submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states ''THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.'' FDA will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on *https://www.regulations.gov.* Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify the information as ''confidential.'' Any information marked as ''confidential'' will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: *https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf.*

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to *https://www.regulations.gov* and insert the docket number, found in brackets in the heading of this document, into the ''Search'' box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240–402–7500.

FOR FURTHER INFORMATION CONTACT: Jessica Seo, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 31, Rm. 2417, Silver Spring, MD 20993–0002, 301–796–7699, email: *ODAC@fda.hhs.gov,* or FDA Advisory Committee Information Line, 1–800–741–8138 (301–443–0572 in the Washington, DC area). A notice in the **Federal Register** about last-minute modifications that impact a previously announced advisory committee meeting cannot always be published quickly enough to provide timely notice. Therefore, you should always check FDA's website at *https://www.fda.gov/AdvisoryCommittees/default.htm* and scroll down to the appropriate advisory committee meeting link, or call the advisory committee information line to learn about possible modifications before the meeting.

SUPPLEMENTARY INFORMATION:

Agenda: The meeting presentations will be heard, viewed, captioned, and recorded through an online teleconferencing and/or video conferencing platform. Amendments made by section 504 of the 2017 FDA Reauthorization Act to section 505B of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355c) required, for original applications submitted on or after August 18, 2020, pediatric investigations of certain targeted cancer drugs with new active ingredients, based on molecular mechanism of action rather than clinical indication. The Committee will discuss perspectives relating to implementation of this legislation and its impact on pediatric cancer drug development to date.

FDA intends to make background material available to the public no later than 2 business days before the meeting. If FDA is unable to post the background material on its website prior to the meeting, the background material will be made publicly available on FDA's website at the time of the advisory committee meeting. Background material and the link to the online teleconference and/or video conference meeting will be available at *https://www.fda.gov/AdvisoryCommittees/Calendar/default.htm.* Scroll down to the appropriate advisory committee meeting link.

The meeting will include slide presentations with audio and video components to allow the presentation of materials in a manner that most closely resembles an in-person advisory committee meeting.

Procedure: Interested persons may present data, information, or views, orally or in writing, on issues pending before the Committee. All electronic and written submissions to the Docket (see **ADDRESSES**) on or before May 8, 2024, will be provided to the Committee. Oral presentations from the public will be scheduled between approximately 1:30 p.m. and 2:30 p.m. Eastern Time. Those individuals interested in making formal oral presentations should notify the contact person and submit a brief statement of the general nature of the evidence or arguments they wish to present, the names and addresses of proposed participants, and an indication of the approximate time requested to make their presentation on or before April 30, 2024. Time allotted for each presentation may be limited. If the number of registrants requesting to speak is greater than can be reasonably accommodated during the scheduled open public hearing session, FDA may conduct a lottery to determine the speakers for the scheduled open public hearing session. The contact person will notify interested persons regarding their request to speak by May 1, 2024.

For press inquiries, please contact the Office of Media Affairs at *fdaoma@fda.hhs.gov* or 301–796–4540.

FDA welcomes the attendance of the public at its advisory committee meetings and will make every effort to accommodate persons with disabilities. If you require accommodations due to a disability, please contact Jessica Seo (see **FOR FURTHER INFORMATION CONTACT**) at least 7 days in advance of the meeting.

FDA is committed to the orderly conduct of its advisory committee meetings. Please visit our website at *https://www.fda.gov/AdvisoryCommittees/AboutAdvisoryCommittees/ucm111462.htm* for procedures on public conduct during advisory committee meetings.

Notice of this meeting is given under the Federal Advisory Committee Act (5 U.S.C. 1001 *et seq.*). This meeting notice also serves as notice that, pursuant to 21 CFR 10.19, the requirements in 21 CFR 14.22(b), (f), and (g) relating to the location of advisory committee meetings are hereby waived to allow for this meeting to take place using an online meeting platform. This waiver is in the interest of allowing greater transparency and opportunities for public participation, in addition to convenience for advisory committee members, speakers, and guest speakers. The conditions for issuance of a waiver under 21 CFR 10.19 are met.

Dated: April 2, 2024.

Lauren K. Roth,

Associate Commissioner for Policy.

[FR Doc. 2024–07273 Filed 4–4–24; 8:45 am]

BILLING CODE 4164–01–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, HHS.

ACTION: Notice.

SUMMARY: This notice sets forth final changes to *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines)* as initially outlined in a **Federal Register** notice issued on August 10, 2023. Following solicitation of public comments, the NIH is amending the *NIH Guidelines* to include specific considerations and requirements for conducting research

involving gene drive modified organisms (GDMOs) in contained research settings. NIH is updating the *NIH Guidelines* to clarify minimum containment requirements, provide considerations for performing risk assessments, and define additional institutional responsibilities regarding Institutional Biosafety Committees (IBCs) and Biological Safety Officers (BSOs).

