SETTLEMENT AGREEMENT

I. PARTIES

This Settlement Agreement ("Agreement") is entered into between the United States of America, acting through the United States Department of Justice and on behalf of the Food and Drug Administration ("FDA") and its Center for Biologics Evaluation and Research ("CBER"), the National Institutes of Health ("NIH"), the Office of Acquisition Management and Policy of the Department of Health and Human Services ("HHS"), and the HHS Office of Inspector General ("OIG-HHS")(collectively the "United States"); and James M. Wilson, M.D., Ph.D. ("Dr. Wilson") (hereafter referred to as "the Parties"), through their authorized representatives.

II. PREAMBLE

As a preamble to this Agreement, the Parties agree to the following:

A. The settlement arises out of Dr. Wilson's participation in the development of an investigational new drug to treat a certain deficiency in an enzyme called ornithine transcarbamylase (OTC). The urea cycle, located in the liver, detoxifies nitrogen and changes it to urea which is nontoxic and can then be excreted as urine. Some individuals are unable to convert nitrogen (ammonia) to urea because they are born with deficient or absent activity of OTC, an essential enzyme for making urea. A high level of ammonia is toxic to the central nervous system and as a result, hyperammonaemic coma and death may occur with OTC deficiency (OTCD).

B. A Phase I safety study of the use of a genetically engineered adenovirus being inserted into human subjects to address OTCD was reviewed by the FDA and NIH. The OTC gene was placed inside a virus called adenovirus and the virus was injected into the liver through blood vessels. The virus then carried the OTC gene into the subject's liver cells and once in the

liver cells, the OTC gene was to produce the OTC enzyme that is missing in OTCD. The studies of the safety of this drug in humans were regulated by the FDA. The research studies were funded by the NIH and by the FDA.

C. Dr. Wilson is a professor at the University of Pennsylvania and was Director of the Institute for Human Gene Therapy at the University of Pennsylvania. Dr. Wilson was a Co-Investigator on the OTC NIH grant and Sponsor/Investigator of the investigational new drug (IND) application.

D. The United States contends that it has certain civil claims against Dr. Wilson as a result of his actions and those of his colleagues, Mark Batshaw, M.D. and Steven Raper, M.D., in their studies of this new investigational drug described in paragraphs A-C above between July 1998 through September1999: false statements and claims in connection with the submission of grant applications, progress reports, and annual reports to, and receipt of federal funds from, the NIH; false statements and claims in connection with submissions to the FDA; false statements and claims in connection with the failure to obtain properly informed consent from human research participants; and false statements made to Institutional Review Boards charged with oversight of this research. In addition, the allegations contained in the FDA's Notice of Opportunity for Hearing issued to Dr. Wilson on February 8, 2002, the FDA Form 483 issued to Dr. Wilson on January 19, 2000, the FDA Form 483 issued to Dr. Wilson on March 1, 2000, the FDA warning letter issued to IHGT on March 3, 2000, the FDA warning letter issued to IHGT on July 3, 2000, the FDA Notice of Initiation of Disqualification Proceedings and Opportunity to Explain (NIDPOE) issued to Dr. Wilson on November 30, 2000, FDA correspondence to Dr. Wilson dated October 27, 2000, November 27, 2000, and March 9, 2001,

and the FDA letter regarding inspection of manufacturing dated March 13, 2001, are incorporated herein by reference. The United States' contentions described above are hereinafter referred to as the "Covered Conduct."

E. Dr. Wilson does not admit the contentions of the United States as set forth in Paragraph D above, and to the contrary, contends that his conduct was at all times lawful and appropriate.

F. In order to avoid the delay, uncertainty, inconvenience and expense of protracted litigation of these claims, the Parties reach a full and final settlement as set forth below.

