**MASTER CLINICAL STUDY AGREEMENT**

THIS MASTER CLINICAL STUDY AGREEMENT is made and entered into as of the 22nd day of July, 2003 (the "Effective Date"), by and among Wyeth Pharmaceuticals Inc., sometimes acting through its division, Wyeth Research, having a business address at 555 East Lancaster Avenue, St. Davids, Pennsylvania 19087 ("Sponsor"), and each of The University of Texas Health Science Center at San Antonio, The University of Texas Health Science Center at Houston, The University of Texas MD Anderson Cancer Center, The University of Texas Health Center at Tyler, The University of Texas Medical Branch at Galveston, and The University of Texas Southwestern Medical Center at Dallas (each an "Institution" and, collectively, the "Institutions"), each with an office and place of business as set forth on Schedule 1 hereto, and each a component institution of The University of Texas System, located at 201 West 7th Street, Austin TX 78701 ("System"), as governed by its Board of Regents ("Regents").

**RECITALS**

WHEREAS, Sponsor conducts business in the research and development, manufacture and marketing of pharmaceutical products; and

WHEREAS, each Institution has the requisite skill and ability in the conduct of clinical research studies with investigational pharmaceutical products and has the requisite experience with the requirements, processes and procedures related to such clinical studies; and

WHEREAS, Sponsor wishes to have the Institutions conduct certain clinical research studies pursuant to this Master Agreement (as defined below) and separate Protocol Agreements (as defined below) which are to be entered into with respect to each such individual research study and incorporated herein by reference; and

WHEREAS, certain of the Protocol Agreements may include a Contract Research Organization (as defined below) who will, in connection with such Protocol Agreement, provide certain services and perform certain functions as delegated to it by Sponsor; and

WHEREAS, the clinical studies contemplated by this Master Agreement are of mutual interest and benefit to the Institutions and Sponsor, and will further the Institutions' instructional, basic science, clinical science and fundamental research objectives and missions.

NOW, THEREFORE, for and in consideration of the above recitals, which are incorporated herein by reference as covenants, and for other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, and intending to be legally bound by the terms, conditions and covenants hereinafter set forth, the parties agree as follows:

 **ARTICLE 1
Definitions**

In addition to the terms defined above and elsewhere in this Master Agreement, the following terms shall have the meanings set forth in this Article 1.

1.1. "Audit" shall mean a systematic examination, by Sponsor or a third party chosen by Sponsor, of study-related activities and documents to determine whether the evaluated study-related activities were conducted, and the data were recorded, analyzed, and accurately reported according to the applicable Protocol (as defined below), the terms of this Master Agreement and the respective Protocol Agreements, Good Clinical Practice, and the applicable regulatory requirement(s).

1.2. "Biological Samples" include, without limitation, blood, serum, fluid and tissue biopsy samples collected from Study Patients (as defined below) enrolled in a study that are not directly related to patient care or safety monitoring, including pharmacokinetic, pharmacogenomic or biomarker testing. Biological Samples further include, without limitation, any tangible material directly or indirectly derived from such blood, fluid or tissue samples, such as: genes, gene fragments, gene sequences, proteins, protein fragments, protein sequences, probes, DNA, RNA, cDNA libraries, plasmids, vectors, expression systems, cells, cell lines, organisms, antibodies or other biological substances; and any constituents, progeny, mutants, variants, derivatives, replications, reagents or chemical compounds thereof or derived therefrom.

1.3. "Case Report Form" or "CRF" shall mean a printed, optical, or electronic document designed to record all of the Protocol-required information to be reported to Sponsor on each Study Patient.

1.4. "Contract Research Organization" or "CRO" shall mean a person or an organization (commercial, academic, or other) contracted by Sponsor to perform one or more of a Sponsor's study-related duties and functions. The CRO for a study, if applicable, will be provided in each respective Protocol Agreement.

1.5. "Debarred or Disqualified Person" means any person subject to limitations or any form of enforcement imposed upon clinical investigators or study sites by the United States Food and Drug Administration (FDA), the European Medicines Evaluation Agency (EMEA), or any Regulatory Authority or other recognized national, multi-national, or industry body.

1.6. "Good Clinical Practice" or "GCP" shall mean any standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of Study Patients are protected as defined by the then current International Conference on Harmonisation ("ICH") Guideline for Good Clinical Practice.

1.7. "Independent Ethics Committee" ("IEC") shall mean an independent body (a review board or a committee, institutional, regional, national or supranational), constituted of medical/scientific professionals and non-medical/non-scientific members, whose responsibility it is to ensure the protection of the rights, safety and well-being of human subjects involved in a clinical trial and to provide public assurance of that protection, by, among other things, reviewing and approving/providing favorable opinion on each Protocol, the suitability of the investigator(s), facilities, and the methods and material to be used in obtaining and documenting the informed consent of Study Patients.

1.8. "Informed Consent" shall mean a process by which a Study Patient voluntarily confirms his or her willingness to participate in a particular study, after having been informed of all aspects of such study that are relevant to the Study Patient's decision to participate. Informed Consent is documented by means of a written, signed, and dated informed consent form as defined by the then-current Guideline for Good Clinical Practice.

1.9. "Institutional Review Board" or "IRB" shall mean an independent body constituted of medical, scientific, and nonscientific members, whose responsibility it is to ensure the protection of the rights, safety, and well-being of human subjects involved in a clinical trial, by, among other things, reviewing, approving, and providing continuing review to be used in protocols and amendments, and of the methods and material to be used in obtaining and documenting informed consent of the Study Patients.

1.10. "Master Agreement" shall mean this Master Clinical Study Agreement and any Exhibits, Protocol Agreements and Schedules incorporated herein by reference, as amended from time to time.

1.11. "Personnel" shall mean other employees of each Institution under Principal Investigator's (as defined below) supervision and direction to whom specific study responsibilities and/or work assignments have been assigned. Personnel includes without limitation, Other Clinical Investigators (as defined in Section 2.4.1 below). All Personnel shall at all relevant times be an employee of Institution.

1.12. "Principal Investigator" shall mean an employee of Institution who actually conducts a study (i.e., under whose immediate direction the Study Drug is administered or dispensed to a Study Patient). In the event a study is conducted by a team of individuals (e.g., study coordinators or Other Clinical Investigators, as defined below), the Principal Investigator is the responsible leader of the team. The Principal Investigator for each respective study shall be as set forth in the applicable Protocol Agreement.

1.13. "Protocol" shall mean, collectively, the scientific, administrative and other written specifications and written requirements under which a particular study shall be conducted, as more particularly set forth in the individual Protocol Agreement applicable thereto, as same may be amended in writing from time to time in accordance therewith.

1.14. "Protocol Agreement" shall mean an agreement entered into among Sponsor, Principal Investigator and an Institution, which sets forth the Protocol and budget for a particular study, which agreement shall be executed for each study to be conducted under this Master Agreement and substantially in the form attached hereto as Exhibit "A". Each such Protocol Agreement is incorporated herein by reference and made a part of this Master Agreement.

1.15. "Regulatory Authority" shall mean: (i) any and all national, multi-national (as used in this Agreement including without limitation the FDA and the EMEA), or other governmental or industry agency or body with authority over the manner in which a clinical trial is conducted in a country; and (ii) any national or multi-national authority responsible for granting regulatory approval in a particular country or multi-national group or union of countries.

1.16. "Study Patient" shall mean an individual who participates in a study, either as a recipient of a Study Drug or as a control.

1.17. "Study Documents" shall mean, with respect to each study, all documents other than the Protocol and Protocol Agreement that are provided by the Sponsor to an Institution, Principal Investigator or Personnel, which instruct, provide information or otherwise explain the conduct of such study. In the event of a conflict between a Study Document and the respective Protocol Agreement, the Protocol Agreement shall control.

1.18. "Study Drug" shall mean, with respect to each study, the drug that is the subject of such study, identified by chemical compound or brand name and as set forth and described more particularly in the Protocol Agreement applicable thereto.

 **ARTICLE 2
Conduct of Study**

2.1. Protocol Agreements. A Protocol and budget for each study to be conducted hereunder shall be separately negotiated and agreed to by Sponsor, Principal Investigator and each Institution, pursuant to a Protocol Agreement to be executed by such parties. This Master Agreement shall be deemed to apply to each such Protocol Agreement so executed as fully and with like effect as though this Master Agreement were re-executed at the time each such Protocol Agreement is executed. If any provisions of any such Protocol Agreement should conflict with any provisions set forth in this Master Agreement, the provisions of this Master Agreement shall control, unless such Protocol Agreement expressly refers to the provision(s) of this Master Agreement that it is intended to replace or modify (and which change shall be limited in force and effect to such Protocol Agreement only).

