NOVARTIS PHARMACEUTICALS CORPORATION
East Hanover, NJ 07936

MASTER CLINICAL TRIAL AGREEMENT

for Institutions

Effective Date: **September 1, 1998**

MASTER CLINICAL TRIAL AGREEMENT

Table of Contents

MASTER CLINICAL TRIAL AGREEMENT

This Master Clinical Trial Agreement ("Agreement") is entered into by and between The University of Texas Health Science Center at San Antonio, The University of Texas Health Science Center at Houston, The University of Texas M.D. Anderson Cancer Center, The University of Texas Southwestern Medical Center at Dallas, The University of Texas Medical Branch at Galveston and The University of Texas Health Center at Tyler each with an office and place of business as set forth in Article 12 and each a component of The University of Texas System located at 201 West 7th Street, Austin, Texas 78701 and ("each an Institution"), and Novartis Pharmaceuticals Corporation, a corporation with its principal office and place of business at 59 Route 10, East Hanover, NJ 07936 ("Novartis").

1. SCOPE OF WORK

During the Agreement Period, Institution shall conduct the research ("Research"), including clinical trials ("Clinical Trials") in accordance with the referenced clinical trial protocol ("Protocol"), as may be modified from time to time, and as set forth in individual Clinical Trial Request Forms, hereinafter described. The terms and conditions of this Agreement shall apply to any Clinical Trial Request Form(s) entered into prior to the end of the Agreement Period.

2. AGREEMENT TERM

The term of this Agreement shall be from September 1, 1998 until five (5) years thereafter ("Agreement Period").

3. CLINICAL TRIAL REQUEST FORM

A. The specific requirements for any Research, including a determination of whether the Research is an "Oncology-related research trial" shall be set forth in Clinical Trial Request Forms ("Clinical Trial Request Form(s)"), in substantially the form attached hereto as Attachment A, including the referenced attachments. Other terms and conditions shall be as set forth in this Agreement. The principal investigator for each Clinical Trial ("Principal Investigator") shall agree in writing to the terms of the Clinical Trial Request Form.

B. A copy of the budget (Schedule A) for each Clinical Trial, including the payment schedule, shall be attached to the applicable Clinical Trial Request Form and shall be a part thereof. The total cost to Novartis for the completion of such Clinical Trial by Institution shall not exceed the amount set forth in the applicable Schedule A. Payment includes all applicable overheads as stated in Schedule A. For partially completed enrolled patients Novartis may, in its sole discretion, pay Institution a prorated amount according to the duration of the patient's participation.

C. Payment shall be made to Institution according to Schedule A All costs as outlined shall remain firm for the duration of the Research unless otherwise agreed to in writing by Institution and Novartis.

D. Checks will be made payable to the applicable Institution(s) and will reference the Agreement number and account name referenced in the applicable Clinical Trial Request Form and will be mailed to the address shown in Schedule A.

4. PRINCIPAL INVESTIGATOR

Institution's Principal Investigator will be responsible for the performance of the Research and Protocol, in accordance with applicable Institution policies, which Institution warrants and represents are not inconsistent with the terms of this Agreement. If for any reason, he/she is unwilling or unable to continue as Principal Investigator and a successor, acceptable to both the Institution and Novartis, is not available, this Agreement shall be terminated as to the Research and Protocol in the applicable Clinical Trial Request Form as provided in Article 15 (B).

5. PERFORMANCE PERIOD

The Research will be initiated and completed by Novartis and Institution within the dates set forth in the applicable Clinical Trial Request Form ("Performance Period"). If the Research is not completed within the Performance Period, Novartis may extend the period by written notification to the Institution.

6. RECORDKEEPING, REPORTING AND ACCESS

A. Novartis' authorized representative(s) and regulatory authorities to the extent required by law, may, during regular business hours, arrange in advance in writing with the Principal Investigator and Institution to:

(1) examine and inspect the Institution's facilities required for performance of the Research; and

(2) inspect and copy all data and work products relating to the Research.

B. The Institution and the Principal Investigator shall perform the following recordkeeping and reporting obligations in a timely fashion:

(1) Prepare and maintain complete, accurate written records, accounts, notes, reports and data of the Research. Federal regulations require that copies of case report forms ("Case Reports") be retained by the Principal Investigator for a period of at least two years following either the approval of the New Drug Application or the withdrawal of the Investigational New Drug Application. Foreign laws and regulations may require longer retention periods.