TERMS AND CONDITIONS

NOW, THEREFORE, in consideration of the mutual promises, covenants, and obligations set forth below, and for good and valuable consideration as stated herein, the Parties agree as follows:

1. For purposes of this Agreement, the following definitions will apply:

A. "Clinical Trial" is (i) a clinical investigation (as defined by 21 CFR Section 56.102(c)) in which Dr. Wilson has been identified on a Form FDA 1572 or investigator agreement for investigational medical devices as the investigator or as a subinvestigator; or (ii) an NIH-funded Clinical Trial, as defined in the NIH Grants Policy Statement (12/03) in which Dr. Wilson has been identified in a pre-award or post-award action as Principal Investigator, Co-Investigator, or Other Significant Contributor as defined in C., D., and E. respectively, and has a direct involvement with human research participants.

B. "Non-Trial Clinical Research" is an Institutional Review Board (IRB) approved study involving non-exempt human subjects' research (as defined by 45 CFR Part 46) in which Dr. Wilson is initially identified to the IRB, or at any point becomes, the Principal Investigator, or Co-Investigator, and has a direct involvement with human research participants.

C. “Principal Investigator” (“PI”) on an NIH-funded grant or cooperative agreement grant (hereafter referred to as “grant”) is that individual who is designated by the grantee as responsible for the scientific or technical aspects of the grant, including Multi-Project Activities, and for day-to-day management of the project or program, whether referred to as the principal investigator, program director, or project leader.

D. “Co-Investigator” on an NIH-funded grant, including Multi-Project Activities, is an individual involved with the PI in the scientific development or execution of a project who devotes a specified percentage of time to the project and is considered “Key Personnel” as defined in the NIH Grants Policy Statement (rev. 12/03). An individual is not a Co-Investigator on an NIH grant if the pre-award or post-award action does not identify him as providing a specified level of effort.

E. “Other Significant Contributor” is defined in the PHS 398 grant application dated September 2004 and refers to individuals who have committed in the pre-award or post-award action to contribute to the scientific development or execution of the project, but are not committing any specified measurable effort to the projects as identified in a pre-award action or post-award action.

F. "Key Personnel" refers to the PI and other individuals who contribute to the scientific development or execution of a project in a substantive, measurable way, whether or not they receive salaries or compensation under the grant. Consultants also may be considered Key Personnel if they meet this definition. An individual is considered Key Personnel if the pre-award or post-award action identifies him as committing a specified amount greater than zero percent effort to the grant.

G. “Grant Affiliation” refers to those situations in which Dr. Wilson is the PI, or Co-Investigator, or when identified as Key Personnel or Other Significant Contributor on an NIH-funded grant. Grant Affiliation does not pertain to those situations in which Dr. Wilson is identified as Key Personnel or Other Significant Contributor in institutional training grants, such as Ruth L. Kirschstein-NRSA grants.

H. “Restricted Clinical Activity” refers to (i) Clinical Trials; (ii) Non-Trial Clinical Research in which some financial support is provided by federal funds; and (iii) any federally funded grant in which Dr. Wilson has a Grant Affiliation and in which Dr. Wilson participates through conducting Clinical Trials or Non-Trial Clinical Research.

I. "Multi-Project Activities" refers to an award that supports the funding of at least two related research projects that are related to a theme with collaboration and interaction among investigators to achieve a common goal.

2. Dr. Wilson represents that, although he was under no government restriction: (a) he has not served as a sponsor of a new IND since September 1999; (b) he has not enrolled patients in any Clinical Trials since January 2000; (c) except with respect to appropriate follow-up on subjects enrolled in then-existing Clinical Trials, he has not conducted research on human subjects, other than to analyze tissue or biologic samples provided by others or secured as part of then existing Clinical Trials, since January 2000. Dr. Wilson agrees that for a five year period beginning on the Effective Date of this Agreement, he will not seek to serve as a sponsor (as described in 21 CFR Parts 312.3(b) and 812.3(n)) of any FDA-regulated Clinical Trial.

3. Dr. Wilson's name will be added to the list of restricted clinical investigators, currently entitled "Restricted List for Clinical Investigators," which is published on FDA's website. The government agrees that, once Dr. Wilson fulfills all of the terms of the Agreement, the government will remove Dr. Wilson's name from the Restricted List for Clinical Investigators and place it on the "Clinical Investigators-Restrictions Removed" website list. Dr. Wilson acknowledges that, once Dr. Wilson fulfills all of the terms of the Agreement, information relating to this Agreement, including the fact that the restrictions have been removed, will continue to be publicly available in accordance with freedom of information laws and FDA's policies and procedures regarding public information.

