Agreement for Research and Education collaboration between Institut de Recherche pour le Développement ("IRD"), Chiang Mai University ("CMU") and the President and Fellows of Harvard College on behalf of the Harvard School of Public Health ("Harvard")

BETWEEN

The Institut de Recherche pour le Développement, hereinafter referred to as the "IRD", is a public scientific and technological research institution. The head office is located at Le Sextant 44, bd de Dunkerque, CS 90009, 13572 Marseille cedex 02, France, and is represented by the Director General, **Prof. Dr. Michel LAURENT**

AND

The President of Chiang Mai University "CMU" on behalf of the Faculty of Associated Medical Sciences, hereinafter referred to as "AMS", located at 110 Intawaroros Road, Tumbol Sripoom, Aumpur Muang, Chiang Mai 50200, Thailand and represented by the President, **Prof. Dr. Pongsak ANGKASITH**

AND

President and Fellows of Harvard College on behalf of the Harvard School of Public Health, Department of Immunology and Infectious Diseases, a non-profit educational institution, hereinafter referred to as "Harvard", with offices at 677 Huntington Ave., Boston, MA 02115 USA represented by the Dean, **Prof. Dr. Julio FRENK**

Hereinafter, all parties, when referred to collectively, shall be referred to as the "Parties";

Considering the 'Parties' common research concerns, particularly regarding the prevention of mother to child transmission of HIV and the care of HIV infected infants and adults in Thailand and their desire to establish a mutual understanding regarding their collaborative ongoing research and educational efforts in the Program for HIV Prevention and Treatment in Thailand [http://www.phpt.org/], currently under the direction of Marc Lallemant.

THE PARTIES AGREE AND STATE AS FOLLOWS:

ARTICLE 1: **PURPOSE**

The Parties agree effective as of January 1st 2010 (the "Effective Date") to create an International Research and Education Unit entitled "Clinical Epidemiology, Mother and Child Health, and HIV in Southeast Asia" (hereinafter referred to the "Research and Education Unit", the "Research Unit" or the "Unit") in order to support, facilitate and provide a decision-making structure for research and educational collaboration between the Parties.

The Parties agree that the Unit shall not have a separate legal status (e.g., as a non-profit, registered in Thailand, France, the United States or otherwise), and, as a non-legal entity, the Unit shall not enter into contracts or sponsored research agreements, purchase real estate, or employ individuals. Each of the Parties shall assign personnel, equipment or other materials to support the Unit in accordance with the terms of this Agreement. The Unit shall be given by IRD the following code: UR 174.

ARTICLE 2: **DURATION, RENEWAL, DISCONTINUATION**

This Agreement is for an initial period of two (2) years from the Effective Date, and can be renewed once by written agreement of the Parties for an additional four (4) year period.

The Agreement may be terminated by mutual agreement of all of the Parties at any time, with an advanced notice of six (6) months. Such termination shall be accomplished by an amendment to this Agreement, signed by authorized representatives of each of the Parties.

Each Party may withdraw from the Agreement at any time by six (6) months advance written notice to the other Parties.

Upon any termination of or withdrawal from this Agreement by a Party or the Parties, the Parties involved will: (i)_ endeavor to finalize the joint activities initiated, (ii) decide upon the modes of liquidation of equipment and/or premises jointly owned by two or more of the Parties, (iii) cease using the names and logos of the Parties, either alone or in combination with any other words (if permission for such use has been granted), and (iv) promptly return to the terminating Party or Parties each Party's materials or property.

ARTICLE 3: **RESEARCH AND EDUCATION UNIT GOALS**

The goals of the Unit are to

1. Conceive and conduct clinical and laboratory research in various areas including but not limited to: HIV, maternal and child health, and HIV-associated infections and conditions such as infectious hepatitis, CMV, papillomavirus, and tuberculosis, and other infectious diseases found in Southeast Asia.

2. Carry out individual and group educational programs (courses, work-shops, tutorials, and exchange programs) for the benefit of students, research workers, and health care providers enrolled in or employed by the Parties.

ARTICLE 4: **RESEARCH AND EDUCATION UNIT MANAGEMENT**

4.1 RESEARCH AND EDUCATION UNIT DIRECTOR

The Research and Education Unit shall be managed by the individual who submitted the Unit proposal on behalf of the research group, the Unit Director ("Director"). The Director for the period of this Agreement is Marc Lallemant, M.D., a *Directeur de Recherche* at the Institut de Recherche pour le Développement and a Harvard School of Public Health Research Associate. If Dr. Lallemant shall for any reason be unable to continue as Director, the Parties may either nominate a replacement Director to be mutually agreed upon by the Parties or may terminate this Agreement by an amendment signed by authorized representatives of the Parties.

4.2 RESPONSIBILITIES OF THE RESEARCH AND EDUCATION UNIT DIRECTOR

The Director shall:

a. On or before sixty (60) days after the Effective Date, submit to the Parties for their review the Research Unit proposal updated as needed detailing the research and educational operations to be conducted by the Unit, sources and amount of funding, personnel involved, and resources that each Party has agreed to devote to support of the Research Unit (the "Workplan"). The initial Workplan and related resources is attached to this Agreement in **Appendix 1**. The Director shall submit to the Parties, for their information, a progress report every year, and two months at least before the end of the contractual duration shall submit to the Parties, the Research and Education Committee and the

Evaluation/Advisory Committee (as defined below) a progress report, as measured against the current Workplan.

b. Be responsible for the management of the administration of the Research and Education Unit.
c. Manage the activities of the Research and Education Unit in accordance with its general objectives, and in accordance with the policies of the Parties and the Sponsors of the Parties' research.
d. Propose partnerships, in particular with institutions or researchers from developing or emerging countries, to reinforce or enrich their research capacities.
e. Encourage research personnel and teams to participate in international conferences and in the dissemination of the results of the research to further the public good.
f. Conceive, develop, and facilitate the educational activities of the Unit.
g. Ensure that the rules of ethics and professional codes of conduct are communicated adequately to the Unit.
h. Establish internal rules and regulations for the Research and Education Unit, including without limitation safety regulations, and ensure that all such rules and regulations are communicated adequately to the Unit.
i. Coordinate the activities of the Evaluation/Advisory Committee, and the Research and Education Committee (as defined below), and act as the main liaison between the Parties and the Unit.