Novartis will advise the Principal Investigator when the applicable retention period begins. Principal Investigator may be subject to a field audit by inspectors of the U.S. Food and Drug Administration ("FDA") or comparable foreign regulatory agencies and/or by Novartis representatives to verify that Research is conducted according to the applicable Protocol, and is in compliance with the federal regulations relating to Investigational New Drugs; and

(2) Prepare and submit to Novartis all original Case Reports and electronic files (if applicable) for each patient participating in the Research ("Research Subject").

7. CONFIDENTIAL INFORMATION

A. Subject to its rights under Article 8, the Institution agrees not to disclose or to use for any purpose other than performance of the Research any and all trade secrets, privileged records, results of the Research, or other confidential or proprietary information (collectively "Information") disclosed to or developed by the Institution pursuant to this Agreement or any previous confidentiality agreement(s) relating to the Research between Novartis and Institution. The obligation of non-disclosure and non-use shall not apply to the following:

(1) information at or after such time that it is or becomes publicly available through no fault of the Institution;

(2) information that is already independently known to the Institution as shown by its prior written records, provided that the Institution promptly advises Novartis that the Information is already independently known to the Institution;

(3) information at or after such time that is disclosed to the Institution on a non-confidential basis by a third party with the legal right to do so;

(4) information required by law or regulation to be disclosed, provided that the Institution notifies Novartis prior to making such disclosure.

(5) information independently developed by Institution as shown by its prior written records.

B. The obligations of the Institution under this Article shall survive and continue for five (5) years after termination of this Agreement.

C. If Novartis comes into contact with Research Subject's medical records, Novartis shall hold in confidence the patient's identity and shall comply with all applicable laws regarding the confidentiality of such records.

D. If the Institution finds it necessary to disclose Information to a proper authority to defend its Research against an allegation of fraud, the Institution shall first notify Novartis and the Institution and Novartis shall agree upon a mutually satisfactory way to disclose such Information for this limited purpose.

8. PUBLICATIONS/PRESENTATIONS

Novartis acknowledges that each Institution is dedicated to a free scholarly exchange and to public dissemination of the results of their scholarly activities. Except as set forth in this Article or in the CONFIDENTIAL INFORMATION and DATA, OTHER INFORMATION, INVENTIONS AND PATENTS Articles, nothing in this Agreement shall restrict the right of each Institution, its physicians, other employees and/or students to publish, disseminate, or otherwise disclose the results of the Research pursuant to this Agreement.

For any publication or presentation, a manuscript of the paper, abstract or other materials must be reviewed by Novartis prior to any outside submission. A period of fifteen (15) working days for presentational materials and abstracts and forty-five (45) working days for manuscripts will be required for Novartis review. These requirements acknowledge Novartis' responsibility to evaluate such publications for their accuracy, to ascertain whether proprietary Information (including trade secrets and patent protected materials) is being utilized and inappropriately released, to provide the investigator with information which may not yet have been available to him/her, and to provide input from co-authors regarding content and conclusions of the publication or presentation.

If an invention is described in a proposed publication which in the opinion of Novartis should be made the subject of a patent application, Novartis shall have four (4) months after full disclosure to Novartis to file such patent application. Institution shall withhold publication respecting that invention until such application is so filed by Novartis.

For multicenter studies it is mandatory that the data be pooled and analyzed as stipulated in the Protocol. Authorship will include representatives from each active trial site and from Novartis. It is agreed that no presentations or publications will be authorized individually or by subgroups participating in the trial without the consent of all the relevant parties prior to publication of the pooled data, but in no event shall any Institution involved in this study be restricted from publishing independently after the expiration of twenty-four (24) months from the completion of the Research covered by the applicable Clinical Trial Request Form.

9. DATA, OTHER INFORMATION, INVENTIONS AND PATENTS

A. All data, other information and inventions resulting from the performance of the Research shall be owned by Novartis and may be used and/or transferred by Novartis for any lawful purpose with no further payment to the Institution.

B. In the event that Novartis decides to file one or more United States and/or foreign patent applications covering one or more inventions resulting from the performance of the Research, the Institution and each Principal Investigator shall, at Novartis' request and expense, assist Novartis in the preparation and prosecution of such patent application(s) and shall execute all documents deemed necessary by Novartis for the filing thereof and/or for the vesting in Novartis of title thereto.

10. PUBLICITY

Neither party shall use the other party's name, nor issue any public statement about this Agreement, including its existence, without the prior written permission of the other party, except as required by law (and, in such case, only with prior notice to the other party). Such prior permission shall not be unreasonably withheld. The parties agree that for Institution to satisfy its reporting obligations, it may identify Novartis as the Research sponsor and the amount of funding received from Novartis for the Research, but will not include any information identifying the name of the Research compound or the therapeutic areas of the Research.