4. Dr. Wilson, if he so elects, will be eligible to participate without restriction in Restricted Clinical Activity on or after a date five years from the Effective Date of this Agreement by completing the educational and practical experience steps described in paragraphs 5 and 6. Dr. Wilson must complete the educational step described in paragraph 5 before completing the practical experience step described in paragraph 6. Upon Dr. Wilson’s successful

completion of these educational and practical experience steps, and the passage of not less than five years from the Effective Date of this Agreement, the parties agree that the restrictions imposed by this Agreement will be removed.

5. Dr. Wilson agrees that before conducting Restricted Clinical Activity, he will complete: (a) "Introduction to the Principles and Practices of Clinical Research" (a course developed by the NIH Clinical Research Center); (b) Clinical Research Training Course (on-line training – five modules); and (c) DHHS Office for Human Research Protections (OHRP) – "Investigator 101" (available on CD Rom). Dr. Wilson agrees to provide a certification to the FDA and NIH evidencing that he has successfully completed each course within 30 days of completion.

6. Dr. Wilson agrees that during the period of restriction, he may conduct Restricted Clinical Activity only in a manner consistent with subparagraphs a through j, below. Moreover, in order to become eligible to participate without restriction, as described in paragraph 4, Dr. Wilson must obtain practical experience by performing Restricted Clinical Activity for at least thirty-six (36) months in a manner consistent with subparagraphs a through j, below:

a. Dr. Wilson may participate in Restricted Clinical Activity one study at a time. However, Dr. Wilson may submit, or be listed on, more than one grant application to the federal government for him to conduct Restricted Clinical Activity.

b. Dr. Wilson will provide a copy of this Agreement to the sponsor of, and the IRB responsible for overseeing, any study in which he participates in Restricted Clinical Activity. Dr. Wilson will ensure that any grant application that identifies Dr. Wilson as participating in Restricted Clinical Activity submitted to the NIH by the grantee will include, in a cover letter, a description of Dr. Wilson's role in the project.

c. Dr. Wilson agrees that he will notify any sponsor and/or recipient of a federal grant in which Dr. Wilson is to conduct Restricted Clinical Activity involving a Clinical Trial that the sponsor or grant recipient must hire an independent contract research organization (CRO) to oversee Dr. Wilson's compliance with applicable regulations and this Agreement. Dr. Wilson will provide a copy of this Agreement to the CRO. No reimbursement by federal funds may be sought for this expense.

d. If the study is federally funded, Dr. Wilson and the grantee will ensure that the CRO complies with all of the provisions set forth in Exhibit 1.

e. If the study is federally funded, Dr. Wilson and the grantee will ensure that the CRO reports to the government, on a semi-annual basis, all findings based on its review. In the event that the government does not receive such a report within 30 calendar days from the end of the 6-month period, Dr. Wilson will be considered to be in breach of this Agreement, and the entire reporting period will not be credited toward the thirty-six month period described in paragraph 6.

f. Dr. Wilson agrees that, while performing Restricted Clinical Activity under this paragraph, he will engage a "Medical Monitor" with expertise in human clinical research and in an area of relevant expertise. Dr. Wilson will provide a copy of this Agreement to the Medical Monitor. The Medical Monitor cannot be affiliated with the University of Pennsylvania or Dr. Wilson's employer and must be approved (i) in the case of a Clinical Trial, by FDA (if a clinical investigation as defined by paragraph 1A(i)) and/or NIH (if an NIH-funded Clinical Trial as defined in paragraph 1A(ii)); and (ii), in the case of Non-Trial Clinical Research, by NIH. Dr. Wilson must obtain such approval of the Medical Monitor before entering any subject into a Clinical Trial and, if applicable, before receiving any federal funds to conduct Restricted Clinical Activity.

