participants of either:

1. Recombinant nucleic acid molecules, or DNA or RNA derived from recombinant nucleic acid molecules, or

2. Synthetic nucleic acid molecules, or DNA or RNA derived from synthetic nucleic acid molecules that meet any one of the following criteria:

a. Contain more than 100 nucleotides; or

b. Possess biological properties that enable integration into the genome (*e.g., cis* elements involved in integration); or

c. Have the potential to replicate in a cell; or

d. Can be translated or transcribed.

No research participant shall be enrolled (see definition of enrollment in Section I–E–7) until the NIH protocol registration process has been completed (see Appendix M–I–B, Selection of Individual Protocols for Public RAC Review and Discussion).

In its evaluation of human gene transfer protocols, the NIH will make a determination, following a request from one or more oversight bodies involved in the review at an initial site(s), whether a proposed human gene transfer experiment has one or more of the characteristics that warrant public RAC review and discussion (See Appendix M–1–B–1). The process of public RAC review and discussion is intended to foster the safe and ethical conduct of human gene transfer experiments. Public review and discussion of a human gene transfer experiment (and access to relevant information) also serves to inform the public about the technical aspects of the proposal, the meaning and significance of the research, and any significant safety, social, and ethical implications of the research.

Public RAC review and discussion of a human gene transfer experiment will be initiated in two exceptional circumstances: (1) Following a request for public RAC review from one or more oversight bodies involved in the review at an initial site(s), the NIH concurs that the submission meets one or more of the following NIH RAC review criteria: (i) The protocol uses a new vector, genetic material, or delivery methodology that represents a first-in-human experience, thus presenting an unknown risk; (ii) the protocol relies on preclinical safety data that were obtained using a new preclinical model system of unknown and unconfirmed value; or (iii) 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 involved in the review at an initial site(s) to evaluate the protocol rigorously. However, if one or more oversight bodies involved in the review at an initial site(s) requests public RAC review, but the NIH does not concur that the submission meets one or more of the RAC review criteria (listed in i, ii, or iii), then the NIH OSP will inform, within 10 working days, the requesting and other oversight bodies involved in the review at an initial site(s) that public RAC review is not warranted. (2) The NIH Director, in consultation (if needed) with appropriate regulatory authorities, determines that the submission: (a) Meets one or more of the NIH RAC review criteria (listed in i, ii, or iii) and that public RAC review and discussion would provide a clear and obvious benefit to the scientific community or the public; or (b) raises significant scientific, societal, or ethical concerns.

For a clinical trial site that is added after completion of the NIH protocol registration process, no research participant shall be enrolled (see definition of enrollment in Section I–E–7) at the clinical trial site until the following documentation has been submitted to the NIH OSP: (1) Institutional Biosafety Committee approval (from the clinical trial site); (2) Institutional Review Board approval; (3) Institutional Review Board-approved informed consent document; and (4) the NIH grant number(s) if applicable.

In order to maintain public access to information regarding human gene transfer (including protocols that are not publicly reviewed by the RAC), the NIH OSP will maintain the documentation described in Appendices M–I through M–II. The information provided in response to Appendix M should not contain any confidential commercial or financial information or trade secrets, enabling all aspects of RAC review to be open to the public.

Note: For specific directives concerning the use of retroviral vectors for gene delivery, consult Appendix B–V–1, Murine, Retroviral Vectors.

Section IV–B–1–f will be amended as follows:

Section IV–B–1–f. Ensure that when the institution participates in or sponsors recombinant or synthetic nucleic acid molecule research involving human subjects: (i) The Institutional Biosafety Committee has adequate expertise and training (using *ad hoc* consultants as deemed necessary), (ii) all aspects of Appendix M have been appropriately addressed by the Principal Investigator; and (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.

None of the other sub-sections under Section IV–B–1. General Information are to be amended.

Section IV–B–2–a–(1) will be amended as follows:

