MINUTES OF MEETINGS BETWEEN THE JAPANESE DETAILED PLANNING SURVEY TEAM AND THE AUTHORITIES CONCERNED OF THE GOVERNMENT OF THE KINGDOM OF THAILAND ON JAPANESE TECHNICAL COOPERATION FOR THE PROJECT FOR ESTABLISHMENT OF THERAPEUTIC PRODUCTS AND TECHNOLOGIES FOR PREVENTIVE APPLICATION FOR EMERGING AND RE-EMERGING INFECTIONS ENVISAGING CLINICAL TRIAL

Japan International Cooperation Agency (hereinafter referred to as "JICA") organized the Detailed Planning Survey Team (hereinafter referred to as "the Team"), headed by Dr. Kishio Ono from December 10 to 22, 2008 for the purpose of discussing the framework of the technical cooperation project entitled "Establishment of Therapeutic Products and Technologies for Preventive Application for Emerging and Re-emerging Infections Envisaging Clinical Trial" (hereinafter referred to as "the Project")

The Team had a series of discussions and exchanged views on the Project with the authorities concerned of Thailand.

During the discussions both sides agreed that it is appropriate to modify the original project title indicated above to "the Project for Research and Development of Therapeutic Products against Infectious Diseases, especially Dengue Virus Infection".

As a result of the discussions, the Team and the Thai authorities concerned agreed on the matters referred to in the document attached hereto.

Nonthaburi, December 22, 2008

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THE ATTACHED DOCUMENT

I OBJECTIVE OF THE DETAILED PLANNING SURVEY

The objectives of the survey are to confirm background and contents of the request from the government of Thailand and to make a cooperation plan (project design) through discussions with the Thai authorities concerned. The survey team will also collect and analyze necessary information for ex-ante evaluation.

The contents of the survey are as follows:

1. To confirm the contents and changed points of the request from the Thai government and the research plan of the Osaka University and to match them.
2. To have discussions with the Thai authorities concerned on the project design including Project Purpose, Implementing Structure, Project Design Matrix, Plan of Operation, Inputs and so on and to reach agreement.
3. To confirm the current situation on ethical consideration of research, system of research approval, implementation and compensation for clinical studies / trials.
4. To confirm actions and schedule up to the Project's commencement.
5. To sign on the Minutes of Meeting so as to confirm the result of the discussions.

II BASIC FRAMEWORK OF THE PROJECT

1. Project Implementation Scheme (Annex I)

Both sides confirmed that the Project was implemented under the 'Science and Technology Research Partnership for Sustainable Development*' promoted by JICA and Japan Science and Technology Agency (hereinafter referred to as "JST") in collaboration.

JICA will take necessary measures for the technical cooperation such as dispatch of Japanese experts, provision of equipment and training of personnel, and other supports related to the Project in Thailand. JST will support the Japanese research institute for the project activities held in Japan.

Thai counterpart research institutes will take necessary measures for technical cooperation, such as research facilities and utilities, personnel, and other support related to the Project.

*' Science and Technology Research Partnership for Sustainable Development' aims to develop new technology and its applications, and also aims at capacity development of researchers and research institutes in both countries.

2. Project Title

Both sides agreed that it was appropriate to modify the original project title

indicated in the application "the Project for Establishment of Therapeutic Products and Technologies for Preventive Application for Emerging and Re-emerging Infections Envisaging Clinical Trial" to "the Project for Research and Development of Therapeutic Products against Infectious Diseases, especially Dengue Virus Infection", which reflected the agreed contents of the Project.

Both sides will propose the title modification to the authorities concerned of each government and, if approved, the title will be changed officially through diplomatic procedure.

3. Term of Cooperation

The duration of the technical cooperation for the Project will be four years from the date, which will be described in the Record of Discussions (hereinafter referred to as "R/D").

4. Administration of the Project

4-1. Administration

The administration of the Project is as follows:

(1) Project Director (who will bear overall responsibility for the administration and implementation of the Project):
Director General, Department of Medical Sciences (hereinafter referred to as "DMSc"), Ministry of Public Health (hereinafter referred to as "MoPH")

(2) Project Manager (who will be responsible for the managerial and technical matters of the Project):
Director, National Institute of Health (hereinafter referred to as "NIH"), DMSc, MoPH

(3) Project Co-managers (who will be responsible for the managerial and technical matters of the Project, supporting the Project Manager):
Dean, Faculty of Tropical Medicine, Mahidol University
Representative from Faculty of Science, Mahidol University

(4) Thai counterpart institutions and personnel: as shown in Annex II.

(5) Thai Project Coordinator (who will coordinate all aspects of the Project on Thai side with the Japanese Project Coordinator):
Representative from DMSc as to be assigned by the Project Director

(6) The Japanese chief advisor will provide necessary recommendations and advice to the Project Director, the Project Manager and the Project Co-managers on any matters pertaining to the implementation of the Project.

(7) The Japanese experts will give necessary technical guidance and advice to Thai counterpart personnel on technical matters pertaining to the implementation of the Project.

4-2. Joint Coordinating Committee

For the effective and successful implementation of technical cooperation for the Project, a Joint Coordinating Committee will be established whose functions and

composition are described as follows:

(1) Functions

1) To formulate and authorize the annual activity plan of the Project
2) To endorse major achievements and products of the Project
3) To monitor and review overall progress and supervise the Project
4) To review and discuss on major issues arising from or concerning the Project

(2) Composition

1) Chairperson:

Director General, DMSc, MoPH

2) Members:

Director, NIH, DMSc, MoPH
Dean, Faculty of Tropical Medicine, Mahidol University
Representative from Faculty of Science, Mahidol University
Senior medical scientists, DMSc, MoPH
Leaders of research groups as shown in Annex II
Representative from Department of Microbiology, Faculty of Medicine Siriraj Hospital, Mahidol University
Japanese long-term experts and representative(s) from Osaka University
Representative(s) from Embassy of Japan
Representative(s) from JICA Thailand Office

3) Observers:

Representatives from JST

4-3. Working Group

A Working Group is established to meet bi-monthly whose functions and composition are described as follows:

(1) Functions

1) To review progress and outputs of research activities
2) To coordinate and exchange information among the counterpart institutions
3) To discuss on issues including technical, ethical and safety matters, arising from or concerning the Project

(2) Composition

1) Chairpersons:

Director, NIH, DMSc, MoPH (Chair)
Dean or representative, Faculty of Tropical Medicine, Mahidol University (Vice-chair)
Representative from Faculty of Science, Mahidol University (Vice-chair)
Representative from Japanese researchers (Vice-chair)

2) Members:

Leaders of Thai counterpart researchers
Sub-leaders of Thai counterpart researchers
Representatives from Department of Disease Control and Government Pharmaceutical Organization, if necessary
Japanese experts

4-4. Monthly Progress Report

For effective monitoring of the research progress and timely feedback of the technical advice from the Japanese and Thai experts, a Monthly Progress Report will be submitted monthly in English by each Thai and Japanese researcher engaged in the Project. The reports will be shared with the Project Director, JICA and JST.

4-5. Ethical approval of the Project

All research activities of the Project involving human subjects must be approved by the ethical committee of Osaka University, DMSc or MoPH, and Faculty of Tropical Medicine of Mahidol University or Mahidol University, as applicable.

All research activities of the Project involving animal subjects must be approved by the relevant committee of Osaka University, DMSc, and Faculty of Tropical Medicine of Mahidol University or Mahidol University, as applicable.

4-6. Biosafety

In order to secure biosafety of research activities, Thai side agreed to clarify who will be responsible and will report and respond in case of emergency such as bio-hazard accidents, blackouts and natural disasters.

5. Contents of Collaborative Research

The contents of collaborative research covered in the Project are as follows:

(1) Establishment of human monoclonal antibodies against
- Dengue virus (first priority)
- Influenza virus
(- Botulinum toxin)

(2) Search for novel bioactive compounds of bacterial origin against
- Dengue virus

6. Project Design Matrix and Tentative Plan of Operation

A basic framework of the Project is as shown in a Project Design Matrix (hereinafter referred to as "PDM") in Annex III. The tentative Plan of Operation as shown in Annex IV.

