SAFETY REPORTS AND ADVERSE EVENTS FOR
HUMAN GENE TRANSFER PROTOCOLS
RECOMBINANT DNA ADVISORY COMMITTEE MEETING
JUNE 28-29, 2000

ID #	OBA Date	Protocol	Description
807	3/21/00	C95-084 Sponsor: Schering	A Phase I Study in Patients with Peritoneal Carcinomatosis Using SCH 58500 (rAd/p53) Administered by Single Intraperitoneal Instillation. Initial; Event: Hospitalization for leukopenia (WBC: 1.8) Pt is F with diagnosis of ovarian cancer. Event is considered grade 3 (NCI) in severity. Event deemed "possibly associated" with IND agent.
809	3/21/00	C95-084	Initial; Events: 1. Vasovagal episode 2. Associated hypotension (both grade 3 severity [NCI]). Pt is F with diagnosed metastatic ovarian cancer. Pt received 500 ml IP of IND product. Resulting abdominal distention is the suspected cause of the event. Deemed "possibly associated" with IND study drug.
812	3/21/00	C95-084	Initial; Events: 1. Fever (40 °C) [gr 2] 2. Hypotension [gr 3] 3. Loss of consciousness [gr. 3]. Pt is F with diagnosis of stage III ovarian cancer. Hospitalized for IP administration of IND agent. Events are deemed "possibly associated" with IND study drug administration
814	3/21/00	C95-084	Initial; Event: Anaphylactic reaction (itching, tachycardia, lightheadedness and hypotension). (Investigator submission of ID#510– reviewed at March RAC meeting) Patient is F with diagnosis of ovarian cancer and advanced peritoneal involvement. Patient had received 2 previous cycles of Adp53 with concurrent chemo (taxol + carboplatin); no complications were noted. For the 3rd cycle, the patient was hospitalized. After receiving 2 doses of Adp53, the patient developed fever, nausea, vomiting, malaise; dosing was interrupted. A 3rd dose was administered later that day followed by chemo (carboplatin). Itching at IV site noted. Within 8 minutes of receiving the chemo, the patient experienced lightheadedness and became agitated; BP fell to: 37/23 with a HR of 140. Chemo was interrupted and 500 ml IV saline was administered. Chemo was resumed within 10 min and was successfully completed. The patient was subsequently treated with IV Dexamethasone and

			Benadryl. BP increased to 121/64 within a matter of hours. The patient was discharged within four days of the treatment. The PI initially reported the event (anaphylaxis) as possibly associated with Adp53. On Follow-Up 1 (F/U1), the sponsor considers anaphylaxis as possibly associated with chemo and unlikely to be associated with Adp53.
820	3/21/00	C95-084	Initial; Events: 1. Pharyngitis. 2. Lymphadenopathy. Pt is F with advanced ovarian carcinoma. Admitted to hospital post administration of study drug for sore throat [gr 1] and painful adenopathy [gr 1]. Events are deemed "possibly associated" with IND study drug administration.
821	3/21/00	C95-084	Initial; Events: Transient Ischemic Attack. Pt is F with advanced ovarian carcinoma. Following IP administration of study drug, pt appeared confused [gr 3] and aphasic [gr 3] and was hospitalized. Pt had no prior history of coronary artery disease, hypertension or venous / arterial thrombosis. Event is considered "possibly associated" to IND study drug administration.
825	3/21/00	C95-084	Initial; Events: 1. Severe nausea. 2. Vomiting. 3. Gastritis. 3. Weakness 4. Fever (38 °C). Pt is F with metastatic ovarian carcinoma. Pt was hospitalized for treatment of nausea (gr 3), vomiting (gr 3), gastritis (gr 2), weakness (gr 2) and fever (gr 1). Events are considered possibly associated with administration of study drug.
827	3/21/00	C95-084	Initial; Events: 1. Fatigue. 2. Malaise 3. Nausea. 4. Vomiting 4. Fever (39.2 °C). 5. Tachycardia Pt is F with metastatic ovarian carcinoma. Pt was hospitalized for treatment of fatigue and malaise (gr 2) nausea (gr 1), vomiting (gr 2), fever (gr 2), and tachycardia (gr 2). Events are considered possibly associated with administration of study drug and chemotherapy (Taxol).
831	3/21/00	C95-084	Initial; Events: 1. Nausea (gr 3), 2. Vomiting (gr 3), 3. Abdominal pain (gr 3), 4. Dehydration (gr 3), 5. Tachycardia (gr 2). Pt is F with metastatic ovarian carcinoma. Pt had previously undergone three cycles of Adp53 /Topotecan treatment. (Last cycle: 2/26/99). Pt was hospitalized on 3/10/99. Suspected cause of event: Bowel obstruction. Events are considered possibly associated to Adp53 administration
1378	5/19/00	Sponsor: Novartis	Gene Therapy for the Treatment of Recurrent Pediatric Malignant Astrocytomas with In Vivo Tumor Transduction with the Herpes Simplex Thymidine Kinase Gene.