4.3 Research and Education Unit Associate Director

Asst. Prof. Dr. Wasna Sirirungsi will act as Associate Director to coordinate the education activities of the research unit with the Faculty of Associated Medical Sciences, and assist in the functions of the Director. He/she may be appointed or replaced by the Director upon consultation with the Research and Education Unit Committee. Generally, the term of the Associate Director shall coincide with that of the Director.

ARTICLE 5: **EVALUATION/ADVISORY COMMITTEE**

The Evaluation/Advisory Committee shall be established within three (3) months of the creation of the Research and Education Unit. The Evaluation/Advisory Committee shall be comprised of two scientific experts selected by each Party each of whom shall serve for the period of this Agreement. Members of the Evaluation/Advisory Committee shall choose a Chairman. The Director shall serve as an ex officio member.

The Evaluation/Advisory Committee shall provide technical and scientific advice as needed and shall make recommendations as to the necessity and/or feasibility of continuing the Research and Education Unit for any additional term. The Evaluation/Advisory Committee may also make recommendations to the Parties regarding the renewal of the Director at the end of his term and candidates for the Director's successor.

The Evaluation/Advisory Committee will review the progress report of the Unit, and, based on this report and Committee discussions among themselves or with Unit members as needed, will issue a letter addressed to the Parties stating the conclusions of their evaluation. They have the option of issuing a longer report at any time if deemed necessary.

ARTICLE 6: **RESEARCH AND EDUCATION COMMITTEE**

The Research and Education Committee shall be established within three (3) months of the creation of the Research and Education Unit.

6.1 Composition

The Research and Education Committee shall be composed of the Director, the Associate Director, a Team Leader (defined below) from each Team (if applicable), and two Unit Personnel representatives (defined below) selected by the personnel. Each member of the Committee shall be empowered with one vote.

All researchers and technical department heads may attend Committee meetings as non-voting members. In addition, the host institution, Chiang Mai University, will select an administrative expert in order to facilitate the insertion of the Unit within the University who may attend Committee meetings as a non-voting member. Associate Dean in Research and International Relations of AMS will assist as administrative expert in order to facilitate the insertion of the Unit within Chiang Mai University.

Personnel hosted by the Research and Education Unit for at least one year and not affiliated with any of the Parties who are participating in a research or educational project of the Unit ("Guests"), may attend Committee meetings as non-voting members. In the event that there are more than five Guests during a given year, the Guests will designate a non-voting delegate to the Research and Education Committee.

6.2 STRUCTURE

The Research and Education Committee is headed by the Director who sets the agenda for each meeting. At the request of one-third of the members of the Research and Education Committee, the Director may add additional items to the agenda.

The Research and Education Committee meets at least twice a year (in person or by other mutually-agreed upon methods), either at the request of the Director or of the majority of its members. Absent members of the Research and Education Committee may give their mandate to other members, to present on their behalf and may express their opinion by any means of communication.

6.3 FUNCTION

The Research and Education Committee is consulted for:

a. Approving the budget, the annual progress report, and other significant decisions related to the resources, organization and functioning of the Research and Education Unit.
b. The composition of Teams, if any, within the Research and Education Unit
c. Work, hygiene and safety conditions at sites of Research and Education Unit work.
d. Issues related to ethics and professional codes of conduct.
e. The ongoing training plan of the Research and Education Unit.
f. Approval of invited Guests.
g. Any other pertinent question that the Director proposes for consideration or debate.

The Committee functions through consensus. If a vote is required (for example, for a. or f. above, or if consensus cannot be reached), then a two-thirds majority is required for approval of a measure.

ARTICLE 7: **TEAMS**

The Research and Education Unit may be organized in teams should the betterment of the organization of the Unit warrant it. A team consists of a voluntary association of researchers, educators, engineers, technicians or administrative staff sharing the same scientific or educational objective. As an integral part of the Research and Education Unit, the Team is directly involved in:

- The scientific, educational, and financial programs of the Research and Education Unit
- The preparation of the activity reports
- The management of the financial resources
- Organizing transfer activities: (promotion and dissemination of research results, information and training)

The Director designates the Team Leaders, after consultation with the members of the team and deliberation by the Research and Education Committee.

With the agreement of the Director, the Team may identify new potential sources of financial support for which a Party may apply.

ARTICLE 8: **ALLOCATION AND MANAGEMENT OF RESOURCES**

During the period of this Agreement, the Parties may provide the Research and Education Unit with either unrestricted material resources to be used as needed in order to achieve the objectives of the Unit and/or with material resources to be used as required by the provider Party(ies) or the outside Sponsors of the work of the Parties. Each Party shall have the right to designate and approve its financial and/or material support for the Unit. None of the Parties to this Agreement will be obligated pursuant to any provisions of this Agreement to provide more or different resources for the support of the Unit or to be used as required by that Party or an outside Sponsor than that Party has agreed upon.

8.1 HUMAN RESOURCES

All members of the Research and Education Unit shall be employed by, or shall serve as an independent contractor to, one of the Parties and assigned to support the Unit for the purposes of this Agreement. Such personnel are referred to herein collectively as Unit Personnel, and individually as Unit Members. The Unit Personnel are subject not only to the rules and regulations of the Unit, but also to all rules, regulations, policies and procedures of their respective institutions. The Unit Members are identified in **Appendix 2** of the present Agreement.

Within budgetary and organizational constraints, the Unit Personnel will be encouraged to participate to the in-house training plan of each Party, without consideration of the institution they respectively belong to.

With the agreement of the Director and the Unit Member's employer, a Unit Member may be assigned or sent to a foreign country in accordance with the policies and procedures of his or her institution, and subject to the policies of the Sponsors of the research.

The Unit may host invited Guests who are not affiliated with any of the Parties. Each Guest will remain an employee of his or her respective institution, and shall not become an employee of the Unit or any of the Parties.

If Unit Member does not reasonably fulfill his or her duties or otherwise engages in misconduct or violation of applicable policies, then the Director may, after consultation with the Party responsible for the Unit Member at issue, request in writing that the Unit Member be removed from the Unit.
Each Party to this Agreement shall be responsible for overseeing and providing financial support (which may include, without limitation, salaries, benefits, and travel expenses) for its own personnel who are participating in this Agreement as Unit Members. Without limiting the foregoing, each Party shall be responsible for disciplining its own personnel in accordance with its own procedures.

8.2 BUILDING AND EQUIPMENT RESOURCES

AMS will provide the Research and Education Unit with research space located at the facility described in 8.3, and maintenance. Each Party shall be responsible for the maintenance and renovation of its buildings and equipment.