Section IV–B–2–a–(1). The Institutional Biosafety Committee must be composed of no fewer than five members so selected that they collectively have experience and expertise in recombinant or synthetic nucleic acid molecule technology and the capability to assess the safety of recombinant or synthetic nucleic acid molecule research and to identify any potential risk to public health or the environment. At least two members shall not be affiliated with the institution (apart from their membership on the Institutional Biosafety Committee) and who represent the interest of the surrounding community with respect to health and protection of the environment (*e.g.,* officials of state or local public health or environmental protection agencies, members of other local governmental bodies, or persons active in medical, occupational health, or environmental concerns in the community). The Institutional Biosafety Committee shall include at least one individual with expertise in plant, plant pathogen, or plant pest containment

principles when experiments utilizing Appendix P, Physical and Biological Containment for Recombinant or Synthetic Nucleic Acid Molecule Research Involving Plants, require prior approval by the Institutional Biosafety Committee. The Institutional Biosafety Committee shall include at least one scientist with expertise in animal containment principles when experiments utilizing Appendix Q, Physical and Biological Containment for Recombinant or Synthetic Nucleic Acid Molecule Research Involving Animals, require Institutional Biosafety Committee prior approval. When the institution conducts recombinant or synthetic nucleic acid molecule research at BL3, BL4, or Large Scale (greater than 10 liters), a Biological Safety Officer is mandatory and shall be a member of the Institutional Biosafety Committee (see Section IV–B–3, Biological Safety Officer). When the institution participates in or sponsors recombinant or synthetic nucleic acid molecule research involving human research participants, the institution must ensure that: (i) The Institutional Biosafety Committee has adequate expertise and training (using ad hoc consultants as deemed necessary); (ii) all aspects of Appendix M have been appropriately addressed by the Principal Investigator; (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); and (iv) final IBC approval is granted only after 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 must be obtained from the clinical trial site.

Note: Individuals, corporations, and institutions not otherwise covered by the *NIH Guidelines,* are encouraged to adhere to the standards and procedures set forth in Sections I through IV (see Section IV–D, Voluntary Compliance. The policy and procedures for establishing an Institutional Biosafety Committee under Voluntary Compliance, are specified in Section IV–D–2, Institutional Biosafety Committee Approval).

None of the other sub-sections under Section IV–B2–a. Membership and Procedures of the IBC are to be amended.

Section IV–B–2–b–(1) will be amended as follows:

Section IV–B–2–b–(1). Reviewing recombinant or synthetic nucleic acid molecule research conducted at or sponsored by the institution for compliance with the *NIH Guidelines* as specified in Section III, Experiments Covered by the *NIH Guidelines,* and approving those research projects that are found to conform to the *NIH Guidelines.* This review shall include: (i) Independent assessment of the containment levels required by the *NIH Guidelines* for the proposed research; (ii) assessment of the facilities, procedures, practices, and training and expertise of personnel involved in recombinant or synthetic nucleic acid molecule research; (iii) ensuring that all aspects of Appendix M have been appropriately addressed by the Principal Investigator (iv) ensuring that no research participant is 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 (from the clinical trial site) has been obtained, Institutional Review Board approval has been obtained, and all applicable regulatory authorizations have been obtained; (v) for human gene transfer protocols selected for public RAC review and discussion, consideration of the issues raised and recommendations made as a result of this review and consideration of the Principal Investigator's response to the RAC recommendations; (vi) ensuring that final IBC approval is granted only after the NIH protocol registration process has been completed (see Appendix M–I–B, Selection of Individual Protocols for Public RAC Review and Discussion); and (vii) ensuring compliance with all surveillance, data reporting, and adverse event reporting requirements set forth in the *NIH Guidelines.*

None of the other sub-sections under Section IV–B–2–b. Functions of the IBC are to be amended.

Section IV–B–6 will be amended as follows:

Section IV–B–6. Human Gene Therapy Expertise. When the institution participates in or sponsors recombinant or synthetic nucleic acid molecule research involving human subjects, the institution must ensure that: (i) The Institutional Biosafety Committee has adequate expertise and training (using ad hoc consultants as deemed necessary) and (ii) all aspects of Appendix M, Points to Consider in the Design and Submission of Protocols for the Transfer of Recombinant or Synthetic Nucleic Acid Molecules into One or More Human Subjects (Points to Consider), have been appropriately addressed by the Principal Investigator prior to its approval.

Section IV–B–7–b–(6) will be amended as follows:

Section IV–B–7–b–(6). Ensure that all aspects of Appendix M have been appropriately addressed prior to submission. 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); IBC approval (from the clinical trial site) has been obtained; Institutional Review Board (IRB) approval has been obtained; and all applicable regulatory authorization(s) have been obtained.

For a clinical trial site that is added after completion of the NIH protocol registration process, no research participant shall be enrolled (see definition of enrollment in Section I–E–7) at the clinical trial site until the following documentation has been submitted to the NIH OSP: (1) IBC approval (from the clinical trial site); (2) IRB approval; (3) IRB-approved informed consent document; and (4) NIH grant number(s) if applicable.

