For WHO Use				
P:	**T:**	**A:**	**E:**	**O:**

#100XXX

RTG-WHO COLLABORATIVE PROGRAMME PROJECT ACTIVITY PROPOSAL

Note: See details on how to prepare the proposal in documents (1) WHO-THA-4.1 ***INSTRUCTIONS*** *FOR SUBMITTING PROJECT ACTIVITY* ***PROPOSALS*** *(Revised 16/02/10) and (2) WHO-THA-5.1* ***Rates.***

PART I. ADMINISTRATIVE INFORMATION

1.1 Full Name of Responsible Officer: Pritaporn Kingkaew

Title: Researcher

Note: Attach your curriculum vitae (CV) or biodata. Use the WHO format if you do not have a current CV.

Full Name of Organization:

Health Intervention and Technology Assessment Program (HITAP)

Address of Organization:

Health Intervention and Technology Assessment Program (HITAP)
6th Floor, 6th Building, Department of Health, Ministry of Public Health
Tiwanon Road, Nonthaburi 11000
Thailand

Telephone Number:	**Fax Number:**	**E-mail Address:**
66 2 5904374-5	66 2 5904369	pritaporn.k@hitap.net

1.2 Title of Project:

An Economic Evaluation of Tetravalent Dengue Vaccine in Thailand

1.3 **Proposed Starting Date:** 15 May 2011

1.4 **Estimated Duration (in months):** 12 months

1.5 Total Budget Requested (Baht): 400,000

II. PROJECT TIMELINE

Title of Project: An economic evaluation of tetravalent dengue vaccine in Thailand

Project Activities	Time Frame (Month)												Budget Required (Baht)
	1	2	3	4	5	6	7	8	9	10	11	12	
Literature review	←	—	→										30,000
Series of consultation meetings with key informants		←	—	→									40,000
Constructing economic model			←	—	→								50,000
Planning for primary data collection			←	—	→								20,000
Ethical review				←	—	→							20,000
Field visits and interviewing with stakeholders					←	—	→						50,000
primary data collection						←	—	→					50,000
Conducting economic analysis							←	—	—	—	→		40,000
Organizing a workshop among experts and stakeholders to gather comments on preliminary findings									←	→			40,000
Report writing										←	—	→	20,000
Producing and disseminating reports												↔	40,000

III. PROJECT DESCRIPTION

3.1 Background:

Dengue is a mosquito-borne infection that has been a major national public health concern in tropical and sub-tropical areas around the world. It has grown dramatically in recent decades approximately two-fifths of world population is now at risk from dengue.[1] Dengue viruses are transmitted to humans through the bites of infective female *Aedes* mosquitoes i.e. *Aedes aegypti* and *Aedes albopictus*. There are four serotypes of dengue viruses (DEN 1, DEN 2, DEN 3, and DEN 4), belonging to the *Flavivirus* genus of the Flaviviridae family, cause dengue infection. There has an assumption that the recovery from infection from one viral serotype provides a lifelong immunity against that particular serotype but confers only partial or transient protection against the other three serotypes. Also, sequential infections post a higher risk of developing dengue hemorrhagic fever (DHF). In Thailand, there are 97,721 reported dengue infected cases and case-fatality rate is 0.12% in 2010.[2] Dengue affects mainly children especially in school-age children as it reported to have the highest incidence of dengue infection in Thailand. It has been suggested that a number of reported dengue cases are considerable underestimated. Therefore, a multiplication factor should be applied to the reported cases in order to gain a better estimation for dengue infected cases because around 75% of the cases are non-hospitalized.[3, 4, 5]

Most dengue infection cases are asymptomatic; therefore, the clinical cases such as dengue fever (DF), DHF and dengue shock syndrome (DSS) only represent a fraction of the total burden of dengue infections.[6] Pediatric dengue vaccine initiative estimated that there are 36 million dengue fever cases and 2.1 million dengue hemorrhagic fever or dengue shock syndrome cases per year with 1% death rate.[7] A small proportion of clinical cases are leading to DHF/DSS and death rate is estimated for 2.5% of patients with this severe state by World Health Organization (WHO).[1] DF is a severe flu-like illness including fever with rash, abrupt high fever onset, severe headache, pain behind the eyes, and muscle and joint pains, but seldom causes death. On the other hand, DHF/DSS is a potentially lethal complication that is characterized by high fever, often with liver enlargement, and fluid circulatory failure in severe cases. In consequence, dengue infection leads to the loss of life, quality of life and productivity.