Depending upon the mode of financing and in accordance with the policies of outside Sponsors of the research where appropriate and the policies of each Party, the equipment provided to or acquired by the Research and Education Unit will be registered in the inventory of one, some or all of the Parties. Maintenance costs of the equipment are supported by one, some or all Parties, by mutual agreement and in accordance with the policies of outside Sponsors of the research where appropriate.

The Parties remain owners of the equipment or buildings/premises they provide. If the Parties buy equipment collectively, property shares will be determined in relation to the financial contribution of each of the Parties for the purchase of equipment.

In case of discontinuation of the present agreement or at its termination/expiration the Parties will dispose of the equipment that is collectively owned in accordance with the policies of the Sponsor(s) of the research. If the equipment was not purchased with funds provided by an outside Sponsor, the Parties will agree upon its disposition.

8.3 LOCATION OF THE UNIT

The Research and Education Unit shall be located at Chiang Mai University Faculty of Associated Medical Sciences, Muang, Chiang Mai 50200, Thailand.

8.4 FINANCING OF THE UNIT

Each Party shall manage the funds for which it is responsible that support the Unit, or Unit Teams if applicable, or to be used as required by the Party or an outside Sponsor, as described in **Appendix 3**, according to its own financial rules and that of the sponsoring institution. However, for the purpose of facilitating the Unit operations, a Party may agree to delegate to another Party all or any of the funds granted the Unit. This delegation is organized through a specific agreement.

8.5 CONTRACTS FOR RESEARCH ACTIVITIES

Contracts made out for joint research or education activities of the Unit, or Unit Teams if applicable, shall be negotiated and executed by either one of the Parties depending on:

- the nature of the activities and the source of funding;
- the planned contributions of each of the Parties in the draft of the contract.

When one Party prepares an application for a research grant or a collaborative agreement that would substantially involve personnel or facilities assigned to the Research and Education Unit, the Party will use reasonable efforts to notify the other parties. Parties, then will have three weeks to provide reasonable comments to the other Party. Silence kept by these Parties over this period shall be considered as a consent to execution.

ARTICLE 9: **RESEARCH RESULTS AND INCREASING THE VALUE OF INTELLECTUAL PROPERTY ("VALORIZATION")**

9.1 KNOW HOW

All technologies, methods, expertise and data provided to a Party by another Party within the framework of the cooperative activities conducted under this Agreement remain its property.

9.2 RESEARCH RESULTS AND INTELLECTUAL PROPERTY

9.2.1 Disclosure and Ownership of Research Results and Inventions

The Parties agree that their mutual objective is to ensure that each invention that is conceived and reduced to practice in the performance of the research under the Workplan during the term of this Agreement (an "Invention") be developed for public use and benefit. The scope and subject of the research will be defined in the Workplan.

Each Party shall notify the others, promptly and in writing, of any Invention of which it becomes aware. A party shall be deemed to be aware of an Invention only after a written invention disclosure form that

describes such Invention has been submitted to its Office of Technology Development or equivalent office. Each Party shall treat as confidential and not disclose to any third party the contents of any notice provided to it under this Section 9.2.1 that discloses an Invention owned by another Party, and shall use such information only as authorized under Section 9.2.2. Each Party shall treat as confidential and not disclose to any third party the contents of any notice provided to it under this Section 9.2.1 that discloses a Joint Invention (as defined below) until the earlier of filing of the first patent application with respect to such Joint Invention in accordance with Section 9.2.3 or publication of such Joint Invention in accordance with Section 11.

Each Party shall own its Results (as defined in 9.2.3). In the case of Results generated under this Agreement by the efforts of more than one Party, the Parties contributing to the Results shall jointly own such Results.

9.2.2 Use of Research Results and Inventions

Each Party can use free of charge and without restriction the Results obtained by any Party under this Agreement for its own research, under condition of respecting the conditions specified in articles 11 and 13 and the other conditions of article 9.

Inventorship of each Invention shall be determined in accordance with patent law of the country where patent applications for such Invention are filed. Any and all Inventions made solely by one Party and patent applications and patents to the extent claiming Inventions made solely by one Party shall be owned solely by that Party. Any and all Inventions made jointly by more than one Party ("Joint Inventions") and patent applications and patents to the extent claiming Joint Inventions shall be owned jointly by those Parties.

Each Party agrees to grant to the other Parties a non-exclusive, non-transferable, royalty-free license for research use under its interest in any patent or patent application to the extent claiming its solely owned Inventions. Each Party granted such a license shall treat as confidential and not disclose to any third party the contents of the solely owned Invention. Each such license agreement will be in the form normally used by the granting Party for non-exclusive licenses and will include, without limitation, indemnity, insurance and limitation on liability provisions.

9.2.3 Valorization of Research Results and Inventions

Each Party shall be responsible for patent prosecution and commercialization of its solely owned Inventions.

In the case of Joint Inventions, the relevant Parties will consider together the opportunity to file a jointly-owned patent application. The Parties which endorse the decision to file such application will make good faith efforts to negotiate a common agreement ("Invention Administration Agreement") governing the conditions of the patent filing and licensing, and the sharing of the costs and expenses associated with these activities. In any case, if a Party does not endorse the filing or support of an application in general or in a specific territory ("Abandoned Joint Patent Rights"), it shall notify the other Party(ies) promptly in writing. In such event, the other Party(ies) shall have the unrestricted right to license such Abandoned Joint Patent Rights to third parties without accounting to the abandoning Party, and the abandoning Party shall have the right to use the subject matter of the Abandoned Joint Patent Rights only for its own research use.

Under the terms of an Invention Administration Agreement, the co-owners of a Joint Invention shall appoint one Party or several of them to be responsible for leading the commercializing of the Joint Invention upon mutual agreement of the inventing Parties. Alternatively, the inventing Parties may agree to jointly designate, via an agreed-upon process in accordance with agreed-upon criteria, a third party who shall be authorized to pursue the commercial exploitation of a Joint Invention for the benefit of the Parties (hereafter "Valorization Representative"). Appropriate compensation, if applicable, for the Valorization Representative shall be determined and agreed upon by the Parties.

When several Parties are appointed to be responsible for leading commercializing of a Joint Invention, each of them shall be entitled to enter into negotiations to commercially exploit the Joint Invention with third

parties, provided the other Parties are informed thereof beforehand. Any agreements resulting from such negotiations must be co-signed by all Parties with an ownership interest in the Joint Invention. No Party shall withhold consent to such agreements absent reasonable cause.

