Appendix M–II–B–3–h. If a treated patient dies, what special post-mortem studies will be performed?

Appendix M–II–B–4. Public Health Considerations

Describe any potential benefits and hazards of the proposed therapy to persons other than the patients being treated. Specifically:

Appendix M–II–B–4–a. On what basis are potential public health benefits or hazards postulated?

Appendix M–II–B–4–b. Is there a significant possibility that the added DNA will spread from the patient to other persons or to the environment?

Appendix M–II–B–4–c. What precautions will be taken against such spread (e.g., patients sharing a room, health-care workers, or family members)?

Appendix M–II–B–4–d. What measures will be undertaken to mitigate the risks, if any, to public health?

Appendix M–II–B–4–e. In light of possible risks to offspring, including vertical transmission, will birth control measures be recommended to patients? Are such concerns applicable to health care personnel?

Appendix M–II–B–5. Qualifications of Investigators and Adequacy of Laboratory and Clinical Facilities

Indicate the relevant training and experience of the personnel who will be involved in the preclinical studies and clinical administration of recombinant DNA. Describe the laboratory and clinical facilities where the proposed study will be performed. Specifically:

Appendix M–II–B–5–a. What professional personnel (medical and nonmedical) will be involved in the proposed study and what is their relevant expertise? Provide a two-page curriculum vitae for each key professional person in biographical sketch format (see Appendix M–I, Submission Requirements).

Appendix M–II–B–5–b. At what hospital or clinic will the treatment be given? Which facilities of the hospital or clinic will be especially important for the proposed study? Will patients occupy regular hospital beds or clinical research center beds? Where will patients reside during the follow-up period? What special arrangements will be made for the comfort and consideration of the patients. Will the research institution designate an ombudsman, patient care representative, or other individual to help protect the rights and welfare of the patient?

Appendix M–II–C. Selection of the Patients

Estimate the number of patients to be involved in the proposed study. Describe recruitment procedures and patient eligibility requirements, paying particular attention to whether these procedures and requirements are fair and equitable. Specifically:

Appendix M–II–C–1. How many patients do you plan to involve in the proposed study?

Appendix M–II–C–2. How many eligible patients do you anticipate being able to identify each year?

Appendix M–II–C–3. What recruitment procedures do you plan to use?

Appendix M–II–C–4. What selection criteria do you plan to employ? What are the exclusion and inclusion criteria for the study?

Appendix M–II–C–5. How will patients be selected if it is not possible to include all who desire to participate?

Appendix M–III. Informed Consent

In accordance with the Protection of Human Subjects (45 CFR Part 46), investigators should indicate how subjects will be informed about the proposed study and the manner in which their consent will be solicited. They should indicate how the Informed Consent document makes clear the special requirements of gene transfer research. If a proposal involves children, special attention should be paid to the Protection of Human Subjects (45 CFR Part 46), Subpart D, Additional Protections for Children Involved as Subjects in Research.

Appendix M–III–A. Communication About the Study to Potential Participants

Appendix M–III–A–1. Which members of the research group and/or institution will be responsible for contacting potential participants and for describing the study to them? What procedures will be used to avoid possible conflicts of interest if the investigator is also providing medical care to potential subjects?

Appendix M–III–A–2. How will the major points covered in Appendix M–II, Description of Proposal, be disclosed to potential participants and/or their parents or guardians in language that is understandable to them?

Appendix M–III–A–3. What is the length of time that potential participants will have to make a decision about their participation in the study?

Appendix M–III–A–4. If the study involves pediatric or mentally handicapped subjects, how will the assent of each person be obtained?

Appendix M–III–B. Informed Consent Document

Investigators submitting human gene transfer proposals must include the Informed Consent document as approved by the local Institutional Review Board. A separate Informed Consent document should be used for the gene transfer portion of a research project when gene transfer is used as an adjunct in the study of another technique, e.g., when a gene is used as a 'marker' or to enhance the power of immunotherapy for cancer.

Because of the relative novelty of the procedures that are used, the potentially irreversible consequences of the procedures performed, and the fact that many of the potential risks remain undefined, the Informed Consent document should include the following specific information in addition to any requirements of the DHHS regulations for the Protection of Human Subjects (45 CFR 46). Indicate if each of the specified items appears in the Informed Consent document or, if not included in the Informed Consent document, how those items will be presented to potential subjects. Include an explanation if any of the following items are omitted from the consent process or the Informed Consent document.

Appendix M–III–B–1. General Requirements of Human Subjects Research

Appendix M–III–B–1–a. Description/ Purpose of the Study

The subjects should be provided with a detailed explanation in non-technical language of the purpose of the study and the procedures associated with the conduct of the proposed study, including a description of the gene transfer component.

Appendix M–III–B–1–b. Alternatives

The Informed Consent document should indicate the availability of therapies and the possibility of other investigational interventions and approaches.

Appendix M–III–B–1–c. Voluntary Participation

The subjects should be informed that participation in the study is voluntary and that failure to participate in the study or withdrawal of consent will not result in any penalty or loss of benefits to which the subjects are otherwise entitled.

Appendix M–III–B–1–d. Benefits

The subjects should be provided with an accurate description of the possible benefits, if any, of participating in the proposed study. For studies that are not reasonably expected to provide a therapeutic benefit to subjects, the