There is no specific anti-viral treatment for dengue infection. Monitoring and maintenance of patient's circulating fluid volume is a goal standard for dengue

hemorrhagic fever. At present, the standard preventive measure against dengue infection is vector control including public education, elimination of larval habitats, and insecticides against mature *Aedes* mosquitoes. Although the vector control has been endorsed in all Thai communities, substantial infected cases in Thailand still remain. This gap opens the room for other alternative preventive intervention. Over the past few years, the increasing spread of the disease and available fund for developing dengue vaccine, have stimulated the interest and investment in the vaccine research. The leading candidate in phase IIb clinical trial is the chimeric tetravalent dengue vaccine (ChimeriVax^{TM}-DEN) while other vaccines are in the first phase or preclinical phase. This promising vaccine is expected to provide a remarkable protection from all serotypes. This randomized clinical trial is currently undergoing in 4,002 of 4 to 11 years old children in Ratchaburi province, Thailand to assess the efficacy and safety of the vaccine.[8]

Decision to adopt new interventions into health benefit package requires various types of information for example the efficacy, the safety and the budget impact of those interventions. Recently, economic evaluation studies have played an important role to support decision makers in Thailand. A recent cost-utility study of hypothetical dengue vaccine was conducted to encourage the development of pediatric dengue vaccine.[9] A deterministic model of dengue transmission was constructed to assess the costs and benefits of dengue vaccination over no vaccination in a hypothetical cohort of children aged 15 months in Southeast Asian countries with the assumption of 95% lifetime protection against the four dengue virus serotype, 0.25% reduction of the annual risk of infection, and no side effects occurred. The study reported that two-dose of dengue vaccine is highly cost-effective at US$ 0.50 per dose in public sector and US$ 10 per dose in private sector. However, the model was based on many assumptions as there is no vaccine available for this crucial infection at the time of analysis. Therefore, it is necessary to conduct an economic evaluation of tetravalent dengue vaccine using actual efficacy data from the ongoing trial and the costs from the Thai context to support the use of evidence-based policy decision making.

3.2 Objectives:

General

To assess the value for money of providing tetravalent dengue vaccine to prevent dengue infection and to provide information on the impact of dengue vaccine as an additional tool to policy makers to aid their decision making on dengue control.

Specific

1. To identify resources used for providing tetravalent dengue vaccine to prevent dengue infection in the Thai health care setting.
2. To conduct economic evaluation of providing tetravalent dengue vaccine measured in cost per disability-adjusted life year (DALY) saved.

3.3 Methodology: *(Provide a conceptual framework and activities to be carried out – each activity with details as to what, how, where, when and by whom it will be undertaken. See Instructions section 3.3 for details on the type of narrative description to include here for your specific project.)*

Study design

This is a model based cost-utility analysis to estimate the incremental cost per disability-adjusted life year (DALY) saved of providing dengue vaccination programme comparing with no vaccination programme in school-age children population. DALY saved represents one year of healthy life gained due to postponement of mortality and/or reduction in rate or severity of morbidity.

Perspective and time horizon

The study will be conducted using costs not only incurred from the health system perspective but also from the societal perspective as the majority of the dengue cases occur at home. Consideration only the costs from the hospital might underestimate the total costs of treatment for the dengue infections. The lifetime horizon will be considered to capture all possible costs and outcomes that might occurred.

Model structure

The dynamic epidemiologic model will be used to obtain the incidence of asymptomatic and symptomatic dengue infections, as well as to evaluate the impact of vaccination programme. Figure 1 shows the epidemiologic model that will be used for assessing costs and consequences of intervention options (vaccination and no vaccination programme). The model presents possible clinical stages and outcomes of dengue infection in each compartment. The Susceptible-Exposed-Infectious-Recovered-Susceptible (SEIRS) was used as those who infected with one serotype of dengue virus

will be able to develop another infection from another serotype. The vaccination programme would make the population moving from the susceptible compartment to immune/recovery compartment directly. The arrows represent probabilities of being in different compartment. The model will incorporate birth rate (b) and death rate (m) into the population since the basic reproduction number, R_0, of dengue infection in available literature is more than 1.[10] By using the differential equations, we can consider the events occurring at continuous time rather than discrete time interval. The mathematical model of each compartment can be described below.