7. Inputs

The inputs from each side are as follows:

7-1. Japanese side

(1) Long-term experts: A Project Coordinator
A researcher, if necessary

(2) Short-term experts: Chief Advisor and researchers to be dispatched several times for each research topic according to a plan to be developed based on mutual agreement of both sides.

(3) Equipment: A tentative list proposed by Thai side is attached in Annex V. The equipment to be provided in the first year will be decided by the signing date of the R/D.

(4) Training in Japan: Several Thai counterpart personnel to be trained.

7-2. Thai side

(1) Counterpart researchers and administrative personnel including a Project Coordinator

(2) Office spaces in NIH, and Faculty of Tropical Medicine and Science, Mahidol University

(3) The existing Biosafety Level (BSL)-2 laboratories in DMSc, MoPH

(4) Space for BSL-2 laboratory in Faculty of Tropical Medicine, Mahidol University

(5) Renovation of the laboratory space in Faculty of Tropical Medicine, Mahidol University

(6) The existing laboratories in Faculty of Science, Mahidol University

(7) Running expenses for research activities

8. Special Issues

8-1. Collaborative Research Agreement between research institutes

Both sides agreed that the research institutes in Japan and Thailand should reach an agreement to execute the collaborative research in accordance with the Master Plan of the Project. The agreed document (e.g. Collaborative Research Agreement*) should contain the following items:

a. Objective and Plan
b. Implementation
c. Confidentiality and Intellectual Property Rights
d. Access to Genetic Resources
e. Publication
f. Dispute Resolution
g. Duration of the Agreement
h. Compliance with Laws and Regulations
i. Other items concerning both institutes

Both sides agreed that DMSc was the representative of Thai side, and Osaka University was that of Japanese side including Medical and Biological Laboratories, Ltd.

*The Collaborative Research Agreement could be made between DMSc and Osaka University; and between DMSc and representative from Faculty of Tropical Medicine

and Faculty of Science of Mahidol University; or The Collaborative Research Agreement could be made among DMSc, Mahidol University, and Osaka University.

8-2. Intellectual Property

Both sides confirmed that matters on intellectual property should follow the Collaborative Research Agreement to be signed between the research institutions.

8-3. Exclusion of Clinical Trials

Both sides agreed that clinical trials shall not be included in the Project.

Even though clinical trials are executed in relation with the activities of the Project, JICA is indemnified for any and all liabilities, losses, and expenses on claims for injury or damages arising out of or resulting from, the actions or omissions by the Thai and Japanese research institutes or of any of their officers, agents, employees, or subcontractors with respect to the clinical trials.

Therefore, JICA will not bear any expenses or honorarium for implementing clinical trials.

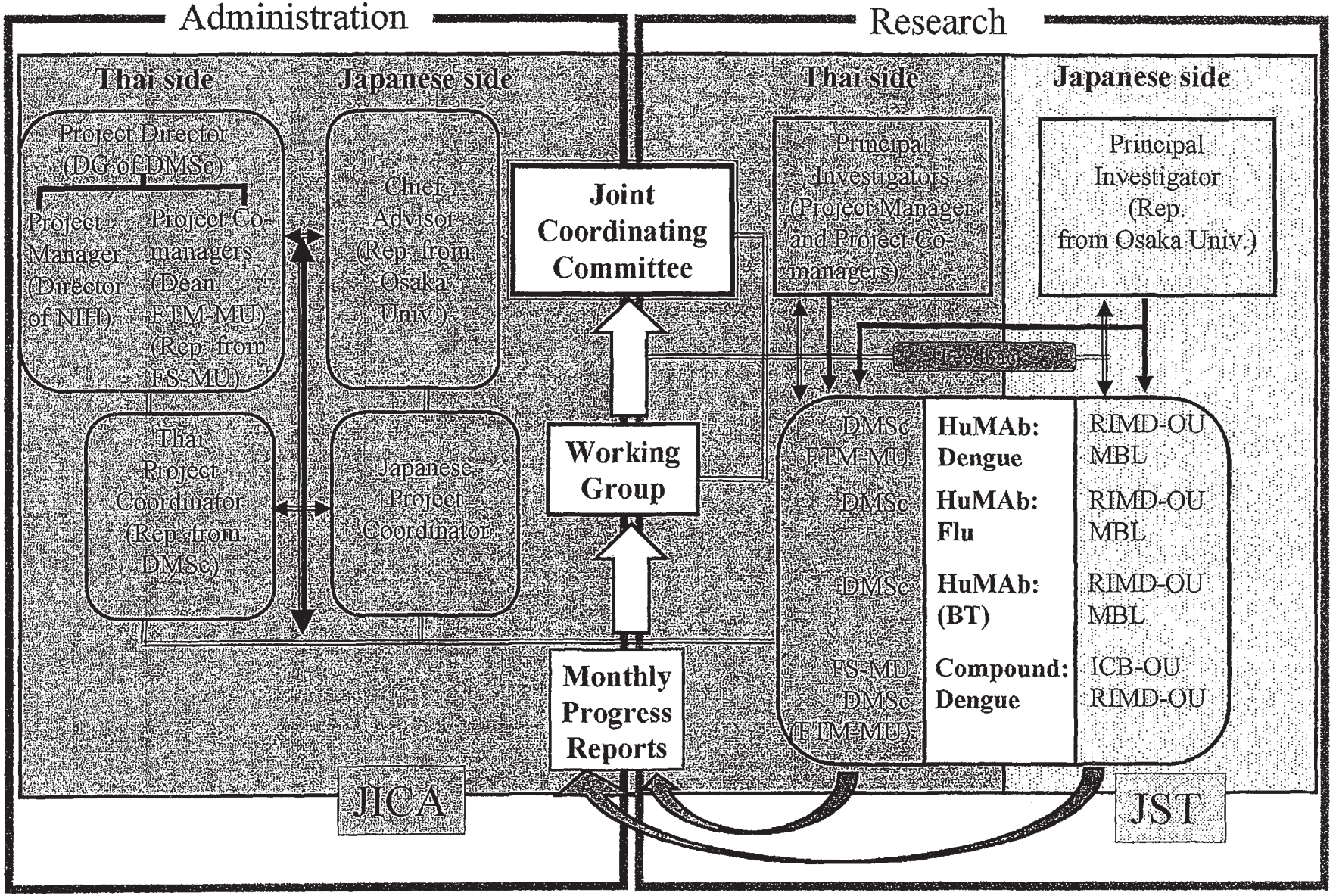
III WAY FORWARD

1. Based on this Minutes of Meeting and the draft R/D as shown in Annex VI, the Thai and Japanese sides will prepare for the final version of the R/D.
2. Before starting the Project, the research institutes of both sides should take necessary actions such as to apply to the relevant ethical committee, to allocate the budget and so on.
3. Based on the mutual agreement reached, the R/D will be signed by both sides around February 2009. The schedule is subject to change in accordance with approval processes of the Project.

