humans or animal models that could be addressed with new technologies.

- Considerations for data sharing infrastructure and policies.
- Areas and topics for research on the ethical implications of BRAIN Initiative-supported emerging neurotechnologies and advancements and their applications.
- Approaches for disseminating new tools and technologies as well as training the broader neuroscience research community.
- Any other topic relevant to the strategic plan of the BRAIN Initiative.

Responses to this RFI are voluntary. Any personal identifiers will be removed when responses are compiled. Individual feedback will not be provided to any responder. Proprietary, classified, confidential, or sensitive information should not be included in your response. This Request for Information (RFI) is for planning purposes only and is not a solicitation for applications or an obligation on the part of the United States (U.S.) Government to provide support for any ideas identified in response to it. Please note that the U.S. Government will not pay for the preparation of any comment submitted or for its use of that comment.

Dated: August 10, 2018.

Lawrence A. Tabak,

Deputy Director, National Institutes of Health.

[FR Doc. 2018–17759 Filed 8–16–18; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institutes of Health (NIH) Office of Science Policy (OSP) Recombinant or Synthetic Nucleic Acid Research: Proposed Changes to the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines)

AGENCY: National Institutes of Health, HHS.

ACTION: Notice.

SUMMARY: The National Institutes of Health (NIH) seeks public comment on its proposal to amend the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines)* to streamline oversight for human gene transfer clinical research protocols and reduce duplicative reporting requirements already captured within the existing regulatory framework. Specifically, NIH proposes amendments to: Delete the NIH protocol registration submission and reporting requirements under Appendix M of the *NIH Guidelines,* and modify the roles and responsibilities of entities that involve human gene transfer or the Recombinant DNA Advisory Committee (RAC).

DATES: To ensure consideration, comments must be submitted in writing by October 16, 2018.

ADDRESSES: Comments may be submitted electronically by visiting: *https://osp.od.nih.gov/comment-form-nih-guidelines/.* Comments may also be sent via fax to 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. All written comments received in response to this notice will be available for public inspection at NIH Office of Science Policy (OSP), 6705 Rockledge Drive, Suite 750, Bethesda, MD 20892–7985, weekdays between the hours of 8:30 a.m. and 5 p.m. and may be posted without change, including any personal information, to the NIH OSP website.

FOR FURTHER INFORMATION CONTACT: If you have questions, or require additional background information about these proposed changes, please contact the NIH by email at *SciencePolicy@od.nih.gov*, or telephone at 301–496–9838. You may also contact Jessica Tucker, Ph.D., Director of the Division of Biosafety, Biosecurity, and Emerging Biotechnology Policy, Office of Science Policy, NIH, at 301–451–4431 or *Jessica.Tucker@nih.gov.*

SUPPLEMENTARY INFORMATION: NIH is proposing a series of actions to the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines)* to streamline oversight of human gene transfer research (HGT), and to focus the *NIH Guidelines* more specifically on biosafety issues associated with research involving recombinant or synthetic nucleic acid molecules. The field of HGT has recently experienced a series of advances that have resulted in the translation of research into clinical practice, including U.S. Food and Drug Administration (FDA) approvals for licensed products. Additionally, oversight mechanisms for ensuring HGT proceeds safely have sufficiently evolved to keep pace with new discoveries in this field.

At this time, there is duplication in submitting protocols, annual reports, amendments, and serious adverse events for HGT clinical protocols to both NIH and FDA that does not exist for other areas of clinical research. Historically, this duplication was conceived as harmonized reporting, enabling FDA to provide regulatory oversight while NIH provided a forum for open dialogue and transparency. However, since these complementary functions were first envisioned, we have now seen several converging systems emerge that provide some of these functions. For instance, *ClinicalTrials.gov* has been instituted, which provides a transparent and searchable database for clinical trials. In addition, the protection of human research subjects was improved through changes that updated provisions of the Common Rule. In 2018, FDA released a suite of draft guidance documents pertaining to gene therapy that includes new guidance on manufacturing issues, long-term follow-up, and pathways for clinical development in certain areas, including hemophilia, ophthalmologic indications, and rare diseases.

While the science and oversight system have evolved, HGT protocols continue to receive special oversight that is not afforded to other areas of clinical research. This observation was also noted in a 2014 Institute of Medicine of the National Academies report, *Oversight and Review of Clinical Gene Transfer Protocols: Assessing the Role of the Recombinant DNA Advisory Committee,* in which it was recommended that NIH begin to limit RAC review to only exceptional HGT protocols that meet certain criteria and that would significantly benefit from RAC review. As very few protocols have been assessed by NIH to merit review under this new system, NIH asserts it is an opportune time to make changes to the *NIH Guidelines* to make oversight of HGT commensurate with oversight afforded to other areas of clinical research given the robust infrastructure in place to oversee this type of research.

Briefly to summarize, NIH proposes amending the *NIH Guidelines* to:

1. Eliminate RAC review and reporting requirements to NIH for HGT protocols.

2. Modify roles and responsibilities of investigators, institutions, IBCs, the RAC, and NIH to be consistent with these goals including:

a. Modifying roles of IBCs in reviewing HGT to be consistent with review of other covered research, and

b. Eliminating references to the RAC, including its roles in HGT and biosafety.

NIH suggests that the series of changes proposed in this Notice is a rational next step in the process of considering appropriate oversight of HGT. Consistent with these proposed changes to the *NIH Guidelines,* Section I–A, the Purpose of the *NIH Guidelines,* is proposed to be amended to clarify that the focus of the policy is biosafety

oversight of research involving recombinant or synthetic nucleic acid molecules. NIH notes that some of the duties of Institutional Biosafety Committees (IBCs) as currently written in the *NIH Guidelines* (*e.g.,* review of informed consent documents) are duplicative with the oversight provided by FDA or Institutional Review Boards (IRBs). NIH proposes that IBCs retain responsibility to review and approve HGT protocols; however, NIH proposes that these responsibilities be modified to be similar to those responsibilities IBCs currently have for review and approval of other research subject to the *NIH Guidelines.*

With the proposed elimination of the requirements for safety reporting under Appendix M, IBC oversight should be completed immediately after the last participant is administered the final dose of product. Additionally, the role of IBC review is proposed to be amended to be consistent with FDA's current guidance regarding individual patient expanded access to investigational drugs. In this way, the role of the IBCs will be focused on providing local biosafety oversight of basic and clinical research involving recombinant or synthetic nucleic acids. In particular, NIH seeks comment on whether the expectations of IBCs, in light of these proposed changes, have been articulated clearly in the proposed revisions to the *NIH Guidelines.*

Notably, the roles and responsibilities of the RAC are proposed to be removed from the *NIH Guidelines.* NIH recognizes the value of the RAC in discussions of science, safety, and ethics. In an effort to use the RAC as a public forum to advise on issues associated with emerging biotechnologies, the RAC's charter will be modified to change the committee's focus from research solely involving recombinant or synthetic nucleic acids to emerging biotechnologies research. In light of this modification to the committee, NIH proposes eliminating references to the RAC in the *NIH Guidelines,* though NIH may continue to seek advice from the RAC on biosafety issues that fall under the purview of the *NIH Guidelines.* Similarly, NIH may choose to seek advice from internal working groups or Federal Advisory Committees on a variety of issues, when warranted.

The proposed changes outlined above will require amendment of multiple portions of the *NIH Guidelines.* Sections and appendices proposed to be deleted from the current *NIH Guidelines* may be accessed at *https://osp.od.nih.gov/biotechnology/nih-guidelines/.* Following deletions, sections and appendices will be relabeled to proceed consecutively throughout the *NIH Guidelines.*

Proposed Amendments to the *NIH Guidelines*

Section I–A currently states:

Section I–A. Purpose

The purpose of the *NIH Guidelines* is to specify the practices for constructing and handling: (i) Recombinant nucleic acid molecules, (ii) synthetic nucleic acid molecules, including those that are chemically or otherwise modified but can base pair with naturally occurring nucleic acid molecules, and (iii) cells, organisms, and viruses containing such molecules.