11. APPLICABLE LAW

This Agreement shall be governed by the laws of the State of Texas.

12. NOTICE

Any notice required or permitted hereunder shall be in writing and shall be deemed given as of the date it is (A) delivered by hand or (B) sent by registered or certified mail, postage prepaid, return receipt request, and addressed to the party to receive such notice at the address set forth below, or such other address as is subsequently specified in writing, as well as any persons so designated under an applicable Clinical Trial Request Form, including the Principal Investigator:

If to Novartis:

For all payment queries, the following information must be provided (please refer to Schedule A):

1. Project (compound)
2. Study #
3. Center #
4. PI name
5. PO # (if available)

and Contact:

Marie Ronca
Novartis Pharmaceuticals Corporation
59 Route 10, Bldg. 419, Rm. 2180
East Hanover, NJ 07936
973-503-8526

The above information must also be included on all invoices.

For Contract Matters:
Insert Grant Managers Name
Novartis Pharmaceuticals Corporation
59 Route 10, Bldg. 419-2
East Hanover, NJ 07936-1080
Phone: 973-781-____

For Medical / Research Related Matters:
(Enter on the Clinical Trial Request Form the Clinical Trial Leader's Name, Address, & Phone)

If to Institution:

For Administrative or Contract Matters:
~~Ms. Janice Hinds~~ Perrie M. Adams, Ph.D.
~~Director, Grants Management~~ Associate Dean for Research
The University of Texas Southwestern
Medical Center at Dallas
5323 Harry Hines Blvd.
Dallas, Texas 75235-~~9105~~ 9007

or

Mr. David Kusnerik
Contract Administrator
The University of Texas Health
Science Center at Houston
P.O. Box 20036
Houston, Texas 77225

or

Ms. Donna Gilberg
Manager, ~~Sponsored Programs~~ Grants and Contracts Accounting
U.T. M.D. Anderson Cancer Center
1515 Holcombe Blvd., Box 202
Houston, Texas 77030

or

Ms. Marcie Padia
Research Administrative Services
The University of Texas Medical
Branch at Galveston
Galveston, Texas 77550-2774

or

Ms. Jane A. Youngers
Director, Grants Management
The University of Texas Health
Science Center at San Antonio
7703 Floyd Curl Drive
San Antonio, Texas 78284-7862

or

Ms. Michelle Hargis
Administrator, Sponsored Programs
The University of Texas Health
Center at Tyler
11937 U.S. Highway 271
Tyler, Texas 75708

13. INDEMNIFICATION AND INSURANCE

A. Novartis shall defend, indemnify and hold harmless the Institution, the Principal Investigator, The University of Texas System, their Regents, officers, any agents and employees of Institution (collectively the "Indemnitees") from any and all liabilities, claims, actions or suits for personal injury or death directly arising out of the activities to be carried out pursuant to the Protocol and to the use by Novartis of the results obtained from performance on the Research provided however:

(1) that the Research is conducted in accordance with the respective Protocol, compliance with the applicable requirements of the Food and Drug Administration, all written instructions delivered by Novartis concerning administration of the Research Study Drugs or devices and Good Clinical Practice regulations;

(2) that such loss does not arise out of the negligence or willful malfeasance of any Indemnitee, exclusive of Novartis employees;

(3) that Novartis is promptly notified in writing no later than ten (10) business days of any complaint, claim or injury relating to any loss subject to this indemnification; and

(4) that Novartis reserves the right to select defense counsel for whose fees it may be liable and to direct, subject to the statutory duties of the Texas Attorney General, the defense or other disposition (including settlement) of any such claim or suit.

B. Deviations from the terms of the Protocol that may arise out of necessity do not constitute negligence or willful malfeasance provided that Institution promptly notifies Novartis in writing of any such deviations.

C. Novartis warrants that it maintains a policy or program of insurance or self-insurance at levels sufficient to support the indemnification obligations assumed herein. Upon request Novartis will provide evidence of its insurance.

D. Institution, as a component of The University of Texas System, is an agency of the State of Texas and is self-insured pursuant to The University of Texas System Professional Medical Malpractice Self-Insurance Plan, under the authority of Section 59.01, Texas Education Code. Institution has and will maintain in force during the term of this Agreement adequate insurance to cover its indemnification obligations hereunder.