LIST OF ANNEXES

Annex I	Implementation Structure Chart
Annex II	Research Contents and Personnel Allocation
Annex III	Project Design Matrix (PDM) Version 0
Annex IV	Tentative Plan of Operation (PO) Version 0
Annex V	Tentative List of Machinery and Equipment
Annex VI	Draft Record of Discussions (R/D)

Annex I Implementation Structure Chart



Annex II Research Contents and Personnel Allocation

Research Subject		Thai side		Research Contents	Japanese side
Human monoclonal antibodies (MAb)	Dengue	DMSc (NIH)	☆ Surapee Anantapreecha Atchareeya A-nuegoonpipat	Clinical sampling	Kazunori Oishi (RIMD)
			† Aree Thattiyaphong Surapee Anantapreecha Atchareeya A-nuegoonpipat	Human MAb preparation	Kazuyoshi Ikuta (RIMD) Motoki Kuhara (MBL)
			† Surapee Anantapreecha Atchareeya A-nuegoonpipat	Evaluation of effectiveness by in vitro models	Kazuyoshi Ikuta (RIMD)
			† Navakanit Sachanonta	Evaluation of effectiveness and safety by in vivo models	Kazuyoshi Ikuta (RIMD) Kazunori Oishi (RIMD)
			† Panadda Dhepakson Apichai Prachasupsap	Human MAb gene cloning	Kazuhito Fujiyama (ICB)
			† Panadda Dhepakson Apichai Prachasupsap	Human MAb gene expression	Kazuyoshi Ikuta (RIMD) Kazuhito Fujiyama (ICB)
		Mahidol University (Tropical Medicine)	☆ Pongrama Ramasoota	Human MAb gene cloning	Kazuhito Fujiyama (ICB)
			Pongrama Ramasoota	Human MAb gene expression	Kazuyoshi Ikuta (RIMD) Kazuhito Fujiyama (ICB)
			† Kriengsak Limkittikul Weerapong Rattanaprapin Pannamas Maneekarn	Clinical sampling	Kazunori Oishi (RIMD)
			† Pornsawan Luergwuttiwong Akanitt Jittmittraphap	Human MAb preparation	Kazuyoshi Ikuta (RIMD) Motoki Kuhara (MBL)
			† Natthanej Luplerdlop	Evaluation of effectiveness by in vitro models	Kazuyoshi Ikuta (RIMD)
			† Jiraporn Ruangsittichai Sungsit Sungvornyothin	Evaluation of effectiveness and safety by in vivo models	Kazuyoshi Ikuta (RIMD) Kazunori Oishi (RIMD)
	Influenza	DMSc (MBC, NIH)	☆ Naphatsawan Boonsathorn Malinee Chittaganpitch	Clinical sampling	Kazuyoshi Ikuta (RIMD) Takaaki Nakaya (RIMD)
			† Naphatsawan Boonsathorn	Human MAb preparation	Kazuyoshi Ikuta (RIMD) Takaaki Nakaya (RIMD) Motoki Kuhara (MBL)
			† Naphatsawan Boonsathorn Malinee Chittaganpitch	Evaluation of effectiveness by in vitro models	Kazuyoshi Ikuta (RIMD) Takaaki Nakaya (RIMD)
			† Naphatsawan Boonsathorn Navakanit Sachanonta Sumolrat Panthong	Evaluation of effectiveness and safety by in vivo models	Takaaki Nakaya (RIMD) Kazunori Oishi (RIMD)
			† Panadda Dhepakson Apichai Prachasupsap Naphatsawan Boonsathorn Watoo Phrompittayarat	Human MAb gene cloning	Kazuhito Fujiyama (ICB)
			† Panadda Dhepakson Apichai Prachasupsap Naphatsawan Boonsathorn	Human MAb gene expression	Takaaki Nakaya (RIMD) Kazuhito Fujiyama (ICB)

Note: ☆:Leader, †: Sub-leader, DMSc: Department of Medical Sciences, NIH: National Institute of Health, MBC: Medical Biotechnology Center, RIMD: Research Institute for Microbial Diseases, Osaka University, ICB: International Center for Biotechnology, Osaka University, MBL: Medical and Biological Laboratories, Ltd.

Annex II Research Contents and Personnel Allocation

Research Subject		Thai side		Research Contents	Japanese side
			Watoo Phrompittayarat		
Human monoclonal antibodies (MAb)	(Botulinum Toxin)	DMSc (NIH)	☆ Piyada Wangroongsarb Chutima Chitaprasertsin	Genetic typing of botulinum toxin + (purification of toxin)	Yasuhiko Horiguchi (RIMD) Yukako Fujinaga (RIMD)
			† Piyada Wangroongsarb Chutima Chitaprasertsin	(Clinical sampling)	Yasuhiko Horiguchi (RIMD) Yukako Fujinaga (RIMD)
			† Aree Thattiyaphong	(Human MAb preparation)	Yasuhiko Horiguchi (RIMD) Yukako Fujinaga (RIMD) Motoki Kuhara (MBL)
			† Aree Thattiyaphong Piyada Wangroongsarb Chutima Chitaprasertsin	(Evaluation of effectiveness by in vitro models)	Yasuhiko Horiguchi (RIMD) Yukako Fujinaga (RIMD)
			† Navakanit Sachanonta Piyada Wangroongsarb	(Evaluation of effectiveness and safety by in vivo models)	Yasuhiko Horiguchi (RIMD) Yukako Fujinaga (RIMD) Kazunori Oishi (RIMD)
			† Panadda Dhepakson Piyada Wangroongsarb Apichai Prachasupsap	(Human MAb gene cloning)	Kazuhito Fujiyama (ICB)
			† Panadda Dhepakson Piyada Wangroongsarb Apichai Prachasupsap	(Human MAb gene expression)	Yasuhiko Horiguchi (RIMD) Yukako Fujinaga (RIMD) Kazuhito Fujiyama (ICB)
New compounds	Dengue	Mahidol University (Science)	☆ Watanalai Panbangred	Search for new compounds from Thai natural microorganisms, including plant- and insect-derived bacteria	Takuya Nihira (ICB)
		DMSc (NIH)	† Surapee Anantapreecha Atchareeya A-nuegoonpipat	Evaluation of effectiveness by in vitro models	Kazuyoshi Ikuta (RIMD)
			† Navakanit Sachanonta Surapee Anantapreecha Atchareeya A-nuegoonpipat	Evaluation of effectiveness and safety by in vivo models	Kazuyoshi Ikuta (RIMD) Kazunori Oishi (RIMD)
		(Mahidol University (Tropical Medicine))	† (Pornsawan Luergwuttiwong) (Akanitt Jittmittraphap)	Evaluation of effectiveness by in vitro models	Kazuyoshi Ikuta (RIMD)
			† (Pornsawan Luergwuttiwong) (Akanitt Jittmittraphap)	Evaluation of effectiveness and safety by in vivo models	Kazuyoshi Ikuta (RIMD) Kazunori Oishi (RIMD)

Note: ☆:Leader, †: Sub-leader, DMSc: Department of Medical Sciences, NIH: National Institute of Health, MBC: Medical Biotechnology Center, RIMD: Research Institute for Microbial Diseases, Osaka University, ICB: International Center for Biotechnology, Osaka University, MBL: Medical and Biological Laboratories, Ltd.

Annex III Project Design Matrix (PDM) (Version 0)

Project Title: Establishment of Therapeutic Products and Technologies for Preventive Application for Emerging and Re-emerging Infections Envisaging Clinical Trial
Date: December 22, 2008
Target Area: Kingdom of Thailand
Project Duration: 4 years from ## 2009
Target group: Researchers

【Department of Medical Sciences (DMSc), Ministry of Public Health】 National Institute of Health (NIH) and Medical Biotechnology Center
【Mahidol University (MU)】 Faculty of Tropical Medicine and Faculty of Science