To implement this new process, the NIH will amend Appendix M, Points to Consider in the Design and Submission of Protocols for the Transfer of Recombinant or Synthetic Nucleic Acid Molecules into One or More Human Research Participants (Points to Consider).

Appendix M will be amended as follows:

Appendix M applies to research conducted at or sponsored by an institution that receives any support for recombinant or synthetic nucleic acid molecule research from NIH. Researchers not covered by the *NIH Guidelines* are encouraged to use Appendix M (see Section I–C, General Applicability).

The acceptability of human somatic cell gene transfer has been addressed in several public documents as well as in numerous academic studies. In November 1982, the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research published a report, *Splicing Life,* which resulted from a two-year process of public deliberation and hearings. Upon release of that report, a U.S. House of Representatives subcommittee held three days of public hearings with witnesses from a wide range of fields

from the biomedical and social sciences to theology, philosophy, and law. In December 1984, the Office of Technology Assessment released a background paper, *Human Gene Therapy,* which concluded that civic, religious, scientific, and medical groups have all accepted, in principle, the appropriateness of gene transfer of somatic cells in humans for specific genetic diseases. Somatic cell gene transfer is seen as an extension of present methods that might be preferable to other technologies. In light of this public support, the NIH is prepared to consider proposals for somatic cell gene transfer.

The NIH will not at present entertain proposals for germ line alterations but will consider proposals involving somatic cell gene transfer. The purpose of somatic cell gene transfer is to treat an individual patient, *e.g.,* by inserting a properly functioning gene into the subject's somatic cells. Germ line alteration involves a specific attempt to introduce genetic changes into the germ (reproductive) cells of an individual, with the aim of changing the set of genes passed on to the individual's offspring.

The NIH continues to explore the issues raised by the potential of *in utero* gene transfer clinical research. However, the NIH concludes that, at present, it is premature to undertake any *in utero* gene transfer clinical trial. Significant additional preclinical and clinical studies addressing vector transduction efficacy, biodistribution, and toxicity are required before a human *in utero* gene transfer protocol can proceed. In addition, a more thorough understanding of the development of human organ systems, such as the immune and nervous systems, is needed to better define the potential efficacy and risks of human *in utero* gene transfer. Prerequisites for considering any specific human *in utero* gene transfer procedure include an understanding of the pathophysiology of the candidate disease and a demonstrable advantage to the *in utero* approach. Once the above criteria are met, the NIH would be willing to consider well rationalized human *in utero* gene transfer clinical trials.

Research proposals involving the deliberate transfer of recombinant or synthetic nucleic acid molecules, or DNA or RNA derived from such nucleic acid molecules, into one or more human subjects (human gene transfer) will be considered through a registration process involving the NIH, oversight bodies involved in the review at an initial site(s), and regulatory authorities, when appropriate. Investigators shall submit the relevant information on the proposed human gene transfer experiment to the oversight bodies involved in the review at an initial site(s) and then to the NIH. The format of the submission is described in Appendix M–I–A, Requirements for Protocol Submission. Submission to the NIH OSP shall be for registration purposes and will ensure continued public access to relevant human gene transfer information conducted in compliance with the *NIH Guidelines.*

Public RAC review and discussion of a human gene transfer experiment will be initiated in two exceptional circumstances: (1) Following a request for public RAC review from one or more oversight bodies involved in the review at an initial site(s), the NIH concurs that the submission meets one or more of the following NIH RAC review criteria: (i) The protocol uses a new vector, genetic material, or delivery methodology that represents a first-in-human experience, thus presenting an unknown risk; (ii) the protocol relies on preclinical safety data that were obtained using a new preclinical model system of unknown and unconfirmed value; or (iii) 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 involved in the review at an initial site(s) to evaluate the protocol rigorously. However, if one or more oversight bodies involved in the review at an initial site(s) requests public RAC review, but the NIH does not concur that the submission meets one or more of the RAC review criteria (listed in i, ii, or iii), then the NIH OSP will inform, within 10 working days, the requesting and other oversight bodies involved in the review at an initial site(s) that public RAC review is not warranted. (2) The NIH Director, in consultation (if needed) with appropriate regulatory authorities, determines that the submission: (a) Meets one or more of the NIH RAC review criteria (listed in i, ii, or iii) and that public RAC review and discussion would provide a clear and obvious benefit to the scientific community or the public; or (b) raises significant scientific, societal, or ethical concerns.

