Institutional Review Board Cooperative Agreement
Between
The Children’s Hospital of Philadelphia
and
The University of Pennsylvania

This agreement is being entered into pursuant to 45 CFR 46 and 21 CFR 50 and 56 and represents the negotiated and agreed to conditions between the Institutional Review Boards (IRBs) of The Children’s Hospital of Philadelphia (CHOP) (FWA #459) and The University of Pennsylvania (Penn) (FWA #4028).

FOR AND IN CONSIDERATION of the terms and conditions contained in this agreement, CHOP and Penn, intending to be legally bound hereby, hereby agree for their mutual and individual as follows and set forth the following:

I. CONTACT INFORMATION:

Any written submissions required under this Agreement shall be addressed and mailed by one party to the other party at the address indicated below:

CHOP
The Children’s Hospital of Philadelphia
Institutional Review Board
3535 Market Street, Suite 1200
Philadelphia, PA 19104
(215) 590-2830

Human Protections Administrator: Barbara Engel, MD, PhD
IRB Chair: Mark Schreiner, M.D.
Institutional Official: Philip Johnson, M.D.,
Chief Scientific Officer,
Joseph Stokes, Jr. Research Institute

Penn
The University of Pennsylvania
Institutional Review Board
3624 Market Street, Suite 301 South
Philadelphia, PA 19104
(215) 898-2614

Human Protections Administrator: Yvonne Higgins, Ph.D.
IRB Executive Chair: Emma Meagher, M.D.
Institutional Official: Steven Fluharty, Ph.D.,
Vice Provost for Research
University of Pennsylvania
II DEFINITIONS

Not Engaged in Research: means those categories of research activities that correspond with Categories B(1) – (9) of the 1999 OHRP Guidance Document “Engagement of Institutions in Research” or its successor(s), which is attached hereto as Exhibit “1” and incorporated herein by reference.

Penn faculty: means individuals whose academic appointment is at the University of Pennsylvania and whose primary hospital appointment is at an institution other than The Children’s Hospital of Philadelphia.

CHOP faculty: means individuals whose academic appointment (if applicable) is at the University of Pennsylvania but whose primary hospital appointment or employment is at The Children’s Hospital of Philadelphia.

Penn: means the University of Pennsylvania.

CHOP: means The Children’s Hospital of Philadelphia®.

III. PERIOD OF AGREEMENT. This agreement shall commence, subject to its signing by both parties, on May 19, 2008 and continue until December 31, 2013 during which period CHOP and Penn shall abide by all terms and conditions contained herein. This agreement may be renewed or amended by written agreement of the parties.

IV. AMENDMENT/TERMINATION.

A. Either CHOP and/or Penn may amend this agreement with the written consent of the other party. Either party may propose an amendment to this agreement to the other party when there is a change in federal, state, or local regulation materially affecting either institution’s Institutional Review Board (“IRB”) or affecting the conduct of human subject research by CHOP and/or Penn provided that the other party shall be under no express or implied obligation to agree to such proposed amendment.

B. Either party within its sole discretion may terminate the agreement at the written request of the other party; if the party receiving such written termination request does not terminate the agreement, the receiving party shall promptly notify the other party in writing of its decision not to terminate.

C. Either party may, after written notice requesting a joint proceeding to consider certain actions of the other party described in subsections C-(1) through (4) individually or in combination and a joint proceeding is convened at which both parties are present and are provided the opportunity to present relevant information, terminate the agreement upon written notice to the other party if the terminating party reasonably finds on the basis of information presented at such joint proceeding that the other party:

(1) is not in material compliance with the agreement; or

(2) is not in material compliance (a) with a regulatory approval that is not superseded
or replaced in whole or in material part by this agreement or (b) with a provision of federal, state or local regulation or law pertaining to either IRB or affecting the conduct of human subject research by CHOP and/or Penn that is not superseded or replaced in whole or in material part by this agreement; or

(3) has unreasonably refused the other party’s request to amend the agreement where such proposed amendment would not be materially prejudicial or harmful to the refusing party, including without limitation, any amendment; proposed by the terminating party under Section IV-A above in response to a change in Federal, state or local law or regulation as specified in such section; or

(4) has misrepresented or failed to fully disclose all relevant information pertaining to this agreement or any information pertaining to this agreement requested by the other party; or

V. ENTIRE AGREEMENT. This agreement, together with specifications, referenced parts, attachments, and effective amendments, shall constitute the entire agreement. Communications or understandings made prior to the signing of this agreement and pertaining to its subject matter are hereby superseded. All revisions to this agreement must be made by a written amendment to this agreement, signed by both parties and issued under the same procedures as this agreement.

VI. COOPERATION. The parties agree to use their respective commercially reasonable best efforts to cooperate in carrying out the terms of this Agreement and to provide mutual assistance to each other in conducting and monitoring human subjects research projects and trials where both parties are jointly involved as specified in Section VI below.

VII. RESEARCH PROTOCOLS COVERED. When only one of the institutions is engaged in human subjects research, as defined by the current Guidance issued by the Office of Human Research Protections (OHRP), then approval and review is not required at the other institution (Section VII). When both institutions are engaged in the research then this agreement provides the framework for establishing which IRB will serve as the IRB of record as part of the Penn-CHOP cooperative agreement.

