APPENDIX 6

Description of the Proposed Experiment in Nontechnical Language

Cystic fibrosis (CF) is the most common inherited disease among the white population of Europe and North America. It is characterized by chronic infection and obstruction of the airways leading to the lungs. Patients usually die from the disease by their mid twenties. The recent discovery and characterization of the inherited material - the gene - that causes the disease has lead to a rapid increase in our knowledge of the basic defect responsible for the disease state, and has raised the possibility of treating CF by giving to the patient a good copy of the CF associated gene. This is a new approach to the treatment of inherited diseases, called gene therapy.

Eventually gene therapy for cystic fibrosis might be achieved by treating the airways of CF patients with a "tailor-made" virus that has been altered to make it less infectious and to include the CF gene. One possible virus to do this is called adenovirus. It is normally associated with minor respiratory infections, such as colds. Although adenoviruses have been used safely in the past as vaccines, we need to test the feasibility and safety of using such an approach.

This proposal is to treat three CF patients with very small amounts CF-adenovirus and to test whether we can measure correction of the basic defect associated with the disease. Virus will be applied to a small area within the nose and a small electrode will be used to measure the tiny voltage that normally exists across the lining of the nose. In patients with CF, this voltage is abnormal because of a defect in the CF gene.

We hope to be able to measure such voltages in CF patients treated with the virus just as we have been able to do using cells taken from the nose of patients and grown in the laboratory. This will be the first step in developing CF gene therapy. We will also do extensive tests to establish whether the treatment was safe. If this is the case, we shall plan to extend the study to treat larger areas of the lung.