If it is determined that a human gene transfer trial will undergo public RAC review, the NIH will immediately notify the Principal Investigator. RAC recommendations following public review on a specific human gene transfer experiment shall be forwarded to the Principal Investigator, oversight bodies involved in the review at an initial site(s), and regulatory authorities, as appropriate. Relevant documentation will be included in the material for the RAC meeting at which the human gene transfer trial is scheduled to be discussed. RAC meetings will be open to the public except where trade secrets and proprietary information are reviewed (see Section IV–D–5, *Protection of Proprietary Data—Voluntary Compliance*). Information provided in response to Appendix M should not contain any proprietary data or trade secrets, enabling all aspects of the review to be open to the public.

Some but not all sections of Appendix M–I Requirements for Protocol Submission, Review, and Reporting—Human Gene Transfer Experiments will be amended to decrease the number and amount of supporting documentation that must be submitted upon protocol registration, and to modify the timing of the registration processes. Principal Investigators must submit the material as outlined below to oversight bodies at the proposed clinical trial sites; however, submission of responses to Appendices M–II through M–V or curriculum vitae will no longer be required.

Appendix M–I–A will be amended as follows:

Appendix M–I–A. Requirements for Protocol Submission

The following documentation must be submitted according to institutional policy, to the appropriate oversight bodies involved in the review at an initial site(s) and subsequently in electronic form to the NIH OSP:

1. A scientific abstract.

2. The proposed clinical protocol, including tables, figures, and any relevant publications.

3. Summary of preclinical studies conducted in support of the proposed clinical trial or reference to the specific section of the protocol providing this information.

4. A description of the product:

a. Describe the derivation of the delivery vector system including the source (*e.g.,* viral, bacterial, or plasmid vector); and modifications (*e.g.,* deletions to attenuate or self-inactivate, encapsulation in any synthetic complex, changes to tropisms, etc.). Please reference any previous clinical experience with this vector or similar vectors.

b. Describe the genetic content of the transgene or nucleic acid delivered including the species source of the sequence and whether any modifications have been made (*e.g.* mutations, deletions, and truncations). What are the regulatory elements contained in the construct?

c. Describe any other material to be used in preparation of the agent (vector and transgene) that will be administered to the human research subject (*e.g.,* helper virus, packaging cell line, carrier particles).

d. Describe the methods for replication-competent virus testing, if applicable.

e. Describe the intended *ex vivo* or *in vivo* target cells and transduction efficiency.

f. Describe the gene transfer agent delivery method.

5. The proposed informed consent document.

6. Specifically for submission to the NIH OSP, the Principal Investigator shall provide additional documentation originating from oversight bodies involved in the review at an initial site(s) regarding their assessment of whether public RAC review is warranted. In the event that review is requested, a justification that the NIH RAC review criteria (see Section III–C–1) are met shall be included.

Note: Any application submitted shall not contain any document that is designated as 'confidential' in its entirety. In the event that a determination has been made that a specific portion of a document should be considered proprietary or trade secret, each specific portion should be clearly identified as such. In the event that a specific portion of the submission is identified to be proprietary or trade secret, the submission to the NIH OSP must contain a letter that: (1) Clearly indicates what select portions of the application contain information considered as proprietary or trade secret, and (2) provides justification as to why this information is considered to be proprietary or trade secret. The justification must be able to demonstrate *with specificity* how release of that information will reveal a trade secret or will result in substantial competitive harm.

Appendix M–I–B, RAC Review Requirements will be amended to change the process and timing of public RAC review. Currently, investigators are informed within 15 working days whether or not the protocol requires public RAC review. Public discussion of selected protocols then occurs at the next quarterly RAC meeting, which occurs, at a minimum of, eight weeks after receipt of a complete protocol submission. Individual RAC members will no longer make a recommendation regarding whether a protocol should be selected for review at a public meeting.

Therefore, Appendix M–1–B–1 and Appendix M–1–B–2 are being amended as follows to form a consolidated Appendix M–1–B:

Appendix M–1–B. Selection of Individual Protocols for Public RAC Review and Discussion

As part of the NIH protocol registration process, documentation originating from all oversight bodies involved in the review at an initial site(s) regarding their assessment of whether public RAC review is warranted must accompany the Principal Investigator's submission to the NIH. If no oversight body involved in the review at an initial site(s) requests public RAC review, then the required documentation to register the protocol (see Appendix M–I–A) shall be submitted to the NIH OSP at any time, but not less than 10 working days prior to the anticipated date of enrollment of the first subject (see definition of enrollment in Section I–E–7). This information shall be provided in electronic form to the Office of Science Policy, National Institutes of Health, 6705 Rockledge Drive, Suite 750, Bethesda, MD 20892–7985 (20817 for non-USPS mail), 301–496–9838, 301–496–9839 (fax), Email: *HGTprotocols@mail.nih.gov*. An acknowledgement that the protocol registration process is complete will occur within the 10 working days period prior to the anticipated date of enrollment. Final IBC approval may then be granted.