The Institution is responsible for the conduct of its employees to the extent provided for in

Texas Tort Claims Act Chapter 101, Texas Civil Practice and Remedies Code.

14. RESEARCH SUBJECT INJURY

A. Novartis shall reimburse for reasonable and necessary medical expenses incurred by Research Subjects for acute medical care, including hospitalization, in the treatment of adverse reactions, illness or injury arising directly from study drugs or devices following their administration or use in accordance with the Protocol, which expenses are not covered by the Research Subject's medical or hospital insurance coverage or other third party payer and are in no way attributable to the negligence or misconduct of any person in the employment of the Institution or to the Research Subject's own failure to follow instructions. No other compensation of any type will be provided by Novartis to the Research Subjects.

15. TERMINATION

A. This Agreement or any Research hereunder may be terminated by either party for any safety and/or efficacy concerns, upon ten (10) days prior written notice.

B. This Agreement or Research under any individual Clinical Trial Request Form may be terminated by Novartis for any other reason, other than those listed in section 15(A) above, upon thirty (30) days written notice.

C. Novartis will pay Institution within sixty (60) days any funds due regarding the terminated Research based on the pro-rata per patient amount based on patients completed and/or accrued under the Clinical Trial Request Form budget terms.

D. The Institution will return within sixty (60) days to Novartis any funds received regarding such terminated Research exceeding the pro rate per patient amount based on patients completed and/or accrued under the Clinical Trial Request Form budget terms.

E. Immediately upon receipt of a notice of termination, the Principal Investigator shall stop entering Research Subjects into the relevant Clinical Trial and as directed by Novartis and to the extent medically permissible shall cease conducting procedures on Research Subjects already entered in the Clinical Trial.

F. Termination of this Agreement by either party shall not affect the rights and obligations of the parties accrued prior to the effective date of the termination. The rights and duties under Articles 6, 7, 8, 9, 10, 11, 13, 14, 20, 21 and 22 survive the termination or expiration of this Agreement.

16. ENTIRE AGREEMENT

This Agreement represents the entire understanding of the parties with respect to the subject matter hereof. In the event of any inconsistency between this Agreement and the Protocol, the terms of this Agreement shall govern. The invalidity or unenforceability of any term or provision of this Agreement shall not affect the validity or enforceability of any other term or provision hereof.

17. ASSIGNMENTS BY INSTITUTION

This Agreement, and all rights and obligations hereunder may not be assigned by Institution without the express written consent of Novartis. However, Novartis, without the consent of Institution, may assign all of its rights and obligations thereunder to an affiliate or to a successor or assign of the business to which this Agreement relates.

18. NO TRANSFER OF PROPRIETARY RIGHTS NOT SPECIFIED

It is agreed that neither party transfers to the other any patent right, copyright right, or other proprietary right of either party, except as specifically set forth herein.

19. CHANGES TO THE PROTOCOL

Novartis may at any time modify a Protocol after approval by the Principal Investigator and, if required, by the Institutional Review Board by written notice to Institution. No financial adjustments shall be made because of such modification unless the parties hereto amend this Agreement accordingly.

20. DELIVERY TO NOVARTIS OF UNUSED MATERIALS

Within thirty (30) days following termination or completion of the Research, all unused compounds, drugs and devices, case reports, whether or not completed, and other related materials that were furnished to the Institution by or on behalf of Novartis shall be returned to Novartis at Novartis' expense.

21. CONFORMANCE WITH LAW AND ACCEPTED PRACTICE

The Institution shall perform the Research in conformance with (i) generally accepted standards of good clinical practice, (ii) the Protocol, and (iii) all applicable local, state, federal and foreign laws and regulations governing the performance of clinical investigations including but not limited, to the Federal Food, Drug and Cosmetic Act and regulations of the FDA and comparable foreign agencies.

22. DEBARMENT CERTIFICATION

Neither the Institution nor any employee directly performing the Research has been debarred under section 306(a) or (b) of the Federal Food, Drug and Cosmetic Act and no debarred person will in the future be employed by the Institution in connection with any work to be performed for or on behalf of Novartis Pharmaceuticals Corporation. If at any time after execution of this Agreement, the Institution becomes aware that the Institution or any employee directly performing the Research is, or is in the process of being, debarred, the Institution hereby certifies that it will so notify Novartis Pharmaceuticals Corporation immediately.

23. ADVERTISEMENTS

Principal Investigator must inform the Institutional Review Board ("IRB") should (s)he propose to utilize advertisements to recruit Research Subjects. Principal Investigator will supply the proposed advertisement to Novartis and the IRB for approval. Any promotional representation or suggestion that an investigational drug is safe or effective for the purposes for which it is offered under investigation, is a violation of federal regulations 21 CFR 312.7 (a).