$$\frac{dS(t)}{dt} = b(1-v)N(t) - \sum_{i=1}^{4} \lambda_i\,(t)S(t) + \rho R(t) - mS(t)$$

$$\frac{dE(t)}{dt} = \sum_{i=1}^{4} \lambda_i\,(t)S(t) - \sum_{j=1}^{2} f_i\,E(t) - mE(t)$$

$$\frac{dI(t)}{dt} = \sum_{j=1}^{2} f_i\,E(t) - rI(t) - mI(t)$$

$$\frac{dR(t)}{dt} = bvN(t) + rI(t) - mR(t) - \rho R(t)$$

$$N(t) = S(t) + E(t) + I(t) + R(t)$$

Where,

$\frac{dS(t)}{dt}$ denoted the rate of change in the number of susceptible individuals at time t;

$\frac{dE(t)}{dt}$ denoted the rate of change in the number of exposed individuals at time t;

$\frac{dI(t)}{dt}$ denoted the rate of change in the number of infectious individuals at time t;

$\frac{dR(t)}{dt}$ denoted the rate of change in the number of recovered (immune) individuals at

$S(t), E(t), I(t), R(t)$ equal the total number of individuals who are susceptible, exposed, infectious and immune/recovery respectively at time t

$N(t)$ is the total population size at time t,

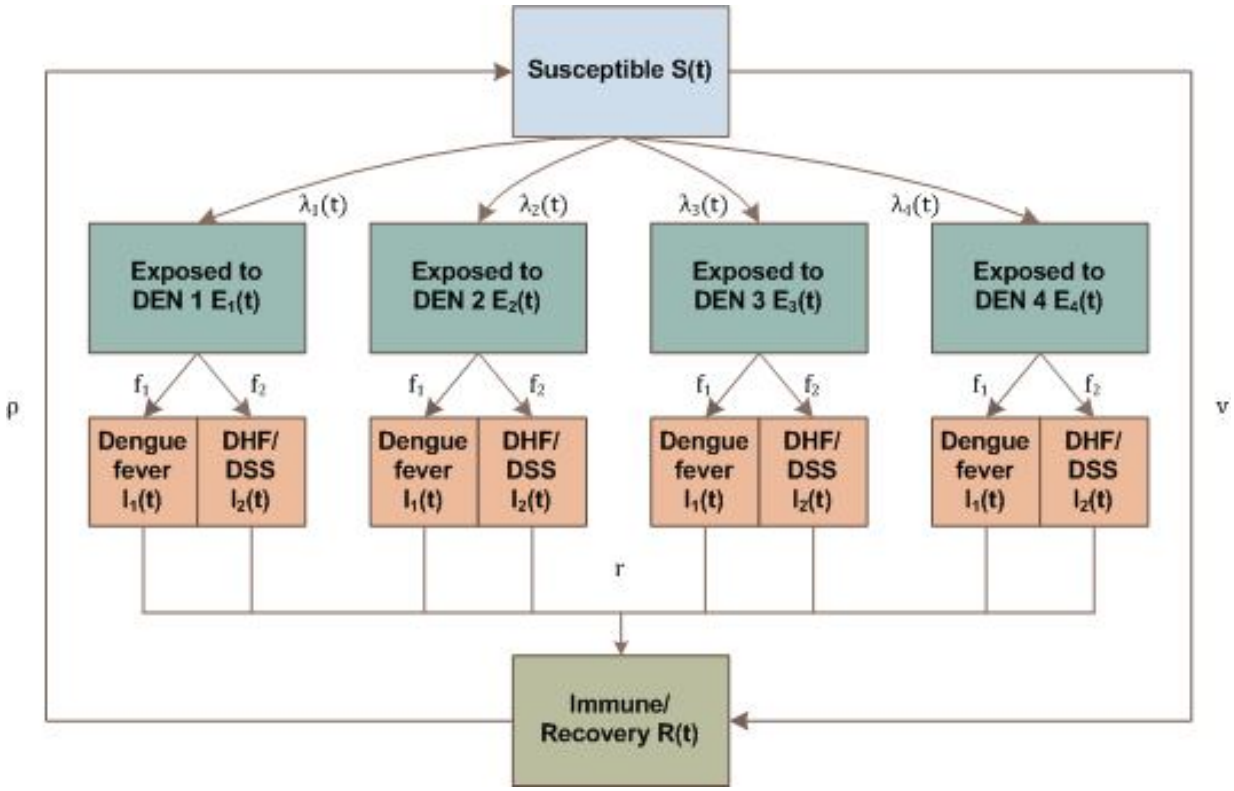
f denotes the rate of onset of infectiousness,