			Initial. Events: 1. Cerebral Edema, 2. Nausea, 3. Vomiting. Pt. had episodes of nausea & vomiting associated w/ concurrent cerebral edema. Event occurred on day 15 (5/23/96) post vector administration (5/8/96). Condition resolved on 5/25/96 w/o residua effects. Event was deemed "possibly associated" with administration of study drug (retrovirus-HSV-TK).
544	2/24/00	6406-079 Roth	Clinical Protocol for Modification of Tumor Suppressor Gene Expression and Induction of Apoptosis in Non-Small Cell Lung Cancer (NSCLC) with an Adenovirus Vector Expressing Wildtype p53 and Cisplatin. Initial; Event: 1. Dyspnea. Pt is M with diagnosis of non small-cell lung cancer (NSCLC). Pt had been previously treated with chemo, radiation and surgery. Pt had numerous occurrences of tumor masses when entering study. New tumors were found in the tracheal area, causing constriction of the airway. Pt rcv'd 5 doses of cisplatin and Ad p53. Two days after last trtmt, pt was admitted to emergency room complaining of increasing dyspnea over the past 48 hrs. Dyspnea was caused by consolidation and collapse of Rt upper lung lobe (RUL) from interstitial fluid accumulation. Pt was removed from study due to disease progression on day 3 post administration. Pt eventually succumbed to his disease. The event dyspnea due to consolidation and collapse of the RUL, was considered possibly associated with the study treatment since fluid accumulation occurred in the injectio field. An autopsy was not performed.
570	2/24/00	079	Initial; Events: 1. Shortness of breath, 2. Pleuritic pain, 3. Rectal incontinence. Pt diagnosed with NSCLC metastasized to brain. Priors included stereotactic radiosurgery w/o chemo. Pt was enrolled in study and treated with cisplatin and Adeno p53 administered to right lower lung lobe (RLL). Four days post-administration of Adp53, pt was hospitalized for SOB, pleuritic pain and rectal incontinence. Chest X-ray revealed atelectasis and edema in the RLL. Blood, stool and sputum cultures negative. Seven days later, lesion was biopsied by bronchoscopy. Edema around injection site and necrosis were noted. Repeat chest X-ray seven days later demonstrated air/fluid and consolidation in the RLL. Pt was treated with steroids and antibiotics. Discharged 21 days post-administration of IND product. Relationship to study treatment is unknown, events are deemed "possibly associated" to study drug by default.
571	2/24/00	079	Initial; Events: 1. Abscess RLL, 2. Dehydration, 3. Productive cough, 4. Hypertension, 5. Pain 6. Diarrhea. *(see ID#570 abve)* Four days following discharge from hospital Pt (see ID #570) was

			readmitted to hospital. CT scan showed evidence of RLL pulmonary abcess, positive for bacterial infection upon culture. Pneumonectomy of the RLL was performed. Pathology report indicated extensive necrosis of tumor tissue. X-ray and CT scan showed that lesion was not regressing with antibiotic treatment. Abcess was continuous with tumor. Right pneumonectomy performed. Relationship to study treatment is unknown, events are deemed "possibly associated" to study drug by default.
572	2/24/00	079	Initial: Event: 1. Hemoptysis Pt was diagnosed with NSCLC. Prior treatments included surgery (RUL and RML removal), radiation, gene transfer, chemo (cisplatin + VP-16; Taxol, Navelbine). At study entry pt had LLL metastases and was treated with Adp53. Pt presented to ER 3 weeks pot treatment for hemoptysis. Condition improved over the 24 hr period and pt was discharged *(see below ID# 573)*
573	2/24/00	079	Initial: Event: 1. Increased hemoptysis Pt *(see ID #572)* readmitted to hospital on same day due to worsening hemoptysis. Bronchio ateriogram and angioembolization performed. Procedure revealed hypervascularity, a small aneurysm shunting in LM & LLL near the tumor mass; presence of infiltrates. Hemoptysis decreased in severity over the next 24 hrs. Bronchoscopy was performed the following day to remove blood clot and mucus plug in the LLL. The pulmonologist felt the hemoptysis was related to the tumor. Pt was removed from study for radiation therapy. The PI indicated that hypervascularity, aneurysm shunting and infiltrate were in the injection area. Because of this association, the event is considered "possibly associated" with study treatment.
1634	5/31/00	9502-099 Sponsor: Novartis	Stereotaxic Injection of Herpes Simplex Thymidine Kinase Vector Producer Cells (PA317/G1TkSvNa.7) and Intravenous Ganciclovir for the Treatment of Recurrent Malignant Glioma. Initial; Event: Fever (gr 2). Pt. developed fever on day of vector administration requiring prolonged hospitalization. Pt recovered w/o residuals *(see ID #1633)*. Event deemed "possibly associated" to study drug.
1633	5/31/00	099	Initial; Events: 1. Headache, 2. Nausea, 3. Vomiting, 4. Right side weakness, 5. Confusion and 6. Meningitis. *(see 1634 above)* Symptoms manifest one day post-vector administration. Condition resolved on day 23 post administration w/o sequelae. Event deemed "possibly associated".
1618	5/31/00	099	Initial; Event: 1. Cerebral edema