Section I–A is proposed to be amended as follows:

Section I–A. Purpose

The purpose of the *NIH Guidelines* is to specify the biosafety practices and containment principles for constructing and handling: (i) Recombinant nucleic acid molecules, (ii) synthetic nucleic acid molecules, including those that are chemically or otherwise modified but can base pair with naturally occurring nucleic acid molecules, and (iii) cells, organisms, and viruses containing such molecules.

Section I–A–1 currently states:

Section I–A–1. Any nucleic acid molecule experiment, which according to the *NIH Guidelines* requires approval by NIH, must be submitted to NIH or to another federal agency that has jurisdiction for review and approval. Once approvals, or other applicable clearances, have been obtained from a federal agency other than NIH (whether the experiment is referred to that agency by NIH or sent directly there by the submitter), the experiment may proceed without the necessity for NIH review or approval. (See exception in Section I–A–1-a regarding requirement for human gene transfer protocol registration.)

Section I–A–1 is proposed to be amended as follows:

Section I–A–1. Any nucleic acid molecule experiment, which according to the *NIH Guidelines* requires approval by NIH, must be submitted to NIH or to another federal agency that has jurisdiction for review and approval. Once approvals, or other applicable clearances, have been obtained from a federal agency other than NIH (whether the experiment is referred to that agency by NIH or sent directly there by the submitter), the experiment may proceed without the necessity for NIH review or approval.

Section I–A–1–a currently states:

Section I–A–1–a. For 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 human research participants (human gene transfer), 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*); Institutional Biosafety Committee (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 the 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 IBC approval and IRB approval from that site have been obtained. 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(s); and (4) NIH grant number(s) if applicable.

Section I–A–1–a is proposed to be amended as follows:

Section I–A–1–a. For 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 human research participants (human gene transfer), no human gene transfer experiment shall be initiated (see definition of initiation in Section I–E–7) until Institutional Biosafety Committee (IBC) approval (from the clinical trial site) has been obtained; and all other applicable institutional and regulatory authorization(s) and approvals have been obtained.

Section I–E. General Definitions is proposed to be amended to delete the current definitions I–E–4, I–E–7 through I–E–12 and to include a new definition for ''initiation.''

Section I–E–4 is proposed to be amended to define initiation as the following: ''Initiation'' of research is the introduction of recombinant or synthetic nucleic acid molecules into organisms, cells, or viruses.

Section III currently states:

Section III. Experiments Covered by the *NIH Guidelines*

This section describes six categories of experiments involving recombinant or synthetic nucleic acid molecules: (i) Those that require Institutional Biosafety Committee (IBC) approval, RAC review, and NIH Director approval before initiation (see Section III–A), (ii) those that require NIH OSP and Institutional Biosafety Committee approval before initiation (see Section III–B), (iii) those that require Institutional Biosafety Committee and Institutional Review Board approvals and RAC review before research participant enrollment (see Section III–C), (iv) those that require Institutional Biosafety Committee approval before initiation (see Section III–D), (v) those that require Institutional Biosafety Committee notification simultaneous with initiation (see Section III–E), and (vi) those that are exempt from the *NIH Guidelines* (see Section III–F).

Note: If an experiment falls into Sections III–A, III–B, or III–C and one of the other sections, the rules pertaining to Sections III–A, III–B, or III–C shall be followed. If an experiment falls into Section III–F and into either Sections III–D or III–E as well, the experiment is considered exempt from the *NIH Guidelines.*

Any change in containment level, which is different from those specified in the *NIH Guidelines,* may not be initiated without the express approval of NIH OSP (see Section IV–C–1–b–(2) and its subsections, Minor Actions).

Section III is proposed to be amended as follows:

Section III. Experiments Covered by the *NIH Guidelines*

This section describes six categories of experiments involving recombinant or synthetic nucleic acid molecules: (i) Those that require Institutional Biosafety Committee (IBC) approval and NIH Director approval before initiation (see Section III–A), (ii) those that require NIH OSP and Institutional Biosafety Committee approval before initiation (see Section III–B), (iii) those that require Institutional Biosafety Committee approval before initiation of human gene transfer (see Section III–C), (iv) those that require Institutional Biosafety Committee approval before initiation (see Section III–D), (v) those that require Institutional Biosafety Committee notification simultaneous with initiation (see Section III–E), and (vi) those that are exempt from the *NIH Guidelines* (see Section III–F).

Note: If an experiment falls into Sections III–A, III–B, or III–C and one of the other sections, the rules pertaining to Sections III–A, III–B, or III–C shall be followed. If an experiment falls into Section III–F and into either Sections III–D or III–E as well, the experiment is considered exempt from the *NIH Guidelines.*

Any change in containment level, which is different from those specified in the *NIH Guidelines,* may not be initiated without the express approval of NIH OSP (see Section IV–C–1–b–(2) and its subsections, Minor Actions).

Section III–A currently states:

Section III–A. Experiments That Require Institutional Biosafety Committee Approval, RAC Review, and NIH Director Approval Before Initiation (See Section IV–C–1–b–(1), Major Actions).

Experiments considered as *Major Actions* under the *NIH Guidelines* cannot be initiated without submission of relevant information on the proposed experiment to the Office of Science Policy, National Institutes of Health, preferably by email to: *NIHGuidelines@od.nih.gov*, the publication of the proposal in the **Federal Register** for 15 days of comment, review by RAC, and specific approval by NIH. The containment conditions or stipulation requirements for such experiments will be recommended by RAC and set by NIH at the time of approval. Such experiments require Institutional Biosafety Committee approval before initiation. Specific experiments already approved are included in Appendix D, *Major Actions Taken under the NIH Guidelines,* which may be obtained from the Office of Science Policy, National Institutes of Health, preferably by submitting a request for this information to: *NIHGuidelines@od.nih.gov*; additional contact information is also available here and on the OSP website (*www.osp.od.nih.gov*).

Section III–A–1–a. The deliberate transfer of a drug resistance trait to microorganisms that are not known to acquire the trait naturally (see Section V–B, *Footnotes and References of Sections I–IV*), if such acquisition could compromise the ability to control disease agents in humans, veterinary medicine, or agriculture, will be reviewed by the RAC.

Consideration should be given as to whether the drug resistance trait to be used in the experiment would render that microorganism resistant to the primary drug available to and/or indicated for certain populations, for example children or pregnant women.

At the request of an Institutional Biosafety Committee, NIH OSP will make a determination regarding whether a specific experiment involving the deliberate transfer of a drug resistance trait falls under Section III–A–1-a and therefore requires RAC review and NIH Director approval. An Institutional Biosafety Committee may also consult with NIH OSP regarding experiments that do not meet the requirements of Section III–A–1–a but nonetheless raise important public health issues. NIH OSP will consult, as needed, with one or more experts, which may include the RAC.

Section III–A is proposed to be amended as follows:

Section III–A. Experiments That Require Institutional Biosafety Committee Approval and NIH Director Approval Before Initiation (See Section IV–C–1–b–(1), Major Actions).

Section III–A–1. Major Actions Under the *NIH Guidelines*

Experiments considered as *Major Actions* as defined in Section III–A–1-a under the *NIH Guidelines* cannot be initiated without submission of relevant information on the proposed experiment to the Office of Science Policy, National Institutes of Health, preferably by email to: *NIHGuidelines@od.nih.gov*, the publication of the proposal in the **Federal Register** for 15 days of comment, and specific approval by NIH. The containment conditions or stipulation requirements for such experiments will be set by NIH at the time of approval. Such experiments require Institutional Biosafety Committee approval before initiation. Specific experiments already approved are included in Appendix D, *Major Actions Taken under the NIH Guidelines,* which may be obtained from the Office of Science Policy, National Institutes of Health, preferably by submitting a request for this information to: *NIHGuidelines@od.nih.gov*; additional contact information is also available here and on the OSP website (*www.osp.od.nih.gov*).