DATES: Changes outlined in this notice will be implemented on September 30, 2024.

FOR FURTHER INFORMATION CONTACT: Caroline Young, ScM, Acting Director of the Division of Biosafety, Biosecurity, and Emerging Biotechnology Policy, Office of Science Policy, at (301) 496–9838 or email at *SciencePolicy@od.nih.gov*.

SUPPLEMENTARY INFORMATION: In a **Federal Register** notice issued on August 10, 2023 (88 FR 54332), NIH proposed a series of actions to the NIH Guidelines for public comment. NIH is amending the *NIH Guidelines* to ensure the continued responsible research involving GDMOs in contained research settings. Specifically, the *NIH Guidelines* will be amended to:

1. clarify minimum containment requirements for research involving GDMOs;
2. provide considerations for risk assessment;
3. define additional institutional responsibilities for IBCs and BSOs.

In addition to the amendments related to contained research involving GDMOs, the *NIH Guidelines* will also be amended to:

1. replace the term ''helper viruses'' with the broader term ''helper systems''; and
2. reclassify WNV and SLEV as risk group 2 agents for consistency with containment guidance provided in the BMBL.

The revisions apply to GDMO research in contained settings, which is subject to the *NIH Guidelines.* These revisions are consistent with the recommendations of the Novel and Exceptional Technology Research Advisory Committee report, *Gene Drives in Biomedical Research* (NExTRAC Report). NIH does not currently support research involving field release of GDMOs and the *NIH Guidelines* pertain to contained research; accordingly, no changes regarding potential field release are included in this Notice. NIH is also revising the *NIH Guidelines* to harmonize with the 6th edition of the *Biosafety in Microbiological and Biomedical Laboratories* (BMBL) regarding the Risk Group (RG) categorization of West Nile Virus (WNV) and Saint Louis Encephalitis Virus (SLEV).

Overview of Comments Received in Response to NIH's Proposal To Amend the NIH Guidelines (88 FR 54332)

The NIH received 28 comments (available at *https://osp.od.nih.gov/wp-content/uploads/2023/11/RFI_Nucleic_Final_508.pdf*) submitted by individuals from the general public, academic institutions, and professional or membership organizations in response to the proposal to amend the *NIH Guidelines* posted to the **Federal Register** on August 10, 2023. All comments were reviewed and considered by the NIH. Most comments did not express general concerns with the proposed amendments, but many included comments or questions on specific sections. These comments, along with NIH responses, are summarized below.

Several of the comments requested additional guidance or resources to accompany any changes. As a source of information in addition to that in the *NIH Guidelines,* the NIH will provide a supplementary reference document, *Biosafety Considerations for Contained Research Involving Gene Drive Modified Organisms,* that institutions, investigators, and the biosafety community can reference as they consider conducting contained gene drive research. The reference document is intended to organize the relevant sections of the *NIH Guidelines* in an accessible format and to provide some additional information and resources. It will be available on the NIH Office of Science Policy (OSP) *NIH Guidelines* website, along with Frequently Asked Questions.

Definition of ''*gene drive*'' *in Section I–E–7.* Several comments requested additional clarification of the definition and that the definition specify ''engineered'' gene drives to exclude natural gene drives. Under the scope of *NIH Guidelines,* only contained research with gene drives involving recombinant or synthetic nucleic acids would be subject to the *NIH Guidelines.* The definition language is based on the definition in the NExTRAC report, *Gene Drives in Biomedical Research.* Other comments asked whether certain research with prokaryotes or viruses could be considered to involve GDMOs. While gene drive technologies are usually applied to sexually reproducing organisms, the risk assessment section of the *NIH Guidelines* will include guidance on the consideration of modifications with properties similar to a gene drive. The supplementary reference document will include sources for additional information on gene drive technologies and capabilities.

Section II–A–3 Risk Assessment. In response to comments seeking additional risk assessment guidance, in particular regarding relevant biosafety data, the reference document will include links to sources with additional information including the NExTRAC report, the National Academy of Sciences report, *Gene Drives on the Horizon,* and other relevant literature sources.

Section III–D Containment

Regarding the requirement of a minimum of biosafety level 2 (BL2) containment for work with GDMOs, several comments asked about appropriate BL2 containment for specific species. Gene drive research may be conducted in a broad range of species, and institutions may wish to consult containment guidance tailored to the specific species or type of organism utilized in a particular protocol. For work with arthropods, the *NIH Guidelines* will be amended to reference the *Arthropod Containment Guidelines* and *Addendum 1 Containment Practices for Arthropods Modified with Engineered Transgenes Capable of Gene Drive.* The reference document will include sources for additional species. In particular, there were comments about *Saccharomyces* and *Kluyveromyces* Host-Vector Systems. The amendments will only affect research involving host vector systems modified by a gene drive and does not pertain to other yeast research.