If a Valorization Representative is designated by the Parties, the Valorization Representative will be authorized, with respect to the Joint Invention designated to him or her to:

- carry out dissemination of relevant data and commercial prospecting operations relating thereto, taking all appropriate measures to safeguard confidential or proprietary information;
- negotiate and draft on behalf of the Parties agreements for the commercial exploitation related thereto. All terms of such potential agreements, especially the financial ones, shall be transmitted to the other Parties which shall have a reasonable time within which to comment and express their consent or opposition; Upon the mutual consent of the Parties, the Valorization Representative shall be authorized to conclude such agreements on behalf of the Parties, provided that the agreement is concluded in a manner that conforms with the Parties' respective policies and practices,
- receive the fruits of the exploitation for distribution to the Parties;
- intervene with the licensees to ensure payment for fees and verify, if necessary, the accuracy of their amount;
- distribute any fees and other financial fruits in accordance with the ownership shares and time frame specified by the particular agreement.

Each Party shall provide the Valorization Representative with reports of data, materials, compositions, methods, processes, analyses, formulae and information that it generates in the performance of the research under the Workplan ("Results"), via an agreed-upon process or schedule. The Valorization Representative shall keep the Parties regularly informed, in writing, of all developments related to the commercial exploitation of Joint Inventions according to a schedule to be specified in a separate written agreement with the Valorization Representative.

9.2.4 Copyright

With respect to any copyrighted work created by one of the Parties Unit Members, such work will be governed by the Party's policy on inventions, patents and copyright and any other individual party's Participation Agreement. Such works that are jointly created[1] by Unit Members from the Parties shall be owned jointly, and the Parties agree that if such works generate royalties that belong to the institutions, such royalties shall be shared, with the size of the shares fairly reflecting the size of the contributions made by authors associated with the Parties.

ARTICLE 10: **RESEARCH ETHICS**

All research activities undertaken at the Unit or otherwise in connection with this Agreement shall be governed by applicable international and Party norms, ethics, codes, principles and guidelines relevant to that research including, where necessary, securing approvals from the Party(ies)'s biosafety committees and institutional review boards.

ARTICLE 11: **PUBLICATIONS**

The mission of all parties is to ensure wide dissemination of the scientific knowledge acquired through the collaborative research. They will provide all assistance possible to that effect. Publications will acknowledge the joint effort of Chiang Mai University Faculty of Associated Medical Sciences, IRD and Harvard University School of Public Health.

It is contemplated that the Parties may publish Results jointly. Nonetheless, each Party reserves the right to publish its Results separately. Each Party shall provide the other Parties with a copy of any manuscript

[1] A "joint work" is a work prepared by two or more authors with the intention that the contributions be merged into inseparable or interdependent parts of a unitary whole (17 U.S.C § 101 of the United States Copyright Act)

disclosing Results at least thirty (30) days prior to submission for publication for the purpose of enabling the other Parties to review the manuscript for potentially patentable Inventions that should be protected by a patent application filing. If, during the thirty (30) day period specified above, a Party notifies the Party wishing to publish that the manuscript reveals a potentially patentable Invention with respect to which it has the right to and would like to file a patent application, the Party wishing to publish shall delay publication for up to thirty (30) additional days for the purpose of enabling a patent application to be filed.

ARTICLE 12: **PUBLICITY**

Any Party's use of another Party's name (alone or as part of another name) or logo in any materials shall be permitted only upon the prior written approval of the Party whose name is sought to be used. Notwithstanding the foregoing, it is understood and agreed that each Party may disclose the existence and nature of their collaboration under this Agreement, and shall have the right to acknowledge the other Parties' support of and participation in the research in scientific publications.

ARTICLE 13: **CONFIDENTIALITY**

The Parties agree not to publish or disclose information that is marked confidential and/or proprietary that they might obtain from the other Party(ies) in the performance of this Agreement or in any manner whatsoever, without the other Party's written consent. Confidential information shall not include information that:

(a) is publicly available prior to the date of the Agreement or becomes publicly available thereafter through no wrongful act of the recipient Party(ies);
(b) was known to recipient Party(ies) prior to the date of disclosure or becomes known to recipient Party(ies) thereafter from a third party having an apparent bona fide right to disclose the information;
(c) is disclosed by recipient Party(ies) in accordance with the terms of the provider Party(ies) written approval;
(d) is disclosed by provider Party(ies) without restriction on further disclosure;
(e) is independently developed by recipient Party(ies);
(f) recipient Party(ies) is obligated to produce pursuant to an order of a court of competent jurisdiction or a valid administrative or Congressional subpoena, provided that recipient Party(ies) (a) promptly notifies the provider Party(ies) and (b) cooperates reasonably with the provider Party(ies) efforts to contest or limit the scope of such order.

Confidential Information shall not include information that is necessary for publication or independent verification of the Results.

ARTICLE 14: **FORCE MAJEURE**

A Party shall be excused from performance of its obligations under this Agreement if and to the extent that such performance is hindered or prevented (directly or indirectly) by reason of any U.S., Thai or French government policy decision fundamentally affecting the ability of a Party to enter into or, having entered into, to maintain, this Agreement, or any labor disturbance, government action, riot, armed conflict, terrorist event, accident, epidemic, pandemic, extremes of weather or event of nature, unavailability of normal means of transport or any other matter unforeseeable or beyond the reasonable control of the Party whose performance is hindered or prevented. If the event of force majeure occurs and continues for a period of more than 30 days, then the Parties shall discuss in good faith whether to terminate this Agreement or extend the term of this Agreement.

ARTICLE 15: **CIVIL LIABILITY**

Except for the intellectual property obligations under Article 9 and the indemnification provisions specified later in this section, each party shall only be responsible and liable for the actions of its own agents or employees (and any related harm to third parties) and shall not look to the other parties for relief.

In the event of an accident that occurs in the workplace and involves one of the Parties' personnel, any Party aware of this accident shall promptly report it to the other Parties.

The Unit Personnel are subject to health and safety regulations enforceable in the Unit and its facilities. They shall comply with the internal regulations and instructions transmitted thereto for the use of equipment.

Each Party (the "Indemnifying Party") shall indemnify the other Parties against all losses, costs, expenses or damages of any kind in connection with any actions, suits, claims or demands arising out of the intentional misconduct or negligence of the Indemnifying Party in the performance of its obligations under this Agreement.

ARTICLE 16**: GENERAL TERMS**

16.1 Status of the Parties. The Parties are independent contractors, and no Party is authorized to act on behalf of any other Party or to bind any other Party to any third party. This Agreement does not establish any agency, partnership or joint venture relationship between the Parties.

