RAC, to other combinations which achieve an equivalent level of containment (see Section IV–C–1–b–(2)–(a).

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

Appendix I–II–A. Responsibility

* * * Proposed host-vector systems will be reviewed by the RAC (see Section IV–C–1–b–(1)–(f). * * * 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). * * * The NIH Director may rescind the certification of a host-vector system (see Section IV–C–1–b–(2)–(g).* * *

Appendix M, The Points to Consider in the Design and Submission of Protocols for the Transfer of Recombinant DNA Molecules into the Genome of One or More Human Subjects (Points to Consider), is proposed to read:

Appendix M. The Points to Consider in the Design and Submission of Protocols for the Transfer of Recombinant DNA Molecules Into the Genome of One or More Human Subjects (Points to Consider)

Appendix M applies to research conducted at or sponsored by an institution that receives any support for recombinant DNA research from the NIH. Researchers not covered by the NIH Guidelines are encouraged to use Appendix M.

The acceptability of human somatic cell gene therapy has been addressed in several public documents as well as in numerous academic studies. In November 1982, the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research published a report, Splicing Life, which resulted from a two-year process of public deliberation and hearings. Upon release of that report, a U.S. House of Representatives subcommittee held three days of public hearings with witnesses from a wide range of fields from the biomedical and social sciences to theology, philosophy, and law. In December 1984, the Office of Technology Assessment released a background paper, Human Gene Therapy, which concluded: civic, religious, scientific, and medical groups have all accepted, in principle, the appropriateness of gene therapy of somatic cells in humans for specific genetic diseases. Somatic cell gene therapy is seen as an extension of present methods of therapy that might be preferable to other technologies. In light of this public support, the Recombinant DNA Advisory Committee (RAC) is prepared to consider proposals for somatic cell gene transfer.

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

In the interest of maximizing the resources of both the NIH and the Food and Drug Administration (FDA) and simplifying the method and period for review, research proposals involving the deliberate transfer of recombinant DNA or DNA or RNA derived from recombinant DNA into human subjects (human gene transfer) will be considered through a consolidated review process involving both the FDA and the NIH. Submission of human gene transfer proposals will be in the format described in Appendices M–I through M–V of the Points to Consider. Investigators must simultaneously submit their human gene transfer proposal to both the FDA and the NIH in a single submission format. This format includes (but is not limited to) the documentation described in Appendices M–I through M–V of the Points to Consider. NIH/ORDA and the FDA will simultaneously evaluate the proposal regarding the necessity for RAC review.

Factors that may contribute to the necessity for RAC review include: (i) new vectors/new gene delivery systems, (ii) new diseases, (iii) unique applications of gene transfer, and (iv) other issues considered to require further public discussion. Among the experiments that may be considered exempt from RAC review are those determined by the FDA and NIH/ORDA not to represent possible risk to human health or the environment (see Appendix M–VII, Categories of Human Gene Transfer Experiments that May Be Exempt from RAC Review). Whenever possible, investigators will be notified within 15 working days following receipt of the submission whether RAC review will be required. In the event that NIH/ORDA and the FDA require RAC review of the submitted proposal, the documentation described in Appendices M–I through M–V of the Points to Consider, will be forwarded to the RAC primary reviewers for evaluation. RAC meetings will be open to the public except where trade secrets and proprietary information are reviewed. The RAC and FDA prefer that information provided in response to Appendix M contain no proprietary data or trade secrets, enabling all aspects of the review to be open to the public. The RAC will recommend approval or disapproval of the reviewed proposal to the NIH Director. In the event that a proposal is contingently approved by the RAC, the RAC prefers that the conditions be satisfactorily met before the RAC's recommendation for approval is submitted to the NIH Director. The NIH Director's decision on the submitted proposal will be transmitted to the FDA Commissioner and considered as a Major Action by the NIH Director.

Public review of human gene transfer proposals will serve to inform the public about the technical aspects of the proposals as well as the meaning and significance of the research.

In its evaluation of human gene transfer proposals, the RAC, NIH/ORDA, and the FDA will consider whether the design of such experiments offers adequate assurance that their consequences will not go beyond their purpose, which is the same as the traditional purpose of clinical investigation, namely, to protect the health and well being of human subjects being treated while at the same time gathering generalizable knowledge. Two possible undesirable consequences of the transfer of recombinant DNA would be unintentional: (i) vertical transmission of genetic changes from an individual to his/her offspring, or (ii) horizontal transmission of viral infection to other persons with whom the individual comes in contact. Accordingly, Appendices M–I through M–V requests information that will enable the RAC, NIH/ORDA, and the FDA, to assess the possibility that the proposed experiment(s) will inadvertently affect reproductive cells or lead to infection of other people (e.g., medical personnel or relatives).

In recognition of the social concern that surrounds the subject of human gene transfer, the RAC, NIH/ORDA, and the FDA, will cooperate with other groups in assessing the possible long-term consequences of the proposal and related laboratory and animal experiments in order to define appropriate human applications of this emerging technology.