			Pt.diagnosed w/ Glioblastoma Multiforme of L parietal occipital brain; Pt Hospitalized for cerebral edema on day 4 post administration of retroviral_HSV-TK vector. Pt showed signs of unsteady gait, disorientation, urinary retention, speech difficulties and confusion. CT scan showed masogenic edema of posterior parietal lobes, cephalad region and centrom. Condition resolved on day 5. Event deemed possibly associated with study drug.
1700	5/26/00	9608-157 Sponsor: Novartis	Prospective, Open-Label, Parallel-Group, Randomized Multicenter Trial Comparing the Efficacy of Surgery, Radiation, and Injection of Murine Cells Producing Herpes Simplex Thymidine Kinase Vector Followed by Intravenous Ganciclovir Against the Efficacy of Surgery and Radiation in the Treatment of Newly Diagnosed, Previoulsy Untreated Glioblastoma. Initial; Event: 1. Fever On day 3 following administration of vector, pt experienced post-operative fever. Blood and urine cultures were negative for growth. PI considered event as a possible chemically-induced meningitis related to vector producer cells. The fever resolved w/ antibiotics and increased glucocorticoids. Event deemed "possibly associated" with IND study drug.
1696	5/26/00	157	Initial; Event: 1. Hemiparesis (left side) Pt experienced L hemiparesis on day of vector administration. Condition improved. Event deemed "possibly associated" with vector administration.
478	2/15/00	9612-170 Sorscher Sponsor: Genzyme	Safety and Efficiency of Gene Transfer of Aerosol Administration of a Single Dose of a Cationic Lipid/DNA Formulation to the Lungs and Nose of Patients with Cystic Fibrosis. Initial; Events: 1. Decrease in Forced Expiratory Volume (FEV) and Forced Vital Capacity (FVC) 2. Myalgia. Pt is F with cystic fibrosis; under medication. One hour after delivery of study drug via nebulizer administration, pt reported wheezing with concomitant drop in FEV and FVC. Pulmonary auscultation indicated bilateral expiratory wheezes from upper lobes. Pt was treated with Albuterol with some improvement although FEV and FVC had decreased further. Pt complained of myalgia localized to upper back. Treatments with Ventolin and analgesics were initiated. Pt improved steadily over the next 48 hrs and was released. Events were considered "probably associated" with delivery of study medication.
479	2/15/00	170	Initial; Events: 1. Supraventricular Tachycardia (SVT), 2. Lightheadedness, 3. Fever (101.4 °F), 4. Myalgia, 5. Headache.

			Pt is F diagnosed w/ CF; under medication and w/ history of heart palpitations. On day of IND study drug administration, pt complained of tachycardia, lightheadedness and flu-like symptoms (fever, myalgia and headache). Heart rate was 160-170 w/ BP at 120-140. Pt was admitted to GCRC for observation; bedside telemetry demonstrated episodes of SVT w/o ischemic changes. Flu symptoms resolved within 6-8 hours. Differential diagnosis: 1. Unrelated chronic SVT, 2. Drug-induced SVT; 3. Exacerbated of chronic SVT. The later is favored based on pt history. Conditions resolved progressively over 15 days post delivery. Events considered "probably associated" with study drug.
475	2/15/00	170	Initial; Events: 1. Fever (102.6 °F), 2. Myalgia. Pt is F with CF; under medication. 12 hrs after receiving test agent (aerosol delivery), pt complained of fever and muscle aches. Symptoms were treated with analgesics. Condition resolved within 24 hrs; no sequelae. Events deemed "probably associated" with IND study drug.
472	2/15/00	170	Initial; Events: 1. Decreased FEV and FVC, 2. Myalgia. Pt is M w/ CF; under medication. Six hrs post delivery, pt complained of respiratory symptoms, mild chest tightness, low grade fever (100.3 °F). Spirogram revealed 20% drop in pulmonary function values which resolved with Albuterol administration. Pt later complained of addominal cramping, generalized malaise and bilateral earache. All symptoms resolved within 36 hours. The pt subsequently reported intermittent myalgias and malaise for 4-7 days. CPK levels were elevated but normalized within one week. Pt had performed strenuous physical exercise in the course of moving to a new residence. All symptoms resolved within a 14 day period. Event: decreased pulmonary function values, and flu-like symptoms were considered "possibly associated" with clinical test material.
477	2/15/00	170	Initial; Events: 1. Fever, 2. Shortness of breath, 3. Headache, 4. Episodes of coughing Pt is M w/ CF; under medication. Pt complained of fever (101.9 °F), SOB, headache, prolonged coughing, O2 saturation was 86-90%, 90 min post administraion of clinical test material. Pt was treated with, Ventolin, Tylenol, and antibiotics. Pt was discharged on day 3; PFTs returned to baseline within 2.5 months.
1102	4/10/00	9701-173 Croop	A Pilot Study of Dose Intensified Procarbazine, CCNU, Vincristine (PCV) for Poor Prognosis Pediatric and Adult Brain Tumors Utilizing Fibronectin-Assisted, Retroviral-Mediated Modification of CD34+ Peripheral Blood Cells with O^6-Methylguanine DNA Methyltransferase Initial: Event: Pruritis (gr 3)

