IBC Considerations in Evaluating Gene Transfer Protocols

Investigational Brochure:

- document produced by the sponsor which summarizes previous findings and data
- may include information about previous animal experiments and clinical trials
- describes previous adverse events(if applicable)

Clinical Protocol:

- is the description of the therapy and will include all participants in a multi-center clinical trial
- describes the scope of the work
- details the procedures to be performed during the therapy

Why

1. Why is this research being done?
   - Appendix M-II-A-1-a,b,c,d
   - Informed consent form
   - Appendix M-III-B-1-a
   - IBC form summaries

Vector/construct

2. Evaluate the potential of risk of the vector to patients (subjects), family members, staff members, or the environment
3. Evaluate the source of the vector (company sponsor, proprietary name, biosafety level)
   - Investigational Brochure
   - IBC form
4. What vector is being used?
   - Appendix M-II-B-1-a-(1)
5. What is the structure of the cloned DNA?
   - Appendix M-II-B-1-a
6. What regulatory elements does the construct contain?
   - Appendix M-II-B-1-a-(2)
7. How is the DNA construct derived?
   - Appendix M-B-1-a-(3)
8. What is the dose:to be given?
   - IBC form
   - Clinical protocol
9. What is the structure of the material to be administered to the research participant?
10. How is it prepared, grown, purified, tested for contamination?
    - Appendix M-II-B-1-b
    - Investigator's Brochure (May)

Risks/Models/Monitoring

11. Evaluate the adverse events in previous clinical trials and animal studies to predict the potential of similar events in future trials
12. Establish the appropriate level of monitoring for potential microbial shedding
13. Evaluate how the animal and cultured cell models are similar to and different from the proposed human treatment
14. Evaluate how the experimental treatment will be monitored for Pathogenicity and the sensitivity of the analyses.

15. What preclinical studies and risk-assessments have been done?
    - Appendix M-II-B-2
16. What are the intended target cells of the recombinant DNA?
    - Appendix M-II-B-2-a
17. How efficient is this delivery system? How will this be monitored? How many copies per cell?
    - Appendix M-II-B-2-a-(2), (3), (4)
18. What animal and cell culture models were used to assess the efficacy of the gene transfer system?
    - Appendix M-II-B-2-b-(1)
19. How will it be determined that new gene sequences have been inserted and that these are being expressed?
    - Appendix M-II-B-3-d
20. Is the gene expressed in cells other than the target cells? If yes, the extent of this expression must be described.
    - Appendix M-II-B-2-b-(6)
21. How will contaminants be detected and effects assessed?
    - Appendix M-II-B-3-e
22. What are the major beneficial and adverse effects of the experimental treatments anticipated?
    - Appendix M-II-3-g
23. If a treated human subject dies, what special post-mortem studies will be performed?
    - Appendix M-II-3-h

Public Health/Exposure Control

24. Evaluate the efficacy or potential benefits of the therapy versus the biohazard or other toxicity risk with regard to alternative therapy
25. Evaluate if any pre-existing patient medical conditions among the recruited subjects may amplify the risks. Appendix M-II-C
26. What are the potential benefits and hazards to persons other than the human subjects receiving the experimental treatment or to the environment? How will the risks be mitigated?
    - Appendix M-II-B-4
    - Informed consent document
    - Exposure control plan
27. Evaluate the containment issues: medical waste disposal, personal protective equipment, disinfection/sterilization, hand washing and other good work practices
    - Exposure control plan
28. Evaluate the training plan
    - Does it describe gene transfer procedures, risks to patient and staff, exposure control plan?
    - Who will be trained (operating room staff, clinic staff, environmental services, pharmacy, infection control, security, facilities management, respiratory therapy, occupational therapy, nutritional services, etc.)

Qualifications of Investigators/Facilities

29. What training and experience do the principal investigators have with gene transfer and with these procedures specifically?
30. What specific facilities (operating rooms, clinics, patient care areas, etc) will the patient be in?
    - Appendix M-II-B-5
    - Informed Consent
        - The IRB is required to approve this and this approval must be sent to the IBC
        - The IBC can review this form and it is also covered in Appendix M-III-B

Privacy Concerns

- Appendix M-IV