16.2 Governmental Approval. AMS/Chiang Mai University shall be responsible for applying for and obtaining all necessary governmental approvals, permits, visas and licenses in Thailand for the Parties to carry out and implement this Agreement.

16.3 Assignment. No Party shall assign (whether voluntarily, involuntarily or by operation of law) all or any part of its rights and obligations under this Agreement without the prior written approval of the other Parties, which approval may be withheld in such Party's sole discretion. Any other assignment whatsoever, direct or indirect, shall be void.

16.4 Authority to Execute and Grant Rights Herein. Each Party to this Agreement represents that this Agreement has been signed and executed by a person with the requisite corporate authority to act on its behalf, to grant these rights, and to enter into this Agreement.

16.5 Notice. Notice under this Agreement shall be given to the Parties in writing by Federal Express (or its equivalent) or facsimile, addressed to the Signatories below. Notices shall be deemed effective upon receipt. Any Party may change the address and recipient of such notice upon written notice to the other Parties, which shall be deemed effective upon receipt.

ARTICLE 17: **CHOICE OF LAW; SETTLEMENT OF DISPUTES**

In the event that a dispute arises from or in connection with this Agreement, the Parties shall attempt to settle the matter by amicable means. Should the Parties be unable to achieve resolution, any dispute arising from or in connection with this Agreement, or out of the execution thereof, shall be decided under the rules of the International Chamber of Commerce by one or more arbitrators appointed in accordance with said rules. The arbitration shall take place in the defendant Party's country). The arbitrator(s) shall be able to read, write and speak English, and the arbitration shall be conducted in English. The arbitral award is final and binding on the Parties, and any Party may apply to a court of competent jurisdiction for enforcement of such award.

ARTICLE 18: **GOVERNING LANGUAGE**

The English language version of this Agreement shall be the official version. A translation may be made for convenience, but the English language version shall govern in the event of conflict between the Parties.

ARTICLE 19: **ENTIRE AGREEMENT**

This Agreement includes the present document and its appendixes, i.e.:

- Appendix 1 : Scientific Workplan of the Unit and Related Resources
- Appendix 2 : List of Unit Members
- Appendix 3 : Unit Resources

This Agreement constitutes the entire understanding among the Parties and supersedes all other understandings among the Parties concerning this Agreement.

IN WITNESS WHEREOF, the Parties have caused this Agreement to be executed as of January 1st, 2010 :

The Institut de Recherche pour le Développement

I. R. D
INSTITUT DE RECHERCHE POUR LE DÉVELOPPEMENT

By :.....

(Prof. Dr. Michel LAURENT)

Date : 21 SEP. 2010

The Harvard School of Public Health, Harvard University

By :.....

(Prof. Dr. Julio FRENK)

Date : April 15, 2010

The Chiang Mai University

By :.....

(Prof. Dr. Pongsak ANGKASITH)

Date : 9 December 2009

Appendix 1: Research and Education Work Plan of the Unit

1. Structure of the Research and Education team

The International Unit is based primarily on the tripartite collaboration between Chiang Mai University, Harvard School of Public Health and French IRD which proved highly productive, particularly since 2003 in the framework of the PHPT-IRD 174 unit. It will be developed within a network of international collaborations with Thai, French, European and US groups.

This International Unit will benefit from the clinical and laboratory platforms progressively developed since the creation of PHPT-IRD program and will keep on the intensive capacity building activities -- education and technology transfer -- which will insure its sustainability.

The staff of this International Unit PHPT-IRD program is multidisciplinary, composed of epidemiologists, public health specialists, statisticians, virologists, immunologists, clinical chemists, hematologists, pharmacologists, counseling experts and clinicians specialized in HIV (internists, pediatricians, and obstetricians). In the framework of PHPT-IRD 174, they will join efforts to conduct research on the prevention and treatment of AIDS in Thailand.

2. Research Programs

In the framework of this International Research Unit, the PHPT-IRD activities will continue to be devoted to improving prevention and care of HIV at the family level. More specifically:

- Improve the efficacy, safety and tolerance of therapies for the prevention of mother to child HIV transmission.
- Minimize the risk of developing resistances to antiretrovirals used for the prevention of mother to child transmission that could limit the response to antiretroviral treatments when mothers and/or infants begin therapy for their own health.
- Develop methods and strategies that maximize the adherence to and the effectiveness and safety of antiretroviral treatments in the family setting.

Several research studies of the International Unit will be the continuation of ongoing programs developed by the PHPT-IRD 174 unit. Programs recently initiated or ready to be implemented are listed below as well as planned programs which, for most of them, will be nested within ongoing cohort programs. Indeed, given the current considerable PHPT workload, the PHPT-IRD 174 Unit, does not consider initiating new cohort programs unless the emergence of new research questions urgently deserves it.

2.1 Clinical Research

Current programs

PHPT-3. A multicenter, randomized strategy trial to compare two HAART switching strategies, one based on the control of the viral load and the other on the maintenance of the CD4 level, to determine which one best preserves patients' therapeutic options

- *Grants: NIH, NICHD, R01 HD 042964*
- IRD-Thai Ministry of Public Health-Chiang Mai University, Faculty of Associated Medical Sciences-Harvard School of Public Health-Harvard Medical School –Columbia University

PHPT-5. A multicenter, phase III, double-blind, randomized, placebo-controlled, trial to evaluate the efficacy of nevirapine administered only to neonates, versus perinatal nevirapine to both mothers and neonates, versus lopinavir/ritonavir in addition to standard zidovudine prophylaxis

- *Grants: NIH, NICHD, R01 HD 05246.*
- IRD-Thai Ministry of Public Health-Chiang Mai University, Faculty of Associated Medical Sciences-Harvard School of Public Health -Harvard Medical School

PACTG 1054-ACTG 5190. Assessment of safety and toxicity among infants born to HIV-1 infected women enrolled in antiretrovirals protocols in diverse areas of the world

- *Grants: NIH (NIAID, PACTG-IMPAACT)*
- IRD-Thai Ministry of Public Health-Chiang Mai University, Faculty of Associated Medical Sciences, Research Institute for Health Sciences, Mahidol University, and the IMPAACT and ACTG networks

PACTG 1056. Comparative pharmacokinetic study of the d4T+3TC+NVP fixed dose combination of antiretrovirals versus liquid formulation for HIV-1 infected children

- *Grants: NIH (NIAID, PACTG-IMPAACT)*
- IRD-Thai Ministry of Public Health-Chiang Mai University, Faculty of Associated Medical Sciences, Research Institute for Health Sciences, Mahidol University, and the IMPAACT network

IMPAACT P1069. Comparative pharmacokinetic study of the ZDV+3TC+NVP fixed dose combination of antiretrovirals versus liquid formulation for HIV-1 infected children

- *Grants: NIH (NIAID, PACTG-IMPAACT)*
- IRD-Thai Ministry of Public Health-Chiang Mai University, Faculty of Associated Medical Sciences, Research Institute for Health Sciences, Mahidol University, and the IMPAACT network

IMPAACT P1077.The PROMISE study (Promoting Maternal and Infant Survival Everywhere).

