EVALUATION OF OPERATIONAL AND RESEARCH NEEDS
OF THE ANTI-MALARIA PROGRAM
IN THAILAND, 1986

by

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TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. EXECUTIVE SUMMARY</td>
<td>1</td>
</tr>
<tr>
<td>II. INTRODUCTION</td>
<td>3</td>
</tr>
<tr>
<td>A. Background to the Malaria Vector Control Program in Thailand</td>
<td>3</td>
</tr>
<tr>
<td>B. Present Situation and Strategy</td>
<td>4</td>
</tr>
<tr>
<td>C. Problems Encountered by the Program</td>
<td>6</td>
</tr>
<tr>
<td>D. Purpose and Terms of Reference of the Consultant Team</td>
<td>7</td>
</tr>
<tr>
<td>III. RECOMMENDATIONS BASED ON CURRENTLY AVAILABLE DATA</td>
<td>9</td>
</tr>
<tr>
<td>A. Discontinuance of House Spraying in Selected Areas, and Assessment</td>
<td>9</td>
</tr>
<tr>
<td>of Impact on Transmission</td>
<td>9</td>
</tr>
<tr>
<td>B. Rational Drug Use</td>
<td>10</td>
</tr>
<tr>
<td>C. Systematized Collection of Adverse Reaction Data for Drugs and</td>
<td>10</td>
</tr>
<tr>
<td>Insecticides</td>
<td></td>
</tr>
<tr>
<td>D. Advanced Training of Scientists and Managers</td>
<td>12</td>
</tr>
<tr>
<td>IV. NEEDS OF THE PROGRAM AS SEEN BY THE CONSULTANT TEAM</td>
<td>12</td>
</tr>
<tr>
<td>A. Identification of the Vectors Responsible for Transmission</td>
<td>12</td>
</tr>
<tr>
<td>B. Control of Transmission by the Identified Vectors</td>
<td>13</td>
</tr>
<tr>
<td>C. Epidemiological/Entomological Data Collection and Interpretation</td>
<td>14</td>
</tr>
<tr>
<td>V. PRIORITY RESEARCH AREAS</td>
<td>16</td>
</tr>
<tr>
<td>A. Identification of Transmission Models</td>
<td>16</td>
</tr>
<tr>
<td>B. Vector Incrimination</td>
<td>18</td>
</tr>
<tr>
<td>C. Value of Control Activities in Vector Reduction</td>
<td>20</td>
</tr>
<tr>
<td>D. Alternative Methods for Anopheles dirus Control</td>
<td>24</td>
</tr>
<tr>
<td>E. Collection and Interpretation of Data</td>
<td>27</td>
</tr>
<tr>
<td>F. Policy for Management of Fever Cases</td>
<td>28</td>
</tr>
<tr>
<td>G. Collection of Background Data Leading to Rational</td>
<td>29</td>
</tr>
<tr>
<td>Development of Alternative Policies</td>
<td></td>
</tr>
<tr>
<td>H. Migration Patterns</td>
<td>34</td>
</tr>
<tr>
<td>VI. MEANS OF APPROACHING THE RESEARCH NEEDS</td>
<td>36</td>
</tr>
<tr>
<td>A. Workshop on Proposal Preparation, July 23-29, 1986</td>
<td>36</td>
</tr>
<tr>
<td>B. Specific Research Proposals Emanating from the Workshop</td>
<td>39</td>
</tr>
<tr>
<td>- &quot;The Hypotheses&quot; Exercise</td>
<td></td>
</tr>
<tr>
<td>C. Identification of Funding Sources</td>
<td>46</td>
</tr>
<tr>
<td>D. Requirements for Consultants</td>
<td>47</td>
</tr>
</tbody>
</table>
TABLE OF CONTENTS (cont.)