g. If the study is federally funded, Dr. Wilson and the grantee will ensure that the Medical Monitor complies with all of the provisions set forth in Exhibit 1.

h. If the study is federally funded, Dr. Wilson and the grantee will further ensure that the Medical Monitor reports to the government, on a semi-annual basis, all findings based on his/her review. Such reports must comply with the requirements set forth in Exhibit 1. In the event that the government does not receive such a report within thirty (30) calendar days from the end of the 6-month period, Dr. Wilson will be considered to be in breach of this Agreement and the entire reporting period will not be

credited toward the three year period described in paragraph 6. No reimbursement by federal funds may be sought for this expense.

i. At least thirty (30) days before Dr. Wilson begins to conduct Restricted Clinical Activity work pursuant to this paragraph, Dr. Wilson will submit to the government: (a) a statement of Dr. Wilson's expected role in the conduct of the research; (b) a copy of the IRB-approved protocol; and (c) a copy of the written agreements in which the Medical Monitor and/or the CRO agree to comply with all terms of this Settlement Agreement

j. Dr. Wilson agrees to attend, throughout this thirty-six month period, at least two educational programs each year sponsored by or conducted by organizations with recognized expertise in the area of clinical research, on subjects relating to Clinical Trials (e.g., dealing with enhancing Clinical Trials, protection of human participants, informed consent, and/or complying with FDA and NIH regulations). Dr. Wilson agrees to provide a certification to the FDA and NIH evidencing that he has successfully completed each course within thirty days of completion.

7. Nothing in this Agreement should be construed as limiting Dr. Wilson's ability to conduct research other than Restricted Clinical Activity, or to discuss such research with individuals engaged in clinical investigations and non-exempt human subjects research. This Agreement also does not apply to situations in which Dr. Wilson provides others with access to a research reagent such as a vector.

8. During the period of restriction, where Dr. Wilson has a Grant Affiliation with a federally funded grant under which he does not conduct Clinical Trials or Non-Trial Clinical Research, but as part of the same grant other individuals with a Grant Affiliation are to conduct Clinical Trials or Non-Trial Clinical Research of greater than minimal risk (as defined in 45 CFR Section 46.102(i)), and the results of his non-Clinical Research could impact on the safety of the participants involved in the Clinical Research as determined by the sponsor of the IND (if a clinical investigation as defined by 21 CFR Section 56.102(c)), or otherwise by the grantee, Dr.

Wilson agrees to arrange for the sponsor or grantee to obtain and utilize the services of a Special Monitor whose function will be to (a) ascertain whether Dr. Wilson's involvement constitutes Restricted Clinical Activity; (b) ascertain whether Dr. Wilson communicates information, developed by Dr. Wilson and related to the safety of human subjects to the sponsor or grantee; and (c) ascertain whether Dr. Wilson complies with applicable regulatory requirements. Such Special Monitor shall report to the government on a semi-annual basis as described in Exhibit 1 as long as Dr. Wilson is subject to the restrictions described in paragraph 6 of this Agreement. If Dr. Wilson's involvement does constitute Restricted Clinical Activity, it shall be limited and governed by the provisions of paragraph 6 of this Agreement. Dr. Wilson will provide a copy of this Agreement to the sponsor and grant recipient and such Special Monitor. No reimbursement by federal funds may be sought for the cost of the Special Monitor.

9. As used for notification purposes in this Agreement, the term "FDA" refers to the Director of the Office of Compliance and Biologics Quality, Center for Biologics Evaluation and Research, United States Food and Drug Administration or the Director's Designee.