r denotes the rate at which individuals recover from being infectious

$\lambda(t)$ denotes the force of infection at time t

v is the introduction of vaccination of a proportion among newborns

ρ is a proportion of immunity waning



DHF, Dengue haemorrhagic fever; DSS, Dengue shock syndrome

Figure 1 Structure for Susceptible-Exposed-Infectious-Recovered-Susceptible (SEIRS) model used to describe the transmission of infections.

Data collections

We utilize efficacy of the vaccine from a randomized controlled trial which is conducting in Thailand setting with assumption that vaccine provides lifetime duration of protection after 3 immunizations at 0, 3-4, and 12 months. Costs consist of direct medical costs, direct non-medical cost and indirect cost when considered the societal perspective. Clinical benefits and costs will be discounted at 3% per year.

Table 1 Data used in the model and their sources

Parameter	Source
Epidemiology	
Probability of dengue infection	Literature reviews
Probability of symptomatic dengue infection	Literature reviews
Probability of DHF/DSS*	Literature reviews
Mortality	
Baseline mortality of Thai population	Burden of disease project
Mortality rate of dengue-infected patients	Literature reviews

Parameter	Source
Intervention effect	
Efficacy and safety of tetravalent dengue vaccine	Phase IIb clinical trial and Expert opinion
Costs	
Cost per dengue-infected patients	Literature reviews
Cost of tetravalent dengue vaccine	Assumption
Outcomes	
Disability of asymptomatic dengue infection	Literature reviews
Disability of patients with dengue fever	Literature reviews
Disability of DHF/DSS patients	Literature reviews

*Dengue Hemorrhagic Fever/Dengue Shock Syndrome

Data analysis and presentation of results

Vaccination has both direct and indirect effect. Vaccination programme directly reduces the prevalence of infectious individuals from the raise in immunity resulting in a reduction in force of infection, λ, and overall number of new infections per unit time in a population. Unvaccinated individuals also benefit from such reductions since the opportunity for them to be infected has decreased. Additionally, the disease can be eliminated, even though the vaccination coverage is less than 100%. This indirect protection is called 'herd immunity'. The application of previous economic evaluation study using static model would reflect in the underestimation of the impact of vaccination. The herd immunity threshold (HIT) or critical vaccination coverage will be calculated to provide a target for immunization programme, using the below formula;

$$HIT = 1 - \frac{1}{R_0}$$

where R_0, the basic reproduction number, is the average number of successful transmissions per infectious person. R_0 can be calculated using the rectangular age distribution;

$$\mathrm{R_0} = \frac{\lambda' \mathrm{L}}{(1-\mathrm{v})(1-\mathrm{e}^{-\lambda' \mathrm{L}})}$$

λ' is the expected average force of infection. L represents the life expectancy and v is the introduction of vaccination of a proportion among newborns. Vaccination is assumed to provide lifelong protection; individuals are assumed to mix randomly (no age patterns).

Cost, effectiveness, and utility parameters will be put into the designed model to estimate the total cost and health gained from each option. The results in terms of value for money will be presented in term of an incremental cost-effectiveness ratio (ICER) where:

$$\text{ICER} = \frac{\text{Cost of vaccination programme} - \text{Cost of current practice}}{\text{Outcome of vaccination programme} - \text{Outcome of current practice}}$$

Sensitivity analysis

Since the outbreak of the disease in the real population might occur under similar conditions; at other time, no outbreak might occur at all. Probabilistic sensitivity analyses of key parameters and assumptions including vaccine efficacy, duration of infection protection, annual risk of infection reduction, vaccine costs will be performed to capture all of the parameter uncertainty in the model. To identify the most sensitive parameters that affect this economic evaluation analysis, a series of one-way sensitivity analysis will be performed. Discount rate of 0 – 6% will be used to observe any changes in the conclusion of results as recommended in the Thai health technology assessment guideline.