Section III–A–1-a. The deliberate transfer of a drug resistance trait to microorganisms that are not known to acquire the trait naturally (see Section V–B, *Footnotes and References of Sections I–IV*), if such acquisition could compromise the ability to control disease agents in humans, veterinary medicine, or agriculture, will require NIH Director approval.

Consideration should be given as to whether the drug resistance trait to be used in the experiment would render that microorganism resistant to the primary drug available to and/or indicated for certain populations, for example children or pregnant women.

At the request of an Institutional Biosafety Committee, NIH OSP will

make a determination regarding whether a specific experiment involving the deliberate transfer of a drug resistance trait falls under Section III–A–1-a and therefore requires NIH Director approval. An Institutional Biosafety Committee may also consult with NIH OSP regarding experiments that do not meet the requirements of Section III–A–1-a but nonetheless raise important public health issues.

Section III–C currently states:

Section III–C. Experiments that Require Institutional Biosafety Committee and Institutional Review Board Approvals and RAC Review (if applicable) Before Research Participant Enrollment

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, 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 meets the requirements for selecting protocols for public RAC review and discussion (See Appendix M–I–B). 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 (a) the individual protocol would significantly benefit from RAC review and (b) 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 and federal regulatory bodies 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 NIH does not concur that (a) the individual protocol would significantly benefit from RAC review and (b) 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 the 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 IBC approval and IRB approval from that site have been obtained. 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(s); and (4) 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 III–C is proposed to be amended as follows:

Section III–C. Experiments Involving Human Gene Transfer That Require Institutional Biosafety Committee Approval Prior to Initiation

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.

Research cannot be initiated until Institutional Biosafety Committee and all other applicable institutional and regulatory authorization(s) and approvals have been obtained.

An individual patient expanded access IND is not research subject to the *NIH Guidelines* and thus does not need to be submitted to an IBC, if the following conditions are met: (i) A PI is submitting an individual patient expanded access IND using Form FDA 3926; (ii) the PI selects the appropriate box on that form to request a waiver under 21 CFR 56.105 of the requirements in 21 CFR 56.108(c); and (iii) the FDA concludes that such a waiver is appropriate.

Section III–D–7–b currently states:

Section III–D–7–b. Highly Pathogenic Avian Influenza H5N1 strains within the Goose/Guangdong/96-like H5 lineage (HPAI H5N1). Experiments involving influenza viruses containing a majority of genes and/or segments from a HPAI H5N1 influenza virus shall be conducted at BL3 enhanced containment, (see Appendix G–II–C–5, Biosafety Level 3 Enhanced for Research Involving Risk Group 3 Influenza Viruses). Experiments involving influenza viruses containing a minority of genes and/or segments from a HPAI H5N1 influenza virus shall be conducted at BL3 enhanced unless a risk assessment performed by the IBC determines that they can be conducted safely at biosafety level 2 and after they have been excluded pursuant to 9 CFR 121.3(e). NIH OSP is available to IBCs to provide consultation with the RAC and influenza virus experts when risk assessments are being made to determine the appropriate biocontainment for experiments with influenza viruses containing a minority of gene/segments from HPAI H5N1. Such experiments may be performed at BL3 enhanced containment or containment may be lowered to biosafety level 2, the level of containment for most research with other influenza viruses. (USDA/APHIS regulations and decisions on lowering containment also apply). In deciding to lower containment, the IBC should consider whether, in at least two animal models (*e.g.,* ferret, mouse, Syrian golden hamster, cotton rat, non-human primates), there is evidence that the resulting influenza virus shows reduced replication and virulence compared to the parental RG3 virus at relevant doses. This should be determined by measuring biological indices appropriate for the specific animal model (*e.g.,* severe weight loss, elevated temperature, mortality or neurological symptoms).

Section III–D–7–b is proposed to be amended as follows:

Section III–D–7–b. Highly Pathogenic Avian Influenza H5N1 strains within the Goose/Guangdong/96-like H5 lineage (HPAI H5N1). Experiments involving influenza viruses containing a majority of genes and/or segments from a HPAI H5N1 influenza virus shall be conducted at BL3 enhanced containment, (see Appendix G–II–C–5, Biosafety Level 3 Enhanced for Research Involving Risk Group 3 Influenza Viruses). Experiments involving influenza viruses containing a minority of genes and/or segments from a HPAI H5N1 influenza virus shall be conducted at BL3 enhanced unless a risk assessment performed by the IBC determines that they can be conducted safely at biosafety level 2 and after they have been excluded pursuant to 9 CFR 121.3(e). NIH OSP is available to IBCs to provide consultation with influenza virus experts when risk assessments are being made to determine the appropriate biocontainment for experiments with influenza viruses containing a minority of gene/segments from HPAI H5N1. Such experiments may be performed at BL3 enhanced containment or containment may be lowered to biosafety level 2, the level of containment for most research with other influenza viruses. (USDA/APHIS regulations and decisions on lowering containment also apply). In deciding to lower containment, the IBC should consider whether, in at least two animal models (*e.g.,* ferret, mouse, Syrian golden hamster, cotton rat, non-human primates), there is evidence that the resulting influenza virus shows reduced replication and virulence compared to the parental RG3 virus at relevant doses. This should be determined by measuring biological indices appropriate for the specific animal model (*e.g.,* severe weight loss, elevated temperature, mortality or neurological symptoms).

Section III–D–7–d currently states:

Section III–D–7–d. Antiviral Susceptibility and Containment. The availability of antiviral drugs as preventive and therapeutic measures is an important safeguard for experiments with 1918 H1N1, HPAI H5N1, and human H2N2 (1957–1968). If an influenza virus containing genes from one of these viruses is resistant to both classes of current antiviral agents, adamantanes and neuraminidase inhibitors, higher containment may be required based on the risk assessment considering transmissibility to humans, virulence, pandemic potential, alternative antiviral agents if available, etc.

Experiments with 1918 H1N1, human H2N2 (1957–1968) or HPAI H5N1 that are designed to create resistance to neuraminidase inhibitors or other effective antiviral agents (including investigational antiviral agents being developed for influenza) would be subject to Section III–A–1 (*Major Actions*) and require RAC review and NIH Director approval. As per Section I–A–1 of the *NIH Guidelines,* if the agent is a Select Agent, the NIH will defer to the appropriate federal agency (HHS or U.S. Department of Agriculture (USDA) Select Agent Divisions) on such experiments.

Section III–D–7–d is proposed to be amended as follows:

Section III–D–7–d. Antiviral Susceptibility and Containment. The availability of antiviral drugs as preventive and therapeutic measures is an important safeguard for experiments with 1918 H1N1, HPAI H5N1, and human H2N2 (1957–1968). If an influenza virus containing genes from one of these viruses is resistant to both classes of current antiviral agents, adamantanes and neuraminidase inhibitors, higher containment may be required based on the risk assessment considering transmissibility to humans, virulence, pandemic potential, alternative antiviral agents if available, etc.

Experiments with 1918 H1N1, human H2N2 (1957–1968) or HPAI H5N1 that are designed to create resistance to neuraminidase inhibitors or other effective antiviral agents (including investigational antiviral agents being developed for influenza) would be subject to Section III–A–1 (*Major Actions*) and NIH Director approval. As per Section I–A–1 of the *NIH Guidelines,* if the agent is a Select Agent, NIH will defer to the appropriate Federal agency (HHS or USDA Select Agent Divisions) on such experiments.