10. All notifications and other communications that Dr. Wilson, the Medical Monitor, the CRO, or the Special Monitor is required to send the government must be addressed as follows:

10.1 To the FDA:

Director
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research
United States Food and Drug Administration
1401 Rockville Pike Suite 200N
Rockville, MD 20852-1448

10. 2 To the NIH:

Director, Division of Grants Compliance and Oversight
Office of Policy for Extramural Research Administration
National Institutes of Health, DHHS
6705 Rockledge Drive, Suite 350
Bethesda, MD 20892-7974

11. Dr. Wilson agrees to author an article regarding lessons of human research participants protections learned from the OTC trial. Dr. Wilson agrees to submit an outline of such article to the United States Attorney's Office for the Eastern District of Pennsylvania (USAO) prior to its publication. Dr. Wilson agrees, in good faith, to support the publication of a written statement authored by those affected by this research in the same venue as his publication. Dr. Wilson also agrees to volunteer to lecture about the lessons of human research participants protections learned from the OTC trial in a public forum, and agrees to submit an outline of such lecture to the USAO.

12. For a five year period, Dr. Wilson agrees to certify to FDA and the NIH, on an annual basis from the date of execution of this Agreement, that he is in compliance with the terms of this Agreement.

13. Subject to the exceptions in Paragraph 15 below, in consideration of the obligations of Dr. Wilson set forth in this Agreement, the United States (on behalf of itself, its officers, agents, agencies and departments) agrees to release Dr. Wilson from any civil or administrative monetary claim the United States has or may have under the False Claims Act, 31 U.S.C. §§ 3729-3733; the Program Fraud Civil Remedies Act, 31 U.S.C. §§ 3801-3812; or the common law theories of payment by mistake, unjust enrichment, breach of contract and fraud, for the Covered Conduct.

14. In consideration of the obligations of Dr. Wilson set forth in this Agreement, HHS agrees to release and refrain from instituting, directing or maintaining any disqualification, debarment, or administrative claim under 21 CFR Part 58, 45 CFR Part 76 or 48 CFR Part 9.4 against Dr. Wilson for the Covered Conduct. In addition, this Agreement terminates the FDA's administrative proceeding against Dr. Wilson, which is captioned In the Matter of James M. Wilson, MD, Ph.D., and HHS agrees that this settlement does not constitute a civil judgment or a present civil charge pursuant to the NIH Grants Policy Statement and 45 CFR Part 76. Nothing in this Paragraph precludes HHS from taking action against entities or persons, or for conduct and practices, for which claims have been reserved in Paragraph 15, below.

15. Notwithstanding any term of this Agreement, specifically reserved and excluded from the scope and terms of this Agreement as to any entity or person are any and all of the following:

(a) Any civil, criminal or administrative claims arising under Title 26, U.S. Code (Internal Revenue Code);

(b) Any criminal liability;

(c) Except as explicitly stated in this Agreement, any administrative liability, including mandatory exclusion from Federal health care programs;

(d) Any liability to the United States (or its agencies) for any conduct other than the Covered Conduct;

(e) Any claims based upon such obligations as are created by this Agreement, including those created by the exhibits attached hereto;

(f) Any claims based on a failure to deliver items or services due;

(g) Any civil or administrative claims against individuals other than Dr. Wilson.

16. In the event that Dr. Wilson fails to comply in good faith with any of the terms of this Settlement Agreement, or should any of Dr. Wilson's representations or warrants be materially false, the United States may, at its sole discretion, exercise one or more of the following rights:

(a) seek specific performance of this Agreement and the prevailing party shall be entitled to an award of reasonable attorneys fees and costs in its favor; or

(b) exercise any other right granted by law.

17. Dr. Wilson waives and will not assert any defenses he may have to any criminal prosecution or administrative action relating to the Covered Conduct, which defenses may be based in whole or in part on a contention that, under the Double Jeopardy Clause in the Fifth Amendment of the Constitution, or under the Excessive Fines Clause in the Eighth Amendment of the Constitution, this Agreement bars a remedy sought in such criminal prosecution or administrative action. Dr. Wilson agrees that this settlement is not punitive or a penalty in purpose or effect.

18. Dr. Wilson fully and finally releases the United States, its agencies, employees, servants, and agents from any claims (including attorneys fees, costs, and expenses of every kind and however denominated) which he has asserted, could have asserted, or may assert in the future against the United States, its agencies, employees, servants, and agents, related to the Covered Conduct and the United States' investigation and prosecution thereof.