2.2. Compliance with Protocol. Institution, Principal Investigator and Personnel shall conduct each study in strict accordance with the Protocol and applicable Study Documents , which may be amended and/or revised in writing by Sponsor on a case-by-case basis. Institution and Principal Investigator may not deviate from the Protocol set forth in a Protocol Agreement without Sponsor's prior written consent except as necessary to protect the safety and welfare of the Study Patients and in conformity with the generally accepted standards of the medical community in which Principal Investigator practices. Institution and Principal Investigator shall immediately notify Sponsor of any such deviation and follow with prompt written confirmation thereof.

2.3. Compliance with laws, regulations and guidelines. Institution, Principal Investigator and Personnel shall comply with all applicable federal, state and local laws, regulations and guidelines, including but not limited to the (i) Federal Food Drug and Cosmetics Act, as amended and regulations promulgated thereunder, (ii) regulations of the Centers for Medicare and Medicaid Services ("CMS"), (iii) regulations and guidances governing the protections of human subjects, including but not limited to the Declaration of Helsinki, (iv) regulations and guidances governing the conduct of clinical research, specifically including but not limited to GCP, (v) laws and regulations governing the purchase and sale of securities in a company while in possession of material, non-public information about that company, (vi) laws, rules and regulations regarding the federal anti-kickback statute (42 U.S.C. 1320a-7(b)) and the related safe harbor regulations, and (vii) the Limitation on Certain Physician Referrals, also referred to as the "Stark Law" (42 U.S.C. 1395nn). Additionally, Institution, Principal Investigator and Personnel shall comply with generally accepted professional clinical and research standards of care.

2.4. Investigators. Each study shall be conducted by and under the direction and supervision of the Principal Investigator named in the Protocol Agreement applicable thereto. Such Principal Investigator shall at all relevant times be an employee of Institution.

2.4.1. Sub-investigator and Co-investigator. Institution and Principal Investigator may recommend the inclusion of any co-investigators or sub-investigators ("Other Clinical Investigators"). Such inclusion is subject to the prior written approval of Sponsor.

2.4.2. Replacement. In the event Principal Investigator or Other Clinical Investigators are unable or unwilling to carry out their duties under this Master Agreement and each respective Protocol Agreement, Institution may nominate a replacement for such Principal Investigator or Other Clinical Investigators. Sponsor, in its sole discretion, may approve or reject such replacements. In the event that such replacements are not approved, Sponsor reserves the right to terminate the respective Protocol Agreement in accordance with Section 13 of this Master Agreement.

2.4.3. Additional Personnel and Material Support. Institution shall arrange for qualified medical, technical, laboratory services, and any Personnel necessary to support its obligations under this Master Agreement and each Protocol Agreement. Institution represents and certifies that such Personnel will abide by the terms and conditions of this Master Agreement that impose confidentiality obligations on such Personnel, as if each were a party hereto, and that any rights such Personnel might otherwise have in the results of their work (excluding their scholarly works) will effectively vest in Institution and Institution will be permitted to assign all such rights to Sponsor.

Institution and Principal Investigator shall be responsible for ensuring that all Personnel are qualified by education, training or experience to perform their respective study responsibilities/work assignments. Institution and Principal Investigator shall provide to all relevant Personnel, subject to the confidentiality provisions of Article 5 of this Master Agreement, copies of the Protocol and all Study Documents which relate to preclinical and prior clinical experience and are furnished to the Institution and Principal Investigator by Sponsor. Institution and Principal Investigator shall be responsible for ensuring, at the beginning of each study and on an ongoing basis during such study, that Personnel are fully informed regarding the Study Drug, including by review and discussion of the above-referenced material, the conduct of the study pursuant to the Protocol Agreement and any amendments thereto, and such Personnel's obligations with respect to this Master Agreement and each respective Protocol Agreement, including compliance with applicable laws and regulations, as defined above.

2.5. Ownership, Delivery, Handling and Return of Study Drug. Sponsor is and shall at all times remain the sole owner of each Study Drug. Sponsor shall provide Institution and Principal Investigator with the required quantities of the Study Drug, at no cost, for Institution and Principal Investigator to conduct each study. Shipment of the Study Drug for each study will be subject to the applicable Protocol Agreement. Institution will handle and store the Study Drug in accordance with the Protocol Agreement, Study Documents, and all applicable laws and regulations and, upon conclusion of the respective study, will return all unused Study Drug to Sponsor or Sponsor's designee at Sponsor's expense or dispose of all unused portions thereof in accordance with Sponsor's written instructions. In case of noncompliance with this Master Agreement, Sponsor reserves the right to require Institution to return all unused Study Drugs immediately at Sponsor's expense. Institution shall maintain records on the receipt and disposition of all Study Drugs, including dates, quantity and use by patients. If requested by Sponsor, all empty Study Drug containers shall be retained and returned to Sponsor or Sponsor's designee at Sponsor's expense.

2.6. Unrelated Research. Institution and Principal Investigator shall not concurrently enroll any Study Patient who is enrolled in a study in any other conflicting clinical trial or perform any unrelated research on any Study Patient without the prior written consent of Sponsor.

2.7. Institutional Review Board/Independent Ethics Committee. Each study shall be conducted under the supervision and with the approval of the IRB/IEC. Institution and Principal Investigator shall conduct the study only after its IRB/IEC has approved the Protocol, Informed Consent, and Study Patient recruitment documents, as applicable, and any amendments to the foregoing, in writing and a copy of these approvals has been received by Sponsor. In the event of any amendment to a Protocol Agreement that requires IRB/IEC review, continuation of the study at the Institution is subject to IRB/IEC approval of the amendment. Sponsor reserves the right to terminate any Protocol Agreement in accordance with Article 13 herein if IRB/IEC does not approve such amendment. Principal Investigator shall keep the IRB/IEC fully informed of the progress of each study. Institution and Principal Investigator shall forward to Sponsor copies of all correspondence to or from the IRB/IEC concerning each study and shall notify Sponsor of any refusal of, withdrawal of, or suspension of IRB/IEC approval within twenty-four (24) hours of receiving such notification. For sake of clarity, use of the phrase "IRB/IEC" here and throughout this Master Agreement means "IRB and/or IEC (if applicable)".

Principal Investigator shall obtain continuing review and approval of each study from the IRB and/or IEC (if applicable) including but not limited to submission of information regarding adverse events and amendments to the Protocol Agreement. Principal Investigator shall submit copies of continuing approvals to Sponsor. Institution and Principal Investigator shall submit an annual report to the IRB and/or IEC regarding each study with a copy to Sponsor.

2.8. Study Patient Consent. Institution and Principal Investigator shall obtain from all Study Patients a signed Informed Consent form, in accordance with applicable laws and regulations, approved by Sponsor and the IRB/IEC, prior to their participation in a study or undergoing any study test, examination or procedure. Institution will ensure that Principal Investigator has obtained a signed Informed Consent from a Study Patient before any Protocol-mandated procedures are performed on that Study Patient at Institution. Additional Informed Consent forms may be required in accordance with any amendments to a Protocol or individual Protocol Agreement.

2.9. Protected Health Information. Institution shall comply with all relevant and applicable laws and regulations governing the privacy and security of health information, including without limitation Title II of the Health Insurance Portability and Accountability Act and applicable regulations promulgated thereunder ("HIPAA"). To the extent required by applicable law, Institution will also require Principal Investigator, all Personnel and any other third parties involved in the conduct of each study to comply with applicable law.

Institution shall treat all information regarding diagnosis, history or treatment that allows unique identification of an individual ("Protected Health Information"), as that term is defined by 45 CFR § 164.501, as confidential. To the extent required by applicable law, Institution and Sponsor will implement and maintain such privacy and security safeguards as are necessary to ensure that Protected Health Information is adequately protected from unauthorized access, and that any disclosure of such information is compliant with applicable HIPAA requirements.