			Pt is F undergoing autologous stem cell reinfusion for treatment of glioblastoma multiforme. Following the fourth cycle of chemo & stem cell reinfusion, the pt developed intermittent urticaria 1 mo post treatment. There was no evidence of rash, fever or other symptoms. Because of the persistence of the condition, pt was placed on systemic steroids; condition reappeared after stopping the short course. SAE is currently ongoing, pt is stable. Similar pruritis has been observed following unmodified stem cell transplantation. Event is deemed "possibly related".
705	3/2/00	9705-189 Belani	Phase I Study of Percutaneous Injections of Adenovirus p53 Construct (Adeno-p53) for Hepatocellular Carcinoma. Follow Up1 (see ID #76, #512 reviewed at March 8-10, 2000 RAC meeting). *[Original event description embedded in an annual report from Investigator. This is an investigator report of the event – No new information provided.]* Pt is a 65+ yo M. Pt liver function tests [LFTs -- ALT & AST] elevated on 8/31/99. He received second dose of treatment (Adp53) on 9/1/99 after which AST levels declined. PI considered elevation of AST as possibly related to IND drug and possibly related to hepatocellular cancer
1455	5/25/00	9708-206 Flowers & Riddell	Infusion of Polyclonal HyTK (hygromycin phosphotransferase and HSV thymidine kinase gene)-transduced Donor T Cells for Adoptive Immunotherapy in Patients with Relapsed CML after Allogeneic Stem Cell Transplant: Phase I-II Clinical Trial. Initial; Event: Fever Patient is M with diagnosis of relapsed chronic myelogenous leukemia (CML) following bone marrow transplantion. About 5 hrs post 2nd infusion of Hy TK – modified T- cells, pt complained of chills; temp 39.3 °C. Pt admitted for third T-cell infusion and observation. Pt was discharged the following day. No causality has been provided by the investigator; the chronology of the event (5 hrs post treatment) would suggest a "possible association".
354	2/11/00	9709-214 Sponsor: Aventis	A Phase II Multi-Center, Open Label, Randomized Study to Evaluate Effectiveness and Safety of Two Treatment Regimens of Ad5CMV-p53 Administered by Intra-Tumoral Injections in 78 Patients with Recurrent Squamous Cell Carcinoma of the Head and Neck (SCCHN). Initial; Event: Pain at injection site. Pt is M undergoing treatment for recurrent SCCHN. Pt was in first cycle of treatment but complained of severe, sharp shooting pain in left neck, ear and side of head at the time of the third injection. Pt

			requested to be removed from study. The event was considered important by investigator. The causality is "possible association" with the clinical trial medication.
317	2/11/00	9709-215 von Mehren Sponsor: CTEP	Phase I/Pilot Study of ALVAC-CEA-B7.1 Immunization in Patients with Advanced Adenocarcinoma Expressing CEA. Initial; Event: Epigastric/abdominal pain (gr 3). Pt is F with diagnosed adenocarcinoma of the colon. Pt presented with severe epigastric discomfort, burning, some nausea 3 weeks following administration of IND agent. EGD: distal esophagitis/gastritis. Pt treated with IV fluids, anti-emetics and analgesics. Discharged 2 days later. Association to administration of IND agent is considered "possible".
311	2/11/00	215	Initial; Events: 1. Fever (gr 3), Lethargy (gr 2), 3. Elevated LFTs, 4. Change in mental status Pt is F diagnosed with stage IV colon cancer, metastasized to liver. Pt has history of mental disorder. 2 days post injection, pt admitted with fever, lethargy, elevated LFT's and change in mental status. Brain MRI was negative. Pt was treated with IV fluids and antibiotics. Pt was removed from study.. Event is considered by investigator to be "possibly associated"
568	3/2/00	9709-216 von Mehren Sponsor: CTEP	Phase I/Pilot Study of p53 Intralesional Gene Therapy with Chemotherapy in Breast Cancer. Initial; Event: elevated liver function tests (LFT), vomiting (gr. 3) and diarrhea (gr. 3) Pt is F diagnosed with breast cancer, metastasized to the chest wall. Pt received two cycles of injections subcutaneously to the chest wall lesions. Following cycle 1, pt exhibited elevated LFTs. On treatment cycle 2, pt experienced episodes of vomiting and diarrhea. The event has been considered by the investigator to be "associated" with administration of the clinical trial medication.
1684	5/31/00	9712-223 Bowman	Phase I Study of Chemokine and Cytokine Gene Modified Allogeneic Neuroblastoma Cells for Treatment of Relapsed/Refractory Neuroblastoma Using a Retroviral Vector. Initial; Event: Pt experienced grade 3 musculoskeletal pain. Deemed "possibly related" to treatment.
1660	5/31/00	9712-224 Brenner	Phase I Study of Chemokine and Cytokine Gene Modified Autologous Neuroblastoma Cells for Treatment of Relapsed/Refractory Neuroblastoma Using an Adenoviral Vector. Initial; Event: Pt experienced malaise, grade 3 redness, swelling and tenderness at injection site. Deemed "definitely related" to study [drug].
387	2/11/00	9712-226	A Phase II, Multi-Center, Open Label, Study to Evaluate