Other comments requested a process for handling requests to lower containment levels for research involving GDMOs. As with requests to lower containment for research involving infectious agents outlined in Section IV–C–b–(2)–(a), OSP will consider containment lowering requests for research involving GDMO on a case-by-case basis.

Section III–D and III–E. Comments were supportive of the terminology shift from ''helper virus'' to ''helper system,'' but several asked that the examples of helper systems that were included in the **Federal Register** notice also be included in the *NIH Guidelines.* To provide that information, the preamble to III–D–3 will state: ''The potential for reversion or generation of replication competent virus should be considered when generating or using defective viruses or vectors in the presence of helper systems (*e.g.,* helper viruses, packaging cell lines, transient transfection systems, replicon systems).''

Section III–E–3 Experiments Involving Transgenic Rodents

Several comments asked whether NIH was proposing to expand Section III–E–3 to include the use of transgenic rodents. There are two instances where transgenic rodents are specifically exempted from the *NIH Guidelines.* Appendix C–VII exempts the purchase or transfer of transgenic rodents and Appendix C–VIII exempts the generation of BL1 rodents by breeding. The use of exempt rodents remains exempt unless the subsequent research involves the use of recombinant or synthetic nucleic acid molecules. The language added to III–E–3 is not an expansion to include the use of *de novo* generated rodents covered under that section. Rodents covered under III–E–3 are not exempt and, as such, their subsequent use is not exempt. The inclusion of the language referring to the use of such rodents is intended to clarify that their subsequent use is not exempt.

Section IV Roles and Responsibilities and V–N. Several comments asked for clarification regarding the requirement for adequate expertise on IBCs reviewing GDMO research including consideration of ecological impacts. Consistent with expectations in the *NIH Guidelines* for the review of research with plants, animals, or human research participants, appropriate expertise regarding ecological impacts may be provided by members of the IBC or ad hoc consultants. An ad hoc consultant with expertise in ecological impacts would only be needed for review of specific GDMO research and, if an institution has multiple IBCs, would only be required to serve on the specific IBC reviewing such research. An ad hoc consultant may be from a partner or unrelated institution and does not need to be local to the institution.

Several comments addressed the additional requirement for a biological safety officer (BSO) to be appointed if research involving GDMOs is to be conducted. Some commenters interpreted this language to mean that a BSO must be appointed if the institution engages in any BL2 research. To clarify, a BSO must be appointed if the institution engages in recombinant or synthetic nucleic acid molecule research that involves GDMOs. Section IV–B–1–c will be revised to clarify this requirement. Others commented on the qualifications of a BSO and the reference to the *Laboratory Safety Monograph*. The duties of a BSO are specifically outlined in Section IV–B–3 of the *NIH Guidelines.*

Appendix B Classification of Human Etiologic Agents on the Basis of Hazard. All comments regarding this proposed change supported the reclassification of West Nile Virus and Saint Louis Encephalitis virus (SLEV) as risk group 2 agents to harmonize with guidance provided by the BMBL. One comment noted that SLEV was improperly classified as an alphavirus. Appendix B will be amended to classify SLEV as a flavivirus. As minor actions under the *NIH Guidelines,* Appendix B–IV–D Risk Group 4 Viral Agents will be amended from ''Hemorrhagic fever agents and viruses as yet undefined'' to ''Hemorrhagic fever viruses as yet undefined'' to prevent possible misinterpretation that all undefined viruses require RG4 containment, and the listing of Ebola and Marburg virus will be pluralized to harmonize with recent changes in taxonomy nomenclature to cover multiple viruses. The amendment to ''Ebola viruses'' and ''Marburg viruses'' will clarify that the virus name applies to the multiple species.

Amendments to the NIH Guidelines

Section I–E will be amended as follows:

Section I–E. General Definitions

Section I–E–7. ''Gene drive'' is defined as a technology whereby a particular heritable element biases inheritance in its favor, resulting in the heritable element becoming more prevalent than predicted by Mendelian laws of inheritance in a population over successive generations.