- *Grants: NIH (NIAID, IMPAACT)*
- IRD-Thai Ministry of Public Health-Chiang Mai University, Faculty of Associated Medical Sciences, Research Institute for Health Sciences, and the IMPAACT network

PREDICT. When to Start Anti-HIV Drugs in Children Infected With HIV.

- *Grants: NIH (NIAID, CIPRA)*
- IRD-Thai Ministry of Public Health-Chiang Mai University, Faculty of Associated Medical Sciences, Research Institute for Health Sciences, Mahidol University, HIVNAT and the CIPRA network

PENTA 11. A randomized clinical trial evaluating structured therapeutic interruptions in HIV infected children. Long term follow-up of children.

- *Grants: European Union, PENTA*
- IRD-Thai Ministry of Public Health-Chiang Mai University, Faculty of Associated Medical Sciences, HIVNAT, Mahidol University, and the PENTA network

Cohorts. Observational cohort of over 2000 adults and children receiving antiretroviral treatment within the PHPT network. This study evaluates clinical, biologic, socio-demographic and economic data collected to inform policy makers at the Ministry of Public Health and international health agencies (WHO, UNICEF).

- *Grants: Global Fund to Fight AIDS, TB and Malaria (GFATM) and Oxfam GB*

- IRD-Thai Ministry of Public Health-Chiang Mai University, Faculty of Associated Medical Sciences, Faculty of Science

Programs in development

HIV – Tuberculosis co-infections and HIV – Hepatitis B and C co-infections: Diagnostic and clinical management

- *Grants: ANRS,12 179, Thai National Research Council, Thai Ministry of Education, French Ministry of Foreign Affairs*
- IRD-Chiang Mai University, Faculty of Associated Medical Sciences *and Tours university*

Evaluation of the pharmacokinetics and safety of new antiretroviral drugs and formulations, as well as co-formulations

- *Grants: European Union, PENTA, NIH (NIAID,IMPAACT)*
- IRD -Chiang Mai University, Faculty of Associated Medical Sciences

Long term toxicities associated with antiretroviral therapy

- *Grants: Global Fund to Fight AIDS, TB and Malaria (GFATM)*
- IRD -Chiang Mai University, Faculty of Associated Medical Sciences, Paris VI University

Impact of antiretroviral treatments on the growth of HIV-infected children in Thailand. Comparison with HIV-infected children in France

- IRD-Chiang Mai University, Faculty of Associated Medical Sciences-Faculty of Science and INSERM

2.2 Physiopathology Research

Current programs

ANRS 12 134. Evaluation of transmitted HIV drug resistance in Cambodia, Vietnam, Thailand, Burkina Faso, Cameroon, Ivory Coast and Senegal.

- *ANRS*
- IRD - Chiang Mai University, Faculty of Associated Medical Sciences, and the ANRS working group on non-B HIV resistance.

In addition to this program, several programs are being developed within the **Franco-Thai and other Education through Research Programs**: Short- and long-term field trainings for students from Thailand and abroad at undergraduate, PhD, and postgraduate levels:

Molecular and immuno-virological determinants of mother-to-child transmission of HIV:

- *Grants: ANRS and Sidaction*
- IRD - Chiang Mai University, Faculty of Associated Medical Sciences - Tours University

ANRS 1284. A study of HIV-1 mother-to-child transmission and disease progression in relation to the genetic polymorphism of the patients. HIV-coreceptors/Chemokine receptors and HLA polymorphism as co-factors of HIV perinatal transmission and disease progression.

- *Grants: ANRS*

- IRD - Chiang Mai University, Faculty of Associated Medical Sciences, Mahidol University, Faculty of Medicine and Faculty of Sciences, INSERM 543.

Pharmacogenomics of antiretroviral drugs in HIV-infected Thai patients: Identification of genetic polymorphisms associated with plasma antiretroviral drug concentrations in the Thai population.

- *Grants: IRD and Ramathibodi Hospital*
- IRD-Chiang Mai University, Faculty of Associated Medical Sciences, Department of Pathology, Faculty of Medicine at Ramathibodi Hospital, Mahidol University;

Development of simplified immunological techniques for the evaluation of antiretroviral plasma drug levels for pharmacokinetics studies and Therapeutic Drug Monitoring (TDM)

- *Grants: IRD, Thai National Research Council, Thai Ministry of Education, French Ministry of Foreign Affairs*
- IRD-Chiang Mai University, Faculty of Associated Medical Sciences, Faculty of Sciences, Laboratoire de Modélisation et Ingéniérie des Protéines, Paris-Sud 11 University

Decay of ARV resistance mutations in women enrolled in PHPT-2

- *Grants: IRD and NIH-IMPAACT*
- IRD-Chiang Mai University, Faculty of Associated Medical Sciences-University of Washington

Genetic analysis of HBV surface antigen variants in HBV/HIV-co-infected patients in Thailand

- *ANRS 12179, IRD, Thai Ministry of Education, French Ministry of Foreign Affairs*
- IRD-Chiang Mai University, Faculty of Associated Medical Sciences-Tours University

Programs in development

Use of monoclonal antibodies for the development of diagnostic tools in the field of HIV and co-infection

- IRD-Chiang Mai University, Faculty of Associated Medical Sciences

HIV - Papilloma virus co-infections

- IRD-Chiang Mai University, Faculty of Associated Medical Sciences-Tours University

Identification of the genetic polymorphisms associated with abnormal lipid profiles in Thai HIV infected patients receiving HAART.