Narrative Summary	Objectively Verifiable Indicators	Means of Verification	Important Assumptions
Project Purpose			Nobody, excluding any concerning organizations in this project, claims the intellectual properties regarding to the products of this project.
Research and development capacity of therapeutic products against infectious diseases, especially dengue hemorrhagic fever is improved in Thai research institutes through the collaborative research.	Candidates for clinical trials against infectious diseases, especially dengue hemorrhagic fever, are produced.	(1)Experts' project records (2)Working group meeting records (3)Monthly progress reports	
Outputs			The Thai side properly allocates necessary budget.
1 Human monoclonal antibodies (MAb) against dengue hemorrhagic fever, influenza and botulism are prepared and evaluated their effectiveness and safety in collaboration between Thai and Japanese researchers.	1-1.Human MAb against dengue virus are prepared by the year of 2010. 1-2.Final candidates of human MAb against infectious diseases, especially dengue virus, are identified by the year of 2012.	(1)Experts' project records (2)Working group meeting records (3)Monthly progress reports	
2 Novel bioactive compounds are explored from Thai natural microorganisms, including plant- and insect-derived bacteria, and evaluated their effectiveness and safety in collaboration between Thai and Japanese researchers.	2-1.Novel bioactive compounds from Thai natural microorganisms, including plant- and insect-derived bacteria, against dengue virus are identified by the year of 2010. 2-2.Final candidate of bioactive compounds against dengue virus is identified by the year of 2012.	(1)Experts' project records (2)Working group meeting records (3)Monthly progress reports	
3 The system on research and pharmaceutical affairs of bioproducts is streamlined.	3-1.SOP in each research subject is made and revised. 3-2.Working group is established to discuss progress of the research, achievements and safety management bi-monthly. 3-3.Monthly progress report is made by Thai and Japanese researchers. 3-4.Annual plan documents for research operation are prepared collaboratively.	(1)Experts' project records (2)Standard operating procedures (3)Working group meeting records (4)Monthly progress reports (5)Annual plan documents for research operation	
Activities	**Inputs**		
1 Human monoclonal antibodies (MAb) against dengue hemorrhagic fever, influenza and botulism are prepared and evaluated their effectiveness and safety in collaboration between Thai and Japanese researchers.	Japan	Thailand	Trained counterparts do not leave their position so as to affect the outputs of the Project.
1-1. Preparation of human MAb against dengue virus and the evaluation of effectiveness and safety 1-1-1. Collect and screen specimens. 1-1-2. Prepare candidates of human MAb from the patients with dengue virus infection. 1-1-3. Establish the experimental system for the evaluation of neutralization activity of human MAb against dengue virus for the screening of the candidates. 1-1-4. Establish the animal study system for the evaluation of effectiveness and safety studies to identify final candidate of human MAb against dengue virus. 1-1-5.* Establish the study system for the cloning of human MAb IgG variable regions to make the human recombinant MAb IgG. 1-1-6.* Establish the system for expressing the human recombinant MAb by Chinese hamster ovary (CHO) cells and/or plant biotechnology. 1-2. Preparation of human MAb against influenza virus and the evaluation of effectiveness and safety	Experts (1) Research Management (Long-term expert) (2) Project Coordinator (Long-term expert) (3) Chief Coordinator, Viral experiments, Microorganisms experiments, identification of novel compounds, Cell manipulation technique, Gene manipulation technique, etc. (Short-term experts) Training in Japan (1)Training for the preparation of human MAb (2)Training for the evaluation of human MAb Equipment and materials (1)Necessary equipment for research activities in the Project Local costs	Counterparts (1) Project Director (2) Project Manager (3) Project Co-managers (4) Project Coordinator (5) Researchers (DMSc and MU) Facilities, equipment and materials (1) Office spaces in NIH, and Faculty of Tropical Medicine and Science, MU (2) The existing Biosafety Level (BSL)-2 laboratories in DMSc, MoPH (3) Space for BSL-2 laboratory in Faculty of Tropical Medicine, MU (4) Renovation of the laboratory space in Faculty of Tropical Medicine, MU (5) The existing laboratories in Faculty of Science, MU Local costs (1) Running expense for research activities	

1-2-1.	Collect and screen specimens.			
1-2-2.	Prepare candidates of human MAb from the patients with influenza.			
1-2-3.	Establish the experimental system for the evaluation of neutralization activity of human MAb against influenza virus for screening of the candidates.			
1-2-4.	Establish the animal study system for the evaluation of effectiveness and safety studies to identify final candidate of human MAb against influenza virus.			
1-2-5.*	Establish the study system for the cloning of human MAb IgG variable regions to make the human recombinant MAb IgG.			
1-2-6.*	Establish the system for expressing the human recombinant MAb by CHO cells.			
1-3.	**(Preparation of human MAb against botulinum toxin and the evaluation of effectiveness and safety)**			
1-3-1.	Identify the genetic types of botulinum (and purify the botulinum toxin).			
1-3-2.	(Establish the experimental system for the evaluation of neutralization activity of human MAb against botulinum toxin for screening of the candidates.)			
1-3-3.*	(Establish the study system for the cloning of human MAb IgG variable regions to make the human recombinant MAb IgG.)			
1-3-4.*	(Establish the system for expressing the human recombinant MAb by CHO cells.)			
2	**Novel bioactive compounds are explored from Thai natural microorganisms, including plant- and insect-derived bacteria, and evaluated their effectiveness and safety in collaboration between Thai and Japanese researchers.**			
2-1.	Identify new compounds by comparing extracts from Thai natural microorganisms, including plant- and insect-derived bacteria, with existing database.			**Pre-Conditions**
2-2.	Screen the candidates of novel bioactive compounds with anti-dengue activity.			The approval is obtained by the ethical committee for the researches including the preparation of human MAb from patients' samples.
2-3.	Establish the animal study system for the evaluation of effectiveness and safety studies to identify the final candidate of novel bioactive compound.			
3	**The system on research and pharmaceutical affairs of bioproducts is streamlined.**			
3-0.	Set up laboratories for the research activities.			
3-1.	Make and revise Standard Operating Procedure (SOP) in each research subject.			
3-2.	Establish working group to discuss progress of the research, achievements and safety management bi-monthly.			
3-3.	Thai and Japanese researchers make monthly progress reports.			
3-4.	Make annual plan documents for research operation.			
3-5.	Guidelines and operating procedures of non-clinical and clinical studies for biopharmaceuticals are documented.			
3-6.	Conduct training and guidance regarding GLP.			

Remarks: * *These activities depend on the success of obtaining effective hybridomas.*

Annex IV Tentative Plan of Operation (PO) (Version 0)

Date: December 22, 2008

Project title: Establishment of Therapeutic Products and Technologies for Preventive Application for Emerging and Re-emerging Infections Envisaging Clinical Trial

Output 1:

Human monoclonal antibodies (MAb) against dengue hemorrhagic fever, influenza and botulism are prepared and evaluated their effectiveness and safety in collaboration between Thai and Japanese researchers.