Section II–A–3 will be amended as follows:

Section II–A–3. Comprehensive Risk Assessment

In deciding on the appropriate containment for an experiment, the first step is to assess the risk of the agent itself. Appendix B, Classification of Human Etiologic Agents on the Basis of Hazard, classifies agents into Risk Groups based on an assessment of their ability to cause disease in humans and the available treatments for such disease. Once the Risk Group of the agent is identified, this should be followed by a thorough consideration of how the agent is to be manipulated. Factors to be considered in determining the level of containment include agent factors such as: virulence, pathogenicity, infectious dose, environmental stability, route of spread, communicability, operations, quantity, availability of vaccine or treatment, and gene product effects such as toxicity, physiological activity, and allergenicity. Any strain that is known to be more hazardous than the parent (wild-type) strain should be considered for handling at a higher containment level. Certain attenuated strains or strains that have been demonstrated to have irreversibly lost known virulence factors may qualify for a reduction of the containment level compared to the Risk Group assigned to the parent strain (see Section V–B, Footnotes and References of Sections I–IV).

While the starting point for the risk assessment is based on the identification of the Risk Group of the parent agent, as technology moves forward, it may be possible to develop an organism containing genetic sequences from multiple sources such that the parent agent may not be obvious. In such cases, the risk assessment should include at least two levels of analysis. The first involves a consideration of the Risk Groups of the source(s) of the sequences and the second involves an assessment of the functions that may be encoded by these sequences (*e.g.,* virulence or transmissibility). It may be prudent to first consider the highest Risk Group classification of all agents that are the source of sequences included in the construct. Other factors to be considered include the percentage of the genome contributed by each parent agent and the predicted function or intended purpose of each contributing sequence. The initial assumption should be that all sequences will function as they did in the original host context.

The Principal Investigator and Institutional Biosafety Committee must also be cognizant that the combination of certain sequences in a new biological context may result in an organism whose risk profile could be higher than that of the contributing organisms or sequences. The synergistic function of these sequences may be one of the key attributes to consider in deciding whether a higher containment level is warranted, at least until further assessments can be carried out. A new biosafety risk may occur with an organism formed through combination of sequences from a number of organisms or due to the synergistic effect of combining transgenes that results in a new phenotype.

A final assessment of risk based on these considerations is then used to set the appropriate containment conditions for the experiment (see Section II–B, Containment). The appropriate containment level may be equivalent to the Risk Group classification of the agent or it may be raised or lowered as a result of the above considerations. The Institutional Biosafety Committee must

approve the risk assessment and the biosafety containment level for recombinant or synthetic nucleic acid experiments described in Sections III–A, Experiments that Require NIH Director Approval and Institutional Biosafety Committee Approval, Before Initiation; III–B, Experiments that Require NIH OSP and Institutional Biosafety Committee Approval Before Initiation; III–C, Experiments Involving Human Gene Transfer that Require Institutional Biosafety Committee Approval Prior to Initiation; III–D, Experiments that Require Institutional Biosafety Committee Approval Before Initiation.

Research involving gene drive modified organisms may require risk assessments that incorporate a broader scope of considerations because of greater uncertainty of the technology and potential uncertainty of the impact of the newly modified organism. Specific attention must be paid to risks of an unintended release from the laboratory and the potential impact on humans, other populations of organisms, and the environment.

Considerations for conducting risk assessments for research involving gene drive modified organisms might include:

1. The specific types of manipulations based on:

a. Function or intended function of the genetic/gene drive construct (*i.e.,* a designed or engineered assembly of sequences);

b. Source of the genetic material (*e.g.,* sequences of transgenes) in the construct;

c. The modifications to the construct;

d. Whether it is possible to predict the consequences of a construct, including the recognition of an unintended gene drive (*i.e.,* construct not specifically designed as a gene drive but nonetheless having properties of a gene drive) and the possible consequences of escape into the environment;

e. The potential ability of the gene drive to spread or persist in local populations;

2. Options for approaches to risk mitigation for specific types of risks in experiments or when dealing with a high degree of uncertainty about risks;

3. Considerations for implementing more stringent containment measures until biosafety data are accrued to support lowering containment.

Careful consideration should be given to the types of manipulation planned for some higher Risk Group agents. For example, the RG2 dengue viruses may be cultured under the Biosafety Level (BL) 2 containment (see Section II–B); however, when such agents are used for animal inoculation or transmission studies, a higher containment level is recommended. Similarly, RG3 agents such as Venezuelan equine encephalomyelitis and yellow fever viruses should be handled at a higher containment level for animal inoculation and transmission experiments.

Individuals working with human immunodeficiency virus (HIV), hepatitis B virus (HBV) or other bloodborne pathogens should consult the applicable Occupational Safety and Health Administration (OSHA) regulation, 29 CFR 1910.1030, and OSHA publication 3127 (1996 revised). BL2 containment is recommended for activities involving all blood-contaminated clinical specimens, body fluids, and tissues from all humans, or from HIV- or HBV-infected or inoculated laboratory animals. Activities such as the production of research-laboratory scale quantities of HIV or other bloodborne pathogens, manipulating concentrated virus preparations, or conducting procedures that may produce droplets or aerosols, are performed in a BL2 facility using the additional practices and containment equipment recommended for BL3. Activities involving industrial scale volumes or preparations of concentrated HIV are conducted in a BL3 facility, or BL3 Large Scale if appropriate, using BL3 practices and containment equipment.