Section III–F–6 currently states:

Section III–F–6. Those that consist entirely of DNA segments from different species that exchange DNA by known physiological processes, though one or more of the segments may be a synthetic equivalent. A list of such exchangers will be prepared and periodically revised by the NIH Director with advice of the RAC after appropriate notice and opportunity for public comment (see Section IV–C–1–b–(1)–(c), *Major Actions*). See Appendices A–I through A–VI, *Exemptions under Section III–F–6—Sublists of Natural Exchangers,* for a list of natural exchangers that are exempt from the *NIH Guidelines.*

Section III–F–6 is proposed to be amended as follows:

Section III–F–6. Those that consist entirely of DNA segments from different species that exchange DNA by known physiological processes, though one or more of the segments may be a synthetic equivalent. A list of such exchangers will be prepared and periodically revised by the NIH Director after appropriate notice and opportunity for public comment (see Section IV–C–1–b–(1)–(c), *Major Actions*). See Appendices A–I through A–VI, *Exemptions under Section III–F–6—Sublists of Natural Exchangers,* for a list of natural exchangers that are exempt from the *NIH Guidelines.*

Section III–F–8 currently states:

Section III–F–8. Those that do not present a significant risk to health or the

environment (see Section IV–C–1–b–(1)–(c), *Major Actions*), as determined by the NIH Director, with the advice of the RAC, and following appropriate notice and opportunity for public comment. See Appendix C, *Exemptions under Section III–F–8* for other classes of experiments which are exempt from the *NIH Guidelines.*

Section III–F–8 is proposed to be amended as follows:

Section III–F–8. Those that do not present a significant risk to health or the environment (see Section IV–C–1–b–(1)–(c), *Major Actions*), as determined by the NIH Director, and following appropriate notice and opportunity for public comment. See Appendix C, *Exemptions under Section III–F–8* for other classes of experiments which are exempt from the *NIH Guidelines.*

Section IV–B–1–f currently states:

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.

Section IV–B–1–f is proposed to 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), and (ii) no human gene transfer experiment shall be initiated until Institutional Biosafety Committee approval has been obtained, and all other applicable institutional and regulatory authorization(s) and approvals 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 proposed to be amended.

Section IV–B–2–a–(1) currently states:

Section IV–B–2–a–(1). The Institutional Biosafety Committee must be comprised 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.

Section IV–B–2–a–(1) is proposed to be amended as follows:

Section IV–B–2–a–(1). The Institutional Biosafety Committee must be comprised 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 the Institutional Biosafety Committee has adequate expertise and training (using *ad hoc* consultants as deemed necessary). Institutional Biosafety Committee approval must be obtained from the clinical trial site.

Section IV–B–2–b–(1) currently states:

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 with 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 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.*

Section IV–B–2–b–(1) is proposed to 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 with 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) for recombinant or synthetic nucleic acid molecule research involving human research participants, assessment focused on biosafety issues (*e.g.,* administration, shedding).

Section IV–B–2–b–(8) currently states:

Section IV–B–2–b–(8). The Institutional Biosafety Committee may not authorize initiation of experiments which are not explicitly covered by the *NIH Guidelines* until NIH (with the advice of the RAC when required) establishes the containment requirement.

Section IV–B–2–b–(8) is proposed to be amended as follows:

Section IV–B–2–b–(8). The Institutional Biosafety Committee may not authorize initiation of experiments which are not explicitly covered by the *NIH Guidelines* until NIH establishes the containment requirement.

None of the other sub-sections under Section IV–B–2. Institutional Biosafety Committee (IBC) are proposed to be amended.

Section IV–B–6 currently states:

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–6 is proposed to be amended as follows:

Section IV–B–6. Human Gene Transfer Expertise

When the institution participates in or sponsors recombinant or synthetic nucleic acid molecule research involving human subjects, the institution must ensure that the Institutional Biosafety Committee has adequate expertise and training (using *ad hoc* consultants as deemed necessary).

Section IV–B–7 currently states:

Section IV–B–7. Principal Investigator (PI)

On behalf of the institution, the Principal Investigator is responsible for full compliance with the *NIH Guidelines* in the conduct of recombinant or synthetic nucleic acid molecule research. A Principal Investigator engaged in human gene transfer research may delegate to another party, such as a corporate sponsor, the reporting functions set forth in Appendix M, with written notification to the NIH OSP of the delegation and of the name(s), address, telephone, and fax numbers of the contact. The Principal Investigator is responsible for ensuring that the reporting requirements are fulfilled and will be held accountable for any reporting lapses.

Section IV–B–7 is proposed to be amended as follows:

Section IV–B–7. Principal Investigator (PI)

On behalf of the institution, the Principal Investigator is responsible for full compliance with the *NIH Guidelines* in the conduct of recombinant or synthetic nucleic acid molecule research.

Section IV–B–7–b–(6) is proposed to be deleted in its entirety

Section IV–B–7–e–(5) is proposed to be deleted in its entirety

None of the other sub-sections under Section IV–B–7. Principal Investigator are proposed to be amended.

Section IV–C currently states:

Section IV–C. Responsibilities of the National Institutes of Health (NIH)

Section IV–C–1. NIH Director

The NIH Director is responsible for: (i) Establishing the *NIH Guidelines,* (ii) overseeing their implementation, and (iii) their final interpretation. The NIH Director has responsibilities under the *NIH Guidelines* that involve OSP and RAC. OSP's responsibilities under the *NIH Guidelines* are administrative. Advice from RAC is primarily scientific, technical, and ethical. In certain circumstances, there is specific opportunity for public comment with published response prior to final action.

Section IV–C–1-a. General Responsibilities

The NIH Director is responsible for:

Section IV–C–1–a–(1). Promulgating requirements as necessary to implement the *NIH Guidelines;*

Section IV–C–1–a–(2). Establishing and maintaining RAC to carry out the responsibilities set forth in Section IV–C–2, *Recombinant DNA Advisory Committee* (RAC membership is specified in its charter and in Section IV–C–2);

Section IV–C–1–a–(3). Establishing and maintaining NIH OSP to carry out the responsibilities defined in Section IV–C–3, *Office of Science Policy;*

Section IV–C–1–a–(4). Conducting and supporting training programs in laboratory safety for Institutional Biosafety Committee members, Biological Safety Officers and other institutional experts (if applicable), Principal Investigators, and laboratory staff.

Section IV–C–1–a–(5). Establishing and convening Gene Therapy Policy Conferences as described in Appendix L, *Gene Therapy Policy Conferences.*

Section IV–C–1–b. Specific Responsibilities

In carrying out the responsibilities set forth in this section, the NIH Director, or a designee shall weigh each proposed action through appropriate analysis and consultation to determine whether it complies with the *NIH Guidelines* and presents no significant risk to health or the environment.

