Administration), representatives of collaborating institutions, vector suppliers, etc., will have access to the subjects' medical records.

Appendix M–IV. Privacy and Confidentiality

Indicate what measures will be taken to protect the privacy of patients and their families as well as to maintain the confidentiality of research data.

Appendix M–IV–A. What provisions will be made to honor the wishes of individual patients (and the parents or guardians of pediatric or mentally handicapped patients) as to whether, when, or how the identity of patients is publicly disclosed?

Appendix M–IV–B. What provisions will be made to maintain the confidentiality of research data, at least in cases where data could be linked to individual patients?

Appendix M-V. Special Issues

Although the following issues are beyond the normal purview of local Institutional Review Boards, investigators should respond to the following questions:

Appendix M–V–A. What steps will be taken, consistent with Appendix M–IV, Privacy and Confidentiality, to ensure that accurate and appropriate information is made available to the public with respect to such public concerns as may arise from the proposed study?

Appendix M–V–B. Do you or your funding sources intend to protect under patent or trade secret laws either the products or the procedures developed in the proposed study? If so, what steps will be taken to permit as full communication as possible among investigators and clinicians concerning research methods and results?

Appendix M–VI. RAC Review—Human Gene Transfer Protocols

Appendix M–VI–A. Categories of Human Gene Transfer Experiments That Require RAC Review

Factors that may contribute to the necessity for RAC review include, but are not limited to: (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. 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 RAC review is deemed necessary by the NIH and FDA, the proposal will be forwarded to the RAC primary reviewers for evaluation. In order to maintain public access to

information regarding human gene transfer protocols, NIH/ORDA will maintain the documentation described in Appendices M–I through M–V (including protocols that are not reviewed by the RAC).

Appendix M–VI–B. RAC Primary Reviewers' Written Comments

In the event that NIH/ORDA or the FDA recommend RAC review of the submitted proposal, the documentation described in Appendices M–I through M–V will be forwarded to the RAC primary reviewers for evaluation.

The RAC primary reviewers shall provide written comments on the proposal to NIH/ORDA. The RAC primary reviewers' comments should include the following:

Appendix M–VI–B–1. Emphasize the issues related to gene marking, gene transfer, or gene therapy.

Appendix M–VI–B–2. State explicitly whether Appendices M–I through M–V have been addressed satisfactorily.

Appendix M–VI–B–3. Examine the scientific rationale, scientific context (relative to other proposals reviewed by the RAC), whether the preliminary in vitro and in vivo data were obtained in appropriate models and are sufficient, and whether questions related to safety, efficacy, and social/ethical context have been resolved.

Appendix M–VI–B–4. Whenever possible, criticisms of Informed Consent documents should include written alternatives for suggested revisions for the RAC to consider.

Appendix M–VI–B–5. Primary reviews should state whether the proposal is: (i) acceptable as written, (ii) expected to be acceptable with specific revisions or after satisfactory responses to specific questions raised on review, or (iii) unacceptable in its present form.

Appendix M–VI–C. Investigator's Written Responses to RAC Primary Reviewers

Appendix M–VI–C–1. Written responses (including critical data in response to RAC primary reviewers' written comments) shall be submitted to NIH/ORDA greater than or equal to 2 weeks following receipt of the review.

Appendix M–VI–D. Oral Responses to the RAC

Investigators shall limit their oral responses to the RAC only to those questions that are raised during the meeting. Investigators are strongly discouraged from presenting critical data during their oral presentations that was not submitted greater than or equal to 2 weeks in advance of the RAC meeting at which it is reviewed.

Appendix M–VI–E. RAC Recommendations to the NIH Director

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.

Appendix M–VII. Categories of Human Gene Transfer Experiments That May Be Exempt From RAC Review

A proposal submitted under one of the following categories may be considered exempt from RAC review unless otherwise determined by NIH/ ORDA and the FDA on a case-by-case basis (see Appendix M–VI–A, Categories of Human Gene Transfer Experiments That Require RAC Review).

Note: In the event that the submitted proposal is determined to be exempt from RAC review, the documentation described in Appendices M–I through M–V will be maintained by NIH/ORDA for compliance with semiannual data reporting and adverse event reporting requirements (see Appendix M–VIII, Reporting Requirements—Human Gene Transfer Protocols). Any subsequent modifications to proposals that were not reviewed by the RAC must be submitted to NIH/ORDA in order to facilitate data reporting requirements.

Appendix M-VII-A. Vaccines

This category includes recombinant DNA vaccines not otherwise exempt from RAC review (see Appendix M–IX–A for exempt vaccines).

Appendix M–VII–B. Lethally Irradiated Tumor Cells/No Replication-Competent Virus

This category includes experiments involving lethally irradiated tumor cells and: (1) vector constructs that have previously been approved by the RAC (or with the incorporation of minor modifications), or (2) a different tumor cell target.

Appendix M–VII–C. New Site/Original Investigator

This category includes the following: (1) initiation of a protocol at an additional site other than the site that was originally approved by the RAC, and (2) the investigator at the new site is the same as the investigator approved for the original study.