- IRD-Chiang Mai University, Faculty of Associated Medical Sciences- Ramathibodi Hospital, Mahidol University-University Paris V

Evaluation of the impact of HIV-1 CRF01_AE protease gene polymorphisms on the virological response to protease inhibitors

- IRD-Chiang Mai University, Faculty of Associated Medical Sciences- Ramathibodi Hospital, Mahidol University- University Paris V

Establishment of a single-cycle pseudotyped virus phenotypic assay and a genotypic bioinformatic-based assay for the determination of CCR5 or CXCR4 coreceptor usage in Thailand

- IRD-Chiang Mai University, Faculty of Associated Medical Sciences- Tours University

Development of an immunodiagnostic test for the diagnosis of latent tuberculosis and Development of immunological techniques for the identification of drug resistant M. tuberculosis

- IRD-Chiang Mai University, Faculty of Associated Medical Sciences-University Paris V

2.3 Social Sciences

<u>Current program</u>

LIWA/ANRS 12-141 (Living with Antiretrovirals). A socio-demographic and economic evaluation of the PHPT-Oxfam community based antiretroviral treatment program in northern Thailand.

- *Grants: ANRS and Oxfam*
- IRD-INED-Chiang Mai University, Social Research Institute

<u>Program in development</u>

Fairness issues in health economics evaluation

Trade off between universal access and incentives to Research & Development (R&D) through Intellectual Property Rights (IPR)

- *Grants: ANRS and Oxfam*
- IRD-INED-Chiang Mai University, Lameta/Université de Montpellier

3. Education and Capacity building

3.1. Training/Education

Graduate Course (in development)
A graduate course including three tracks in "Clinical Trial Design and Implementation" (30 hours) is planned for 2009 with the collaboration of AMS, Faculty of Medicine (Department of Community Medicine), and the Faculty of Science (Department of Statistics), and is to be hosted by the Faculty of Associated Medical Sciences. This course is aimed at providing students with a theoretical and practical understanding of the issues involved in the design, conduct, analysis and interpretation of randomized controlled trials for health interventions with a focus on AIDS treatment and care.

Graduate Research Seminar: "Research Projects Development"

This seminar will be open to all students and faculty as a forum for the development of research proposals for graduate and post-doctoral students. At each session, the progress of the development of one idea into a formal research proposal is presented by the investigator and discussed by all participants: presentation of the review of the literature, research hypotheses, methodology, partnerships, technical platform and funding needs. The objective is to help the participants in thinking through the process of developing an independent research project at the master, PhD, or post-doctoral level.

The Franco-Thai Collaboration Program in Higher Education and Research / Hubert Curien

The Franco-Thai Collaboration Program in Higher Education and Research "Optimizing the Prevention of Mother to Child Transmission of HIV and the Care for HIV Infected Infants and Adults in Thailand", initiated in 2005 ended in 2008. A new application was submitted in 2008 to continue this very productive training program (particularly its PhD component). This project provides opportunities for doctoral candidates, young researchers, and young lecturers to spend significant time in French academic research units to pursue individual research projects developed within and with the support of the research unit. It also allows mentors, lecturers and advanced students or postdoctoral fellows from France to come to Thailand for short times to lecture, participate in workshops or help research projects or technology transfers.

(1). Complexities of antiretroviral treatments: drug toxicities and pharmacology, HBV and HIV co-infection and resistance to drugs.

- Genetic polymorphisms associated with abnormal lipid profiles in Thai HIV infected patients receiving HAART.
- CYP2B6 genetic polymorphisms and efavirenz drug concentrations
- HIV-1 CRF01_AE protease gene polymorphisms and virological response to protease inhibitors
- HBV variants, HBV vaccine escape mutants, HBV resistance to lamivudine, and therapeutic possibilities of Tenofovir

(2). Innovative approaches for the diagnosis of HIV co-infections and the monitoring of therapy

- Immunodiagnostic test for latent tuberculosis, drug resistant M. tuberculosis
- Detection and typing of HPV: real-time PCR, enzyme restriction analysis or probe hybridization assays.
- Screening tests for CCR5 or CXCR4 coreceptor usage in Thailand
- Candidate molecules interfering with the processing of the HIV gag polyprotein
- I*n vitro* model to screen for inhibitors of the HIV Gag maturation process

The Esther mentoring program and regional trainings, workshops, and scientific meetings

The research unit and Chiang Mai University will continue to host regional training programs for the Greater Maekong Subregion, such as (1) the Esther – Laos - France mentoring program for HIV care teams which allows physicians, nurses, laboratory technicians, counselors and patient network participants to benefit from the experience of Thai medical teams of the Chiang Mai province and from advanced trainings in France; (2) The International HIV medicine Symposia series; (3) The HIV prevention and care Workshops for the Greater Maekong Subregion.

The team will also participate to the following courses as needed:

508701 Advanced Clinical Microbiology 4(2/2-2/P)
Cellular and molecular level interactions between microorganisms and hosts leading to pathology.

508731 Special Techniques in Clinical Microbiology 2(1/1-1/P)
Techniques in clinical microbiology: theory, concepts, application in bacteriology, virology and mycology.

508732 Special Topics in Clinical Microbiology 2(2/2-0/0)
Emerging micro organisms or diseases and progress in the diagnostic technology.

510713 Research Methodology and Biostatistics 2(1/1-1/P)
Research organization, methodology, planning, data collection, analysis, and publication.

510791 Seminar in Medical Technology 1(1/1-0/0)
Presentation and discussion of fundamental articles in medical technology.

510793 Selected topics in Biomedical Sciences 2(2/2-0/0)
Lectures and round table discussions on newly acquired knowledge and technology in clinical and diagnostic immunology, blood banking, microbiology, haematology, microscopy, chemistry, oncology, molecular biology/genetics.

3.2. Technological Transfers

To decrease the price of HIV RNA load, the laboratory will establish within the first months of 2009 the ANRS HIV RNA quantification technique using the real-time PCR technique.