Section IV–C–1–b–(1). Major Actions

To execute *Major Actions,* the NIH Director shall seek the advice of RAC and provide an opportunity for public and federal agency comment. Specifically, the Notice of Meeting and *Proposed Actions* shall be published in the **Federal Register** at least 15 days before the RAC meeting. The NIH Director's decision/recommendation (at his/her discretion) may be published in the **Federal Register** for 15 days of comment before final action is taken. The NIH Director's final decision/recommendation, along with responses to public comments, shall be published in the **Federal Register**. The RAC and Institutional Biosafety Committee Chairs shall be notified of the following decisions:

Section IV–C–1–b–(1)–(a). Changing containment levels for types of experiments that are specified in the *NIH Guidelines* when a *Major Action* is involved;

Section IV–C–1–b–(1)–(b). Assigning containment levels for types of experiments that are not explicitly considered in the *NIH Guidelines* when a *Major Action* is involved;

Section IV–C–1–b–(1)–(c). Promulgating and amending a list of classes of recombinant or synthetic nucleic acid molecules to be exempt from the *NIH Guidelines* because they consist entirely of DNA segments from species that exchange DNA by known physiological processes or otherwise do not present a significant risk to health or the environment;

Section IV–C–1–b–(1)–(d). Permitting experiments specified by Section III–A, *Experiments that Require Institutional Biosafety Committee Approval, RAC Review, and NIH Director Approval Before Initiation;*

Section IV–C–1–b–(1)–(e). Certifying new host-vector systems with the exception of minor modifications of already certified systems (the standards and procedures for certification are described in Appendix I–II, *Certification of Host-Vector Systems*). Minor modifications constitute (*e.g.,* those of minimal or no consequence to the properties relevant to containment); and

Section IV–C–1–b–(1)–(f). Adopting other changes in the *NIH Guidelines.*

Section IV–C–1–b–(2). Minor Actions

NIH OSP shall carry out certain functions as delegated to it by the NIH Director (see Section IV–C–3, *Office of Science Policy*). *Minor Actions* (as determined by NIH OSP in consultation with the RAC Chair and one or more RAC members, as necessary) will be transmitted to RAC and Institutional Biosafety Committee Chairs:

Section IV–C–1–b–(2)–(a). Changing containment levels for experiments that are specified in Section III, *Experiments Covered by the NIH Guidelines* (except when a *Major Action* is involved);

Section IV–C–1–b–(2)–(b). Assigning containment levels for experiments not explicitly considered in the *NIH Guidelines;*

Section IV–C–1–b–(2)–(c). Revising the *Classification of Etiologic Agents* for the purpose of these *NIH Guidelines* (see Section V–A, *Footnotes and References of Sections I–IV*).

Section IV–C–1–b–(2)–(d). Interpreting the *NIH Guidelines* for experiments to which the *NIH Guidelines* do not specifically assign containment levels;

Section IV–C–1–b–(2)–(e). Setting containment under Sections III–D–1–d, *Experiments Using Risk Group 2, Risk Group 3, Risk Group 4, or Restricted Agents as Host-Vector Systems,* and III–D–2–b, *Experiments in which DNA from Risk Group 2, Risk Group 3, Risk Group 4, or Restricted Agents is Cloned into Nonpathogenic Prokaryotic or Lower Eukaryotic Host-Vector Systems;*

Section IV–C–1–b–(2)–(f). Approving minor modifications of already certified host-vector systems (the standards and procedures for such modifications are described in Appendix I–II, *Certification of Host-Vector Systems*);

Section IV–C–1–b–(2)–(g). Decertifying already certified host-vector systems;

Section IV–C–1–b–(2)–(h). Adding new entries to the list of molecules toxic for vertebrates (see Appendix F, *Containment Conditions for Cloning of Genes Coding for the Biosynthesis of Molecules Toxic for Vertebrates*); and

Section IV–C–1–b–(2)–(i). Determining appropriate containment conditions for experiments according to case precedents developed under Section IV–C–1–b–(2)–(c).

Section IV–C is proposed to be amended as follows:

Section IV–C. Responsibilities of the National Institutes of Health (NIH)

Section IV–C–1. NIH Director

The NIH Director is responsible for: (i) Establishing the *NIH Guidelines,* (ii) overseeing their implementation, and (iii) their final interpretation. The NIH Director has responsibilities under the *NIH Guidelines* that involve OSP. OSP's responsibilities under the *NIH Guidelines* are administrative. In certain circumstances, there is specific opportunity for public comment with published response prior to final action.

Section IV–C–1–a. General Responsibilities

The NIH Director is responsible for:

Section IV–C–1–a–(1). Promulgating requirements as necessary to implement the *NIH Guidelines;*

Section IV–C–1–a–(2). Establishing and maintaining NIH OSP to carry out the responsibilities defined in Section IV–C–3, *Office of Science Policy;*

Section IV–C–1–a–(3). Conducting and supporting training programs in laboratory safety for Institutional Biosafety Committee members, Biological Safety Officers and other institutional experts (if applicable), Principal Investigators, and laboratory staff.

Section IV–C–1–b. Specific Responsibilities

In carrying out the responsibilities set forth in this section, the NIH Director or a designee shall weigh each proposed action through appropriate analysis and consultation to determine whether it complies with the *NIH Guidelines* and presents no significant risk to health or the environment.

Section IV–C–1–b–(1). Major Actions

To execute *Major Actions,* the NIH Director shall provide an opportunity for public and Federal agency comment. The NIH Director's decision/recommendation (at his/her discretion) may be published in the **Federal Register** for 15 days of comment before final action is taken. The NIH Director's final decision/recommendation, along with responses to public comments, shall be published in the **Federal Register**. Institutional Biosafety Committee Chairs shall be notified of the following decisions:

Section IV–C–1–b–(1)–(a). Changing containment levels for types of experiments that are specified in the *NIH Guidelines* when a *Major Action* is involved;

Section IV–C–1–b–(1)–(b). Assigning containment levels for types of experiments that are not explicitly considered in the *NIH Guidelines* when a *Major Action* is involved;

Section IV–C–1–b–(1)–(c). Promulgating and amending a list of classes of recombinant or synthetic nucleic acid molecules to be exempt from the *NIH Guidelines* because they consist entirely of DNA segments from species that exchange DNA by known physiological processes or otherwise do not present a significant risk to health or the environment;

Section IV–C–1–b–(1)–(d). Permitting experiments specified by Section III–A, *Experiments that Require Institutional Biosafety Committee Approval, and NIH Director Approval Before Initiation;*

Section IV–C–1–b–(1)–(e). Certifying new host-vector systems with the exception of minor modifications (*e.g.,* those of minimal or no consequence to the properties relevant to containment) of already certified systems (the standards and procedures for certification are described in Appendix I–II, *Certification of Host-Vector Systems;* and

Section IV–C–1–b–(1)–(f). Adopting other changes in the *NIH Guidelines.*

Section IV–C–1–b–(2). Minor Actions

NIH OSP shall carry out certain functions as delegated to it by the NIH Director (see Section IV–C–3, *Office of Science Policy*). *Minor Actions* will be transmitted to Institutional Biosafety Committee Chairs:

Section IV–C–1–b–(2)–(a). Changing containment levels for experiments that are specified in Section III, *Experiments Covered by the NIH Guidelines* (except when a *Major Action* is involved);

Section IV–C–1–b–(2)–(b). Assigning containment levels for experiments not explicitly considered in the *NIH Guidelines;*

Section IV–C–1–b–(2)–(c). Revising the *Classification of Etiologic Agents* for the purpose of these *NIH Guidelines* (see Section V–A, *Footnotes and References of Sections I–IV*).

Section IV–C–1–b–(2)–(d). Interpreting the *NIH Guidelines* for experiments to which the *NIH Guidelines* do not specifically assign containment levels;

Section IV–C–1–b–(2)–(e). Setting containment under Sections III–D–1–d, *Experiments Using Risk Group 2, Risk Group 3, Risk Group 4, or Restricted Agents as Host-Vector Systems,* and III–D–2–b, *Experiments in which DNA from Risk Group 2, Risk Group 3, Risk Group 4, or Restricted Agents is Cloned into Nonpathogenic Prokaryotic or Lower Eukaryotic Host-Vector Systems;*

Section IV–C–1–b–(2)–(f). Approving minor modifications of already certified host-vector systems (the standards and procedures for such modifications are described in Appendix I–II, *Certification of Host-Vector Systems*);

Section IV–C–1–b–(2)–(g). Decertifying already certified host-vector systems;

Section IV–C–1–b–(2)–(h). Adding new entries to the list of molecules toxic for vertebrates (see Appendix F, *Containment Conditions for Cloning of Genes Coding for the Biosynthesis of Molecules Toxic for Vertebrates*); and

Section IV–C–1–b–(2)–(i). Determining appropriate containment conditions for experiments according to case precedents developed under Section IV–C–1–b–(2)–(c).