Institution and Principal Investigator shall ensure that all consents and authorizations required by applicable law are obtained from Study Patient, such that Sponsor and each of Sponsor's contractors are permitted to access the Protected Health Information of any Study Patient for the purpose of fulfilling any obligation under this Master Agreement or a Protocol Agreement, or for the purpose of complying with any requirement under applicable law or any other legal or regulatory requirement to which Sponsor is subject.

In the event that this Master Agreement, a Protocol Agreement, or any practices which could be or are employed in exercising rights under this Master Agreement or any Protocol Agreement are inconsistent with or do not satisfy the requirements of applicable law relating to the privacy of Protected Health Information, the parties shall take any action necessary to bring performance under this Master Agreement or any Protocol Agreement into compliance with such applicable law, including amending or modifying this Master Agreement or any such Protocol Agreement.

2.10. Records and Reporting.

2.10.1. Complete and Accurate Records. Institution and Principal Investigator shall maintain complete and accurate records of the status and progress of each study, all Study Patient information and all other data and information related to such study, including, but not limited to CRFs, Informed Consent Forms, Principal Investigator or Other Clinical Investigator's study notebook, Study Drug disposition forms and any documents deemed essential documents as defined by ICH Guideline for Good Clinical Practice Section 8, and shall provide such documents, data or information to Sponsor upon written request. Institution and Principal Investigator shall promptly complete, and allow Sponsor access to, Sponsor supplied CRFs for all Study Patients and any original source documents for all Study Patients. Institution and Principal Investigator shall comply with Sponsor's written instructions regarding the direct data flow process (in accordance with the applicable Study Documents). Upon Sponsor's written request, Institution, Personnel and Principal Investigator shall correct any CRF errors and/or omissions. At all times Sponsor shall remain the sole owner of all CRFs. Subject to the Confidentiality and Publication restrictions set forth in this Master Agreement, nothing herein, however, shall prevent Institution and Principal Investigator from using information or data, generated solely by Institution and/or Principal Investigator and provided to Sponsor hereunder, for non-commercial research and educational purposes of a state university.

2.10.2. Periodic Reports and Meetings. At Sponsor's written request, Institution and Principal Investigator shall advise Sponsor of the status of a study through regular telephone conversations, written correspondence, and meetings with Sponsor.

2.10.3. Final Report. Institution shall complete a final report on each study, in accordance with the Protocol Agreement applicable thereto. If a study is suspended or terminated prior to completion, Institution shall provide Sponsor with a final report of the results of such study through the date of suspension or termination. At all times Sponsor shall remain the sole owner of the final report. Subject to the Confidentiality and Publication restrictions set forth in this Master Agreement, nothing herein, however, shall prevent Institution and Principal Investigator from using information or data, generated solely by Institution and/or Principal Investigator and provided to Sponsor hereunder, for non-commercial research and educational purposes of a state university.

2.10.4. Retention of Records. Institution shall retain and preserve one (1) copy only of all data generated in the course of a study for the longer of: (i) two (2) years after the last marketing authorization for the Study Drug has been approved or Sponsor has discontinued its research with respect to such drug or (ii) such longer period as required by applicable global regulatory requirements or as required by law. At the end of such period, Institution and Principal Investigator shall notify Sponsor of their intent to destroy all such material. Sponsor shall have thirty (30) days to respond to Institution's notice, and Sponsor shall have a further opportunity to retain such materials at Sponsor's expense.

2.10.5. Communication of Study Results to Study Patients. Principal Investigator is encouraged to disclose a summary of the results of each study to Study Patients in accordance with Article 6 of this Master Agreement.

2.11. Sponsor Auditing and Source Document Verification (SDV). Institution and Principal Investigator shall reasonably cooperate and make all necessary documents (including but not limited to source data/documents) and Personnel available to Sponsor to permit Sponsor to examine, analyze, verify, monitor and audit the Study as necessary. Sponsor shall have the right to monitor and audit each study, including access to records and Personnel and Principal Investigator involved in the conduct of the study. Institution, Principal Investigator and Personnel shall also participate as necessary in follow-up to monitoring visits and Audits to ensure compliance with all applicable laws and regulations.

2.12. Inspections and Audits. Institution, Principal Investigator and Personnel shall also make all necessary data and documents available to a Regulatory Authority or other governmental authorities or the IRB/IEC for inspection or auditing. In the event Institution or Principal Investigator receives notice that the activities of it or the IRB/IEC relating to a Protocol shall be the subject of an inspection, investigation or Audit by a Regulatory Authority, Institution or Principal Investigator receiving such notice shall promptly notify Sponsor. In the event Institution or Principal Investigator does not receive prior notice of said inspection, investigation or Audit, Institution or Principal Investigator shall notify Sponsor as soon as practicable after receiving notice of said inspection, investigation or Audit. Institution and Principal Investigator shall provide Sponsor with copies of any documents received from or provided to a Regulatory Authority or other governmental authorities related to a Protocol.

2.13. Non-Exclusive Relationships. Nothing in this Master Agreement will limit or prohibit Institution or any Personnel, including Principal Investigator, from conducting any research or for performing research for or with any entity or person, including any other outside sponsors. Sponsor acknowledges that this provision is intended to preserve the academic freedom and integrity of Institution and its faculty and to ensure that Institution and its faculty are not regarded as captive researchers for Sponsor.

2.14. E-Clinical Representations . Institution acknowledges and agrees that if a Protocol Agreement so provides, the research to be performed under such Protocol Agreement shall be conducted in whole or in part using Sponsor's Web-based Clinical Information System ("eClinical System"), and Institution will record some or all of the clinical data electronically.

Institution represents for itself and on behalf of Principal Investigator and all Personnel that:

2.14.1. all data entered into the eClinical System shall be complete, accurate and reliable;

2.14.2. access to the eClinical System shall be restricted, by means of assigned user identification and password, to the Principal Investigator and Personnel;

2.14.3. with respect to all data gathered pursuant to the applicable Protocol Agreement, Institution, Principal Investigator and Personnel shall at all times comply with the Confidential Disclosure Agreement executed between the parties, if applicable, the confidentiality and data ownership provisions of this Master Agreement and all applicable federal, state and foreign laws (as applicable), rules and regulations;

2.14.4. Institution, Principal Investigator and Personnel shall not use any data collected pursuant to this Master Agreement in any way outside the scope of this Master Agreement, including without limitation, in a manner that would infringe upon Sponsor's proprietary rights therein; and

2.14.5. Neither Institution nor Principal Investigator nor any Personnel shall cause the eClinical System or any data entered thereon to be corrupted or otherwise compromised by means of a computer virus, worm, or lock-out mechanism, or any other similar means.

 **ARTICLE 3
Serious Adverse Event (SAE) and Adverse Event (AE) Reporting**

For each study conducted, Institution and Principal Investigator shall report all SAEs and AEs as set forth in the Protocol Agreement applicable thereto.

 **ARTICLE 4
Compensation**

4.1. Payment. Sponsor shall pay Institution for the conduct of each study in accordance with the budget attached to and incorporated in each respective Protocol Agreement. Institution shall be fully and solely responsible for making any and all payments to any and all parties to this Master Agreement, as well as Principal Investigator, Other Clinical Investigators, or any other third parties or agents thereof who provide services hereunder. Except as may be otherwise set forth in this Master Agreement or the applicable Protocol Agreement, it is expressly understood and agreed that such payments constitute the full compensation for the work performed under the applicable Protocol and Protocol Agreement, including treatments, evaluations, procedures or any supplies, along with overhead and administrative services. Institution shall monitor expenditures, in accordance with its institutional policies, to ensure that the funds provided by Sponsor are spent in connection with the performance of each study. Institution and Principal Investigator, shall not seek payment or accept reimbursement, and similarly shall advise any other individual or entity associated with the Institution and/or Principal Investigator not to seek reimbursement or accept payment from any third party payer, including but not limited to any governmental entity, insurance plan or other third party for any examinations, procedures, testing, Study Drug, or supplies or other requirements of a study which are paid for by Sponsor or its designated agent in connection with the Protocol Agreement. It is expressly agreed that no payments made by Sponsor under this Master Agreement or the applicable Protocol Agreement shall be used for any examinations, procedures, testing, Study Drug, or supplies or other requirements of any Protocol Agreement for which a governmental entity, insurance plan or other third party has provided payment or reimbursement to the Institution or Principal Investigator. The Principal Investigator and/or Institution may not charge any Study Patient for the Study Drug that has been provided by the Sponsor. In addition to the foregoing, Principal Investigator and Institution each represents that the compensation provided for the services under the terms of this Master Agreement and any related Protocol Agreement shall be consistent with fair market value in arm's length transactions and has not been determined in a manner which takes into account the volume or value of any referrals or other business otherwise generated between the parties for which payment may be made in whole or in part under any federal or state health care program, including Medicare and/or Medicaid, and the payment thereof has not been made in exchange for any explicit or implicit agreement that Principal Investigator purchase, recommend or otherwise arrange for the use of any of Sponsor's product(s).