3.4 Utilization of Results: *(Describe how the results of this project will contribute to delivering the **product** as stated in the Work Plans of WHO Thailand for the current biennium.)*

With the ever-increasing utilization of economic evaluation study as a tool for the evidence-based decision making, this research will help to inform policy makers in Thai health care sector whether it is worthwhile to provide tetravalent dengue vaccine in a national vaccination programme. The result of this project will be disseminate through stakeholder meetings and publish reports both in Thai and English.

PART IV. BUDGET (Baht)

Note: See details on how to prepare this section in documents WHO-THA-4.1 ***INSTRUCTIONS FOR SUBMITTING PROJECT ACTIVITY PROPOSALS*** *(Revised 12/10/05), especially Part IV (Budget), and* ***WHO-THA-5.1 Rates.***

4.1 Budget Details *(attach additional sheets if necessary)*:

Category — **Budget Requested (Baht)**

1. Personnel* *(Salary support or honoraria will not be provided to Principal Investigators of research projects.)*

Name	Position	% of Time on Project	Budget Required, Baht
Surachai Kotirum	Research assistant	60%	158,400
Adun Mohara	Researcher	20%	60,000
Yot Teerawattananon	Senior researcher	10%	30,000
Total Personnel			248,400

2. Equipment* *(It is not WHO policy to provide funding for equipment purchases, as this is the type of input that should be covered by the host organization.)*

Category	Quantity	Unit Cost	Total, Baht
-	-	-	-
-	-	-	-
Total Equipment			-

3. Supplies

Category	Quantity	Unit Cost	Total, Baht
Paper	30	102	3,060
Ink cartridges	3	4,500	13,500
CD	2	300	600
Recording material	1	3,500	3,500
Folders	3	300	900
Total Supplies			**21,560**

4. Data Entry and Data Processing

Category	Quantity	Unit Cost	Total, Baht
Berkeley Madonna license fee	1	10,500	10,500
Total Data			**10,500**

5. Per Diem Costs* (number of persons x rate x number of days = total)

Types of attendees/staff	Local or non-local	No. of persons	Rate	No. of days	Total, Baht
Resource persons	Local	10	1,000	3	30,000
	Non-local	-	-	-	-
Participants	Local	-	-	-	-
	Non-local	-	-	-	-
Secretarial staff	Local	3	500	7	10,500
	Non-local	-	-	-	-
Total Per Diem					**40,500**

6. Transportation Costs* (number of travellers x cost per person x trips = total)

Types of travellers	No. of travellers	Cost per person	No. of trips	Total, Baht
Resource persons	10	500	3	15,000
Participants	-	-	-	-
Secretarial staff	3	500	5	7,500
Field trips	-	-	-	-
Other transport (specify)	-	-	-	-
Total Transportation				**22,500**

7. Documents/Printing

Category	Quantity	Unit Cost	Total, Baht
Meeting minutes	50	50	2,500
Preliminary report	20	300	6,000
Final report	50	500	25,000
Total Documents			**33,500**

8. Miscellaneous* (*Specify*)

Category	Quantity	Unit Cost	Total, Baht
Photocopying (30 sets)	30	100	3,000
Transcribing interview records	10 (30 hr)	1,500	15,000
Total Miscellaneous			**18,000**

Grand Total	**394,960**

Notes:

a. ***These items require written justification in Section 4.2*** (i.e. why they are needed, the rates used, and how they are calculated).

b. For other items, if **large amounts** of funds are requested, justification for each amount should also be provided in Section 4.2.

c. ***Per diem*** *in WHO terms covers both lodging, meals, and incidental expenses (i.e. local taxi fare). Per diem or honoraria are not payable for attendance at meetings in connection with work undertaken in the course of normal duties. WHO per diem is payable only in cases where the activity is for a full working day and the participant does not receive per diem and/or accommodation payments from the RTG or other sources.*

d. Per diem rates vary according to the types of personnel and types of area (Areas A, B, or C) – see ***WHO-THA-5.1 Rates.***

e. **Local** participants or resource persons are those residing in the area of the venue of the Group Educational Activities (GEA) and not requiring paid accommodation for an overnight stay. For example, residents of the Greater Bangkok Metropolitan area would be considered "local" participants for any activity conducted in Bangkok and Nonthaburi.

f. **Flexibility**: Up to **10% of an existing budget line item** may be transferred to another existing budget line item due to minor adjustments in project implementation. Any budget line item changes exceeding 10% must be documented (with justification) and agreed to by WHO *before* transferring or committing funds for such a purpose.