Section IV–C–2. Recombinant DNA Advisory Committee (RAC) is proposed to be deleted in its entirety.

Section IV–C–3. Office of Science Policy (OSP) is proposed to be amended as follows:

Sections IV–C–3–a through IV–C–3–f are proposed to be deleted in their entirety. Section IV–C–3–h is proposed to be deleted in its entirety. Section IV–C–3–g will be renumbered to Section IV–C–3–a. Section IV–C–i will be renumbered to Section IV–C–3–b; Section IV–C–3–i–(1), Section IV–C–3–i–(2) and Section IV–C–3–i–(3) are proposed to be deleted in their entirety. Section IV–C–3–j will be renumbered to Section IV–C–3–c.

Section IV–C–3 is proposed to be amended as follows:

Section IV–C–3. Office of Science Policy (OSP)

OSP shall serve as a focal point for information on recombinant or synthetic nucleic acid molecule activities and provide advice to all within and outside NIH including institutions, Biological Safety Officers, Principal Investigators, Federal agencies, state and local governments, and institutions in the private sector. OSP shall carry out such other functions as may be delegated to it by the NIH Director. OSP's responsibilities include (but are not limited to) the following:

Section IV–C–3–a. Reviewing and approving experiments involving the cloning of genes encoding for toxin molecules that are lethal for vertebrates at an LD_{50} of less than or equal to 100 nanograms per kilogram body weight in organisms other than *Escherichia coli* K–12 (see Section III–B–1, *Experiments Involving the Cloning of Toxin Molecules with LD_{50} of Less than 100 Nanograms Per Kilogram Body Weight,* Appendix F, *Containment Conditions for Cloning of Genes Coding for the Biosynthesis of Molecules Toxic for Vertebrates*);

Section IV–C–3–b. Publishing in the **Federal Register**, as needed.

Section IV–C–3–c. Reviewing and approving the membership of an institution's Institutional Biosafety Committee, and where it finds the Institutional Biosafety Committee meets the requirements set forth in Section IV–B–2, *Institutional Biosafety Committee (IBC),* giving its approval to the Institutional Biosafety Committee membership.

Section IV–D–5 currently states:

Section IV–D–5. Protection of Proprietary Data—Voluntary Compliance

Section IV–D–5–a. General

In general, the Freedom of Information Act requires federal agencies to make their records available to the public upon request. However, this requirement does not apply to, among other things, ''trade secrets and commercial or financial information that is obtained from a person and that is privileged or confidential.'' Under 18 U.S.C. 1905, it is a criminal offense for an officer or employee of the U.S. or any federal department or agency to publish, divulge, disclose, or make known ''in any manner or to any extent not authorized by law any information coming to him in the course of his employment or official duties or by reason of any examination or investigation made by, or return, report or record made to or filed with, such department or agency or officer or employee thereof, which information concerns or relates to the trade secrets, (or) processes . . . of any person, firm, partnership, corporation, or association.'' This provision applies to all employees of the federal government, including special Government

employees. Members of RAC are ''special Government employees.''

Section IV–D–5 is proposed to be amended as follows:

Section IV–D–5–a. General

In general, the Freedom of Information Act requires federal agencies to make their records available to the public upon request. However, this requirement does not apply to, among other things, ''trade secrets and commercial or financial information that is obtained from a person and that is privileged or confidential.'' Under 18 U.S.C. 1905, it is a criminal offense for an officer or employee of the United States or any federal department or agency to publish, divulge, disclose, or make known ''in any manner or to any extent not authorized by law any information coming to him in the course of his employment or official duties or by reason of any examination or investigation made by, or return, report or record made to or filed with, such department or agency or officer or employee thereof, which information concerns or relates to the trade secrets, (or) processes . . . of any person, firm, partnership, corporation, or association.'' This provision applies to all employees of the federal government, including special Government employees.

None of the other sub-sections under Section IV are proposed to be amended.

Section V currently states:

Section V. Footnotes and References of Sections I through IV

Section V–A. The NIH Director, with advice of the RAC, may revise the classification for the purposes of the *NIH Guidelines* (see Section IV–C–1–b–(2)–(e), *Minor Actions*). The revised list of organisms in each Risk Group is reprinted in Appendix B, *Classification of Human Etiologic Agents on the Basis of Hazard.*

Section V–B. Section III, *Experiments Covered by the NIH Guidelines,* describes a number of places where judgments are to be made. In all these cases, the Principal Investigator shall make the judgment on these matters as part of his/her responsibility to ''make the initial determination of the required levels of physical and biological containment in accordance with the *NIH Guidelines*'' (see Section IV–B–7–c–(1)). For cases falling under Sections III–A through III–E, *Experiments Covered by the NIH Guidelines,* this judgment is to be reviewed and approved by the Institutional Biosafety Committee as part of its responsibility to make an ''independent assessment of the containment levels required by the *NIH Guidelines* for the proposed research'' (see Section IV–B–2–b–(1), *Institutional Biosafety Committee*). The Institutional Biosafety Committee may refer specific cases to NIH OSP as part of NIH OSP's functions to ''provide advice to all within and outside NIH'' (see Section IV–C–3). NIH OSP may request advice from the RAC as part of the RAC's responsibility for ''interpreting the *NIH Guidelines* for experiments to which the *NIH Guidelines* do not specifically assign containment levels'' (see Section IV–C–1–b–(2)–(f), *Minor Actions*).

Section V is proposed to be amended as follows:

Section V–A. The NIH Director may revise the classification for the purposes of the *NIH Guidelines* (see Section IV–C–1–b–(2)–(e), *Minor Actions*). The revised list of organisms in each Risk Group is reprinted in Appendix B, *Classification of Human Etiologic Agents on the Basis of Hazard.*

Section V–B. Section III, *Experiments Covered by the NIH Guidelines,* describes a number of places where judgments are to be made. In all these cases, the Principal Investigator shall make the judgment on these matters as part of his/her responsibility to ''make the initial determination of the required levels of physical and biological containment in accordance with the *NIH Guidelines*'' (see Section IV–B–7–c–(1)). For cases falling under Sections III–A through III–E, *Experiments Covered by the NIH Guidelines,* this judgment is to be reviewed and approved by the Institutional Biosafety Committee as part of its responsibility to make an ''independent assessment of the containment levels required by the *NIH Guidelines* for the proposed research'' (see Section IV–B–2–b–(1), *Institutional Biosafety Committee*). The Institutional Biosafety Committee may refer specific cases to NIH OSP as part of NIH OSP's functions to ''provide advice to all within and outside NIH'' (see Section IV–C–3).

Appendix A currently states:

Appendix A. Exemptions Under Section III–F–6—Sublists of Natural Exchangers

Certain specified recombinant or synthetic nucleic acid molecules that consist entirely of DNA segments from different species that exchange DNA by known physiological processes, though one or more of the segments may be a synthetic equivalent are exempt from these *NIH Guidelines* (see Section III–F–6, *Exempt Experiments*). Institutional Biosafety Committee registration is not required for these exempt experiments. A list of such exchangers will be prepared and periodically revised by the NIH Director with advice from the RAC after appropriate notice and opportunity for public comment (see Section IV–C–1-b-(1)-(c), *NIH Director—Specific Responsibilities*). For a list of natural exchangers that are exempt from the *NIH Guidelines,* see Appendices A–I through A–VI, *Exemptions under Section III–F–6 Sublists of Natural Exchangers.* Section III–F–6, *Exempt Experiments,* describes recombinant or synthetic nucleic acid molecules that are: (1) Composed entirely of DNA segments from one or more of the organisms within a sublist, and (2) to be propagated in any of the organisms within a sublist (see *Classification of Bergey's Manual of Determinative Bacteriology;* 8th edition, R.E. Buchanan and N.E. Gibbons, editors, Williams and Wilkins Company; Baltimore, Maryland 1984). Although these experiments are exempt, it is recommended that they be performed at the appropriate biosafety level for the host or recombinant/synthetic organism (see Biosafety in Microbiological and Biomedical Laboratories, 5th edition, 2007, U.S. DHHS, Public Health Service, Centers for Disease Control and Prevention, Atlanta, Georgia, and NIH Office of Biosafety, Bethesda, Maryland).