4.2. Initial Payment. Sponsor or its designated agent will pay Institution an initial payment in accordance with each Protocol Agreement upon the execution thereof. This amount shall be applied against Institution's first Study Patient payment. In the event that Institution does not enroll a patient into the study, Institution shall return this initial payment to Sponsor upon completion or termination of the study.

4.3. Payment for Study Visits. Following the initial payment, Institution shall thereafter be eligible to receive payment in accordance with the budget and payment schedule set forth in the respective Protocol Agreement.

4.4. Final Payment. Final payment shall be made in accordance with each Protocol Agreement and related budget and payment schedule thereunder, following the Study Patient's completion of all Study Patient visits and Sponsor's verification that all CRFs have been retrieved and verified and all queries have been resolved for each patient visit.

4.5. Screen Failures. Sponsor shall not pay for screen failures for patients who are found to be ineligible for participation in a study except as otherwise provided according to the terms of the applicable Protocol Agreement. Institution shall provide the results of all screening examinations and tests that are required in a Protocol and complete any CRFs required.

4.6. IRB/IEC Fees. Institution shall invoice Sponsor directly for IRB/IEC fees. Sponsor or its designated agent shall reimburse Institution for such IRB/IEC fee payments upon receipt of an invoice and in accordance with the Protocol Agreement.

4.7. No Payment. Sponsor shall not pay Institution for any Study Patient whose enrollment in a study materially deviates from the applicable Protocol's eligibility criteria or from whom data cannot be analyzed because of material Protocol deviations, lack of proper records or incomplete, uncorrected or unverifiable CRFs.

4.8. Partial Payment. Sponsor or its designated agent shall pay Institution on a prorated basis for any Study Patient who does not complete all treatments and evaluations in accordance with the applicable Protocol or who prematurely withdraws or is removed from the study. Payment amounts will be based on the number of completed study visits and in accordance with the applicable Protocol Agreement.

4.9. Payee Information. All payments shall be made to Institution at the address listed in the applicable Protocol Agreement.

 **ARTICLE 5
Confidentiality**

"Confidential Information" shall mean all unpublished material and information that is disclosed in connection with this Master Agreement or any related Protocol Agreement, including, but not limited to, Study Documents, investigator's brochures, study protocols or synopses thereof and related materials, any data or other information provided by Sponsor, as well as all information generated or developed by Institution or Principal Investigator in the course of the performance of their work on a study and/or providing other research services in connection therewith. Notwithstanding the foregoing, Sponsor grants Principal Investigator the right to publish the results of a study in accordance with Article 6 of this Master Agreement.

5.1. Institution and/or Principal Investigator shall not reveal results of a study to any third party except in accordance with Article 6 of this Master Agreement. Except as expressly authorized herein, Institution and Principal Investigator shall not disclose to any third party or use for its/his/her own benefit or that of any third party any Confidential Information received from Sponsor or its agent, or developed by Institution and Principal Investigator in the performance of their work on a study and/or providing other research services in connection therewith. Institution and Principal Investigator shall protect and safeguard Sponsor's Confidential Information in at least the same manner as their own confidential information, but in no event shall less than reasonable care be used.

5.2. Such information shall not be considered confidential nor subject to this Master Agreement to the extent that it:

5.2.1. was rightfully in the possession of Institution or Principal Investigator prior to the date of disclosure of such information to Institution or Principal Investigator as demonstrated by competent evidence; or

5.2.2. was in the public domain prior to the date of disclosure to Institution or Principal Investigator; or

5.2.3. becomes part of the public domain by publication or otherwise through no fault or unauthorized act or omission on the part of Institution or Principal Investigator; or

5.2.4. is developed by Institution or Principal Investigator independently of any disclosure by Sponsor, as demonstrated by competent evidence; or

5.2.5. is acquired directly or indirectly by Institution or Principal Investigator from a source having the right to disclose such information, as demonstrated by competent evidence; or
5.2.6. is disclosed for the safety and well being of a Study Patient in connection with medically necessary treatment; or

5.2.7. is necessary to disclose in order to file a patent application or enforce a patent related to this Master Agreement; or

5.2.8. is reasonably requested by a prospective Study Patient during the process of obtaining Informed Consent, provided, however, that the information will be disclosed only to the extent necessary and Confidential Information will not be provided to answer unsolicited inquiries by telephone or to individuals who are not eligible study candidates.

5.3. Institution may disclose Confidential Information to a governmental authority upon written request or by order of a court of competent jurisdiction, or as otherwise required to be disclosed by law or applicable regulation, provided that reasonable advance notice, if legally permissible, is provided to Sponsor, and Institution takes all reasonable steps to limit the scope of such required disclosure, including, without limitation, assisting Sponsor in seeking all applicable governmental or judicial protection available for such material and providing Sponsor with an opportunity to comment on such disclosure.

5.4. Nothing in this Master Agreement, any Protocol Agreement or the disclosure of information hereunder shall be deemed by implication or otherwise to vest in the receiving party any rights or licenses to any patents, trade secrets, or other property of the disclosing party.

5.5. The confidentiality obligations of this Article 5 shall survive the termination or expiration of each Protocol Agreement for a period of five (5) years after its termination or expiration.

 **ARTICLE 6
Publication**

6.1. If a study is part of a multicenter study, then neither Institution nor Principal Investigator shall publish or present data from such study center until the earlier of (a) the complete multicenter study publication has been presented in full, (b) Sponsor confirms that there will be no multi-center publication or presentation, (c) or eighteen (18) months have elapsed since the termination of the multicenter study. Subsequent publications and presentations must refer to the multicenter findings. Thereafter, or in the event a study is not part of a multicenter study, if Institution or Principal Investigator expects to participate in the publication or presentation of data generated in the performance of such study, Institution and/or Principal Investigator shall submit reports, abstracts, manuscripts and or other presentation materials to Sponsor for review prior to submission for publication or presentation. Sponsor shall have thirty (30) calendar days to respond with any requested revisions in order to protect Sponsor's Confidential Information. Principal Investigator shall consider in good faith such requested revisions, and Principal Investigator shall delete from such proposed publication any Confidential Information provided to Institution by Sponsor. Principal Investigator shall delay submission of such publication or presentation materials for up to an additional sixty (60) calendar days in order to have a patent application(s) filed pursuant to Article 7 of this Master Agreement.

 **ARTICLE 7
Inventions and Discoveries**

7.1. Inventorship shall be determined in accordance with U.S. patent law.

7.2. Any inventions or discoveries (whether patentable or not), innovations, suggestions, ideas, improvements, enhancements, and reports made or developed by Institution, Principal Investigator and/or Personnel during the course of a study conducted in accordance with the Protocol, which directly relate to a Study Drug, including without limitation, its composition or the composition of its derivatives; the use of it or its derivatives; the administration of it or its derivatives; or any formulations or methods of manufacture of a Study Drug or its derivatives shall be promptly disclosed to Sponsor and shall become the sole and exclusive property of Sponsor ("Sponsor Inventions"). Upon Sponsor's written request and at Sponsor's expense, Institution and/or Principal Investigator shall take such actions as Sponsor deems necessary or appropriate to obtain patent or other proprietary protection in Sponsor's name with respect to any of the foregoing.