If one or more oversight bodies involved in the review at an initial site(s) requests public RAC review, but the NIH does not concur that the submission meets one or more of the RAC review criteria, the NIH OSP will notify the Principal Investigator, oversight bodies involved in the review at an initial site(s), and regulatory authorities, as appropriate, that public RAC review is not warranted. An acknowledgement that the protocol registration process is complete will accompany this decision. Final IBC approval may then be granted.

If an oversight body involved in the review at an initial site(s) determines that: (1) A protocol submission would significantly benefit from public RAC review and discussion and (2) that one or more of the following NIH RAC review criteria are met: (i) The protocol uses a new vector, genetic material, or delivery methodology that represents a first-in-human experience, thus presenting an unknown risk; or (ii) the protocol relies on preclinical safety data that were obtained using a new preclinical model system of unknown and unconfirmed value; or (iii) 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 local and federal regulatory bodies to evaluate the protocol rigorously, and is therefore requesting RAC review and public discussion, the Principal Investigator shall submit the documentation as outlined in Appendix M–I–A at least 8 weeks prior to the next scheduled meeting in order to be reviewed at that RAC meeting. The submission shall include documentation originating from oversight bodies involved in the review at an initial site(s) regarding their assessment of whether public RAC review is warranted and that one or both have justified their request according the NIH RAC review criteria listed above. The submission shall be provided to the NIH in electronic form to the Office of Science Policy, National Institutes of Health, 6705 Rockledge Drive, Suite 750, Bethesda, MD 20892–7985 (20817 for non-USPS mail), 301–496–9838, 301–496–9839 (fax), Email: *HGTprotocols@mail.nih.gov*. If the NIH concurs that the submission meets one or more of the following NIH RAC review criteria above, the protocol will undergo public RAC review and discussion.

Even if an oversight body involved in the review at an initial site(s) does not request public RAC review, the NIH Director, after consultation (if needed) with appropriate regulatory authorities, may initiate public RAC review if (a) the protocol has one or more of the characteristics listed above (i, ii, or iii) and public RAC review and discussion would provide a clear and obvious benefit to the scientific community or public; or (b) the protocol otherwise raises significant scientific, societal, or ethical concerns. If a protocol is to undergo RAC public discussion a complete human gene transfer protocol package must be submitted at least 8 weeks before a scheduled RAC meeting to be reviewed at that upcoming meeting.

After a human gene transfer experiment is publicly reviewed by the full RAC at a regularly scheduled meeting, the NIH OSP will send a letter summarizing the RAC's comments and recommendations (if any) regarding the protocol to the Principal Investigator(s), oversight bodies involved in the review at an initial site(s), and regulatory authorities as appropriate. Unless the NIH determines that there are exceptional circumstances, the NIH will send this letter to the Principal Investigator within 10 working days after the completion of the RAC meeting at which the experiment was reviewed. Receipt of this letter concludes the

protocol registration process. Final IBC approval may then be granted.

RAC meetings will be open to the public except where trade secrets or confidential commercial information are reviewed. To enable all aspects of the protocol review process to be open to the public, information provided in response to Appendix M–I–A should not contain trade secrets or confidential commercial or financial information. Documentation submitted to the NIH OSP shall not be designated as 'confidential' in its entirety. In the event that a determination has been made that a specific portion of a document submitted should be considered as proprietary or trade secret, each specific portion should be clearly identified as such. The cover letter (attached to the submitted material) shall: (1) Clearly indicate what select portions contain information considered as proprietary or a trade secret; and (2) provide justification as to why this information is considered to be proprietary or trade secret. This justification must be able to demonstrate *with specificity* how release of that information will reveal a trade secret or will result in substantial competitive harm.

Appendix M–I–C–2 currently states:

Appendix M–I–C–2. Additional Clinical Trial Sites

No research participant shall be enrolled (see definition of enrollment in Section I–E–7) at a clinical trial site until the following documentation has been submitted to NIH OBA: (1) Institutional Biosafety Committee approval (from the clinical trial site); (2) Institutional Review Board approval; (3) Institutional Review Board-approved informed consent document; (4) curriculum vitae of the Principal Investigator(s) (no more than two pages in biographical sketch format); and (5) NIH grant number(s) if applicable.