A. The following research is covered by this agreement:

(1) When Penn faculty and CHOP faculty participate in the same human subjects research activity, then both institutions will be considered engaged in the research. Under the following scenarios, either the Penn IRB or the CHOP IRB will be the IRB of record for both institutions.

   a) Where all research activities take place at CHOP, and the only involvement of Penn is the participation of a Penn faculty member involved in the research as a sub-investigator; in this circumstance CHOP will be the IRB of record.

   b) Where all research activities take place at Penn, and the only involvement of CHOP is the participation of a CHOP-based faculty member involved in the research as a sub-investigator; in this circumstance, Penn will be the IRB of record.
c) Other scenarios as agreed upon on a case-by-case basis (examples below):

i. When the primary grantee is at one institution (CHOP or Penn) but most or all of the human subjects research activity will take place at the other institution, the institution that receives the award may designate the other institution’s IRB as the IRB of record.

ii. Collaborative research involving neonates and taking place at CHOP and either Penn or the Pennsylvania Hospital or both may designate CHOP as the IRB of record;

iii. When greater than minimal risk study procedures involving adults subjects take place at Penn and research activities at CHOP are limited to those considered not greater than minimal risk, CHOP may designate Penn as the IRB of record.

iv. When research involves both children and adults subjects, the IRBs at Penn and CHOP may agree to designate one IRB the IRB of record.

(2) When the criteria for either Penn or CHOP to serve as the IRB of record have been met (1a, 1b or 1c) the other IRB will document that they have designated the other IRB as the IRB of record in accordance with institutional policies and procedures. When invoking this agreement, the principal investigator shall submit required documentation materials which may consist of the following:

a) The approval letter from the IRB of record;

b) A copy of the approved study protocol;

c) A copy of the approved informed consent form;

d) A list of investigative team members;

e) Copies of Continuing Review approval letters.

B. The following are examples of research activities that are not subject to the provisions of this agreement:

(1) When Penn or CHOP’s facilities are utilized but only for commercial or clinical procedures available outside of the research context and there are no faculty at the institution who are involved as collaborators in the research, then the institution will not be considered engaged in the research. For example:

a) Where all human subjects research activities take place at Penn, and the only involvement of CHOP is the performance of a procedure or test available outside of the research context (for example a DEXA scan) or that involves coded blood or other specimens obtained from research subjects enrolled at Penn but analyzed at CHOP, then CHOP will not be considered engaged in the research and Penn will be the IRB of record.
b) Where all human subjects research activities take place at CHOP, and the only involvement of Penn is the performance of a procedure or test available outside of the research context or that involve coded blood or other specimens obtained from research subjects enrolled at CHOP but analyzed at Penn, then Penn will not be considered engaged in the research and CHOP will be the IRB of record.

(2) When Penn faculty or CHOP faculty participate in research but their involvement does not constitute human subjects research, then their institution will not be considered engaged in the research and there will be no requirement for IRB submission. The following are examples where Penn or CHOP would not be considered engaged in research:

a) When recruitment will be conducted at Penn and research, including obtaining consent, takes place at CHOP: then Penn will not be considered engaged in the research and CHOP will be the IRB of record.

b) When recruitment will be conducted at CHOP and research, including obtaining consent, is done at Penn: then CHOP will not be considered engaged in the research and Penn will be the IRB of record.

VIII. PERFORMANCE EVALUATION AND MEASUREMENT. Each party agrees to conduct a performance evaluation of the parties’ performance under this Agreement within ninety (90) days of the effective date of this agreement. Each party shall repeat this evaluation annually not later than September 1 of each year. Results of all performance evaluations shall be shared in full with the other party promptly upon completion of the evaluation. Each party shall maintain a record of its own administrative issues associated with the agreement.

IX. NOTIFICATION REQUIREMENTS. Penn and CHOP each shall promptly disclose to the other party all material information pertinent to the terms of this Agreement and the obligations of the disclosing party hereunder. Without limiting the generality of the foregoing, Penn and CHOP agree to notify each other of all communications to and from the FDA, Office of Human Research Protection (OHRP) and other applicable federal and state regulatory agencies regarding the research activities to which this Agreement applies and related IRB matters, including communication concerning investigators who have research activities governed by this agreement. Institution further agrees to notify the other when forwarding notification letters described below relating to research activities to which this Agreement applies:

A. any unanticipated problems involving risks to subjects or others;
B. any serious or continuing noncompliance with 45 CFR Part 46 or the requirements or determinations of IRB at Penn or the IRB at CHOP;
C. any suspension or termination of IRB approval; and
D. any reports of Penn or CHOP IRB actions that require forwarding to OHRP and/or any Department or Agency head.

X. GOVERNING LAW AND VENUE. The laws of the Commonwealth of Pennsylvania shall govern this agreement and any action pertaining to this Agreement shall be brought in the Court of Common Pleas for Philadelphia County, Pennsylvania or in the US District Court for the

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Eastern District of Pennsylvania. Except as provided herein, each party shall at all times comply
with all Federal, State, and Local laws, ordinances and regulations in effect and pertaining to the
subject matter of this Agreement during the period of this agreement including without
limitation the Terms of Assurance of the Office of Human Research Protection of the US
Department of Health and Human Services, which is attached hereto as Exhibit "2" and
incorporated herein be reference.

In witness whereof, the parties have executed this Agreement effective as of May 19, 2008.

[Signature]

Signed for and on behalf of CHOP
Philip R. Johnson, M.D.
Chief Scientific Officer, Joseph Stokes, Jr. Research Institute

Date: May 12, 2008

[Signature]

Signed for and on behalf of Penn
Steven Fluharty, Ph.D.
Vice Provost for Research

Date: May 28, 2008