7.3. Institution shall promptly notify Sponsor of all other inventions or discoveries (whether patentable or not), innovations, suggestions, ideas, improvements, enhancements, and reports made or developed by Institution, Principal Investigator and/or Personnel in the performance of a study (whether or not jointly with Sponsor's employees or using Sponsor's information) ("Institution Inventions"). Sponsor shall notify Institution in writing within two (2) months of its receipt of full written disclosure of an Institution Invention if Sponsor wishes to have a patent application filed by Institution with respect to the subject matter of such disclosure. Institution shall prepare and file such patent application and subsequently see to the prosecution, issuance and maintenance of such application or resulting patent, including divisions, continuations and reissues thereof. Sponsor shall pay all reasonable costs and expenses related to such patent application, including, but not limited to, search fees, filing fees, prosecution costs and fees, issuance fees, and maintenance fees. Sponsor shall be responsible for such patent costs and fees so long as the option pursuant to Article 7.4.2 has not terminated or expired. Sponsor shall be consulted concerning the preparation, filing, prosecution, issuance and maintenance of all such patent applications, including receiving copies of a draft patent application, prior to filing, and of all correspondence from and to the particular patent office. Within nine (9) months of the first filing of any patent application in the U.S. Patent and Trademark Office, Sponsor shall notify Institution in writing of its desire to have said application filed in particular foreign countries by appropriate local, regional or international applications. Sponsor shall likewise bear such patent costs and expenses and have such patent consulting rights for such foreign applications until the termination or lapse of its option or license to the particular subject matter.

7.4. For all Institution Inventions, Institution on its own behalf and on behalf of the Principal Investigator and Personnel, hereby grants Sponsor:

7.4.1. an irrevocable, non-exclusive, worldwide, royalty-free license for internal research purposes to Institution's and Principal Investigator's rights and interests in Institution Inventions; and

7.4.2. an exclusive option to negotiate an exclusive, worldwide, royalty-bearing license (including the right to grant sublicenses) to make, have made, use, offer to sell, sell, distribute or otherwise commercialize Institution Inventions owned, in whole or in part, by Institution and/or Principal Investigator, under terms to be negotiated in good faith between the parties.

7.5. Sponsor shall have nine (9) months from the filing of a patent application under Article 7.3 to notify Institution in writing of its desire to negotiate a license agreement, pursuant to Article 7.4.2. The parties shall negotiate the terms of such license agreement in good faith within a period not to exceed three (3) months from Sponsor's notification to Institution of its desire to negotiate a license agreement, or such period of time as to which the parties shall mutually agree. The parties shall also negotiate a commercially reasonable royalty rate. If Sponsor and Institution fail to enter into a license agreement during that period of time, then Institution may offer rights to such Institution Invention to third parties; provided, however, for a period of three (3) months from the termination of license agreement negotiations, Sponsor shall have the right of first refusal to any license, that offers more favorable terms, negotiated between Institution and any third party.

7.6. The Protocol Agreement defines the research to be performed by Institution and Principal Investigator under the applicable Protocol set forth therein. In the event that Institution and/or Principal Investigator perform(s) any research not authorized by the applicable Protocol including, without limitation, any research that utilizes any unused or otherwise discarded Study Drug or any other material provided to Institution and/or Principal Investigator by Sponsor pursuant to such Protocol, the results of such unauthorized research, and any discoveries or inventions which arise from any such unauthorized research, whether patentable or not, shall belong solely and exclusively to Sponsor.

7.7. It is expressly agreed that neither Sponsor nor Institution transfers to the other party, by operation of this Master Agreement or any Protocol Agreement, any patent right, copyright, or other proprietary right either party owns as of the commencement date of this Master Agreement and the respective Protocol Agreement. Sponsor does not transfer to Institution or Principal Investigator by operation of this Master Agreement or any Protocol Agreement any future patent right, copyright or other proprietary right of Sponsor, except as expressly provided herein.

7.8. Institution represents that, as a condition of employment, each Principal Investigator and all Personnel agree to assign all of their rights in any patents, copyrights and/or other intellectual property that may result from their employment by Institution. Institution represents that Institution has full power and authority to enforce each of its, Principal Investigator's and Personnel's obligations to Sponsor under this Article 7.

 **ARTICLE 8
Data Ownership and Copyright**

8.1. Sponsor shall have exclusive ownership of all data and compilations of data generated in the performance of each study and shall have the exclusive right to use all data and compilations of data, including but not limited to the right to use data and information in submissions to governmental or regulatory authorities. Institution shall only have the right to use the information it has generated from a study for publication purposes, or for internal educational, clinical or non-commercial research purposes, subject to the Confidentiality and Publications restrictions herein. All medical records on Study Patients shall remain the property of Institution.

8.2. All rights, title and interest to the data and compilations of data which are created for a study and the related Protocol, CRFs and operations manual provided by Sponsor used at Institution, as well as the final report of such study, including copyright therein, shall belong to and remain the sole and exclusive property of Sponsor, provided that Institution may retain and use copies of such information as permitted in this Master Agreement. Principal Investigator has the right to publish the data generated from a study in accordance with Article 6 of this Master Agreement. Any scholarly work created under this Master Agreement is owned by its author.

8.3. Biological Samples. If and to the extent so specified in a particular Protocol, Principal Investigator may collect and provide to Sponsor or its designee, Biological Samples (as defined above) obtained from Study Patients for testing that is not directly related to patient care or safety monitoring, such testing includes but is not limited to pharmacokinetic, pharmacogenomics or biomarker testing.

8.3.1. Institution's Collection, Retention and Use of Biological Samples. Institution will collect, retain and use Biological Samples in accordance with the applicable Protocol. Institution may collect and/or reserve additional quantities of Biological Samples ("Secondary Biological Samples") for use in research not described in such Protocol ("Non-Protocol Research"), provided that (a) such collection complies with all applicable laws, regulations and acceptable clinical trial practices, including, but not limited to, applicable patient privacy and informed consent laws, and (b) no Confidential Information or any other information which links the Secondary Biological Samples to any Confidential Information is available to Principal Investigator or Personnel for such Non-Protocol Research (for example, without limitation, Institution may annotate such Secondary Biological Samples with a Study Patient's demographic information (e.g., age, gender and clinical diagnosis), but not with information related to administration of, or response to, or adverse events associated with, a Study Drug).

8.3.2. Sponsor's Receipt and Use of Biological Samples.

a. Sponsor or its designee may receive pre-determined quantities of Biological Samples from Institution, as set forth in the applicable Protocol, for use in research as described in such Protocol, provided that such research complies with all applicable laws and regulations, including, but not limited to, applicable patient privacy and informed consent laws. Sponsor will ensure that if it uses a designee that its designee agrees to follow the terms, conditions and obligations of this Master Agreement.

b. Sponsor will disclose to Principal Investigator all raw data generated by Sponsor from its research using such Biological Samples ("Biological Samples Raw Data"). Sponsor reserves the right to withhold any such Biological Samples Raw Data on any such genes which are pre-obligated and/or encumbered in any manner. Such Biological Samples Raw Data (i) shall be treated by Institution as Confidential Information under this Master Agreement, and (ii) Principal Investigator may use such Biological Samples Raw Data for the purpose of generating for non-commercial purposes, a manuscript to be published in a scientific peer-reviewed journal, and (iii) Principal Investigator may use such Biological Samples Raw Data for non-commercial research and academic purposes, either within Institution or, with prior written notice to Sponsor, may disclose such Biological Samples Raw Data to academic investigators outside Institution; provided that Institution provides written notice to the recipient of such Biological Samples Raw Data (with a copy to Sponsor) that such Biological Samples Raw Data is Sponsor's Confidential Information.

c. In the event that Principal Investigator desires to conduct further research in collaboration with Sponsor with respect to such Biological Samples Raw Data, Sponsor agrees to consider any such request. Any such further research agreed upon by Sponsor shall be subject to the terms of a separate research agreement.

 **ARTICLE 9
Publicity/Use Of Name**

9.1. Except as required by law or government regulation, no party hereto shall use in advertising, publicity, news releases, reports or any promotional activities, whether oral or written, any name, trade name, trademark, or other designation of another party hereto, including any contraction, abbreviation, or simulation of any of the foregoing, without the express prior written permission of that party whose name is to be disclosed. Notwithstanding the foregoing, Institution may use the name of Sponsor and the title of a study in accordance with Institution's internal reporting requests, and Institution may use the title of a study on the Institution's Internet web site to help in the recruitment of Study Patients.

9.2. For purposes of this Article 9, the term "party" includes Principal Investigator and Personnel.

 **ARTICLE 10
Study Patient Injury**

Sponsor shall pay for the medical expenses of reasonable and necessary medical treatment if a Study Patient is injured during a study and the injury is a direct result of his/her participation in such study, and/or research procedures required and conducted in accordance with the applicable Protocol, provided that the Study Patient followed the instructions of the Principal Investigator and Institution and Principal Investigator have complied with all material obligations in this Master Agreement, the Protocol and applicable regulations in conformity with the generally accepted standards of the medical community in which Principal Investigator and Personnel practice.