		Sponsor: Aventis	Effectiveness and Safety of Ad5CMV-p53 Administered by Intra-Tumoral Injections in 39 Patients with Recurrent Squamous Cell Carcinoma of the Head and Neck (SCCHN). Initial: Events: 1. Pain at injection/tumor site, 2. Nausea, 3. Vomiting, 4. Dehydration Pt is M w/ recurrent SCCHN. On day of injection pt complained of pain, developed nausea, vomiting and dehydration. Pt was hospitalized 5 days until stable. Pt chose to be removed from study and subsequently expired as a result of disease progression.
1491	5/25/00	9802-233 Sponsor: Vical	Phase II Study of Direct Gene Transfer of HLA-B7 Plasmid DNA/DMRIE/DOPE Lipid Complex (Allovectin-7) as an Immunotherapeutic Agent in Patients with Stage III or IV Melanom with No Treatment Alternatives. Follow Up3: Additional information re: ID #1031, #1032 (discussed at March 8-10 RAC meeting). Additional data provided by sponsor to investigators. Events: 1. Ascites, 2. Death. Pt diagnosed w/ metastatic melanoma received clinical trial study drug by direct intralesional injection. Pt had received 2 cycles of treatment and began to complain of discomfort and severe malaise. The pt was hospitalized 2 weeks (7/15/99) after receiving the last injection (ID #1031) for GI bleeding and severe ascites. The pt was diagnosed at discharge with gastritis and upper GI bleeding secondary to non-steroidal anti-inflammatory drug use. The cause of the ascites was unknown and considered to be unassociated with study drug use. Two weeks later (8/2/99) the pt was readmitted (ID #1032) for ascites / intense abdominal pain. Cultures remained negative; repea paracentesis and cytology remained negative but demonstrated the presence of many reactive cells in the ascites fluid. There was a suspicion of a melanoma mass around the colon although prior biopsy was negative. The pt was discharged (8/7/99) after pain control; the SAE was ongoing. The pt was removed from study on 8/13/99 due to disease progression and was put on a course of antibiotics and chemobiotherapy. The pt still had significant ascites. At the time, the PI indicated that the ascites was "possibly associated" (although that option was not available on the reporting form – the PI indicated "probably associated") with the study drug; the sponsor felt the attribution to be associated with underlying melanoma disease. Pt was treated with combination IL-2, IFN, cis-platin, vinblastine chemobiotherapy and within 10 days became pancytopenic and febrile. He was then treated with G-CSF and antibiotics. The pt was noted to be thrombocytopenic and received platelet transfusions. The pt failed to improve; the family issued a

			DNR order and the pt expired shortly thereafter
1363	5/19/00	9802-235 Markert Sponsor: NeuroVir	A Dose Escalating Phase I Study of the Treatment of Malignant Glioma with G207, a Genetically Engineered HSV-1. Initial; Event: Fever Three days post-injection, patient developed fever >102 °F possibly due to chemical meningitis related to vector producer cells. Cause of fever is indeterminate, occurring post-operatively. Event is considered "possibly associated" with study medication.
662	3/10/00	235	Initial; Event: 1. Neurological trauma Pt is diagnosed w/ glioblastoma multiforme and was treated with study agent by stereotactic injection into the tumor site. Post-operatively, pt exhibited decreased level of spontaneity. CT scan showed patchy hemorrhage. Pt recovered fully. Event: trauma from surgery due to multiple needle passes or virus effect was considered "possibly associated" with study drug.
1353	5/19/00	235	Initial; Event: Left-sided neglect and weakness post-injection. Pt is diagnosed w/ glioblastoma multiforme and was treated with study agent by stereotactic injection into the tumor site. On day of treatment pt exhibited neurological impairment post-operatively. Pt is improving but full recovery is unlikely. Event is deemed "possibly associated" with study medication.
60	2/25/00	9802-238 Lee Sponsor: Berlex	Phase 1/2 Study of the Effects of Ascending Doses of Adenovirus Mediated Human FGF-4 Gene Transfer in Patients with Stable Exertional Angina. Follow Up1 to ID #438; Event: Renal carcinoma Pt had a one-month history of diarrhea with occasional blood. Colonoscopy showed evidence of colon adenocarcinoma, and presence of additional masses (kidney and lung). CT guided biopsy of renal mass led to diagnosis of renal cell carcinoma (2/00).
1136	4/17/00	238	Follow Up 2 to ID #438: Event: Chest pain Pt was diagnosed with metastatic colorectal adenocarcinoma to lung, liver and right kidney. Pt was admitted (4/00) for chest pain resulting from a pulmonary embolism and possible L basilar infiltrates.
1224	5/8/00	9803-240 Rom & Salvio	Phase I Trial of Adenoviral Vector Delivery of the Herpes Simplex Thymidine Kinase Gene by Intratumoral Injection Followed by Intravenous Ganciclovir in Patients with Advanced Non-Small Cell Lung Cancer. Initial; Event: 1. Fever, 2. Breathlessness, 3. R-side chest pain and coughing, 4. Small L pleural effusion.