4.2 Budget Justification:

Budget Category (See sub-part 4.1)	**Justification** See Instructions, Part IV, section 4.2 (Provide details to the extent feasible as to why they are needed, the rates used, and how they are calculated)
1. Personnel	1. Mr. Surachai Kotirum, Health Intervention and Technology Assessment Program-Research assistant Role: - Review literatures regarding current data of dengue-infected consequences and dengue vaccine effectiveness - Collect relevant data for performing the model-based cost-utility analysis - Manage the consultation meetings with the identified specialists - Draft and finalize the meeting minutes, preliminary report, and final report Compensation estimation : Part-time contribution 60% of current salary (0.6 x 22,000 baht x 12 months) = 158,400 baht 2. Mr. Adun Mohara, Health Intervention and Technology Assessment Program-Researcher Role: - Review literatures regarding current data of dengue-infected consequences and dengue vaccine effectiveness - Collect relevant data for performing the model-based cost-utility analysis Compensation estimation : Part-time contribution 20% of current salary (0.2 x 25,000 baht x 12 months) = 60,000 baht 3. Dr. Yot Teerawattananon, Health Intervention and Technology Assessment Program-Senior researcher Role: - Supervise on the decision model for performing the cost-utility analysis - Supervise and edit the research report - Advice and Identify the resource persons (specialists) Compensation estimation : Part-time contribution 10% of current salary (0.1 x 25,000 baht x 12 months) = 30,000 baht
2. Equipment	-
3. Supplies	Some part of methods for conducting this research are literature reviews and consultation meetings with the specialists; therefore, the proposed supplies such as papers, ink, folders, CDs and recording material are required throughout the entire project. The quantities and prices of the items are based on HITAP's records.

4. Data entry/processing	The computer programme for modeling (i.e., Berkeley Madonna) license will be obtained in order to analyse results from the mathematical dynamic modeling.
5. Per diem costs	A series of expert consultation meetings will be organized at the Ministry of Public Health, Nonthaburi. This workshop will include 3 HITAP secretarial staff, 10 local resource persons. The per diem rates are based on WHO/RTG Collaborative Programme (1,000 baht for local expert).
6. Transportation costs	Consultation meetings will be organized. Thus, transportation costs are for 10 local resource persons who have the expertise in dengue discipline to attend such events in the Ministry of Public Health. The other transportation costs are for HITAP secretarial staff to visit varied libraries and relevant institutions throughout the country to gather both primary and secondary data. The rate based on HITAP's records (500 baht for transportation in Bangkok)
7. Documents & printing	Document and printing costs can be divided into 3 parts; meeting minutes, preliminary reports, and final report respectively. The quantity and rate of 50, 300, and 500 baht per copy of the identified documents are based on HITAP's records.
8. Miscellaneous	As some part of methods for conducting this research are literature review and consultation meetings with the specialists; therefore, there is demand for these activities, photo copying and tape records, and transcribed verbatim (1,500 baht per 1.30 hours of transcription).

4.3 Resources and Facilities of Participating Institution Dedicated to Project:

4.3.1 Personnel

Name of Contact Person	Address	Tel/fax/e-mail
Dr. Yot Teerawattananon, M.D. Director of Health Intervention and Technology Assessment Program and senior researcher	Health Intervention and Technology Assessment Program (HITAP) 6th Floor, 6th Building, Department of Health Ministry of Public Health Tiwanon Road, Nonthaburi 11000	+662 590 4373/ +662 590 4369/ yot.t@hitap.net
Dr. Sripen Tantivess Senior researcher	Health Intervention and Technology Assessment Program (HITAP) 6th Floor, 6th Building, Department of Health Ministry of Public Health Tiwanon Road, Nonthaburi 11000	+662 590 4374-5/ +662 590 4369/ sripen.t@hitap.net
Mr. Nuttawut Pimsawan Project Manager	Health Intervention and Technology Assessment Program (HITAP) 6th Floor, 6th Building, Department of Health Ministry of Public Health Tiwanon Road, Nonthaburi 11000	+662 590 4549/ +662 590 4369/ nattawut.p@hitap.net