Activities	Plan																	Person in Charge		Remarks
	2009				2010				2011				2012				2013			
	Feb- Mar	Apr - Jun	Jul - Sep	Oct - Dec	Jan - Mar	Apr - Jun	Jul - Sep	Oct - Dec	Jan - Mar	Apr - Jun	Jul - Sep	Oct - Dec	Jan - Mar	Apr - Jun	Jul - Sep	Oct - Dec	Jan			
	2008 (J.F.Y.)	2009 (J.F.Y.)			2010 (J.F.Y.)				2011 (J.F.Y.)				2012 (J.F.Y.)							
	4Q	1Q	2Q	3Q	4Q	1Q	2Q	3Q	4Q	1Q	2Q	3Q	4Q	1Q	2Q	3Q	4Q			
1-1. Preparation of human MAb against dengue virus and the evaluation of effectiveness and safety																				
1-1-1. Collect and screen specimens.																		Oishi (RIMD)	Surapee (NIH) Atchareeya (NIH) Kriengsak (FTM-MU) Weerapong (FTM-MU) Panisamas (FTM-MU)	
1-1-2. Prepare candidates of human MAb from the patients with dengue virus infection.																		Ikuta (RIMD) Kuhara (MBL)	Aree (NIH) Surapee (NIH) Atchareeya (NIH) Panisawan (FTM-MU) Akanitt (FTM-MU)	
1-1-3. Establish the experimental system for the evaluation of neutralization activity of human MAb against dengue virus for the screening of the candidates.																		Ikuta (RIMD)	Surapee (NIH) Atchareeya (NIH) Natthanej (FTM-MU)	
1-1-4. Establish the animal study system for the evaluation of effectiveness and safety studies to identify final candidate of human MAb against dengue virus.																		Ikuta (RIMD) Oishi (RIMD)	Navakanit (NIH) Jiraporn (FTM-MU) Sangsit (FTM-MU)	
1-1-5.* Establish the study system for the cloning of human MAb IgG variable regions to make the human recombinant MAb IgG.																		Fujiyama (ICB)	Panadda (MBC) Apichai (MBC) Pongrama (FTM-MU)	* This activity depends on the success of obtaining effective hybridomas.
1-1-6.* Establish the system for expressing the human recombinant MAb by Chinese hamster ovary (CHO) cells and/or plant biotechnology.																		Ikuta (RIMD) Fujiyama (ICB)	Panadda (MBC) Apichai (MBC) Pongrama (FTM-MU)	* This activity depends on the success of obtaining effective hybridomas.
1-2. Preparation of human MAb against influenza virus and the evaluation of effectiveness and safety																				
1-2-1. Collect and screen specimens.																		Ikuta (RIMD) Nakaya (RIMD)	Naphatsawan (MBC) Malinee (NIH)	
1-2-2. Prepare candidates of human MAb from the patients with influenza.																		Ikuta (RIMD) Nakaya (RIMD) Kuhara (MBL)	Naphatsawan (MBC)	
1-2-3. Establish the experimental system for the evaluation of neutralization activity of human MAb against influenza virus for screening of the candidates.																		Ikuta (RIMD) Nakaya (RIMD)	Naphatsawan (MBC) Malinee (NIH)	
1-2-4. Establish the animal study system for the evaluation of effectiveness and safety studies to identify final candidate of human MAb against influenza virus.																		Nakaya (RIMD) Oishi (RIMD)	Naphatsawan (MBC) Navakanit (NIH) Sumolrat (MBC)	
1-2-5.* Establish the study system for the cloning of human MAb IgG variable regions to make the human recombinant MAb IgG.																		Fujiyama (ICB)	Panadda (MBC) Apichai (MBC) Watoo (MBC) Naphatsawan (MBC)	* This activity depends on the success of obtaining effective hybridomas.
1-2-6.* Establish the system for expressing the human recombinant MAb by CHO cells.																		Nakaya (RIMD) Fujiyama (ICB)	Panadda (MBC) Apichai (MBC) Watoo (MBC) Naphatsawan (MBC)	* This activity depends on the success of obtaining effective hybridomas.
1-3. (Preparation of human MAb against botulinum toxin and the evaluation of effectiveness and safety)																				
1-3-1. Identify the genetic types of botulinum (and purify the botulinum toxin).																		Horiguchi (RIMD) Fujinaga (RIMD)	Piyada (NIH) Chutima (NIH)	
1-3-2. (Establish the experimental system for the evaluation of neutralization activity of human MAb against botulinum toxin for screening of the candidates.)																		Horiguchi (RIMD) Fujinaga (RIMD) Oishi (RIMD)	Piyada (NIH) Chutima (NIH) Aree (NIH) Navakanit (NIH)	
1-3-3.* (Establish the study system for the cloning of human MAb IgG variable regions to make the human recombinant MAb IgG.)																		Fujiyama (ICB)	Panadda (MBC) Apichai (MBC) Piyada (NIH)	* This activity depends on the success of obtaining effective hybridomas.
1-3-4.* (Establish the system for expressing the human recombinant MAb by CHO cells.)																		Horiguchi (RIMD) Fujinaga (RIMD) Fujiyama (ICB)	Panadda (MBC) Apichai (MBC) Piyada (NIH)	* This activity depends on the success of obtaining effective hybridomas.

Output 2:

Novel bioactive compounds are explored from Thai natural microorganisms, including plant- and insect-derived bacteria, and evaluated their effectiveness and safety in collaboration between Thai and Japanese researchers.

Activities	Plan																Person in Charge		Remarks
	2009				2010				2011				2012				2013	Japan	Thailand	
	Feb- Mar	Apr - Jun	Jul - Sep	Oct - Dec	Jan - Mar	Apr - Jun	Jul - Sep	Oct - Dec	Jan - Mar	Apr - Jun	Jul - Sep	Oct - Dec	Jan - Mar	Apr - Jun	Jul - Sep	Oct - Dec	Jan			
	2008 (J.F.Y.)	2009 (J.F.Y.)			2010 (J.F.Y.)				2011 (J.F.Y.)				2012 (J.F.Y.)							
	4Q	1Q	2Q	3Q	4Q	1Q	2Q	3Q	4Q	1Q	2Q	3Q	4Q	1Q	2Q	3Q	4Q			
2-1. Identify new compounds by comparing extracts from Thai natural microorganisms, including plant- and insect-derived bacteria with existing database.																		Nihira (ICB)	Watanalai (FS-MU)	
2-2. Screen the candidates of novel bioactive compounds with anti-dengue activity.																		Ikuta (RIMD)	Surapee (NIH) Atchareeya (NIH) Pornsawan (FTM-MU) Akanitt (FTM-MU)	
2-3. Establish the animal study system for the evaluation of effectiveness and safety studies to identify the final candidate of novel bioactive compound.																		Ikuta (RIMD) Oishi (RIMD)	Navaknitt (NIH) Surapee (NIH) Atchareeya (NIH) Pornsawan (FTM-MU) Akanitt (FTM-MU)	

Output 3:

The system on research and pharmaceutical affairs of bioproducts is streamlined.

Activities	Plan																Person in Charge		Remarks
	2009				2010				2011				2012				2013	Japan	Thailand	
	Feb- Mar	Apr - Jun	Jul - Sep	Oct - Dec	Jan - Mar	Apr - Jun	Jul - Sep	Oct - Dec	Jan - Mar	Apr - Jun	Jul - Sep	Oct - Dec	Jan - Mar	Apr - Jun	Jul - Sep	Oct - Dec	Jan			
	2008 (J.F.Y.)	2009 (J.F.Y.)			2010 (J.F.Y.)				2011 (J.F.Y.)				2012 (J.F.Y.)							
	4Q	1Q	2Q	3Q	4Q	1Q	2Q	3Q	4Q	1Q	2Q	3Q	4Q	1Q	2Q	3Q	4Q			
3-0. Set up laboratories for the research activities.																		Ikuta (RIMD) Horiguchi (RIMD) Nihira (ICB)	Pathom (NIH) Pratap (FTM-MU)	
3-1. Make and revise Standard Operating Procedure (SOP) in each research subject.																		Ikuta (RIMD) Horiguchi (RIMD) Nihira (ICB)	Jotika (NIH) Pongrama (FTM-MU) Watanalai (FS-MU)	
3-2. Establish working group to discuss progress of the research, achievements and safety management monthly.																		Ikuta (RIMD) Horiguchi (RIMD) Nihira (ICB)	Pathom (NIH) Pratap (FTM-MU)	
3-3. Thai researchers make monthly progress reports.																		Ikuta (RIMD) Horiguchi (RIMD) Nihira (ICB)	Jotika Pongrama (FTM-MU) Watanalai (FS-MU)	
3-4. Make annual plan documents for research operation.																		Ikuta (RIMD) Horiguchi (RIMD) Nihira (ICB)	Jotika (NIH) Pongrama (FTM-MU) Watanalai (FS-MU)	
3-5. Document guidelines and operating procedures of non-clinical and clinical studies for biopharmaceuticals.																		Oishi (RIMD)	Pathom (NIH) Pratap (FTM-MU)	
3-6. Conduct training and guidance regarding GLP.																		Oishi (RIMD)	Pathom (NIH) Pratap (FTM-MU)	

Abbreviations:

RIMD: Research Institute for Microbial Diseases, Osaka University; ICB: International Center for Biotechnology, Osaka University; MBL: Medical and Biological Laboratories, Ltd.
DMSc: Department of Medical Sciences; NIH: National Institute of Health, DMSc; MBC: Medical Biotechnology Center, DMSc; MU: Mahidol University; FTM-MU: Faculty of Tropical Medicine, MU; FS-MU: Faculty of Science, MU
J.F.Y.: Japanese Fiscal Year (starting from April 1 to March 31)