			Pt is M with diagnosis of stage IV lung cancer. Admitted to hospital for fever, shortness of breath (gr2), R side chest pain associated w/ coughing (gr1). Low grade fever (100 °F) and a small L pleural effusion (gr2). New consolidation noted in right middle lung lobe. Considered to be rapid progression of lung cancer, rapidly increasing malignant pleural effusion and post-obstructive pneumonia with possible bacterial pneumonia. Severe systemic infection highly unlikely. Events are deemed possibly associated with clinical test material.
42	2/16/00	Crystal et al Sponsor: GenVec	Phase I Study of Direct Administration of a Replication Deficient Adenovirus vector (Ad_{GV}VEGF121.10) Containing the VEGF121 cDNA to the Ischemic Lower Limb of Individuals with Peripheral Vascular Disease. Initial; Event: Gross, painless hematuria, Pt has history of severe peripheral vascular disease, coronary artery disease, hypertension and nicotine abuse. Pt underwent ureteropyelography, urinary cytology and cystoscopy. Bladder papillary lesions were believed to be transitional cell carcinoma (grade I/III); a kidney lesion was identified. Initial attribution was "possible association" to study medication.
713	2/29/00	243	Follow Up 1 to ID #42: Investigator and sponsor consider the attribution of the event as "unknown" with regard to the study medication: AdVEGF 121.10.
420	2/11/00	9804-250 Swisher Sponsor: Aventis	An Efficacy Study of Adenoviral Vector Expressing Wildtype p53 (Ad5CMV-p53) Administered Intralesionally as an Adjunct to Radiation Therapy in Patients with Non-Small Cell Lung Cancer Initial; Event: Fever, SOB, pain in left upper chest a few hours afte receiving the second dose. Admitted with DX of pneumonia. CXR showed infiltrate localized in the RLL, left pleural effusion and LUL collapse. Pt's tumor located in LUL. ABG's WNL, O2 sat 88%, tx with antibiotics, O2, dexamethasone.
520	2/29/00	9806-255 Muller Sponsor: CTEP	Phase I Trial of Intraperitoneal Adenoviral p53 Gene Therapy in Patients with Advanced Recurrent or Persistent Ovarian Cancer. Initial. Event: hyponatremia with progressive edema, decreased urine output, decreased albumin, increased coags, increased WBC's, acute respiratory event progressing to death. Awaiting post-mortem report
1205	4/21/00	255	Initial; Event: Pt unexpectedly expired two days after receiving 1st

			dose of third course. On day after dosing, pt complained of increased dyspnea - CXR showed bilateral pleural effusions and pulmonary nodules consistent with metastasis. Thoracentesis done with resolution of symptoms. However, that evening pt c/o chest and side pain. Next morning pain worsened, pt transported to hospital. Pt had cardiopulmonary arrest in the car, resuscitation attempts in the field and ER failed.
1206	5/2/00	255	Follow Up1 to ID #1205: Preliminary autopsy report Evidence of metastatic ovarian carcinoma, left ventricular hypertrophy and lipomatous infiltration of intra-arterial septum. Awaiting results of microscopy, microbiology and brain cutting.
52	2/23/00	255	Initial; Event: admitted for increase in bilateral LE edema, hyponatremia. Unable to correct hyponatremia - taken off study
711	3/2/00	255	Initial; Event: Mild abdominal cramping after initial IP treatment. Resolved 4 days post-treatment.
1277	5/12/00	9807-262 Wolf	A Phase I Study of Ad-p53 (NSC#683550) for Patients with Platinum- and Paclitaxel-Resistant Epithelial Ovarian Cancer. Initial; Event: Admission for myalgia, fever, nausea, increased WBC's. Believed to be possibly related to vector
1255	5/12/00	262	Initial; Event: Admission for fever, increased WBC, general malaise, nausea, intermittent abdominal discomfort. Treated with IV antibiotics and fluids. Discharged home afebrile on oral antibiotics.
1187	3/24/00	262	Follow Up1 to ID #1255: Report from sponsor stating infection, nausea, anorexia, abdominal pain and anemia may have been due to the vector, the disease process or the IP catheter.
1286	5/12/00	262	Initial; Event: Admission for fever, nausea and vomiting. Readmitted 7 days later (see ID #1256)
1256	5/12/00	262	Initial; Event: Re-admission (see ID #1286) for nausea, vomiting, no bowel movement X2 days, lower abdominal and back pain, fever, and anorexia. No obstruction noted, cultures negative. Intraperitoneal catheter removed. IV antibiotics and fluids given. Discharged afebrile, no nausea or vomiting.