Exotic plant pathogens and animal pathogens of domestic livestock and poultry are restricted and may require special laboratory design, operation and containment features not addressed in *Biosafety in Microbiological and Biomedical Laboratories* (see Section V–C, Footnotes and References of Sections I through IV). For information regarding the importation, possession, or use of these agents see Sections V–G and V–H, Footnotes and References of Sections I through IV.

A portion of 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 introduction of stable genetic modifications into the genome (*e.g.,* cis elements involved in integration, gene editing); or

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

d. Can be translated or transcribed.

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

Section III–F–1 Exempt Experiments

Section III–F–1. Those synthetic nucleic acids that: (1) can neither replicate nor generate nucleic acids that can replicate in any living cell (*e.g.,* oligonucleotides or other synthetic nucleic acids that do not contain an origin of replication or contain elements known to interact with either DNA or RNA polymerase), and (2) are not designed to introduce a stable genetic modification, and (3) do not produce a toxin that is lethal for vertebrates at an LD50 of less than 100 nanograms per kilogram body weight. If a synthetic nucleic acid is deliberately transferred into one or more human research participants and meets the criteria of Section III–C, it is not exempt under this section.

Section III–D–4 will be amended as follows:

Section III–D–4. Experiments Involving Whole Animals

This section covers experiments involving deliberate transfer of recombinant or synthetic nucleic acid molecules, DNA or RNA derived from recombinant or synthetic nucleic acid molecules, or recombinant or synthetic nucleic acid molecule-modified microorganisms into whole animals and experiments involving whole animals in which the animal's genome has been altered by recombinant or synthetic nucleic acid molecules, or nucleic acids derived therefrom, into the germ-line (transgenic animals). Experiments involving gene drive modified animals or experiments involving viable recombinant or synthetic nucleic acid molecule-modified microorganisms, except for viruses that are only vertically transmitted, may *not* be conducted at BL1–N containment. A minimum containment of BL2 or BL2–N is required (see Section III–D–8).

Caution—Special care should be used in the evaluation of containment conditions for some experiments with transgenic animals. For example, such experiments might lead to the creation of novel mechanisms (*e.g.,* a gene drive; refer to Section III–D–8) or increased transmission of a recombinant pathogen

or production of undesirable traits in the host animal. In such cases, serious consideration should be given to increasing the containment conditions.

Section III–D–4–a. Recombinant or synthetic nucleic acid molecules, or DNA or RNA molecules derived therefrom, from any source except for greater than two-thirds of eukaryotic viral genome may be transferred to any non-human vertebrate or any invertebrate organism and propagated under conditions of physical containment comparable to BL1 or BL1–N and appropriate to the organism under study (see Section V–B, Footnotes and References of Sections I–IV). Animals that contain sequences from viral vectors, which do not lead to transmissible infection either directly or indirectly as a result of complementation or recombination in animals, may be propagated under conditions of physical containment comparable to BL1 or BL1–N and appropriate to the organism under study. Experiments involving the introduction of other sequences from eukaryotic viral genomes into animals are covered under Section III–D–4–b, Experiments Involving Whole Animals. For experiments involving recombinant or synthetic nucleic acid molecule-modified Risk Groups 2, 3, 4, or restricted organisms, see Sections V–A, V–G, and V–L, Footnotes and References of Sections I–IV. It is important that the investigator demonstrate that the fraction of the viral genome being utilized does not lead to productive infection. A U.S. Department of Agriculture permit is required for work with plant or animal pathogens (see Section V–G, Footnotes and References of Sections I–IV).

Section III–D–4–b. For experiments involving recombinant or synthetic nucleic acid molecules, or DNA or RNA derived therefrom, involving whole animals, including transgenic animals, and not covered by Section III–D–1, Experiments Using Human or Animal Pathogens (Risk Group 2, Risk Group 3, Risk Group 4, or Restricted Agents as Host-Vector Systems), or Section III–D–4–a, the appropriate containment shall be determined by the Institutional Biosafety Committee. Experiments involving gene drive modified animals generated by recombinant or synthetic nucleic acid molecules shall be conducted at a minimum of BL2 or BL2–N (see Section III–D–8).

Section III–D–4–c. Exceptions under Section III–D–4, Experiments Involving Whole Animals

Section III–D–4–c–(1). Experiments involving the generation of transgenic rodents that require BL1 containment are described under Section III–E–3, Experiments Involving Transgenic Rodents.