Annex V Tentative list of Machinery and Equipment (DMSc)

Year	Item (priority	Description	Quantity	Estimated Unit price	Estimated Total amount (Thai Baht)	Remarks
1	1	CO2 incubator	3	500,000.00	1,500,000.00	K. Surapee(2),K.Aree
	2	Cage washer, Tunnel type	1	14,000,000.00	14,000,000.00	K. Raywadee
	3	Freezer-80'c	1	1,200,000.00	1,200,000.00	K. Surapee
	4	Freezer-20'c	1	100,000.00	100,000.00	K.Piyada
	5	Incubator	1	70,000.00	70,000.00	K.Piyada
	6	3 kg Liquid Nitrogen tank	4	40,000.00	160,000.00	K.Surapee
	7	Microplate washer	2	300,000.00	600,000.00	K. Malinee,Naphatsawan
	8	50 kg liquid Nitrogen tank	2	150,000.00	300,000.00	K.Aree, K.Naphatsawan
					17,930,000.00	
Year	Item (priority	Description	Quantity	Estimated Unit price	Estimated Total amount (Thai Baht)	Remarks
2	1	CO2 incubator	1	500,000.00	500,000.00	K Naphasawan
	2	Software for GLP	1	300,000.00	300,000.00	Shared by partlcipating laboratorles
	3	Freezer-80'c	1	1,200,000.00	1,200,000.00	K. Naphasawan
	4	Microplate washer	2	300,000.00	600,000.00	K.Aree,K.Surapee
	5	3 kg Liquid Nitrogen tank	4	40,000.00	160,000.00	K. Surapee
	6	Microplate dispenser	1	500,000.00	500,000.00	K.Aree
	7	Bedding Dispenser	1	6,000,000.00	6,000,000.00	K. Raywadee
	8	Individually-ventilated isolators for ABSL-3	1	8,000,000.00	8,000,000.00	K. Raywadee
	9	High speed centrifuge	1	1,000,000.00	1,000,000.00	K.Piyada
					18,260,000.00	

Grand total **36,190,000.00**

Annex V Tentative List of Machinery and Equipment (FTM-MU)

List of Equipment (First year)

No.	List	Price/each	Amount	Price	Use Application
1	Larminar Flow	420,000.00	2	840,000.00	Tissue culture
2	Shaking Incubator	600,000.00	2	1,200,000.00	vecter and vecter-free cell culture
3	Electroporator	440,000.00	1	440,000.00	gene cloning
4	CO2 incubator	450,000.00	4	1,800,000.00	Tissue culture
7	Inverted microscope	300,000.00	1	300,000.00	Evalution of Mab
8	ELISA washing machine	350,000.00	1	350,000.00	Screening of Mab
9	ELISA Reader machine	400,000.00	1	400,000.00	Screening of Mab
10	Refrigerated centrifuge with adapter (Max 12,000 rpm)	870,000.00	1	870,000.00	Evalution of Mab
11	Eppendorf-type centrifuge machine	170,000.00	2	340,000.00	Tissue culture, gene cloning
12	Refrigerated centrifuge with rotor (Max 20,000 rpm)	1,000,000.00	1	1,000,000.00	phage-free centrifuge
13	96-well plate centrifuge machine	400,000.00	1	400,000.00	Phage screening
14	PCR (Gradient)	500,000.00	1	500,000.00	Gene cloning
15	Real time PCR	4,500,000.00	1	4,500,000.00	Evalution of Mab
16	Distill water apparatus	1,000,000.00	1	1,000,000.00	Preparation of Reagent and Medium
17	Western blot apparatus with blotting transfer and power	300,000.00	2	600,000.00	Western blotting and Epitope analysis
18	Deep freezer -20°C >350 L with Rack	150,000.00	2	300,000.00	Store of virus isolates
19	Deep freezer (-70C)	700,000.00	1	700,000.00	Store of hybridoma, Patient's sample
20	Deep freezer (-135C)	1,450,000.00	1	1,450,000.00	Store of hybridoma
21	Refrigerator 18 Q (General Use)	25,000.00	3	75,000.00	Store of reagents and medium
22	Liquid nitrogen tank 35 L	214,000.00	2	428,000.00	Store of hybridoma
23	Liquid nitrogen transfer tank	100,000.00	2	200,000.00	transportation of samples
24	pH meter	65,000.00	1	65,000.00	Reagent preparation
25	Analytical balance (2 digits)	40,000.00	1	40,000.00	Reagent preparation
26	Analytical balance (4 digits)	54,000.00	1	54,000.00	Reagent preparation
27	PCR cabinet	20,000.00	2	40,000.00	Evalution of Mab
29	Gel documentation system	720,000.00	1	720,000.00	Evalution of Mab
30	Sonicator (break cell)	400,000.00	1	400,000.00	Antigen preparation
31	Waterbath sonicator	150,000.00	1	150,000.00	Ultrawave cleaners

Annex V Tentative List of Machinery and Equipment (FTM-MU)

No.	List	Price/each	Amount	Price	Use Application
32	NanoDrop	700,000.00	1	700,000.00	Analyze microliter protein/DNA
33	Spectrophotometer	500,000.00	1	500,000.00	Cell culture
34	Hot air oven	500,000.00	1	500,000.00	Heat sterilizer
35	Autoclave	450,000.00	2	900,000.00	Steam Sterilizer
36	Water bath	90,000.00	2	180,000.00	Tissue culture
37	Fume hood	500,000.00	1	500,000.00	Hazardous chemical handling
38	Syringe stainless steel 1 ml. with needle	7,500.00	2	15,000.00	Tissue culture
39	Syringe stainless steel 5 ml. with needle	7,500.00	2	15,000.00	Tissue culture
40	Mini magnetic stirrer	7,000.00	1	7,000.00	Reagent preparation
41	Hotplate stirrer	30,000.00	2	60,000.00	Reagent preparation
42	Platform shaker	45,000.00	2	90,000.00	Tissue culture
43	Block heater	35,000.00	1	35,000.00	Reagent preparation
44	High speed vacuum	500,000.00	1	500,000.00	gene cloning
45	UV transilluminator	500,000.00	1	500,000.00	gene cloning
46	Fire boyd	30,000.00	5	150,000.00	Sterilization
47	Freeze-Dry lyophilized machine	600,000.00	1	600,000.00	Prepared freerzed dried protein
48	Autopipette P2	10,000.00	10	100,000.00	Multipurpose use
49	Autopipette P10	10,000.00	10	100,000.00	Multipurpose use
50	Autopipette P20	10,000.00	10	100,000.00	Multipurpose use
51	Autopipette P100	10,000.00	10	100,000.00	Multipurpose use
52	Autopipette P200	10,000.00	10	100,000.00	Multipurpose use
53	Autopipette P1000	10,000.00	10	100,000.00	Multipurpose use
	TOTAL			**25,014,000.00**	**Baht**

Annex V Tentative List of Machinery and Equipment (FTM-MU)

List of Equipment (Second year)

No.	List	Price/each	Amount	Price
1	Deep freezer (-70C)	700,000.00	1	700,000.00
2	PCR (Gradient)	500,000.00	2	1,000,000.00
3	Eppendorf-type centrifuge machine	170,000.00	2	340,000.00
4	Digital Imaging Microscopes; fluorescence	3,200,000.00	1	3,200,000.00
5	Largscale Culturing system	4,000,000.00	1	4,000,000.00
6	Flow cytometry 4 color with sorter	5,700,000	1	5,700,000.00
7	Two-dimensional gel electrophoresis	1,800,000	1	1,800,000.00
8	Biacore [Label-free surface plasmon resonance (SPR)]	6,000,000	1	6,000,000.00
				22,740,000 Baht

ANNEX VI Draft Record of Discussions (R/D)

(Draft)

RECORD OF DISCUSSIONS BETWEEN JAPAN INTERNATIONAL COOPERATION AGENCY AND AUTHORITIES CONCERNED OF THE GOVERNMENT OF THE KINGDOM OF THAILAND ON JAPANESE TECHNICAL COOPERATION FOR THE PROJECT FOR <Project title>

In response to the proposal of the Government of Thailand, the Government of Japan has decided to cooperate on the Project for "<Project title>" (hereinafter referred to as "the Project") in accordance with the Agreement on Technical Cooperation between the Government of Japan and the Government of the Kingdom of Thailand signed on November 5, 1981 (hereinafter referred to as "the Agreement") and the Embassy of Japan's Note No. xx/xx dated xx xx, 200x and the Ministry of Foreign Affairs Note No. xx/xx dated xx xx, 200x.