VII. LIST OF REFERENCES CITED 50

VIII. ANNEXES

(1) Program for VBC/USAID Consultant Team 53
(2) List of People Met During the Evaluation 55
(3) List of Places Visited During the Evaluation 57
(4) Schedule for the Workshop on Proposal Preparation 58
(5) List of Participants in the Workshop on Proposal Preparation 60
(6) Telegram Requesting Consultants for the Program 61
(7) Number and Distribution of Malaria Clinics 62
(8) Number and Distribution of Village Voluntary Malaria Collaborators 63

IX. ADDENDA

(1) Unpublished Document "The Current Situation of the Anti-malaria Program in Thailand" (1985) 64
(2) Unpublished Document "The Practice of Antimalarial Drug Usage in the Field and in a Large Scale Trial with Mefloquine and its Combination in Thailand" 75
(3) Unpublished Document "ABATE as a Larvicide Against Anopheles minimus, the Main Vector of Malaria in Thailand" (1985) 84
(4) Comments Concerning a Request for a Leishmaniasis Consultant in Thailand 96
I. EXECUTIVE SUMMARY

Three consultants, Drs. R. G. Andre, E. B. Doberstyn and D. F. Clyde, visited Thailand between June 22 and August 1, 1986 with terms of reference to assess current malaria vector control strategies of the Ministry of Public Health, to determine needs for operational research over the next five years and formulate a plan for implementation, to train Malaria Division personnel in research design, implementation and report writing, to advise on techniques for mosquito identification and separation of sibling species, and to recommend a plan and schedule for short-term assistance to the program by the VBC Project. These points were addressed and are dealt with in this report.

Based on currently available information, the consultants made recommendations in four areas. There is a need to:

1. Stop residual indoor insecticide spraying in a few carefully selected areas, as a test to assess impact on malaria transmission, augmenting the measurement of entomological parameters and malaria incidence. These areas should have ready access to Malaria Clinics;

2. Develop a more rational policy of antimalarial chemotherapy, in particular, the cessation in large-scale distribution of drugs for presumptive treatment in view of potential toxicity to patients and spread of parasite resistance to the drugs;

3. Systematize collection and notification of data on adverse human reactions to drugs (especially sulfonamides) and insecticides (especially OP compounds such as fenitrothion), and improve the relevant monitoring systems; and

4. Promote and provide advanced training of mid-level administrative and technical Malaria Division staff, at recognized centers in the United States.

The principal problems of the program as seen by the Malaria Division are the widespread resistance of malaria parasites to the standard drugs, difficulty in controlling exophilic vectors, and migration of laborers to and from malarious areas. The consultants concurred in the importance of these, but stressed three major needs: 1. identification of the species/sibling species of Anopheles that are currently (rather than formerly) the main vectors (while recognizing that An. minimus was no doubt the main vector in earlier days, it is felt that An. dirus may now have assumed this position); 2. based on identification of the current vectors, the control methodology may have to be altered, probably with less dependence on the residual insecticides DDT and fenitrothion; and 3. revision of the epidemiological reporting system is urgently needed, at all
levels from the field to the center, and will involve use of a microcomputer system.

Eight priority research areas were identified by the consultants, which would provide the anti-malaria program with information essential to improvement of the control operations. These areas were:

1. Identification of transmission models
2. Vector incrimination with particular reference to An. dirus vs. An. minimus
3. Value of control activities in vector reduction, including the utility of insecticide spraying, repellents, bednets impregnated or non-impregnated, and coils, and anti-larval measures both chemical and biological
4. Alternative methods for An. dirus control, including those indicated in the previous item
5. Collection and interpretation of data
6. Policy for management of fever cases, with attention to the place of Malaria Clinics, referral, and reinterpretation of the role of volunteers
7. Collection of background data leading to a rational development of alternative policies, with particular reference to integration of the anti-malaria program with primary health care
8. Migration patterns, both within the country and across the borders.

Outline protocols with budgets were formulated for each of these, and a list of appropriate potential consultants drawn up.