19. Dr. Wilson agrees that all costs (as defined in 45 C.F.R. § 74.27, 45 C.F.R. Part 74 and 45 C.F.R. Part 92), where applicable, whether direct or indirect incurred by or on behalf

of Dr. Wilson in connection with: (1) the matters covered by this Agreement; (2) the Government's audit(s) and civil and any criminal investigation(s) of the matters covered by this Agreement; (3) Dr. Wilson's investigation, defense, and corrective actions undertaken in response to the Government's audit(s) and civil and any criminal investigation(s) in connection with the matters covered by this Agreement (including attorney's fees), (4) the negotiation of this Agreement, and (5) any payment made pursuant to this Agreement, are unallowable costs under the cost principles applicable to government grants, contracts, cooperative Agreements, and other Agreements to which 45 C.F.R. Part 74 and 45 C.F.R. Part 92 applies (hereafter, "unallowable costs"). These unallowable costs will be separately estimated and accounted for by Dr. Wilson and Dr. Wilson will not charge such unallowable costs directly or indirectly to any grants, contracts, cooperative Agreements, or other Agreements with the United States or seek payment for such unallowable costs through any cost report, cost statement, information statement or payment request submitted by Dr. Wilson or any of its departments or agencies. The parties agree that nothing in this Agreement shall constitute a waiver of any rights the United States may have under 45 C.F.R. § 74.27, 45 C.F.R. Part 74 and 45 C.F.R. Part 92.

20. This Agreement is intended to be for the benefit of the Parties only, and by this instrument the Parties do not release any claims against any other person or entity.

21. Each party to this Agreement will bear its own legal and other costs incurred in connection with this matter, including the preparation and performance of this Agreement.

22. Dr. Wilson represents that this Agreement is freely and voluntarily entered into without any degree of duress or compulsion whatsoever.

23. This Agreement is governed by the laws of the United States. The Parties agree that the exclusive jurisdiction and venue for any dispute arising between and among the Parties under this Agreement will be the United States District Court for the Eastern District of Pennsylvania.

24. This Agreement constitutes the complete Agreement between the Parties. This Agreement may not be amended except by written consent of the Parties. The terms of this Agreement do not apply to situations in which Dr. Wilson has been listed without his knowledge as Key Personnel without effort or as Other Significant Contributor before the Effective Date of this Agreement.

25. The undersigned individuals signing this Agreement on behalf of Dr. Wilson represent and warrant that they are authorized to execute this Agreement. The undersigned United States signatories represent that they are signing this Agreement in their official capacities and that they are authorized to execute this Agreement.

26. This Agreement may be executed in counterparts, each of which constitutes an original and all of which constitute one and the same Agreement.

27. This Agreement is effective on the date of signature of the last signatory to the Agreement ("Effective Date").

28. All Parties consent to the United States' disclosure of this Agreement, and information about this Agreement, to the public.

THE UNITED STATES OF AMERICA

PATRICK L. MEEHAN
United States Attorney
Eastern District of Pennsylvania

DATED:_____ BY: _____
JAMES G. SHEEHAN
Associate United States Attorney
United States Attorney's Office
Eastern District of Pennsylvania

DATED:_____ BY: _____
DAVID R. HOFFMAN
Assistant United States Attorney
Eastern District of Pennsylvania

DATED:_____ BY: _____
LEWIS MORRIS
Chief Counsel
Office of Inspector General
United States Department of
Health and Human Services

DATED:_____ BY: _____
MARC R. WEISMAN
Director, Acquisition and
Management Policy
United States Department of
Health and Human Services

BY: _____
MARY MALARKEY
Director
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research
Food and Drug Administration

BY: _____
NORKA RUIZ BRAVO, Ph.D.
Deputy Director for Extramural Research
National Institutes of Health

FOR JAMES M. WILSON, M.D., Ph.D.

DATED:_____ BY: _____
JAMES M. WILSON, M.D., Ph.D.

DATED:_____ BY: _____
DAVID M. HOWARD, ESQ.
DECHERT LLP