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**Serious and Other Selected Adverse Events  
Reported for Human Gene Transfer Protocols  
Recombinant DNA Advisory Committee Meeting  
December 2008**

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Protocol Number: **480**

Protocol Title: **A Phase II, Open-Label, Ascending Dose Study of the Safety and Efficacy of Trinam™ (EG004) in Stenosis Prevention at the Graft-Vein Anastomosis Site in Dialysis Patients.**

<b>DocID#</b>	<b>Receipt Date</b>	<b>Event Description</b>
9932	01/10/2008	Twelve weeks after receiving the gene transfer product, a scheduled test revealed narrowing in the arteriovenous graft (dialysis access) that required an angioplasty (opening of the graft). This is a known complication of arteriovenous fistulas.
9933	01/10/2008	The subject underwent angioplasty of the arteriovenous graft due to narrowing twelve weeks after receiving the gene transfer. The event was possibly related to the gene transfer but such narrowing is also a known complication of such grafts.
9934	01/10/2008	Approximately one week after the subject had a procedure done to open up a narrowing in the arteriovenous (A-V) graft, the subject developed a clot in the A-V graft necessitating surgery and removal of part of the A-V graft. An alternative dialysis access was established. This is a known complication of A-V grafts.
9935	01/10/2008	Four weeks after the gene transfer the subject had a study to assess the patency of the arteriovenous graft. It revealed a narrowing that had to be opened with opened by angioplasty. This is a known complication of arteriovenous grafts.

Protocol Number: 530

Protocol Title: **A Randomized, Phase II/III Study of TNFerade™ Biologic with 5-FU and Radiation Therapy for First-Line Treatment of Unresectable Locally Advanced Pancreatic Cancer.**

DocID#	Receipt Date	Event Description
10020	10/27/2008	Elderly subject admitted with significant gastrointestinal bleeding approximately 2 months after receiving the last dose of TNFerade. The subject had been admitted for gastrointestinal bleeding about 4 weeks prior to this admission. Endoscopy was limited by active bleeding but it is postulated that the bleeding was from the duodenal bulb which is located at the end of the stomach and connects to the pancreatic head. Subject died secondary to the gastrointestinal bleed.
e-Filed	08/01/2008	Approximately 6 weeks after the last dose of the TNFerade, the subject underwent a post study treatment computed tomography scan and a blood clot in the lung was discovered. The subject was asymptomatic. The subject was hospitalized to initiate treatment with medicines to prevent a new clot. Further testing revealed an asymptomatic deep vein thrombosis in the lower right extremity.
9919	09/08/2008	Two months after receiving the final dose of the TNFerade the subject was found to have a deep vein thrombosis in the lower extremity. The subject was treated and recovered.
10022	10/28/2008	Subject experienced vomiting and dark maroon colored stools approximately 4 months after the last dose of the study agent. The subject was taken to a local hospital and received a blood transfusion after losing blood from the gastrointestinal tract.
9980	10/08/2008	Approximately 2 months after the last dose of the TNFerade, this elderly subject was admitted for treatment of back pain and underwent an injection into the lower back nerves to stop the pain. It was thought that the pain might be related to the locally advanced cancer. A magnetic resonance image of the thoracic and lumbar spine did not show any metastatic disease. The principal investigator judged the event as possibly related to TNFerade.

Protocol Number: 585

Protocol Title: **A Phase I Study of Sequential Vaccinations with Fowlpox-CEA(6D)-TRICOM (B7.1/ICAM/LFA3) and Vaccinia-CEA(6D)-TRICOM, in Combination with GM-CSF and Interferon-Alfa-2B in Patients with CEA Expressing Carcinomas.**

DocID#	Receipt Date	Event Description
9941	09/19/2008	Approximately one month after the first gene transfer vaccine, subject presented to clinic for the second vaccine and reported having had a brief episode of chest pain three days earlier. Blood tests were suggestive of myocardial injury. Subject was found to have a severe stenosis in a coronary artery and had a stent placed to open the narrowing. Subject was a former smoker. The subject recovered.

Protocol Number: 661

Protocol Title: **A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Multicenter, Dose-Selection Study of Ad2/Hypoxia Inducible Factor (HIF)-1 $\alpha$ /VP16 in Patients with Intermittent Claudication.**

DocID#	Receipt Date	Event Description
9923	09/15/2008	433 days after receiving blinded study treatment (gene transfer agent or placebo), the subject was diagnosed with lymphoma. A whole body positron emission scan done for initial staging of lymphoma showed multiple lymph nodes in the chest, abdomen and inguinal area. These were consistent with lymphoma. A relationship to the blinded study agent could not be ruled out.
9966	09/30/2008	Approximately one year after receiving either the study agent or placebo, the subject developed bilateral lower extremity ulcers that failed to heal.
10031	11/04/2008	Subject had an abnormal mammogram about a year after receiving the gene transfer or placebo. The subject was asked to have a follow-up mammogram in six months. Less than 2 years after dosing the subject was admitted to the hospital for resection of a low grade ductal carcinoma in situ of the right breast. The surgery and postoperative course went as expected without complications and the subject was discharged home.

Protocol Number: 680

Protocol Title: **A Phase I Study of Regulatory T Cell Depletion with Denileukin Diftitox Followed by Active Immunotherapy with Autologous Dendritic Cells Infected with CEA-6D Expressing Fowlpox-TRICOM in Patients with Advanced or Metastatic Malignancies Expressing CEA.**

DocID#	Receipt Date	Event Description
e-Filed	08/11/2008	The subject reported to the clinic to receive the second of four vaccines. The subject was on two medications to treat hypertension. Prior to receiving the vaccine the subject had a blood pressure that was low but still within normal range. After the vaccination, the subject had a drop in blood pressure below 100 systolic. The subject was asymptomatic. The subject was taken to hospital, give fluids intravenously, the blood pressure returned to baseline and the subject was discharged.