Name of Financial Officer	Address	Tel/fax/e-mail
Ms. Rojalek Leksomboon	Health Intervention and Technology Assessment Program (HITAP) 6th Floor, 6th Building, Department of Health Ministry of Public Health Tiwanon Road, Nonthaburi 11000	+662 590 4549/ +662 590 4369/ rojalek.l@hitap.net
Ms. Pornpimol Sansa-ard	Health Intervention and Technology Assessment Program (HITAP) 6th Floor, 6th Building, Department of Health Ministry of Public Health Tiwanon Road, Nonthaburi 11000	+662 590 4549/ +662 590 4369/ pornpimol.s@hitap.net

Name of Other Personnel	Address	Tel/fax/e-mail

4.3.2 Facilities

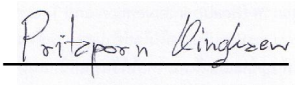
Please check relevant items

Vehicles _____
Office Facilities _____*_____
Computer Facilities _____*_____
Laboratory Facilities _____
Equipment _____
Clinical Facilities _____
Field Facilities _____

General Conditions

The Responsible Officer agrees to accept responsibility for the technical conduct of the project. If a grant is awarded as a result of the proposal application the Responsible Officer shall provide periodic progress reports and financial statements as stipulated in the Agreement, and a final report and statement of accounts upon completion of the study. The Responsible Officer shall also provide an abstract of the project results upon completion of the study. This abstract may be published in WHO publications. If the Responsible Officer publishes the results of the study in a journal, acknowledgement shall be made for the support provided by the WHO Thailand Country Programme. Copies of any such articles shall be forwarded to the WHO Thailand Office for further dissemination. All rights in the work of the project, including ownership of the original work and copyright there of, shall be vested in WHO, which reserves the right (a) to revise the work after consultation with you, (b) to use the work in a different way from that originally envisaged, or (c) not to publish or use the work.

Signature:

Responsible Officer: 

Name: Pritaporn Kingkaew

Title: Researcher

Date: May 6, 2011

References

1. World Health Organization (WHO). Dengue and dengue haemorrhagic fever march 2009 fact sheet, [Access on: Oct 29, 2010]. Available from: http://www.who.int/mediacentre/factsheets/fs117/en/

2. Thai vector borne disease, Department of Disease Control, Ministry of Public Health. Dengue infection surveillance. [Access on: Oct 29, 2010]. Available from: http://dhf.ddc.moph.go.th/Status/2553/week41.pdf

3. Endy TP, Chunsuttiwat S, Nisalak A, Libraty DH, Green S, Rothman AL, Vaughn DW, Ennis FA. Epidemiology of inapparent and symptomatic acute dengue virus infection: a prospective study of primary school children in Kamphaeng Phet, Thailand. Am J Epidemiol 2002;156(1):40-51.

4. Halstead SB, Suaya JA, Shepard DS. The burden of dengue infection. Lancet 2007;369(9571):1410-1.

5. Anderson KB, Chunsuttiwat S, Nisalak A, Mammen MP, Libraty DH, Rothman AL, Green S, Vaughn DW, Ennis FA, Endy TP. Burden of symptomatic dengue infection in children at primary school in Thailand: a prospective study. Lancet 2007;369(9571):1452-9.

6. Endy TP, Yoon IK, Mammen MP. Prospective cohort studies of dengue viral transmission and severity of disease. Curr Top Microbiol Immunol 2010;338:1-13.

7. Pediatric Dengue Vaccine Initiative (PDVI). Global Burden of Dengue, [Access on: Oct 29, 2010]. Available from: http://www.pdvi.org/about_dengue/GBD.asp

8. Webster DP, Farrar J, Rowland-Jones S. Progress towards a dengue vaccine. Lancet Infect Dis 2009;9(11):678-87.

9. Shepard DS, Suaya JA, Halstead SB, Nathan MB, Gubler DJ, Mahoney RT, Wang DN, Meltzer MI. Cost-effectiveness of a pediatric dengue vaccine. Vaccine 2004;22(9-10):1275-80.

10. Nishiura H. Mathematical and Statistical Analyses of the Spread of Dengue. Dengue Bulletin. 2006;30:51-67.