The rest of Section IV-C-1-b-(2) would be renumbered.

Section IV–C–3, Office of Recombinant DNA Activities (ORDA), is proposed 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 FDA and NIH 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,

In Section V, Footnotes and References of Sections I through IV, the following sections are proposed to be 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 would be 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.

In Appendix C, Exemptions under Section III–E–6, the following sections are proposed 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. \* \* \*

#### Appendix C–II–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.

Appendix C–III–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. \* \* \*

#### Appendix C–IV–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. \* \* \*

## Appendix C-V-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. \* \* \*

Appendix C–VI–A–1. 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). \* \* \*

In Appendix F, Containment Conditions for Cloning of Genes Coding for the Biosynthesis of Molecules Toxic for Vertebrates, the following sections are proposed to be amended due to reference changes:

## Appendix F-I. General Information

. . . The results of such tests shall be forwarded to NIH/ORDA, which will consult with *ad hoc* experts, prior to inclusion of the molecules on the list (see Section IV–C–1–b–(2)–(c)).

Appendix F–III. Cloning of Toxic Molecule Genes in Organisms Other Than *Escherichia coli* K–12

Requests involving the cloning of genes coding for toxin molecules for vertebrates at an  $LD_{50}$  of <100 nanograms per kilogram body weight in host-vector systems other than *Escherichia coli* K–12 will be evaluated by NIH/ORDA in consultation with *ad hoc* toxin experts (see Sections III–B–1 and IV–C–1–b–(2)–(c)).

In Appendix G, Physical Containment, the following section is proposed to be amended due to a reference change:

## Appendix G–II. Physical Containment Levels

\* \* \* Consideration will be given by the NIH Director, with the advice of the