 **ARTICLE 11
Indemnification**

11.1. By Sponsor:

11.1.1. Scope. Sponsor agrees to defend, indemnify and hold harmless System, Institution, their Regents, officers, agents and employees, Principal Investigator and Personnel ("Indemnitee(s)"), against any and all claims, lawsuits and judgments thereon, which may be brought as a result of Indemnitees' administration of Study Drug in the performance of a study or the performance of any medical procedure called for by and administered pursuant to the applicable Protocol, or the use by Sponsor of the results of the study.

Notwithstanding the foregoing, Sponsor shall not be liable for any such claim, lawsuit or judgment (i) if Indemnitee failed to comply with the material terms of this Master Agreement, the applicable Protocol, Study Documents or Sponsor's (or its agent's) written instructions concerning the use of the Study Drug, (ii) if Indemnitee failed to comply with applicable laws, regulations or applicable standards of care, such as GCP, or (iii) if and to the extent that Indemnitee's negligence, or willful or intentional malfeasance or misconduct caused the personal injury or property damage.

11.1.2. Process. In the event any claim is made or a lawsuit is initiated , those Indemnitees against whom such lawsuit is brought or a claim is made shall notify Sponsor in writing within fifteen (15) business days after such a claim or lawsuit has been served upon them or such time as does not materially prejudice the rights of Sponsor. Such notice should be rendered via overnight mail to the attention of Legal Division, Wyeth Pharmaceuticals Inc., 150 North Radnor-Chester Road, St. Davids, PA 19087. However, noncompliance by the Institution with the conditions set forth in this Section 11.1.2 will not diminish Sponsor's obligations to defend, indemnify or reimburse the Indemnitees, unless such noncompliance by the Institution directly contributed to the injury or which defense, indemnity, or reimbursement is sought.
Subject to the statutory duties of the Texas Attorney General, the Indemnitees against whom such claim or lawsuit is brought agree to cooperate fully with Sponsor in the defense of any such claim or lawsuit as requested, including, but not limited to, attending hearings and trials and assisting in securing and giving evidence in testimony, and in obtaining the attendance of necessary and proper witnesses at such hearings and trials.

Subject to the statutory duties of the Texas Attorney General, Sponsor shall have the right to fully control the defense of any claim or lawsuit to which this indemnity provision applies, including, but not limited to, the selection of counsel and negotiation and completion of any settlement. In the event that representation of Indemnitees and Sponsor by the same counsel would be a conflict of interest for such counsel, Indemnitees may select separate counsel without relieving Sponsor of its obligations of indemnification and defense as set forth above.

11.2. By Institution.

To the extent authorized under the Constitution and the laws of the State of Texas, Institution agrees to indemnify and hold harmless Sponsor, its affiliates, directors, employees, agents and subcontractors against any and all claims, lawsuits and judgments thereon resulting from the negligent acts or omissions of Institution, its agents or employees pertaining to the activities to be carried out pursuant to the obligations of this Master Agreement; provided, however, that Institution shall not hold Sponsor harmless from claims arising out of the negligence or willful malfeasance of Sponsor, its officers, agents, or employees or any person or entity not subject to Institution's control.

Institution agrees to be responsible to the extent stated above.

11.3. Survival.
The provisions of this Article shall survive any termination of a specific Protocol Agreement or this Master Agreement. Notwithstanding the foregoing, in the event of the termination of a study and related Protocol Agreement, no party shall be liable for indemnification for any claim arising from the Study Drug being administered after the effective date of such termination.

 **ARTICLE 12
Insurance**

12.1. Institution, as a component of The University of Texas System, is an agency of the State of Texas and provides professional liability insurance for its faculty physicians pursuant to The University of Texas System Professional Medical Malpractice Self Insurance Plan, under the authority of Section 59.01, Texas Education Code. Institution shall ensure the Principal Investigator has and will maintain in force during the term of this Agreement adequate insurance to cover his/her indemnification obligations hereunder. Institution, as an agency of the State of Texas, is subject to the provisions of Title 5, Chapter 101 of the Texas Civil Practice and Remedies Code, and the Institution's Personnel or employees are subject to Title 5, Chapter 104 of the Texas Civil Practice and Remedies Code, also known as the Texas Tort Claims Act.

Institution shall maintain such coverage for the duration of this Master Agreement and for two (2) years thereafter.

 **ARTICLE 13
Termination**

13.1. Termination of Master Agreement. The term of this Master Agreement shall begin upon the Effective Date and shall continue for the longer of (a) five (5) years from the Effective Date or (b) until the obligations under all Protocol Agreements are fully performed, unless sooner terminated in accordance with this Article 13. Either party may terminate this Master Agreement at any time by giving thirty (30) calendar days prior written notice to the other party. Upon termination of this Master Agreement, all then on-going Protocol Agreements shall continue under the terms of this Master Agreement and the applicable Protocol Agreement until all obligations in connection therewith are fully performed, unless sooner terminated in accordance with this Article 13.

13.2. Termination of Protocol Agreements. Sponsor may terminate any Protocol Agreement at any time by giving thirty (30) calendar days prior written notice to Institution. Institution may terminate any Protocol Agreement if Sponsor breaches a material obligation of this Master Agreement and if Sponsor fails to cure such breach within thirty (30) days from the receipt of written notice thereof from Institution. Notwithstanding the foregoing, either party shall have the right to terminate a Protocol Agreement effective immediately upon written notice to Institution (if applicable) for the appearance of serious adverse events associated with a Study Drug or related products. Sponsor also reserves the right to terminate a Protocol Agreement upon fourteen (14) calendar days prior written notice for any of the following reasons:

13.2.1. Non-adherence to a Protocol or the material terms outlined in this Master Agreement or applicable Protocol Agreement.

13.2.2. Failure to start a study or progress as stated within the applicable Protocol Agreement.

13.2.3. Study Patient protection and safety considerations within the Sponsor's judgment.

13.2.4. Determination by Sponsor that there are no further benefits to be achieved from a study.

13.2.5. Determination by Sponsor that the continuation of a study would be unethical.

13.2.6. Non-conformance with any applicable standard of care or applicable laws or regulations, including but not limited to Good Clinical Practices.

13.2.7. Failure to allow Audits as provided for herein.

13.2.8. Failure to comply with Articles 2.7 and 2.9 of this Master Agreement.

13.2.9. If Sponsor rejects such replacements as provided for in Section 2.4.2 above.

13.3. Effect of Termination of Protocol Agreements. In the event of early termination of a Protocol Agreement by Sponsor, compensation due to Institution shall be determined as set forth in Article 4 if such Protocol Agreement is terminated for reasons other than Institution's, Principal Investigator's or Personnel's negligence, willful or intentional misconduct or malfeasance, or non-adherence to a Protocol, this Master Agreement and/or written instructions from Sponsor. Institution shall submit a final report of actual expenses and non-cancelable obligations incurred up to the termination date and shall deliver to Sponsor any excess funds received by Institution in advance of work performed. As soon as is practical upon receipt of written notice of termination of a Protocol Agreement, Institution and Principal Investigator shall stop enrolling patients into such study. Institution and Principal Investigator shall cease conduct of such study as soon as is medically practical and in a manner consistent with good medical practice; provided that Institution and Principal Investigator, in their sole discretion, may continue to provide care and treatment to any Study Patient as medically necessary or appropriate and the provisions of this Master Agreement and the respective Protocol Agreement shall continue to govern such care and treatment. Notwithstanding the foregoing, to ensure, among other things, the safety and welfare of Study Patients, Institution and Principal Investigator shall, upon request of Sponsor, conduct such follow-up visits, and record and report such data as required by the applicable Protocol Agreement for such visits. Such follow-up visits shall be performed in accordance with the terms of the Protocol Agreement.

13.4. Survival. The following provisions shall survive the termination or expiration of this Master Agreement: Articles 2.9 (Protected Health Information); 2.11 (Monitoring/Auditing); 2.12 (Inspections and Audits); 5 (Confidentiality); 6 (Publication); 7 (Inventions and Discoveries); 8 (Data Ownership and Copyright); 9 (Publicity/Use of Names); 10 (Study Patient Injury); 11 (Indemnification); and 12 (Insurance).