IN WITNESS WHEREOF, the parties hereto have executed this Agreement by proper persons thereunto duly authorized.

NOVARTIS PHARMACEUTICALS CORPORATION

By _____ SCOTT McDONALD
(signature) VICE PRESIDENT
Print name _____ INTERNATIONAL CLINICAL
Title _____ RESEARCH OPERATIONS
Date 10/16/98 (U.S.)

THE UNIVERSITY OF TEXAS HEALTH SCIENCE CENTER AT SAN ANTONIO

By _____
(signature)
Jane A. Youngers
Director
Grants Management

Date 10-12-98

THE UNIVERSITY OF TEXAS M.D. ANDERSON CANCER CENTER

By _____
(signature)
Donna S. Gilberg, CPA
Manager, ~~Sponsored Programs~~
Grants and Contracts Accounting
Date 9/25/98

THE UNIVERSITY OF TEXAS HEALTH SCIENCE CENTER AT HOUSTON

By _____
(signature)
David E. Kusnerik
Contract Administrator

Date 10/5/98

THE UNIVERSITY OF TEXAS MEDICAL BRANCH AT GALVESTON

By _____
(signature)
~~George M. Bernier, Jr., M.D.~~ Wayne Patterson, Ph.D.
~~Vice President for Academic Affairs and~~ Director,
~~Dean of Medicine~~ Institutional Review Coordinatio
Date 10/7/98

THE UNIVERSITY OF TEXAS SOUTHWESTERN MEDICAL CENTER AT DALLAS

By _____
(signature)
~~Peter H. Fitzgerald~~ Perrie M. Adams, Ph.D.
Associate Dean for Research
~~Executive Vice President for Business Affairs~~
Date 9/16/98

THE UNIVERSITY OF TEXAS HEALTH CENTER AT TYLER

By _____
(signature)
~~George A. Hurst~~ Ronald F. Garvey, M.D., MBA
Chief Administrative Officer and Director
Date 9-18-98

NOVARTIS PHARMACEUTICALS CORPORATION
East Hanover, NJ 07936

ATTACHMENT A: Clinical Trial Request Form

This Clinical Trial Request Form shall be binding upon the undersigned upon its execution by the duly authorized representatives of the parties as of the day and year first above written. It is subject to the terms of the Master Clinical Trial Agreement attached hereto.

1. CLINICAL TRIAL-RELATED INFORMATION

Date:

Principal Investigator:

Account No.

Test Compound:

Brief Description of Clinical Trial [Protocol Title]:

Is This a Multi-Center Trial? [Yes or No]

Is this an Oncology-Related Research Trial? [Yes or No]:

Clinical Trial Dates (Performance Period) Initiation:

Completion:

Number of Research Patients To Be Enrolled:

Agreement No. _____

3. MODIFICATIONS AND ADDITIONAL TERMS FOR THIS CLINICAL TRIAL:
*[**CAUTION**: The provisions of this section supersede any conflicting provisions of the Master Clinical Trial Agreement.]*

4. LIST OF ATTACHMENTS AND PROTOCOL:

Protocol: [Code Number and Title]:

Schedule A

Copy Of Master Clinical Trial Agreement

5. COST AND PAYMENT

A. As consideration for performance under the terms of this Agreement, Novartis agrees to pay the Institution up to a total sum of $_____. Actual charges shall be based upon a rate of $_____ per completed, evaluable Research Subject(s). (The maximum sum assumes completion of ____ Research Subjects in accordance with the scope of work set forth in the Protocol.) Payment includes all applicable overheads. (See Schedule A).

Checks should be made payable to: _____

Checks should be sent to:

Institution Tax Identification Number: _____

In Witness Whereof, the parties hereto have executed this Clinical Trial Agreement in duplicate by proper persons thereunto duly authorized

NOVARTIS PHARMACEUTICALS CORPORATION

By ***SAMPLE***
(signature)

_____
(print or type name)

Title: _____

Date _____

INSTITUTION *{ENTER INSTITUTION NAME}*

By ***SAMPLE***
(signature)

_____
(print or type name)

Title: _____

Date _____

PRINCIPAL INVESTIGATOR

I have read this Clinical Trial Request, including the copy of the Master Clinical Trial Agreement, and understand my obligations hereunder

By ***SAMPLE***
(signature)

_____
(print or type name)

Title _____

Date _____