

*C. Amendments to Section IV, Roles and Responsibilities*

In Section IV-B-4-b, Submissions by the Principal Investigator to the NIH/ORDA, the following sections are amended to read:

Section IV-B-4-b-(3). Petition NIH/ORDA, with concurrence of the Institutional Biosafety Committee, for approval to conduct experiments specified in Sections III-A-1 and III-B of the NIH Guidelines;

In Section IV-B-4-e, Responsibilities of the Principal Investigator During the Conduct of the Research, the following section is added:

Section IV-B-4-e-(5). Comply with semiannual data reporting and adverse event reporting requirements for NIH and FDA-approved human gene transfer experiments (see Appendix M-VIII, Reporting Requirements—Human Gene Transfer Protocols).

In Section IV-C-b-(1), Major Actions, the first paragraph is amended to read:

To execute Major Actions, the NIH Director shall seek the advice of the 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)-(e) is amended to read:

Section IV-C-1-b-(1)-(e). Recommendations made by the NIH Director to the FDA Commissioner regarding RAC-reviewed human gene transfer experiments (see Appendix M-VI-E, RAC Recommendations to the NIH Director);

Except for renumbering, the rest of the Section IV-C-1-B-(1) remains unchanged.

In Section IV-C-1-b-(2), Minor Actions, the following sections are deleted:

Section IV-C-1-b-(2)-(a). Reviewing and approving certain experiments involving the deliberate transfer of recombinant DNA or DNA or RNA derived from recombinant DNA into one or more human subjects that qualify for the Accelerated Review process (see Section III-B-2);

Section IV-C-1-b-(2)-(b). Reviewing and approving minor changes to human

gene transfer protocols under Section III-A-2 and III-B-2;

The rest of the section has been renumbered.

Section IV-C-3, Office of Recombinant DNA Activities (ORDA), will be amended to read:

Section IV-C-3. Office of Recombinant DNA Activities (ORDA)

ORDA shall serve as a focal point for information on recombinant DNA 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. ORDA shall carry out such other functions as may be delegated to it by the NIH Director. ORDA's responsibilities include (but are not limited to) the following:

Section IV-C-3-a. Evaluating human gene transfer protocols for the necessity for RAC review (see Appendix M-VI-A);

Section IV-C-3-b. Serving as the focal point for data management of NIH and FDA approved human gene transfer protocols (see Appendix M-VIII, Reporting Requirements—Human Gene Transfer Protocols);

Section IV-C-3-c. Administering the semiannual data reporting requirements (and subsequent review) for human gene transfer experiments, including experiments that are reviewed solely by the FDA (see Appendix M-VI, Categories of Human Gene Transfer Experiments that May Be Exempt from RAC Review);

Section IV-C-3-d. Maintaining an inventory of NIH and FDA-approved human gene transfer experiments (including subsequent modifications);

Section IV-C-3-e. Reviewing and approving experiments in conjunction with ad hoc experts involving the cloning of genes encoding for toxin molecules that are lethal for vertebrates at an LD<sub>50</sub> 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 and Appendices F-I and F-II);

Section IV-C-3-f. Serving as the executive secretary of the RAC;

Section IV-C-3-g. Publishing in the **Federal Register**:

Section IV-C-3-g-(1). Announcements of RAC meetings and agendas at least 15 days in advance (NOTE—If the agenda for a RAC meeting is modified, ORDA shall make the revised agenda available to anyone upon request in advance of the meeting);

Section IV-C-3-g-(2). Proposed Major Actions (see Section IV-C-1-b-(1)) at least 15 days prior to the RAC meeting; and

Section IV-C-3-h. 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 will give its approval to the Institutional Biosafety Committee membership;

*D. Amendments to Section V, Footnotes and References of Section I through IV*

The following sections are deleted:

Section V-U. Human studies in which the induction or enhancement of an immune response to a vector-encoded microbial immunogen is the major goal, such an immune response has been demonstrated in model systems, and the persistence of the vector-encoded immunogen is not expected, are not covered under Sections III-A-2, III-B-2, or III-B-3. Such studies may be initiated without RAC review and NIH approval if approved by another Federal agency.

Section V-V. For recombinant DNA experiments in which the intent is to modify stably the genome of cells of one or more human subjects (see Sections III-A-2, III-B-2, and III-B-3).

Section V-W has been renumbered to Section V-U:

Section V-U. In accordance with accepted scientific and regulatory practices of the discipline of plant pathology, an exotic plant pathogen (e.g., virus, bacteria, or fungus) is one that is unknown to occur within the U.S. (see Section V-R). Determination of whether a pathogen 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 plant diseases, crops, and ecosystems in the geographic area of the research.

*E. Amendments to Appendix C, Exemptions under Section III-E-6*

The following sections are amended to read:

Appendix C-I-A. Exceptions

The following categories are not exempt from the NIH Guidelines: (i) experiments described in Section III-A which require Institutional Biosafety Committee approval, RAC review, and NIH Director approval before initiation.