Corrected Table (Incorrect protocol number was reported at the Sept. meeting for the 5-14-97 event. Correct number is below.)

SAFETY REPORTS, ADVERSE EVENTS AND UPDATES FOR HUMAN GENE TRANSFER PROTOCOLS RECOMBINANT DNA ADVISORY COMMITTEE MEETING SEPTEMBER 12, 1997

5-14-97	**9403-069 Walker**	**A Study of the Safety and Survival of the Adoptive Transfer of Genetically Marked Syngeneic Lymphocytes in HIV Infected Identical Twins.** **Update:** *Follow up to 2/28/97 report of hospitalization.* Dr. Walker previously reported on a patient who was hospitalized in February for pulmonary infiltrates and azotemia. "Subsequent evaluation led to the diagnosis of lymphoproliferative process on the basis of an axillary lymph node biopsy, and chemotherapy was begun. The final diagnosis monoclonal lymphoproliferative disorder with plasmacytoid differentiation (monoclonal lambda light chain expressing), not consistent with EBV-associated lymphoma. In addition to the histopathology and immunocytochemistry, we performed DNA PCR for murine retrovirus on fresh-frozen tissue samples from lung and lymph node obtained from the outside hospital. No murine retrovirus sequences were detected, arguing against a role played by the retroviral vector in inducing this process. This patient will continue to be followed in our clinic, but will not receive any further infusions of genetically engineered cells on the protocol due to the development of this lymphoproliferative disorder. Lymphomas and lymphoproliferative processes are well-documented complications of HIV-1 infection."
8-12-97	**9403-069 Walker**	**A Phase I/II Pilot Study of the Safety of the Adoptive Transfer of Syngeneic Gene-Modified Cytotoxic T-Lymphocytes in HIV-Infected Identical Twins** *(study closed to new patient accrual as of 2-97)* **Update on the status of the protocol:** To date a total of 86 patients have been enrolled in the protocol out of a maximum of 100 (50 sets of twins). The study is divided into four cohorts and three treatment periods. In Treatment Period 1, patients received a single dose of either unmodified or up to 10^{10} modified T-cells. Fifty-four patients (27 sets of twins) participated in period 1. In period 2, patients received repeated infusions (every 8 weeks for a total of 6 infusions over one year) of 10^{10} modified, the maximum dose from period 1 that was deemed safe, or 10^{10} control cells. Thirty-three patients are participating in the portion of the study; the final cell infusion was performed on 6-30-97, and all of the patients are in long-term follow-up. Data analysis will begin shortly to evaluate period 2. A third treatment period (protocol extension) that employed gene modified CD4 and CD8 cells (the first periods used only CD8 cells) was added as an amendment, dated 3-17-97. Eighteen patients out of the 33 who participated in period 2 are participating in period 3. As of this date, four of the 18 patients have received one or more cell infusions. In general, Dr. Walker reports that "the cell infusions have been extremely well tolerated. Most of the adverse events that have occurred on the study are attributable to advanced HIV infection, to antiretroviral therapy, or to IL-2."

8-13-97	**9610-164 Sung and Woo**	**Phase I Trial of Adenoviral Vector Delivery of the Herpes Simplex Thymidine Kinase Gene by Intratumoral Injection Followed by Intravenous Ganciclovir in Patients with Hepatic Metastases** **One adverse event:** Possibly related to major concomitant medication. Patient received a dose of 1 x 10^9 pfu of Adv.RSV-tk into hepatic metastasis. Intravenous ganciclovir (5 mg/kg) was administered every 12 hours starting one day after vector injection. Patient had a decreased white blood count (3.6/uL) one day after initial ganciclovir administration. Hemoglobin and platelet count were normal. Ganciclovir was continued and white blood count was normal (5.7/ul) two days after vector injection. Adverse reaction was determined by PI as hematological grade 1 (WBC). Reaction was deemed to be possibly related to ganciclovir administration. The rapid onset of decreased white blood count and rapid resolution with continuation of ganciclovir is not usual for ganciclovir-related myelosuppression. Changes were not made to the study protocol or informed consent document due to this adverse event.