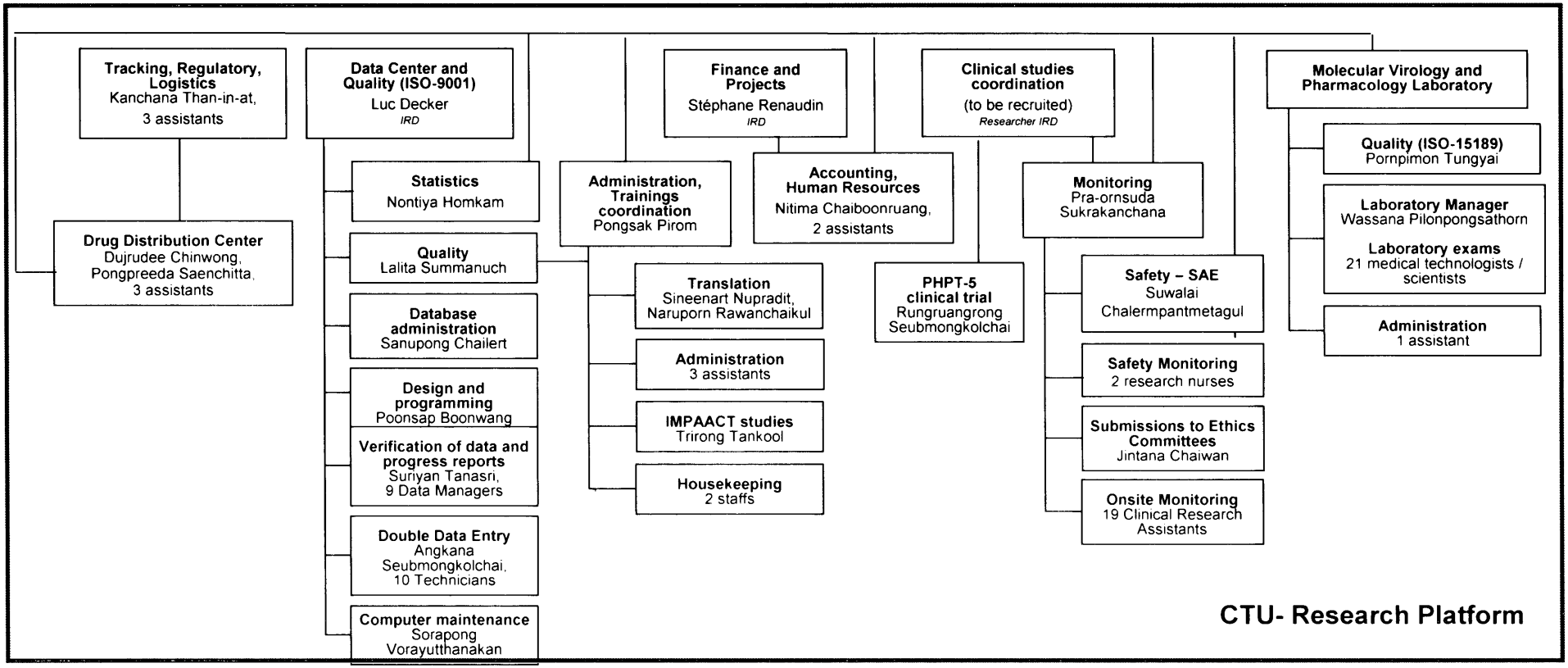
Since more and more ARV drugs will be available in Thailand, technology transfer concerning resistance mutations will continue.

The establishment of a technique to evaluate the HIV co-receptor usage will be needed. Also, evaluation of neutralizing antibodies may be critical in the prospect of vaccine programs. The latter technique requires a biosafety level-3 laboratory which will be of important significance in further development of the PHPT programs but also for other programs to be developed at AMS.

Appendix 2: The Unit members

Clinical Research: CMU-Harvard-IRD-MOPH-Mahidol

Marc Lallemant
Gonzague Jourdain
Audomsark Haesungcharern (CMU)
Virat Klinbuayam (Sanpatong Hospital)
Suparat Kanjanavanit (Nakornping Hospital)
Rudiwilai Samakoses (Phramongkutklao Hospital)
Boonmee Sathapatayavongs (Mahidol University)
Ruengpung Sutthent (Mahidol University)
Kovit Pattanapanyasat (Mahidol University)
Suwachai Intaraprasert (Thai OBJYN R. Society)
Wiput Phoolcharoen (MoPH)



Physio-pathology Research CMU-Harvard-IRD-Mahidol

Wasna Sirirungsi
Nicole Ngo-Giang-Huong
Pranee Leechanachai
Tanawan Samleerat
Sorasak Intorasoot
Tim Cressey
Warunee Kunachiwa
Watchara Kasinrerk
Chatchai Tayapiwatana
Sakorn Pornprasert
Khanittha Taney-Hill
Ratchada Cressey
Suchart Punjaisee
Yuttana Mundee
Chonlaphat Sukasem
Wasun Chantratita
Kuntida Kitidee (PhD student)
Sawittree Nangola (PhD student)
Ponrut Punpae (PhD student)
Sornranun Chantarangsu (PhD student)
Woottichai Khamduang (PhD student)

Social Sciences Research: CMU-IRD-Mahidol U

Suporn Koetsawang
Sophie LeCoeur
Intira Collins (PhD student)
Sukon Prasitwattanaseree
Patrinee Traisatit
Julie Pannetier (PhD student)
Hélène Lepinay (PhD student)
Suwalai Chalermpantmetagul
Cheeraya Kannabkaew
Sineenart Nupradit
Wipada Chanthaweethip

Appendix 3: Unit resources

Clinical Research: CMU-Harvard-IRD-MOPH-Mahidol U

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Suwachai Intaraprasert (Thai OBJYN R. Society)
Wiput Phoolcharoen (MoPH)

Resources in USD$ June 2009

	Management by	Budget CTU*	Budget Sites **
GFATM RCC Year 1	IRD	212,381	1,145,750
IMPAACT Core Y3	IRD	428,644	1,024,780
Penta EU Y4	IRD	26,079	
Penta Labnet period 1	IRD	22,664	
PHPT-3 Y5	Harvard	464,823	358,686
PHPT-5a Y3	Harvard	293,502	363,812
PHPT-5b Y2	Harvard	81,580	376,439

*CTU: Clinical Trial Unit – Research platform; ** sites: network of ~ 50 hospitals around Thailand

	Management by	Budget
GFATM RCC Year 1	IRD	301,098
GFATM RCC Year 1	AMS	30,110
ANRS 12179	AMS	26,230
Thai National Research Council	AMS	34,286
Hubert Curien France 2009	Egide	32,206
Hubert Curien Thailand 2009	AMS	8,571
French Ministry of Foreign Affairs	AMS	16,825

	Management by	Budget
Oxfam 2 Y5	IRD	245,463
LIWA Lab B	IRD	28,999
ANRS workshop	IRD	5,241

Physio-pathology Research CMU-Harvard-IRD-Mahidol

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Tim Cressey
Warunee Kunachiwa
Watchara Kasinrerk
Chatchai Tayapiwatana
Sakorn Pornprasert
Khanittha Taney-Hill
Ratchada Cressey
Suchart Punjaisee
Yuttana Mundee
Chonlaphat Sukasem
Wasun Chantratita
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Sawittree Nangola (PhD student)
Ponrut Phunpae (PhD student)
Sornranun Chantarangsu (PhD student)
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