Appendix A is proposed to be amended as follows:

Appendix A. Exemptions Under Section III–F–6—Sublists of Natural Exchangers

Certain specified recombinant or synthetic nucleic acid molecules that consist entirely of DNA segments from different species that exchange DNA by known physiological processes, though one or more of the segments may be a synthetic equivalent are exempt from these *NIH Guidelines* (see Section III–F–6, *Exempt Experiments*). Institutional Biosafety Committee registration is not required for these exempt experiments. A list of such exchangers will be prepared and periodically revised by the NIH Director after appropriate notice and opportunity for public comment (see Section IV–C–1-b-(1)-(c), *NIH Director—Specific Responsibilities.* For a list of natural exchangers that are exempt from the *NIH Guidelines,* see Appendices A–I through A–VI, *Exemptions under Section III–F–6 Sublists of Natural Exchangers.* Section III–F–6, *Exempt Experiments,* describes recombinant or synthetic nucleic acid molecules that are: (1) Composed entirely of DNA segments from one or more of the organisms within a sublist, and (2) to be propagated in any of the organisms within a sublist (see *Bergey's Manual of Systematic Bacteriology;* 2nd edition, Springer-Verlag; New York, NY). Although these experiments are exempt, it is recommended that they be performed at the appropriate biosafety level for the host or recombinant/synthetic organism (see Biosafety in Microbiological and Biomedical Laboratories, 5th edition, 2007, U.S. DHHS, Public Health Service, Centers for Disease Control and Prevention, Atlanta, Georgia, and NIH Office of Biosafety, Bethesda, Maryland).

Appendix C–IX–A currently states:

Appendix C–IX–A

The NIH Director, with advice of the RAC, may revise the classification for the purposes of these *NIH Guidelines* (see Section IV–C–

1–b–(2)–(b), *Minor Actions*). The revised list of organisms in each Risk Group is located in Appendix B.

Appendix C–IX–A is proposed to be amended as follows:

Appendix C–IX–A

The NIH Director may revise the classification for the purposes of these *NIH Guidelines* (see Section IV–C–1–b–(2)–(b), *Minor Actions*). The revised list of organisms in each Risk Group is located in Appendix B.

None of the other sub-sections under Appendix C–IX. Footnotes and References of Appendix C are proposed to be amended.

Appendix D currently states in part:

Appendix D. Major Actions Taken Under the NIH Guidelines

As noted in the subsections of Section IV–C–1–b–(1), the Director, NIH, may take certain actions with regard to the *NIH Guidelines* after the issues have been considered by the RAC. Some of the actions taken to date include the following:

Appendix D is proposed to be amended as follows:

Appendix D. Major Actions Taken Under the NIH Guidelines

As noted in the subsections of Section IV–C–1–b–(1), the Director, NIH, may take certain actions with regard to the *NIH Guidelines.* (Entries up to and including D–118 were approved using a process that involved the RAC.) Some of the actions taken to date include the following:

Appendix I–II currently states:

Appendix I–II. Certification of Host-Vector Systems

Appendix I–II–A. Responsibility

Host-Vector 1 systems (other than *Escherichia coli* K–12) and Host-Vector 2 systems may not be designated as such until they have been certified by the NIH Director. Requests for certification of host-vector systems may be submitted to the Office of Science Policy, National Institutes of Health, preferably by email to: *NIHGuidelines@od.nih.gov;* additional contact information is also available here and on the OSP website (*www.osp.od.nih.gov*). Proposed host-vector systems will be reviewed by the RAC (see Section IV–C–1–b–(1)–(f), *Major Actions*). Initial review will based on the construction, properties, and testing of the proposed host-vector system by a subcommittee composed of one or more RAC members and/or *ad hoc* experts. The RAC will evaluate the subcommittee's report and any other available information at the next scheduled RAC meeting. The NIH Director is responsible for certification of host-vector systems, following advice of the RAC. Minor modifications to existing host-vector systems (*i.e.,* those that are of minimal or no consequence to the properties relevant to containment) may be certified by the NIH Director without prior RAC review (see Section IV–C–1–b–(2)–(f), *Minor Actions*). Once a host-vector system has been certified by the NIH Director, a notice of certification will be sent by NIH OSP to the applicant and to the Institutional Biosafety Committee Chairs. A list of all currently certified host-vector systems is available from the Office of Science Policy, National Institutes of Health, preferably by submitting a request for this information to: *NIHGuidelines@od.nih.gov;* additional contact information is also available here and on the OSP website (*www.osp.od.nih.gov*). The NIH Director may rescind the certification of a host-vector system (see Section IV–C–1–b–(2)–(g), *Minor Actions*). If certification is rescinded, NIH will instruct investigators to transfer cloned DNA into a different system or use the clones at a higher level of physical containment level, unless NIH determines that the already constructed clones incorporate adequate biological containment. Certification of a host-vector system does not extend to modifications of either the host or vector component of that system. Such modified systems shall be independently certified by the NIH Director. If modifications are minor, it may only be necessary for the investigator to submit data showing that the modifications have either improved or not impaired the major phenotypic traits on which the containment of the system depends. Substantial modifications to a certified host-vector system requires submission of complete testing data.

Appendix I–II–B. Data To Be Submitted for Certification

Appendix I–II–B–1. Host-Vector 1 Systems Other than *Escherichia coli* K–12

The following types of data shall be submitted, modified as appropriate for the particular system under consideration: (i) A description of the organism and vector; the strain's natural habitat and growth requirements; its physiological properties, particularly those related to its reproduction, survival, and the mechanisms by which it exchanges genetic information; the range of organisms with which this organism normally exchanges genetic information and the type of information is exchanged; and any relevant information about its pathogenicity or toxicity; (ii) a description of the history of the particular strains and vectors to be used, including data on any mutations which render this organism less able to survive or transmit genetic information; and (iii) a general description of the range of experiments contemplated with emphasis on the need for developing such an Host-Vector 1 system.

Appendix I–II–B–2. Host-Vector 2 Systems

Investigators planning to request Host-Vector 2 systems certification may obtain instructions from NIH OSP concerning data to be submitted (see Appendices I–III–N and O, *Footnotes and References of Appendix I*). In general, the following types of data are required: (i) Description of construction steps with indication of source, properties, and manner of introduction of genetic traits; (ii) quantitative data on the stability of genetic traits that contribute to the containment of the system; (iii) data on the survival of the host-vector system under non-permissive laboratory conditions designed to represent the relevant natural environment; (iv) data on transmissibility of the vector and/or a cloned DNA fragment under both permissive and non-permissive conditions; (v) data on all other properties of the system which affect containment and utility, including information on yields of phage or plasmid molecules, ease of DNA isolation, and ease of transfection or transformation; and (vi) in some cases, the investigator may be asked to submit data on survival and vector transmissibility from experiments in which the host-vector is fed to laboratory animals or one or more human subjects. Such *in vivo* data may be required to confirm the validity of predicting *in vivo* survival on the basis of *in vitro* experiments. Data shall be submitted 12 weeks prior to the RAC meeting at which such data will be considered by the Office of Science Policy, National Institutes of Health, preferably by email to: *NIHGuidelines@od.nih.gov;* additional contact information is also available here and on the OSP website (*www.osp.od.nih.gov*). Investigators are encouraged to publish their data on the construction, properties, and testing of proposed Host Vector 2 systems prior to consideration of the system by the RAC and its subcommittee. Specific instructions concerning the submission of data for proposed *Escherichia coli* K–12 Host-Vector 2 system (EK2) involving either plasmids or bacteriophage in *Escherichia coli* K–12, are available from the Office of Science Policy, National Institutes of Health, preferably by submitting a request for this information to: *NIHGuidelines@od.nih.gov;*additional contact information is also available here and on the OSP website (*www.osp.od.nih.gov*).

