RESPONSES TO APPENDIX M-I-C-1
HUMAN GENE TRANSFER PROTOCOLS

RECOMBINANT DNA ADVISORY COMMITTEE MEETING
March 2002

ID #	Letter	Protocol #	Response
		0010-427	**Effect of Ad_{GV}CFTR.10 on the Cystic Fibrosis Phenotype.**
346	11/28/2001		*Response to M-I-C-1:* Based upon recommendations from the FDA, the clinical protocol and consent (if applicable) have been amended as follows: 1) Clarification has been made that Group B will be started one month after Group A is finished. 2) An additional follow-up visit has been added at day 14. The day 14 visit will include a physical exam, routine blood work (identical to that required at day 30), sweat chloride and sweat rate tests (as for day 30), testing for anti-adeno antibodies, and an optional skin biopsy. 3) Mention of the inability of the vector to reproduce itself has been removed due to the potential of the study agent to recombine with "...another adenovirus and thus reacquire the ability to reproduce." 4) Mention of the death of a study participant in a previous adenovirus trial has been re-worded to remove the phrases: "not relevant to you" and "it was a higher dose [of study agent]." 5) At list of the efficacy measurements and parameters that will be taken and used has been added.
		0101-453	**A Multi-Center, Open Label, Two Part, Dose Escalation Study to Determine the Tolerability of Interferon-beta Gene Transfer in the Treatment of Recurrent or Progressive Glioblastoma Multiforme. Sponsor: Biogen.**
358	12/17/2001		*Response to M-I-C-1:* Received a copy of the clinical protocol containing changes based upon the FDA's review.
		0101-457	**An Open-Label, Phase I, Dose-Escalation Study of TNFerade™ Biologic with Radiation Therapy as an Adjunct to Surgery or for Palliation of Soft Tissue Sarcoma of the Extremities. Sponsor: GenVec.**
331	01/16/2002		*Response to M-I-C-1:* Received a copy of the IBC and IRB approvals and IRB-approved informed consent for Dr. Hanna at the University of Kentucky.

ID #	Letter	Protocol #	Response
		0104-463	**Phase I Double Blind, Parallel-Group, Multi-Center, Gene Expression (Synthesis of FGF-1 mRNA), Safety and Tolerability Study of Increasing Single Doses of NV1FGF Administered by Intra-Muscular Injection in Patients with Severe Peripheral Artery Occlusive Disease (PAOD) Planned to Undergo Amputation Above the Ankle. Sponsor: Aventis Pharma Recherche-Development.**
367	01/31/2002		*Response to M-I-C-1:* Received copies of the IBC and IRB approvals for all trial sites currently registered (Temple Univ., Hennepin County Medical Center, and Atlanta Cardiovascular Research Institute). Also received a copy of the approved informed consent for the Atlanta Cardiovascular site. Questions raised by individual RAC members during the initial RAC review (this protocol was not selected for RAC public review) were addressed. The FDA did not require any modifications to the protocol. Therefore, version of the clinical protocol submitted is the same one as that submitted for initial RAC review. There has been, however, an amendment (number 2) to this protocol; summarized in "Trial Design." The first individual entered into this study on January 7, 2002.
		0106-479	**Vaccination in Peripheral Stem Cell Transplant Setting for Acute Myelogenous Leukemia: The Use of Autologous Tumor Cells with an Allogeneic GM-CSF Producing Bystander Cell Line. Sponsor: Cell Genesys, Inc.**
364	01/29/2002		*Response to M-I-C-1:* Received a copy of the IBC and IRB approvals and informed consent for the trial site identified with the initial submission.

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		0107-481	**An Open-Label, Phase Ib/II Study of the Safety, Tolerability and Efficacy of G207, a Genetically Engineered Herpes Simplex Type-1 Virus, Administered Intracerebrally to Subjects with Recurrent Malignant Glioma. Sponsor: MediGene, Inc.**
323	01/10/2002		*Response to M-I-C-1:* Copies of IBC and IRB approvals and informed consent document. Trial was initiated on December 12, 2001. No NIH grant numbers are applicable. This protocol was not selected for RAC public discussion. Changes were made to the clinical protocol based upon internal review; changes were not recommended by the FDA. Changes were made to clarify that the maximum tolerated dose may not be reached and that a measurement for the optimal biologic dose does not exist. In addition, the exclusion criteria have been clarified to indicate that individuals with multiple lesions are not eligible for surgical resection and therefore are not eligible for this study. The definition of the maximum tolerated dose (MTD) has been clarified. MTD is now defined as being reached when one of three individuals in any cohort experiences a grade 3 or 4 toxicity that is probably related to the study agent. Previously, the MTD was defined as a grade 3 or 4 event "likely attributable" to the study agent.
		0110-506	**Treatment of Patients with Metastatic Melanoma using Lymphocytes Transduced with an Interleukin-2 (IL-2) Gene Following the Administration of a Nonmyeloablative but Lymphocyte Depleting Regimen.**
355	01/02/2002		*Response to M-I-C-1:* Received a copy of the IBC approval.