1273	5/12/00	262	Initial; Event: Admission for significant angioedema, swelling of tongue, hands, feet. Condition reported by pt one day post-injection. Possibly related to vector
730	3/16/00	9808-263 Lang & Yung Sponsor: CTEP	Phase I Trial of Adenovirus-Mediated Wild Type p53 Gene Therapy for Malignant Gliomas. Initial, Event: Granulocytopenia (gr1). Values: Onset (1.8); 2.28 on 2/3/00
708	2/28/00	263	Initial; Event: Post-op experienced grade 1 lethargy
732	3/16/00	263	Initial; Event: Fatigue 1 day after biopsy, recovered 9/8/99
738	3/16/00	263	Initial; Event: Fever, headache and generalized fatigue for a period of 10 days. Blood and cerebro-spinal fluid cultures negative.
710	2/29/00	263	Initial; Event: increasing aphasia, increased word finding difficulty. MRI showed extensive edema and striking progression of tumor around cavity. Compression of left lateral ventricle. Increased signal along injection tracts
1442	5/30/00	263	Initial; Event: Pt admitted for decreased level of consciousness. (See ID #1441) Pt transferred to an extended care facility 5/9/00 unresponsive to auditory or painful stimuli.
1441	5/30/00	263	Initial; Event: refer to ID #1442. Pt expired most likely due to tumor progression, but the gene therap cannot be excluded as a possible contributing factor. Awaiting additional post-mortem information.
1061	3/31/00	263	Initial; Event: pt developed moderately severe headache post craniotomy for direct infusion. Headache resolved within 1 day following treatment with analgesics
733	3/16/00	263	Initial; Event: Post craniotomy, pt experienced nausea, vomiting. Continued into next day
646	3/9/00	9808-264 Gitlitz Sponsor: Transgene	Phase I/II Trial of Antigen-Specific Immunotherapy in MUC-1 Positive Patients with Advanced Non-Small Cell Lung Cancer Using Vaccina-Virus-MUC1-IL2 (TG1031). Initial; Event: admitted for severe pain less than 24 hrs post delivery
1162	4/20/00	9811-271	A Randomized, Double-Blind, Placebo-Controlled, Dose-Escalating

		Isner Sponsor: Vascular Genetics	Study of Intramuscular Vascular Endothelial Growth Factor-2 (VEGF-2) Gene Therapy in Patients with Moderate-Risk Critical Limb Ischemia. Follow Up1 to ID #75; - Initial attribution was classified as "not associated"; subsequently changed to "unknown/possibly associated". Pt diagnosed with metastases to brain, liver + others organs (10/99), new mets found 1/00.
785	3/21/00	9901-280 Sponsor: Schering	A Phase II/III Trial of Chemotherapy Alone Versus Chemotherapy Plus SCH 58500 in Newly Diagnosed Stage III Ovarian and Primary Peritoneal Cancer Patients with ≥0.5 cm and ≤2 cm Residual Disease Following Surgery. Follow Up1 to ? (No initial report on file). Pt complained of intractable nausea and vomiting. Abdominal x-ray showed no obstruction, however, barium did not pass through the duodenum. Pt was hydrated, and intubated (naso-gastric). Pt underwent surgery to release small bowel obstruction possibly. Event was attributed as "possibly associated" with the IND product.
1141	4/18/00	280	Follow Up2 to ID #785; Same data provided by investigator.
48	2/18/00	280	Initial; Event: abdominal wall infection Fistula (cutaneous opening not contiguous with the intra-abdominal cavity), hospitalization for IV antibiotics and drainage catheter placement
1217	5/5/00	280	Follow Up1 to ID #48: Investigator and sponsor believe fistula was related to an inflammatory reaction to the trial medication: SCH58500
1242	5/10/00	280	Initial; Event: Admission for fever, 103.6 °F, vomiting, 1 day post vector administration. N/G tube placed, IV's, TPN, IV antibiotics. Gradually improved discharged to home 5/9/00 afebrile. Dx with ileus secondary to surgical IP port placement, cellulitis probably secondary to extravasation from improper needle placement, and fever secondary to cellulitis or vector administration.
1243	5/10/00	280	Follow Up1 to ID #1242. Corrected lab values provided.
784	3/21/00	280	F1 to ? (No initial report on file).

			Pt complained of post-prandial vomiting, abdominal pain, dehydration tachycardia. Small bowel obstruction possibly associated with IND drug administration. Pt underwent lysis of adhesions, release of small bowel obstruction and small bowel resection. Inflammatory rind over small intestine and cavity was resected Pt was discharged after improvement.
1140	4/18/00	280	Follow Up2 to ID #784: Pt had lysis of adhesion and release of small bowel obstruction with resection 3/15/99. P/O DX inflammatory small bowel obstruction D/T confined inflammatory collection in abdomen with necrosis and intraperitoneal catheter infusion. CT 4/2/99 showed disease progression. Pt taken off study.
1069	4/4/00	280	Initial; Event: Pt admitted for hypotension, shortness of breath, R/O PE, sepsis and acute renal failure.
1072	4/3/00	280	Follow Up1 to ID #1069. Investigator Initially considered the event as not associated to IND drug administration. Sponsor changed the attribution to possibly associated with the IND drug - severe chronic inflammation of the bowel wall possibly caused by IND drug may have weakened the bowel wall making it more susceptible to perforation.
1148	4/18/00	280	Follow Up2 to ID #1069: Chest X-ray showed pulmonary infiltrates, increased ascites. Ascitic fluid tested positive for gram (-) rods.
1123	4/12/00	280	Follow Up3 to ID #1069: Pt did not meet protocol definition of progressive disease. Investigator felt DIC, HTN, renal failure DT sepsis from intestinal perforation and acute bacterial peritonitis. Investigator believes pancytopenia and renal failure D/T chemotherapy. The investigator considers the perforation D/T combination of intraperitoneal catheter, the malignant disease and the inflammatory effects of SCH58500.
1126	4/13/00	280	Follow Up4 to ID #1069: Corrected cover letter from sponsor.
632	3/6/00	280	Initial; Event: pt hospitalized for nausea and vomiting. Obstruction diagnosed mid jejunum. Pt was treated and discharged 2/8/00
633	3/6/00	280	Initial; Event: pt readmitted (632) for reevaluation. Small bowel obstruction in distal duodenum/proximal jejunum. Exploratory laparotomy showed markedly thickened peritoneum, TPN and IV antibiotics started, G-tube placed.