 **ARTICLE 14
Entire Agreement And Modifications**

14.1. With regard to the subject matter herein, this Master Agreement, along with any Exhibits and Schedules incorporated herein by reference and the Protocol Agreements, supersede any and all other discussions, negotiations and representations of any kind and constitutes the entire understanding of the Sponsor and the Institution.

14.2. No changes, amendments, or alterations to this Master Agreement shall be effective unless designated in writing and signed by all parties.

 **ARTICLE 15
Notice**

15.1. Any notice, request, approval or consent under this Master Agreement, other than the reporting of claims covered by Article 11 Indemnification and Article 3 Serious Adverse Events, Adverse Events, shall be sufficiently given if in writing and delivered in person or by recognized overnight courier or mailed, postage-prepaid to the appropriate party at the address below, as well as in each Protocol Agreement, where the address of Sponsor's study team and Institution's Principal Investigator shall be set forth, unless, by notice to the other parties, a different address shall have been designated:

Sponsor: Wyeth Pharmaceuticals Inc.
Attn.: Legal Department
170 North Radnor-Chester Road
St. Davids, PA 19087
Tel: 610-902-2600
Fax: 610-964-3876

If to an Institution, to the address shown on Schedule 1.

15.2. Notice given by personal delivery or delivered by overnight courier under this Master Agreement shall be deemed effective upon receipt. Notice given by United States mail service shall be deemed effective five (5) days after being delivered to the United States postal service.

 **ARTICLE 16
Debarment and Disqualification**

16.1. Institution represents and certifies that neither it nor the Principal Investigator, nor any Personnel, have ever been and are not currently debarred or otherwise disqualified by the FDA or any other Regulatory Authority, nor will Institution employ any Debarred or Disqualified Persons as defined herein, to provide services under this Master Agreement. Institution and/or Principal Investigator shall notify Sponsor immediately of any contrary information. Institution represents and certifies that Principal Investigator and Personnel have not engaged in any conduct or activity which could lead to any of the above mentioned disqualification or debarment actions and that it has no notice that the FDA or other Regulatory Authority intends to seek disqualification or debarment. If during the term of this Master Agreement, Institution, Principal Investigator or Personnel (i) comes under investigation by FDA for debarment action or disqualification, (ii) is debarred or disqualified, or (iii) engages in any conduct or activity which could lead to any of the above mentioned disqualification or debarment actions, Institution shall promptly notify Sponsor of same.

 **ARTICLE 17
Conflict of Interest**

17.1. Institution represents and certifies that Principal Investigator shall disclose any conflict(s) of interest with respect to financial holdings, proprietary interests or significant equity interests in Sponsor, its affiliates or other companies that are supplying products or services under this Master Agreement or the Protocol Agreement. Institution shall cause Principal Investigator to represent and certify that neither Principal Investigator nor any Other Clinical Investigator, nor anyone in Principal Investigator's or any Other Clinical Investigator's immediate family, has a direct ownership interest in any Study Drug. Institution represents and certifies that it has not received any significant payments of other sorts from Sponsor, its affiliates or other companies that are supplying products or services under this Master Agreement or the Protocol Agreement to support the activities of Principal Investigator. Principal Investigator and Institution are cognizant that full disclosure of ties to such companies is required. Institution further represents and certifies that it has a system in place to manage, eliminate or otherwise resolve conflicts of interest.

17.2. For purposes of this Master Agreement, the terms "significant equity interests", "proprietary interests", and "significant payments of other sorts" shall have the same meanings and interpretations given such terms in 21 CFR § 54.

17.3. Institution, Principal Investigator and Personnel shall comply with all other disclosure requirements of FDA or other regulatory or governmental authority related to conflicts of interest.

 **ARTICLE 18
Assignment and Delegation**

This Master Agreement, and the rights and obligations hereunder, may not be assigned or transferred by any party hereto without the prior written consent of the other parties hereto, except that Sponsor may, with written notice to Institution, assign this Master Agreement to an affiliated company or in connection with the merger, consolidation or sale of all or substantially all of its assets which agrees to be bound by all terms and conditions of this Master Agreement without any material modifications thereto. With Sponsor's prior written consent, Institution may delegate the performance of certain activities under this Master Agreement to qualified third parties, provided however, (i) that such third parties perform such activities in a manner consistent with the terms and conditions contained in this Master Agreement; (ii) that Institution remains fully liable for its and such third parties' performance; (iii) that Principal Investigator or Other Clinical Investigators have no conflict of interest with respect to such third party; and (iv) all payments made to third parties by Institution shall be made in accordance with Article 4.9 (Payee Information) of this Master Agreement.

 **ARTICLE 19
Independent Contractor**

The relationship of Institution, Principal Investigator and Personnel to the Sponsor in the performance of this Master Agreement is that of an independent contractor, and not a partner or joint venture. It shall not confer upon Institution, Principal Investigator and/or Personnel any benefits available to employees of Sponsor.

 **ARTICLE 20
Applicable Law**

This Article is intentionally left silent.

 **ARTICLE 21
General**

21.1. No Third Party Rights. This Master Agreement shall not create, and does not create, enforceable legal rights as a third party beneficiary or through any other legal theory on the part of Institution, Principal Investigator, Personnel or any other person, including Study Patients, except as otherwise provided by Article 10 of this Master Agreement.

21.2. Freedom to Contract. Sponsor and Institution each represents and certifies that it is under no obligation, including but not limited to an agreement, license, or contract, that would cause it to be unable to fulfill any part of this Master Agreement, nor will it enter into any such obligation during the term of this Master Agreement. Institution represents that Principal Investigator is under no obligation, including but not limited to an agreement, license, or contract, that would cause Principal Investigator to be unable to fulfill any part of this Master Agreement, nor will Principal Investigator enter into any such obligation during the term of this Master Agreement. Sponsor acknowledges and agrees that, subject to each of their respective obligations hereunder, Principal Investigator and Institution shall have the right to engage in other research and development and consulting activities during the term of this Master Agreement.

21.3. Severability. If any provision of this Master Agreement is determined to be invalid or unenforceable, the parties shall negotiate in good faith such revisions to said provision as may be required in order to render them valid and enforceable. In the event the parties are unable to agree to such new or modified terms, the remainder of this Master Agreement shall not be affected thereby if capable of performance in the absence of the invalid or unenforceable provision(s).

21.4. Non-waiver. The waiver of or acquiescence by any party hereto to any terms or provision hereunder, or the failure of any party to insist upon strict compliance with any warranty, certification, representation, agreement, term or condition in this Master Agreement or a Protocol Agreement, shall not constitute a waiver of any subsequent waiver, acquiescence, default or failure, whether similar or dissimilar.

21.5. Conflict Between Protocol Agreement and this Master Agreement. Subject to Article 2 hereof, in the event of conflict between the provisions of a Protocol Agreement and this Master Agreement, the Protocol Agreement shall prevail only with respect to matters of science, medical practice, and patient safety. For all other matters the provisions of this Master Agreement shall prevail.

21.6. Force Majeure. No party shall be liable for failure or delay in performing any of its obligations under this Master Agreement if the failure or delay is required in order to comply with any governmental regulation, request or order, or necessitated by other circumstances beyond the reasonable control of the party so failing or delaying, including but not limited to acts of God, or of the public enemy, acts of the government in either its sovereign or contractual capacity, fire, flood, epidemics, quarantine restrictions, freight embargoes, accident, FDA or IRB/IEC action, or inability to obtain raw materials, supplies, power or equipment necessary to enable a party to perform its obligations. Notwithstanding the above, strikes, work stoppage or slowdown, and labor disputes, whether or not such labor event is in the control of the parties, shall not constitute an excusable delay for either party under this Master Agreement or a Protocol Agreement.

21.7. Other Institution Certification. Institution hereby represents and certifies to Sponsor that it possesses the skill, experience and personnel to perform its obligations hereunder, and that it has obtained all consents or other approvals from any third party, including without limitation any hospital or other institution at which Institution will conduct a study, which are necessary to enable Institution to fulfill its respective obligations hereunder.

21.8. Titles. Titles to Articles of this Master Agreement are solely for convenience and do not constitute a substantive part of this Master Agreement.

21.9. Terms. Words importing the singular include the plural and vice versa. Words importing one gender include both genders, and references to persons include bodies corporate or noncorporate.