Appendix M–1–C–2 will be amended as follows:

Appendix M–I–C–2. Additional Clinical Trial Sites

Within 30 days of enrollment (see definition of enrollment in Section I–E–7) at a clinical trial site, the following documentation shall be submitted to NIH OSP: (1) Institutional Biosafety Committee approval (from the clinical trial site); (2) Institutional Review Board approval; (3) Institutional Review Board-approved informed consent document; and (4) NIH grant number(s) if applicable.

There are no amendments to Appendix M–I–D, Safety Assessments in Human Gene Transfer Research.

The current appendices Appendix M–II, Description of the Proposal; Appendix M–III, Informed Consent; Appendix M–IV, Privacy; and Appendix M–V, Special Issues will be deleted in their entirety, except for Appendix M–III–B–2–b, Long Term Follow-Up which will be updated to include a reference to FDA's current guidance on this issue and will become Appendix M–II.

Appendix M–II will be amended as follows:

Appendix M–II. Long Term Follow-Up

To permit evaluation of long-term safety and efficacy of gene transfer, prospective subjects should be informed that they are expected to cooperate in long-term follow-up that extends beyond the active phase of the study. A list of persons who can be contacted in the event that questions arise during the follow-up period should be provided to the investigator. In addition, the investigator should request that subjects continue to provide a current address and telephone number.

The subjects should be informed of any significant findings resulting from the study will be made known in a timely manner to them and/or their parent or guardian including new information about the experimental procedure, the harms and benefits experienced by other individuals involved in the study, and any long-term effects that have been observed.

Additional guidance is available in the FDA Guidance for Industry: Gene Therapy Clinical Trials—Observing Subjects for Delayed Adverse Events (available at the following URL: *http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/CellularandGeneTherapy/default.htm).*

Appendix M–VI Footnotes of Appendix M will be renumbered to Appendix M–III. Footnotes of Appendix M. There will be no amendment to the language.

Dated: March 15, 2016.

Francis S. Collins,

Director, National Institutes of Health.

[FR Doc. 2016–06448 Filed 3–21–16; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Office of the Director, National Institutes of Health Notice of Meeting

Pursuant to section 10(a) of the Federal Advisory Committee Act, as amended (5 U.S.C. App.), notice is hereby given of a meeting of the Advisory Committee to the Director, National Institutes of Health.

This meeting is open to the public but is being held by teleconference only. No physical meeting location is provided for any interested individuals to listen to and/or participate in the meeting. Any individual interested in listening to the meeting discussions must call 800–779–9040 and use Participant Passcode 5055308 for access to the meeting. Individuals needing special assistance should notify the Contact Person listed below in advance of the meeting.

Name of Committee: Advisory Committee to the Director, National Institutes of Health.

Date: April 21, 2016.

Time: 4:00 p.m. to 6:00 p.m. EDT.

Agenda: The HeLa Genome Data Access working group will report on the evaluation of requests to access HeLa cell genome sequence data. The Clinical Center working group will present their final report to the Advisory Committee to the Director, NIH.

Place: National Institutes of Health, (Telephone Conference Call), Dial In Number 800–779–9040, Participant Passcode: 5055308.

Contact Person: Gretchen Wood, Staff Assistant, National Institutes of Health, Office of the Director, One Center Drive, Building 1, Room 126, Bethesda, MD 20892, Telephone: 301–496–4272, Email: *woodgs@od.nih.gov.*

Any interested person may file written comments with the committee by forwarding their statement electronically to the Contact Person at *woodgs@od.nih.gov.* The statement should include the name, address, telephone number and when applicable, the business or professional affiliation of the interested of the interested person.

Additional information for this meeting including both working group reports will be posted, when available, on the Advisory Committee to the Director, NIH, Web site (*http://acd.od.nih.gov*). Additional information about the HeLA Genome Data Access working group is available at *http://acd.od.nih.gov/hlgda.htm* and additional information about the Clinical Center working group is available at *http://acd.od.nih.gov/redteam.htm.*

Dated: March 15, 2016.

Anna Snouffer,

Deputy Director, Office of Federal Advisory Committee Policy.

[FR Doc. 2016–06333 Filed 3–21–16; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Center for Scientific Review, Notice of Closed Meetings

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. App.), notice is hereby given of the following meetings.

The meetings will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), title 5 U.S.C., as amended. The grant applications and the discussions could disclose confidential trade secrets or commercial property such as patentable material,