Appendix I–II is proposed to be amended as follows:

Appendix I–II. Certification of Host-Vector Systems

Appendix I–II–A. Responsibility

Host-Vector 1 systems (other than *Escherichia coli* K–12) and Host-Vector 2 systems may not be designated as such until they have been certified by the NIH Director. Requests for certification of host-vector systems may be submitted to the Office of Science Policy, National Institutes of Health, preferably by email to: *NIHGuidelines@od.nih.gov;* additional contact information is also available here and on the OSP website (*www.osp.od.nih.gov*). Proposed host-vector systems will be reviewed based on the construction, properties, and testing of the proposed host-vector system by *ad hoc* experts. The NIH Director is responsible for certification of host-vector systems. Once a host-vector system has been certified by the NIH Director, a notice of certification will be sent by NIH OSP to the applicant and to the Institutional Biosafety Committee Chairs. A list of all currently certified host-vector systems is available from the Office of Science Policy, National Institutes of Health, preferably by submitting a request for this information to: *NIHGuidelines@od.nih.gov;*

additional contact information is also available here and on the OSP website (*www.osp.od.nih.gov*). The NIH Director may rescind the certification of a host-vector system (see Section IV–C–1–b–(2)–(g), *Minor Actions*). If certification is rescinded, NIH will instruct investigators to transfer cloned DNA into a different system or use the clones at a higher level of physical containment level, unless NIH determines that the already constructed clones incorporate adequate biological containment. Certification of a host-vector system does not extend to modifications of either the host or vector component of that system. Such modified systems shall be independently certified by the NIH Director. If modifications are minor, it may only be necessary for the investigator to submit data showing that the modifications have either improved or not impaired the major phenotypic traits on which the containment of the system depends. Substantial modifications to a certified host-vector system requires submission of complete testing data.

Appendix I–II–B. Data To Be Submitted for Certification

Appendix I–II–B–1. Host-Vector 1 Systems Other than *Escherichia coli* K–12

The following types of data shall be submitted, modified as appropriate for the particular system under consideration: (i) A description of the organism and vector; the strain's natural habitat and growth requirements; its physiological properties, particularly those related to its reproduction, survival, and the mechanisms by which it exchanges genetic information; the range of organisms with which this organism normally exchanges genetic information and the type of information is exchanged; and any relevant information about its pathogenicity or toxicity; (ii) a description of the history of the particular strains and vectors to be used, including data on any mutations which render this organism less able to survive or transmit genetic information; and (iii) a general description of the range of experiments contemplated with emphasis on the need for developing such an Host-Vector 1 system.

Appendix I–II–B–2. Host-Vector 2 Systems

Investigators planning to request Host-Vector 2 systems certification may obtain instructions from NIH OSP concerning data to be submitted (see Appendices I–III–N and O, *Footnotes and References of Appendix I*). In general, the following types of data are required: (i) Description of construction steps with indication of source, properties, and manner of introduction of genetic traits; (ii) quantitative data on the stability of genetic traits that contribute to the containment of the system; (iii) data on the survival of the host-vector system under non-permissive laboratory conditions designed to represent the relevant natural environment; (iv) data on transmissibility of the vector and/or a cloned DNA fragment under both permissive and non-permissive conditions; (v) data on all other properties of the system which affect containment and utility, including information on yields of phage or plasmid molecules, ease of DNA isolation, and ease of transfection or transformation; and (vi) in some cases, the investigator may be asked to submit data on survival and vector transmissibility from experiments in which the host-vector is fed to laboratory animals or one or more human subjects. Such *in vivo* data may be required to confirm the validity of predicting *in vivo* survival on the basis of *in vitro* experiments. Data shall be submitted to the Office of Science Policy, National Institutes of Health, preferably by email to: *NIHGuidelines@od.nih.gov;* additional contact information is also available here and on the OSP website (*www.osp.od.nih.gov*). Investigators are encouraged to publish their data on the construction, properties, and testing of proposed Host Vector 2 systems prior to consideration of the system by NIH. Specific instructions concerning the submission of data for proposed *Escherichia coli* K–12 Host-Vector 2 system (EK2) involving either plasmids or bacteriophage in *Escherichia coli* K–12, are available from the Office of Science Policy, National Institutes of Health, preferably by submitting a request for this information to: *NIHGuidelines@od.nih.gov;* additional contact information is also available here and on the OSP website (*www.osp.od.nih.gov*).

Appendix L, GENE THERAPY POLICY CONFERENCES (GTPCS), is proposed to be deleted in its entirety.

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), is proposed to be deleted in its entirety.

Dated: August 7, 2018.

Lawrence A. Tabak,

Deputy Director, National Institutes of Health.

[FR Doc. 2018–17760 Filed 8–16–18; 8:45 am]

BILLING CODE 4140–01–P

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, 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, and personal information concerning individuals associated with the grant applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: Center for Scientific Review Special Emphasis Panel; PAR–17–144: Limited Competition: National Primate Research Centers (P51).

Date: September 11–14, 2018.

Time: 8:00 a.m. to 12:00 p.m.

Agenda: To review and evaluate grant applications.

Place: Hotel Vintage Portland, 422 SW Broadway, Portland, OR 97205.

Contact Person: Brian H. Scott, Ph.D., Scientific Review Officer, National Institutes of Health, Center for Scientific Review, 6701 Rockledge Drive, Bethesda, MD 20892, 301–827–7490, *brianscott@mail.nih.gov.*

Name of Committee: Brain Disorders and Clinical Neuroscience Integrated Review Group; Pathophysiological Basis of Mental Disorders and Addictions Study Section.

Date: September 13–14, 2018.

Time: 8:00 a.m. to 5:00 p.m.

Agenda: To review and evaluate grant applications.

Place: Renaissance Orlando at SeaWorld, 6677 Sea Harbor Drive, Orlando, FL 32821.

Contact Person: Boris P. Sokolov, Ph.D., Scientific Review Officer, Center for Scientific Review, National Institutes of Health, 6701 Rockledge Drive, Room 5217A, MSC 7846, Bethesda, MD 20892, 301–408–9115, *bsokolov@csr.nih.gov.*

(Catalogue of Federal Domestic Assistance Program Nos. 93.306, Comparative Medicine; 93.333, Clinical Research, 93.306, 93.333, 93.337, 93.393–93.396, 93.837–93.844, 93.846–93.878, 93.892, 93.893, National Institutes of Health, HHS)

Dated: August 13, 2018.

Sylvia L. Neal,

Program Analyst, Office of Federal Advisory Committee Policy.

[FR Doc. 2018–17785 Filed 8–16–18; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Draft Report on Carcinogens Monograph on Night Shift Work and Light at Night; Availability of Document; Request for Comments; Notice of Peer-Review Meeting

AGENCY: National Institutes of Health, HHS.

ACTION: Notice.

SUMMARY: The National Toxicology Program (NTP) announces a meeting to peer review the Draft Report on Carcinogens Monograph on Night Shift Work and Light at Night. NTP has conducted a literature-based assessment to determine whether night shift work (*e.g.,* working at least three hours between 12 a.m. and 6 a.m.) and light at night are cancer hazards and should