Section III–D–4–c–(2). The purchase or transfer of BL1 transgenic rodents is exempt from the *NIH Guidelines* under Section III–F, Exempt Experiments (see Appendix C–VII, The Purchase or Transfer of Transgenic Rodents).

Section III–D–4–c–(3). Experiments involving the generation or use of gene drive modified animals require a minimum of BL2 containment and are covered under III–D–8, Experiments Involving Gene Drive Modified Organisms.

A portion of Section III–D–5 will be amended as follows:

Section III–D–5. Experiments Involving Whole Plants

Experiments to genetically engineer plants by recombinant or synthetic nucleic acid molecule methods, to use such plants for other experimental purposes (*e.g.,* response to stress), to propagate such plants, or to use plants together with microorganisms or insects containing recombinant or synthetic nucleic acid molecules, may be conducted under the containment conditions described in Sections III–D–5–a through III–D–5–e. If experiments involving whole plants are not described in Section III–D–5 and do not fall under Sections III–A, III–B, III–D or III–F, they are included in Section III–E. Experiments involving the generation or use of gene drive modified organisms require a minimum of BL2 containment and are described under Section III–D–8, Experiments Involving Gene Drive Modified Organisms.

Section III–D–8 will be added as follows:

Section III–D–8. Experiments Involving Gene Drive Modified Organisms

Experiments involving gene drive modified organisms generated by recombinant or synthetic nucleic acid molecules shall be conducted at a minimum of Biosafety Level (BL) 2, BL2–N (Animals) or BL2–P (plant) containment.

A portion of Section III–E–3 will be amended as follows:

Section III–E–3. Experiments Involving Transgenic Rodents

This section covers experiments involving the generation or use of rodents in which the animal's genome has been altered by stable introduction of recombinant or synthetic nucleic acid molecules, or nucleic acids derived therefrom, into the germ-line (transgenic rodents). Only experiments that require BL1 containment are covered under this section; experiments that require BL2, BL3, or BL4 containment are covered under Section III–D–4, Experiments Involving Whole Animals or Section III–D–8, Experiments Involving Gene Drive Modified Organisms.

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

Section IV–B–1–c. Appoint a Biological Safety Officer (who is also a member of the Institutional Biosafety Committee) if the institution: (i) conducts recombinant or synthetic nucleic acid molecule research at Biosafety Level (BL) 3 or BL4, (ii) engages in large-scale (greater than 10 liters) research or (iii) conducts any research involving gene drive modified organisms, which all must be conducted at BL2 or higher containment. The Biological Safety Officer carries out the duties specified in Section IV–B–3.

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

Section IV–B–2–a–(1). The Institutional Biosafety Committee must comprise 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 L, 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 M, Physical and Biological Containment for Recombinant or Synthetic Nucleic Acid Molecule Research Involving Animals, require Institutional Biosafety Committee prior approval. When the institution conducts research involving

gene drive modified organisms, the institution must ensure that the Institutional Biosafety Committee has adequate expertise (*e.g.,* specific species containment, ecological or environmental risk assessment) using ad hoc consultants if necessary. When the institution conducts recombinant or synthetic nucleic acid molecule research at BL3, BL4, or Large Scale (greater than 10 liters) or research involving gene drive modified organisms, 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 conducts research with gene drive modified organisms, the impact on ecosystems should be assessed by the Institutional Biosafety Committee (see Section V–N, Footnotes and References of Sections I–IV). 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 if necessary). Institutional Biosafety Committee approval must be obtained from the clinical trial site. Section IV–B–3, Biological Safety Officer (BSO), will be amended as below in Section IV–B–3–a along with the addition of a new Section IV–B–3–c and re-lettering of the current Section IV–B–3–c to IV–B–3–d as follows:

Section IV–B–3–a. The institution shall appoint a Biological Safety Officer if it engages in large-scale research or production activities involving viable organisms containing recombinant or synthetic nucleic acid molecules. The Biological Safety Officer shall be a member of the Institutional Biosafety Committee.

Section IV–B–3–c. The institution shall appoint a Biological Safety Officer if it engages in recombinant or synthetic nucleic acid molecule research that involves gene drive modified organisms. The Biological Safety Officer shall be a member of the Institutional Biosafety Committee.

A new footnote and reference for Sections I through IV will be to be added as follows:

Section V–N. Determination of whether a gene drive modified organism has a potential for serious detrimental impact on managed (agricultural, forest, grassland) or natural ecosystems should be made by the Principal Investigator and the Institutional Biosafety Committee, in consultation with scientists knowledgeable of gene drive technology, and of the environment, and ecosystems in the geographic area of the research.