Protocol Number: 694

Protocol Title: **Phase I Trial of a PSA Based Vaccine and an Anti-CTLA-4 Antibody in Patients with Metastatic Androgen Independent Prostate Cancer.**

DocID#	Receipt Date	Event Description
9869	08/01/2008	Subject had been receiving the gene transfer vaccines for 5 months when he was admitted with complaints of a rash, weakness and fatigue. The rash responded to steroid creams. The subject was diagnosed with a urinary tract infection and subject's blood lab levels indicated possible early adrenal insufficiency. The subject was started on oral steroids, antibiotics and was then discharged. The principal investigator could not rule out the possibility that the fatigue was caused by the gene transfer agent.

Protocol Number: 708

Protocol Title: **A Phase 3 Randomized, Open-Label Study of Docetaxel in Combination with CG1940 and CG8711 versus Docetaxel and Prednisone in Taxane-Naive Patients with Metastatic Hormone-Refractory Prostate Cancer with Pain.**

DocID#	Receipt Date	Event Description
9854	07/24/2008	Approximately one week after the first dose of the gene transfer cancer vaccine by injection into the leg, the subject was admitted with swelling and redness of the entire lower extremity. The subject was admitted for cellulitis (skin infection) and was noted to have lymph nodes that were compressing a vein in the leg and may have therefore contributed to the swelling. It is unclear as to whether this was an infection or an injection site reaction to the vaccine. Subject responded to treatment and was discharged.

Protocol Number: 721

Protocol Title: **A Phase I Trial for the Treatment of Purine Analog-Refractory Chronic Lymphocytic Leukemia Using Autologous T Cells Genetically Targeted to the B Cell Specific Antigen CD19**

DocID#	Receipt Date	Event Description
e-Filed	11/11/2008	Subject had extensive previous treatments for chronic lymphocytic leukemia prior to enrolling in the trial. The day of infusion of the modified T-cells, the subject's labs were stable. That night the subject developed a fever that persisted. Antibiotics were started. By the following morning the subject developed low blood pressure and difficult breathing. The subject developed kidney failure. Subject continued to have worsening difficulty with breathing and low blood pressure and passed away that night. The clinical picture appeared to be consistent with sepsis leading to renal failure and death. The investigator felt the evidence did not support a role for the T-cells leading to extensive tumor destruction and renal failure, however, due to the temporal relationship between dosing and the subject's death a possible contribution could not be ruled out.

Protocol Number: 785

Protocol Title: **TRIST (TroVax Renal Immunotherapy Survival Trial) An International, randomized, double-blind, placebo controlled, parallel group study to investigate whether TroVax added to first-line standard of care therapy, prolongs the survival of patients with locally advanced or metastatic clear cell renal adenocarcinoma**

DocID#	Receipt Date	Event Description
9969	10/01/2008	Shortly after starting on the study, this subject, who was receiving anticoagulation with coumadin, was found to have an elevation in the prothrombin time above what was the goal for anticoagulation with warfarin. This was thought to be due to an interaction between sunitinib and warfarin. The subject also had a transient ischemic attack (TIA). A reason for the TIA was not found as a brain magnetic resonance imaging study, an echocardiogram, electrocardiogram and carotid dopplers were all normal. The subject recovered. The principal investigator felt that the TIA was possibly related to the blinded trial medication (i.e. the gene transfer or placebo) and/or the sunitinib.
9894	08/22/2008	Subject had completed over 30 weeks of vaccine when subject was found to have a blood clot in the lung on a computed tomography scan done to evaluate for disease progression. The subject was asymptomatic and received medication to prevent further blood clots.

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Protocol Number: 828

Protocol Title: **A Phase I, Open-Label, Dose Escalation Study of the Safety and Preliminary Efficacy of EGEN 001 in Combination with Carboplatin and Docetaxel in Women with Recurrent, Platinum-Sensitive, Epithelial Ovarian Cancer**

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DocID#	Receipt Date	Event Description
10002	10/21/2008	Subject experienced hypotension and low oxygen levels starting approximately 12 hours after receiving the study agent. The subject also developed a fever. Antibiotics were administered but cultures done during admission did not reveal a source of infection. Subject recovered with intravenous fluid administration and oxygen therapy. The principle investigator believed this "systemic inflammatory response" was probably related to the study agent.

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Protocol Number: 853

Protocol Title: **A Phase 1, Open-Label, Dose-Escalation, Multiple Dose Study of the Safety, Tolerability, and Immune Response of CRS-207 in Adult Subjects with Selected Solid Tumors Who Have Failed or Who Are Not Candidates for Standard Treatment**

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DocID#	Receipt Date	Event Description
9896	08/26/2008	Subject was infused with CRS-207, the study agent. The subject developed a fever to 38.8 degrees celsius, chills, and shaking (rigors) on the day of infusion for which subject was given ibuprofen. Subject also given a muscle relaxant for the rigors. Overnight, subject experienced heartburn and later during the evening developed bilateral flank pain. In the morning the subject had nausea and vomited on three occasions and was given medications for these symptoms. The flank pain worsened over the course of the day requiring narcotic pain medication. The subject admitted to having at least 4 similar previous episodes of abdominal pain and cramping in the past, which were related to constipation. With laxatives subject was able to have a bowel movement and the abdominal pain abated. The Investigator coded the event as possibly related to study product. This was based on the close temporal relationship of the event to study drug administration along with the induction of rigors, fever, and possible dehydration. In addition, the investigator reported that although the subject felt that some of the symptoms were similar to previous episodes at home, the vomiting was more severe.

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