IN WITNESS WHEREOF, the parties hereto have caused this Master Agreement to be executed in duplicate as of the date indicated above.

ACCEPTED AND AGREED TO:

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| --- | --- |
| **WYETH PHARMACEAUTICALS INC.** By: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Victoria Kusiak, M.D. Vice President, Global Affairs/ North America Medical DirectorDate: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_  | **The University of Texas M. D. Anderson Cancer Center**By: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_Leonard A. Zwelling, M.D., M.B.A.Vice President for Research AdministrationDate: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |
|  **The University of Texas Health Science Center at Houston**By: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_Title:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_Date: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |  **The University of Texas Southwestern Medical Center at Dallas**By: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_Perrie M. Adams, Ph.D.Associate Dean for ResearchDate: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |
| **The University of Texas Medical Branch at Galveston**By: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_Title:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_Date: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ | **The University of Texas Health Center at Tyler**By: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_Title: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_Date: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |
| **The University of Texas Health Science Center at San Antonio**By: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_Jane Youngers Director, Grants ManagementDate:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |   |

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**Schedule 1**

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| --- | --- |
| Melinda Mathis, MPADirector Sponsored Programs and ComplianceOffice of Research AdministrationUT M.D. Anderson Cancer Center1515 Holcombe Boulevard, Unit 307Room B8.4453Houston, TX 77030phone: 713-745-3468fax: 713-794-4535 | Perrie Adams, Ph.D.Assoc. Dean for ResearchThe University of Texas Southwestern Medical Center at Dallas5323 Harry Hines Blvd., B1.204Dallas, TX 75390-9016phone: 214-648-6449fax: 214-648-3362  |
| Ms. Susan E. RamseyContract AdministratorThe University of Texas HealthScience Center at HoustonP.O. Box 20036Houston, TX 77225phone: 713-500-3268fax: 713-500-3275Overnight address is:7000 Fannin Street, Suite 1460Houston, TX 77030  | Mr. Rick HefnerVice President for Finance and Administration The University of Texas Health Center at Tyler11937 U.S. Hwy. 271Tyler, TX 75708phone: 903-877-7720fax: 903-877-7899     |
| Lively WilliamsClinical Trial Specialist The University of Texas Medical Branch at GalvestonOffice of Clinical Trials 301 University Boulevard2.234 Gail BordonGalveston, TX 77555-0671phone: (409) 772-1538fax: (409) 747-3793 | Ms. Jane A. YoungersDirector, Grants ManagementThe University of Texas Health Science Center at San Antonio7703 Floyd Curl Drive, Mail Code 7828San Antonio, TX 78229-3900phone: 210-567-2333fax: 210-567-2344  |



**Exhibit "A"
SAMPLE FORM OF PROTOCOL AGREEMENT

PROTOCOL AGREEMENT**

Drug Name: [\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_]
Protocol Number: [\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_]
Protocol Title: [\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_]
Institution Name: [\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_]
Principal Investigator Name: [\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_]
Study Site Address: [\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_]

NO CHANGES, AMENDMENTS OR ALTERATIONS TO THIS PROTOCOL AGREEMENT SHALL BE EFFECTIVE UNLESS DESIGNATED IN WRITING IN THE FORM OF AN AMENDMENT HERETO AND SIGNED BY ALL PARTIES, INCLUDING "READ AND UNDERSTOOD" BY PRINCIPAL INVESTIGATOR.

This Protocol Agreement is made effective as of the \_\_\_\_ day of \_\_\_\_\_\_\_\_\_, 200\_\_, by and between Wyeth Pharmaceuticals Inc., acting through its division, Wyeth Research ("Wyeth") and [\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_] ("Institution"). This Protocol Agreement is an addendum to that certain Master Clinical Study Agreement between Wyeth and Institution, effective [\_\_\_\_\_\_\_\_] (the "Master Agreement"). The parties agree and acknowledge that the Master Agreement remains in full force and effect and that this Protocol Agreement is governed by and is subject to the terms and conditions of the Master Agreement. If any provisions of this Protocol Agreement should conflict with any provisions set forth in the Master Agreement, the provisions of the Master Agreement shall control, unless this Protocol Agreement expressly refers to the provision(s) of the Master Agreement that it is intended to replace or modify (and which change shall be limited in force and effect to this Protocol Agreement only) and shall be approved by all parties.

This Protocol Agreement confirms the terms and conditions under which Institution has agreed to conduct a certain clinical research study, pursuant to Protocol No. \_\_\_, attached hereto as Exhibit A, entitled "Name of Protocol", and all future amendments thereto, all of which are incorporated herein by reference and made a part of this Protocol Agreement (the "Protocol"), so as to evaluate [compound name/Brand Name®] in accordance with the Protocol (the "Study"). It is estimated that it will take {\_\_\_} months to complete the Study and that Institution expects to be able to provide {\_\_\_} completed subjects for the Study.
The Study will be conducted under the direction of:

{Name of Principal Investigator}
{Address}
{Telephone}

The Study will also be conducted by the following Other Clinical Investigators:

Other Clinical Investigator
and Address
{List Other Clinical Investigator}

Wyeth will pay Institution as detailed in the Investigator Budget and Payment Schedule, attached hereto as Exhibit B, which is incorporated herein by reference and made a part of this Protocol Agreement (the "Study Budget").

All funds under this Protocol Agreement shall be paid by Wyeth to [\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_] (Federal Tax Identification Number \_\_\_\_\_\_\_\_\_\_\_\_\_\_) and shall be sent by corporate check to the attention of \_\_\_\_\_\_\_\_\_\_\_\_ at the following address:

{Address}
{Attn.: \_\_\_\_\_\_\_\_}

All payments hereunder will reference the number of this Protocol Agreement and Principal Investigator's name. Wire transfers may also be used pursuant to a mutually acceptable procedure.

For purposes of the Study, all communications (other than legal or other notices under the Master Agreement) should be sent to the following persons:

If to Institution, to: [\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_]

Attn.:

If to Wyeth, to: Wyeth
{Address}
Attn.: {Name of Wyeth Medical Director for the
Study}

The maximum Study grant and the payment schedule for same, the number of patients to be enrolled, randomized, and completed, and the financial terms and conditions pertaining to the Study are as set forth in the Study Budget attached to this Protocol Agreement. All funds to be paid by Wyeth for the conduct of the Study shall be paid by Wyeth to Institution in accordance with the Study Budget as attached to this Protocol Agreement.

The undersigned Principal Investigator has been informed of the purpose of Source Documentation Verification (SDV) and fully understands this is part of the Sponsor's monitoring process. Principal Investigator understands which studies and items must be included in the source documents and for which data and/or items the CRF may be used as the sole source document.

The undersigned Principal Investigator hereby agrees (i) to supervise the conduct of the Study at the site(s) indicated herein, (ii) to be responsible for leading any Personnel (as defined in the Master Agreement), and (iii) to abide by the terms and conditions of the Master Agreement and this Protocol Agreement. The undersigned Other Clinical Investigators (if applicable) agree to conduct the Protocol in accordance with the terms and conditions of this Protocol Agreement and the Master Agreement.

Promptly upon receipt or delivery by Institution, as applicable, of a notice of termination, Principal Investigator shall stop entering patients or subjects participating in research into the Study and shall cease conducting procedures on such patients already entered in the Study as directed by Wyeth, and to the extent medically and legally permissible and appropriate. To the extent it is medically or legally required or appropriate for Institution to continue to treat subjects according to the Protocol, this Protocol Agreement, including without limitation Wyeth's payment obligations hereunder, shall continue in full force and effect.

IN WITNESS WHEREOF, the parties have caused this Protocol Agreement to be executed in duplicate as of the date indicated above.

ACCEPTED AND AGREED TO:

WYETH PHARMACEUTICALS INC.

By: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_
Name: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_
Title: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_
Date: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

[INSTITUTION]

By: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_
Name: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_
Title: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_
Date: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

I HAVE READ AND UNDERSTAND THE ABOVE PROTOCOL
AGREEMENT AND RELATED MASTER AGREEMENT, AND AGREE
TO ABIDE BY THE TERMS THEREOF:

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_
Signature of the Principal Investigator

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_
Print Name of the Principal Investigator

Date \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_
Signature of the Other Clinical Investigator(s)

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_
Print Name of the Other Clinical Investigator(s)

Date \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_