Appendices C–III–A Exceptions and C–IV–A Exceptions will be amended as follows:

The following categories are not exempt from the *NIH Guidelines:* (i) experiments described in Section III–B, which require NIH OSP and Institutional Biosafety Committee approval before initiation; (ii) experiments involving DNA from Risk Groups 3, 4, or restricted organisms (see Appendix B, Classification of Human Etiologic Agents on the Basis of Hazard, and Sections V–G and V–L, Footnotes and References of Sections I through IV) or cells known to be infected with these agents may be conducted under containment conditions specified in Section III–D–2 with prior Institutional Biosafety Committee review and approval; (iii) large-scale experiments (*e.g.,* more than 10 liters of culture), (iv) experiments involving the deliberate cloning of genes coding for the biosynthesis of molecules toxic for vertebrates (see Appendix F, Containment Conditions for Cloning of Genes Coding for the Biosynthesis of Molecules Toxic for Vertebrates), and (v) experiments involving gene drive modified organisms (Section III–D–8).

Appendix G–III–A will be amended as follows:

Appendix G–III–A. Biosafety in Microbiological and Biomedical Laboratories, 6th edition, U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, Atlanta, Georgia, and National Institutes of Health, Bethesda, Maryland.

Appendix G–III–B will be amended as follows:

Appendix G–III–B. Arthropod Containment Guidelines, Version 3.2, 2019, and *Addendum 1 Containment Practices for Arthropods Modified with Engineered Transgenes Capable of Gene Drive,* 2022, American Committee of Medical Entomology, American Society of Tropical Medicine and Hygiene, Arlington, Virginia.

Appendix L–III–C will be amended as follows:

Appendix L–III–C. Biological Containment Practices (Macroorganisms)

Appendix L–III–C–1. Effective dissemination of arthropods and other small animals can be prevented by using one or more of the following procedures: (i) use non-flying, flight-impaired, or sterile arthropods; (ii) use non-motile or sterile strains of small animals; (iii) conduct experiments at a time of year that precludes the survival of escaping organisms; (iv) use animals that have an obligate association with a plant that is not present within the dispersal range of the organism; or (v) prevent the escape of organisms present in run-off water by chemical treatment or evaporation of run-off water. Containment for arthropods is described in the *Arthropod Containment Guidelines* and *Addendum 1 Containment Practices for Arthropods Modified with Engineered Transgenes Capable of Gene Drive* (see Appendix G–III–B).

Appendix M–III–D will be amended as follows:

Appendix M–III–D. Research with animals, which may not appropriately be conducted under conditions described in Appendix M, may be conducted safely by applying practices routinely used for controlled culture of these biota. In aquatic systems, for example, BL1 equivalent conditions could be met by utilizing growth tanks that provide adequate physical means to avoid the escape of the aquatic species, its gametes, and introduced exogenous genetic material. A mechanism shall be provided to ensure that neither the organisms nor their gametes can escape into the supply or discharge system of the rearing container (*e.g.,* tank, aquarium, etc.). Acceptable barriers include appropriate filtration, irradiation, heat treatment, chemical treatment, etc. Moreover, the top of the rearing container shall be covered to avoid escape of the organism and its gametes. In the event of tank rupture, leakage, or overflow, the construction of the room containing these tanks should prevent the organisms and gametes from entering the building's drains before the organism and its gametes have been inactivated.

Other types of animals (*e.g.,* nematodes, arthropods, and certain forms of smaller animals) may be accommodated by using the appropriate BL1 through BL4 or BL1–P through BL4–P containment practices and procedures as specified in Appendices G and L. Containment for arthropods is described in the *Arthropod Containment Guidelines* and *Addendum 1 Containment Practices for Arthropods Modified with Engineered Transgenes Capable of Gene Drive* (see Appendix G–III–B).

Section III–D–3 will be amended as follows:

Section III–D–3. Experiments Involving the Use of Infectious DNA or RNA Viruses or Defective DNA or RNA Viruses in the Presence of a Helper System in Tissue Culture Systems

Caution: The potential for reversion or generation of replication competent virus should be considered when generating or using defective viruses or vectors in the presence of helper systems (*e.g.,* helper viruses, packaging cell lines, transient transfection systems, replicon systems). Special care should be used in the evaluation of containment levels for experiments which are likely to either enhance the pathogenicity (*e.g.,* insertion of a host oncogene) or to extend the host range (*e.g.,* introduction of novel control elements) of viral vectors under conditions that permit a productive infection. In such cases, serious consideration should be given to increasing physical containment by at least one level.