652	3/14/00	280	Follow Up1 to ID #633. Unable to remove NG tube because of vomiting. UGI showed re-obstruction.
649	2/10/00	280	Follow Up1 to ID #15. Pt admitted for esophagitis. Tx with IV fluids, IV antiemetics, Maalox Lidocaine, Morphine, Droperidol and Lorazepam. Discharged 1/7/00.
1064	1/14/00	9902-287 Schiller & Carbone Sponsor: CTEP	Phase I Pilot Trial of Adenovirus p53 in Bronchioloalveolar Cell Lung Carcinoma (BAC) Administered by Bronchoalveolar Lavage. Initial; Event: Pt suffered a hypoxic episode.
1065	1/24/00	287	Follow Up1 to ID #1064. Pt became progressively more difficult to oxygenate and required high dose sedation. Bronchoscopy revealed herpes infection. Started on acyclovir.
441	2/17/00	287	Initial; Follow Up2 to ID #1064: Report from CTEP Event: Shortness of breath, dyspnea on exertion, hypoxia, bilateral infiltrates, cultures negative. No new information.
1143	2/17/00	287	Follow Up3: (Xrefs: 1066, 442, 1067, 1128). Same information; multiple submissions from different sources.
1128	2/23/00	287	F4 to 1066: (Xrefs: 442, 1067, 1143). Same information; multiple submissions from different sources
1127	2/28/00	287	Follow Up4 to ID #1064: Despite treatment with steroids and antibiotics, the respiratory insufficiency progressed and pt ultimately died (ID #1066). The respiratory deterioration was attributed primarily to bronchioloaveolar carcinoma possibly in association with superimposed inflammation resulting from the Ad-p53 treatment.
838	3/24/00	287	Follow Up5 to ID #442: Investigators attribute pt's respiratory deterioration and death as probably due to bronchioloalveolar carcinoma possibly in association with superimposed inflammation resulting from the IND treatment.
1182	4/25/00	287	Initial; Event: Fatigue (gr3). Pt unable to get dressed post vector administration, required 2 nights hospitalization.
1185	4/25/00	287	Initial; Event: post instillation O_2 sats to 87%,

			Pt c/o fatigue, unable to get dressed. Hospitalized for 3 nights. Discharged on home O2 ventilator due to continued SOB.*(report very similar to ID #1182 slightly different data provided*
1208	5/2/00	287	Follow Up1 to ID #1185: Additional information about Event. Event believed to be probably related to vector instillation. *(Most likely a duplicate submission; reported data differs slightly).*
1184	4/25/00	287	Initial; Event: Shortness of breath (gr4), Fever >100 °F, vomiting, poor appetite, intermittent cough, fatigue. Arterial Blood gas data: pO2 75, pCO2 30
1207	5/2/00	287	Follow Up1 to ID #1184: Event attribution: "Possibly associated" with vector instillation.
1186	4/25/00	287	Initial; Event: Post-obstructive pneumonia (gr3) possibly associate with vector instillation
1183	4/25/00	287	Initial; Event: Lymphopenia. Pt dropped from baseline of 1500 to nadir of 300. Returned to baseline
637	3/8/00	287	Initial; Event: Elevated LDH (gr1 – value: 650) 2 weeks after last dose.
634	3/7/00	287	Initial; Event: hyponatremia (gr1) approx 1 month after 5th dose
783	3/21/00	9903-301 Sponsor: Vascular Genetics	A Randomized, Double-Blind, Placebo-Controlled, Dose-Escalating Study of Intramuscular Vascular Endothelial Growth Factor-2 (VEGF-2) Gene Therapy in Patients with High-Risk Critical Limb Ischemia. Initial; Event: admitted to hosp with severely worsened peripheral artery disease, unstable congestive heart failure. Bilateral amputation expected, but awaiting pt's congestive heart failure to stabilize
1155	4/19/00	9905-314 Kaufman Sponsor: CTEP	A Phase I Trial of Intralesional RV-B7.1 Vaccine in the Treatment of Malignant Melanoma Initial: Event: Pt developed approximately 16 papular nodules, 0.5-1.0 cm in size in left anterior axilla. Occurred within first 30 days of receiving vaccine.
1298	5/16/00	314	Follow Up1 to ID #1155: Corrections to original submission: Source of IND drug is NCI; the "Non-IND" attribution originally provided by the PI has been marked "not applicable" (N/A) for this trial.

412	5/25/00	0002-391 Sponsor: Vical	A Phase I Trial of Intralesional RV-B7.1 Vaccine in the Treatment of Malignant Melanoma Initial; Event: After receiving 5th dose, pt complained of increasing fatigue and shortness of breath. Pt found to be tachypneic and tachycardic. Pt admitted for hydration, was discharged the next day and has subsequently received 6th dose without incidence.