Accordingly, Japan International Cooperation Agency (hereinafter referred to as "JICA"), the implementation agency responsible for the implementation of the technical cooperation program of the Government of Japan, will cooperate with the authorities concerned of the Government of Thailand for the Project.

JICA and the Thai authorities concerned had a series of discussions on the framework of the project. As a result of discussions, JICA and Thai authorities concerned agreed on the matters referred to in the document attached hereto.

Nonthaburi, <date, month, year>

Mr. Katsuji ONODA
Chief Representative
Thailand Office
Japan International Cooperation Agency
Japan

Dr. Manit Teeratantikanont
Director General
Department of Medical Sciences
Ministry of Public Health
Kingdom of Thailand

Witnessed by

Professor Dr. Kazuyoshi Ikuta
Research Institute for Microbial Diseases
Osaka University
Japan

Dr. Pathom Sawanpanyalert
Director, National Institute of Health
Department of Medical Sciences
Ministry of Public Health
Kingdom of Thailand

Professor Dr. Skorn Mongkolsuk
Dean, Faculty of Science
Mahidol University
Kingdom of Thailand

Associate Professor Dr. Pratap Singhasivanon
Dean, Faculty of Tropical Medicine
Mahidol University
Kingdom of Thailand

Annex V Tentative List of Machinery and Equipment (FS-MU)

Necessary equipment for FS-MU

Year	Equipments	Company etc	Estimated cost	Justification
1st year	Ultrafine analytical HPLC with accessories, spare parts, and columns 1 system	Agilent 1200 HPLC system	9.5 M + 2 M + 2 M = 12.5 M	Analyze crude extracts from bacterial culture broth, and compare retention times, UV spectra with those of known compounds in order to eliminate known compounds and locate probable candidates having novel structure
2nd year	Preparative HPLC with accessories, spare parts and columns 1 system	Agilent 1200 Preparative HPLC system	5.9 M + 1.3 M + 4 M = 10.2 M	After locating the candidate compounds by ultrafine analytical HPLC, purify the compound into pure stage
	Solvent tolerant fraction collector 4 sets	Gilson model FC203 x 2 FC204 x1 PrepFC x1	1.0 M + 0.7M +1.2 M = 2.9 M	To fractionate samples for small-scale and large-scale purification from normal column chromatography
3rd year	Refrigerated incubator shaker with accessories 1sets		2.7 M	Cultivate target microorganisms in large number of flasks for large scale purification
4th year	-	-	-	-

Total 28.3 M JPY

Consumables (chemicals, solvents, separation resins, small apparatuses) for short-term experts

2 times per year x 4 years = 8 times

1.5 M per each visit

} = 12M

Sum = 40.3 M JPY

ANNEX VI Draft Record of Discussions (R/D)

THE ATTACHED DOCUMENT

I. COOPERATION BETWEEN BOTH COUNTRIES

1. The Government of the Kingdom of Thailand will implement the Project in cooperation with JICA.
2. The Project will be implemented in accordance with the Master Plan which is given in Annex I.

II. MEASURES TO BE TAKEN BY JICA

In accordance with the laws and regulations in force in Japan and the provisions of Article III of the Agreement, JICA, as the executing agency for technical cooperation by the Government of Japan, will take, at its own expense, the following measures according to the normal procedures of its technical cooperation scheme.

1. DISPATCH OF JAPANESE EXPERTS
   JICA will provide the services of the Japanese experts as listed in Annex II. The provision of Article IV of the Agreement will be applied to the above-mentioned experts.

2. PROVISION OF MACHINERY AND EQUIPMENT
   JICA will provide such machinery, equipment and other materials (hereinafter referred to as "the Equipment") necessary for the implementation of the Project as listed in Annex III. The provision of Article VIII of the Agreement will be applied to the Equipment.

3. TRAINING OF THAI PERSONNEL IN JAPAN
   JICA will receive the Thai personnel connected with the Project for technical training in Japan.

III. MEASURES TO BE TAKEN BY THE GOVERNMENT OF THE KINGDOM OF THAILAND

1. The Government of the Kingdom of Thailand will take necessary measures to ensure that the self-reliant operation of the Project will be sustained during and after the period of Japanese technical cooperation, through full and active involvement in the Project by all related authorities, beneficiary groups and

institutions.

2. The Government of the Kingdom of Thailand will ensure that the technologies and knowledge acquired by the Thai nationals as a result of the Japanese technical cooperation will contribute to the economic and social development of the Kingdom of Thailand.

3. In accordance with the provisions of Article IV, V, VI of the Agreement, the Government of the Kingdom of Thailand will grant in the Kingdom of Thailand privileges, exemptions and benefits to the Japanese experts referred to in II-1 above and their families.

4. In accordance with the provisions of Article VIII of the Agreement, the Government of the Kingdom of Thailand will take the measures necessary to receive and use the Equipment provided by JICA under II-2 above and equipment, machinery and materials carried in by the Japanese experts referred to in II-1 above.

5. The Government of the Kingdom of Thailand will take necessary measures to ensure that the knowledge and experience acquired by the Thai personnel from technical training in Japan will be utilized effectively in the implementation of the Project.

6. In accordance with the provision of Article IV-(b) of the Agreement, the Government of the Kingdom of Thailand will provide the services of Thai counterpart personnel and administrative personnel as listed in Annex IV.

7. In accordance with the provision of Article IV-(a) of the Agreement, the Government of the Kingdom of Thailand will provide the buildings and facilities as listed in Annex V.

8. In accordance with the laws and regulations in force in the Kingdom of Thailand, the Government of the Kingdom of Thailand will take necessary measures to supply or replace at its own expense machinery, equipment, instruments, vehicles, tools, spare parts and any other materials necessary for the implementation of the Project other than the Equipment provided by JICA under II-2 above.

9. In accordance with the laws and regulations in force in the Kingdom of Thailand, the Government of the Kingdom of Thailand will take necessary measures to

meet the running expenses necessary for the implementation of the Project.

IV. ADMINISTRATION OF THE PROJECT

1. Director General, Department of Medical Sciences (hereinafter referred to as "DMSc"), Ministry of Public Health (hereinafter referred to as "MoPH"), as the Project Director, will bear overall responsibility for the administration and implementation of the Project.

2. Director, National Institute of Health (hereinafter referred to as "NIH"), DMSc, MoPH, as the Project Manager, will be responsible for the managerial and technical matters of the Project.

3. Dean, Faculty of Tropical Medicine, Mahidol University and Representative from Faculty of Science, Mahidol University, as the Project Co-managers, will be responsible for the managerial and technical matters of the Project, supporting the Project Manager.

4. The Japanese Chief Advisor will provide necessary recommendations and advice to the Project Director, the Project Manager and the Project Co-managers on any matters pertaining to the implementation of the Project.

5. The Japanese experts will give necessary technical guidance and advice to Thai counterpart personnel on technical matters pertaining to the implementation of the Project.

6. For the effective and successful implementation of technical cooperation for the Project, a Joint Coordinating Committee will be established whose functions and composition are described in Annex VI.

V. JOINT EVALUATION

Evaluation of the Project will be conducted jointly by JICA and the Thai authorities concerned, at the middle and during the last six months of the cooperation term in order to examine the level of achievement.