Note: Recombinant or synthetic nucleic acid molecules or nucleic acid molecules derived therefrom, which contain less than two-thirds of the genome of any eukaryotic virus (all viruses from a single Family (see Section V–J, *Footnotes and References of Sections I–IV*) being considered identical (see Section V–K, *Footnotes and References of Sections I–IV*)), are considered defective and may be used in the absence of helper systems under the conditions specified in Section III–E–1, *Experiments Involving the Formation of Recombinant or Synthetic Molecules Containing No More than Two-Thirds of the Genome of any Eukaryotic Virus.*

Section III–D–3–a. Experiments involving the use of infectious or defective Risk Group 2 viruses (see Appendix B–II, *Risk Group 2 Agents*) in the presence of a helper system may be conducted at BL2.

Section III–D–3–b. Experiments involving the use of infectious or defective Risk Group 3 viruses (see Appendix B–III–D, *Risk Group 3 (RG3)—Viruses and Prions*) in the presence of a helper system may be conducted at BL3.

Section III–D–3–c. Experiments involving the use of infectious or defective Risk Group 4 viruses (see Appendix B–IV–D, *Risk Group 4 (RG4)—Viral Agents*) in the presence of a helper system may be conducted at BL4.

Section III–D–3–d. Experiments involving the use of infectious or defective restricted poxviruses (see Sections V–A and V–L, *Footnotes and References of Sections I–IV*) in the presence of a helper system shall be determined on a case-by-case basis following NIH OSP review. A U.S. Department of Agriculture permit is required for work with plant or animal pathogens (see Section V–G, *Footnotes and References of Sections I–IV*).

Section III–D–3–e. Experiments involving the use of infectious or defective viruses in the presence of a helper system which are not covered in Sections III–D–3–a through III–D–3–d may be conducted at BL1.

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

Section III–E–1. Experiments Involving the Formation of Recombinant or Synthetic Nucleic Acid Molecules Containing No More Than Two-Thirds of the Genome of Any Eukaryotic Virus

Recombinant or synthetic nucleic acid molecules containing no more than two-thirds of the genome of any eukaryotic virus (all viruses from a single Family being considered identical [see Section V–J, *Footnotes and References of Sections I–IV]*) may be propagated and maintained in cells in tissue culture using BL1 containment. For such experiments, it must be demonstrated that the cells lack a helper system for the specific Families of defective viruses being used. If a helper system is present, procedures specified under Section III–D–3, *Experiments Involving the Use of Infectious Animal or Plant DNA or RNA Viruses or Defective Animal or Plant DNA or RNA Viruses in the Presence of Helper Systems in Tissue Culture Systems,* should be used. The DNA may contain fragments of the genome of viruses from more than one Family but each fragment shall be less than two-thirds of a genome.

Appendix B–II–D will be amended as follows:

Appendix B–II–D. Risk Group 2 (RG2)—Viruses

Flaviviruses—Group B Arboviruses
—Saint Louis Encephalitis Virus (SLEV)
—West Nile virus (WNV)

Appendix B–IV–D Risk Group 4 (RG4)—Viruses

Filoviruses
—Ebola viruses
—Marburg viruses
Hemorrhagic fever viruses as yet undefined

Dated: March 25, 2024.

Lawrence A. Tabak,

Principal Deputy Director, National Institutes of Health.

[FR Doc. 2024–07082 Filed 4–4–24; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute of Allergy and Infectious Diseases; Notice of Closed Meeting

Pursuant to section 1009 of the Federal Advisory Committee Act, as amended, notice is hereby given of the following meeting.

The meeting 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: National Institute of Allergy and Infectious Diseases Special Emphasis Panel; NIAID Clinical Trial Planning Grants (R34 Clinical Trial Not Allowed).

Date: May 1, 2024.

Time: 2:00 p.m. to 4:00 p.m.

Agenda: To review and evaluate grant applications.

Place: National Institute of Allergy and Infectious Diseases, National Institutes of Health, 5601 Fishers Lane, Room 3G22, Rockville, MD 20852 (Virtual Meeting).

Contact Person: Michael M. Opata, Ph.D., Scientific Review Officer, Scientific Review Program, Division of Extramural Activities, National Institute of Allergy and Infectious Diseases, National Institutes of Health, 5601 Fishers Lane, Room 3G22, Rockville, MD 20852, 240–627–3319, *michael.opata@nih.gov.*

(Catalogue of Federal Domestic Assistance Program Nos. 93.855, Allergy, Immunology, and Transplantation Research; 93.856, Microbiology and Infectious Diseases Research, National Institutes of Health, HHS)

Dated: April 2, 2024.

Lauren A. Fleck,

Program Analyst, Office of Federal Advisory Committee Policy.

[FR Doc. 2024–07277 Filed 4–4–24; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute of Diabetes and Digestive and Kidney Diseases; Notice of Closed Meeting

Pursuant to section 1009 of the Federal Advisory Committee Act, as