VI. CLAIMS AGAINST JAPANESE EXPERTS

In accordance with the provision of Article VII of the Agreement, the Government of the Kingdom of Thailand undertakes to bear claims, if any arises, against the Japanese experts engaged in technical cooperation for the Project resulting from, occurring in the course of, or otherwise connected with the discharge of their official functions in the Kingdom of Thailand except for those arising from the willful misconduct or gross negligence of the Japanese experts.

VII. MUTUAL CONSULTATION

There will be mutual consultation between JICA and the Government of the Kingdom of Thailand on any major issues arising from, or in connection with this Attached Document.

VIII. MESURES TO PROMOTE UNDERSTANDING OF AND SUPPORT FOR THE PROJECT

For the purpose of promoting support for the Project among the people of the Kingdom of Thailand, the Government of the Kingdom of Thailand will take appropriate measures to make the Project widely known to the people of the Kingdom of Thailand.

IX. TERM OF COOPERATION

The duration of the technical cooperation for the Project under this Attached Document will be four years from <date, month, year>.

ANNEX I MASTER PLAN
ANNEX II LIST OF JAPANESE EXPERTS
ANNEX III LIST OF MACHINERY AND EQUIPMENT
ANNEX IV LIST OF THAI COUNTERPART AND ADMINISTRATIVE PERSONNEL
ANNEX V LIST OF BUILDINGS AND FACILITIES
ANNEX VI JOINT COORDINATING COMMITTEE

ANNEX VI Draft Record of Discussions (R/D)

ANNEX I MASTER PLAN

Project Purpose

Research and development capacity of therapeutic products against infectious diseases, especially dengue hemorrhagic fever is improved in Thai research institutes through the collaborative research.

Outputs

1. Human monoclonal antibodies (MAb) against dengue hemorrhagic fever, influenza and botulism are prepared and evaluated their effectiveness and safety in collaboration between Thai and Japanese researchers.
2. Novel bioactive compounds are explored from Thai natural microorganisms, including plant- and insect-derived bacteria, and evaluated their effectiveness and safety in collaboration between Thai and Japanese researchers.
3. The system on research and pharmaceutical affairs of bioproducts is streamlined.

Activities

1-1. Preparation of human MAb against dengue virus and the evaluation of effectiveness and safety

- 1-1-1. Collect and screen specimens.
- 1-1-2. Prepare candidates of human MAb from the patients with dengue virus infection.
- 1-1-3. Establish the experimental system for the evaluation of neutralization activity of human MAb against dengue virus for the screening of the candidates.
- 1-1-4. Establish the animal study system for the evaluation of effectiveness and safety studies to identify final candidate of human MAb against dengue virus.
- 1-1-5. *Establish the study system for the cloning of human MAb IgG variable regions to make the human recombinant MAb IgG.
- 1-1-6. *Establish the system for expressing the human recombinant MAb by Chinese hamster ovary (CHO) cells and/or plant biotechnology.

1-2. Preparation of human MAb against influenza virus and the evaluation of effectiveness and safety

- 1-2-1. Collect and screen specimens.
- 1-2-2. Prepare candidates of human MAb from the patients with influenza.
- 1-2-3. Establish the experimental system for the evaluation of neutralization activity of human MAb against influenza virus for screening of the

candidates.

1-2-4. Establish the animal study system for the evaluation of effectiveness and safety studies to identify final candidate of human MAb against influenza virus.

1-2-5. *Establish the study system for the cloning of human MAb IgG variable regions to make the human recombinant MAb IgG.

1-2-6. *Establish the system for expressing the human recombinant MAb by CHO cells.

1-3. (Preparation of human MAb against botulinum toxin and the evaluation of effectiveness and safety)

1-3-1. Identify the genetic types of botulinum (and purify the botulinum toxin).

1-3-2. Establish the experimental system for the evaluation of neutralization activity of human MAb against botulinum toxin for screening of the candidates.

1-3-3. *Establish the study system for the cloning of human MAb IgG variable regions to make the human monoclonal recombinant antibody IgG.

1-3-4. *Establish the system for expressing the human recombinant MAb by CHO cells.

2-1. Identify new compounds by comparing extracts from Thai natural microorganisms, including plant- and insect-derived bacteria, with existing database.

2-2. Screen the candidates of novel bioactive compounds with anti-dengue activity.

2-3. Establish the animal study system for the evaluation of effectiveness and safety studies to identify the final candidate of novel bioactive compound.

3-0. Set up laboratories for the research activities.

3-1. Make and revise Standard Operating Procedure (SOP) in each research subject.

3-2. Establish working group to discuss progress of the research, achievements and safety management bi-monthly.

3-3. Thai and Japanese researchers make monthly progress reports.

3-4. Make annual plan documents for research operation.

3-5. Document guidelines and operating procedures of non-clinical and clinical studies for biopharmaceuticals.

3-6. Conduct training and guidance regarding GLP.

Remarks: * These activities depend on the success of obtaining effective hybridomas.

ANNEX II LIST OF JAPANESE EXPERTS

1. Long-term experts
(1) Project Coordinator
(2) Research Management, if necessary

2. Short-term experts
(1) Chief Advisor
(2) Viral experiments
(3) Microorganisms experiments
(4) Identification of novel compounds
(5) Cell manipulation technique
(6) Gene manipulation technique
(7) Other researchers to be dispatched several times for each research topic according to a plan to be developed based on mutual agreement of both sides

ANNEX III LIST OF MACHINERY AND EQUIPMENT

ANNEX VI Draft Record of Discussions (R/D)

ANNEX IV LIST OF THAI COUNTERPART AND ADMINISTRATIVE PERSONNEL

1. Project Director:
   Director General, Department of Medical Sciences (hereinafter referred to as "DMSc"), Ministry of Public Health (hereinafter referred to as "MoPH")
2. Project Manager:
   Director, National Institute of Health (hereinafter referred to as "NIH"), DMSc, MoPH
3. Project Co-managers :
   Dean, Faculty of Tropical Medicine, Mahidol University
   Representative from Faculty of Science, Mahidol University
4. Project Coordinator:
   Representative from DMSc as to be assigned by the Project Director
5. Researchers of NIH and Medical Biotechnology Center, DMSc, MoPH
6. Researchers of Faculty of Tropical Medicine, Mahidol University
7. Researchers of Faculty of Science, Mahidol University

ANNEX V LIST OF BUILDINGS AND FACILITIES

1. Office spaces in National Institute of Health, and Faculty of Tropical Medicine and Science, Mahidol University
2. The existing Biosafety Level (BSL)-2 laboratories in Department of Medical Sciences, Ministry of Public Health
3. Space for BSL-2 laboratory in Faculty of Tropical Medicine, Mahidol University
4. Renovation of the laboratory space in Faculty of Tropical Medicine, Mahidol University
5. The existing laboratories in Faculty of Science, Mahidol University

ANNEX VI JOINT COORDINATING COMMITTEE

1. Functions
   (1) To formulate and authorize the annual activity plan of the Project
   (2) To endorse major achievements and products of the Project
   (3) To monitor and review overall progress and supervise the Project
   (4) To review and discuss on major issues arising from or concerning the Project

2. Composition
   (1) Chairperson:
   Director General, Department of Medical Sciences (hereinafter referred to as "DMSc"), Ministry of Public Health (hereinafter referred to as "MoPH")
   (2) Members:
   Director, National Institute of Health, DMSc, MoPH
   Dean, Faculty of Tropical Medicine, Mahidol University
   Representative from Faculty of Science, Mahidol University
   Senior medical scientists, DMSc, MoPH
   Leaders of research groups
   Representative from Department of Microbiology, Faculty of Medicine Siriraj Hospital, Mahidol University
   Japanese long-term experts and representative(s) from Osaka University
   Representative(s) from Embassy of Japan
   Representative(s) from JICA Thailand Office
   3) Observers:
   Representatives from Japan Science and Technology Agency