The Workshop on Proposal Preparation occurred July 23-29, 1986. It was attended by 26 senior personnel of the Malaria Division, and two national coordinators. The participants were instructed in the step-wise preparation of applied research proposals based on their own suggestions, the most promising of which they developed during the course and produced in draft form.
Distinct from the anti-malaria program, the question of leishmaniasis was examined by Dr. Andre, who concluded that transmission was most unlikely to occur in Thailand from the small number of cases among workers returning from the Middle East. The epidemiology of the disease is such that these individuals would not form a reservoir for infection of sandflies. Dr. Andre provided the concerned national staff with the literature necessary for identification of potential vectors, while noting that the local sandflies are not known to be man-biters.

II. INTRODUCTION

The team focused its evaluation and subsequent recommendations on problems of malaria transmission, rather than chemotherapy, as requested by the Malaria Division of the Ministry of Public Health and in accordance with the U.S. Agency for International Development's terms of reference.

A. Background to the Malaria Vector Control Program in Thailand

The malaria vector control program in Thailand is a part of the Anti-Malaria Program of the Malaria Division, Department of Communicable Disease Control, Ministry of Public Health. The program is undertaken at two main levels - national and regional - using decentralized units and sectors to implement it. The Division headquarters is located in Bangkok, and its activities include administration, health education and training, vector control operational planning and evaluation, epidemiology, applied research, entomology, and laboratory services. There are five regional offices, each directed by a malariologist, and each region contains six to seven units which themselves contain 5 to 14 sectors.

The Director of the Malaria Division is Dr. Surin Pinichpongse and the head of the applied research unit in the Division is an entomologist, Dr. Chusak Prasittisuk. Both of these officials and their staff were most helpful in providing the consultants with available reports and data relating to the assignment.

Prior to 1951, malaria was the leading cause of death in Thailand, with a mortality rate of around 350 per 100,000. The encouraging results of a WHO/UNICEF-assisted pilot project in Chiangmai Province 1949-51, using DDT as an intradomiciliary residual spray, led in the latter year to development of a country-wide malaria control program by the Government, assisted
by USAID. In 1964 this was converted into a malaria eradication program and although complete coverage by DDT spraying was not achieved, large areas were cleared of endemic malaria and the mortality reduced to 22.8 per 100,000 population. By 1970 this had fallen to 10.1. In 1971 the WHO-revised strategy led to a change in policy in order to protect the gains already made and prevent the increase in new problem areas. The plan of operations for 1971-1976 was designed to meet the costs of the project in the face of budget reductions by adjusting the phasing of operations, and by developing criteria for implementing activities. By 1981, 79 percent of the population inhabited areas where residual insecticide was no longer used for malaria control.

B. Present Situation and Strategy

One consequence of the necessary modification of the eradication program in 1971 was a small increase in the mortality rate, which rose to 15.8 per 100,000 population in 1974, and a steady rise in the incidence of malaria, from a fluctuating figure around 3.0 per thousand population in the decade before 1972 to 10.6 in 1981. The figures have, however, decreased since those years. In 1984, the mortality was 4.4 per 100,000. The morbidity, as shown by surveillance activities from 1980 through 1984, has been as follows:

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<td>Population</td>
<td>44.23 m</td>
<td>44.82 m</td>
<td>46.03 m</td>
<td>46.92 m</td>
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<td>Blood Smears Examined</td>
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<td>6,094,665</td>
<td>5,365,960</td>
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<td>Positives</td>
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<td>473,210</td>
<td>420,799</td>
<td>243,910</td>
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<td>SPR</td>
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<td>7.0</td>
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<td>4.6</td>
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<tr>
<td>ABER</td>
<td>8.1</td>
<td>8.9</td>
<td>9.1</td>
<td>8.2</td>
<td>8.2</td>
</tr>
<tr>
<td>API</td>
<td>8.9</td>
<td>10.6</td>
<td>9.1</td>
<td>5.2</td>
<td>6.3</td>
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</tbody>
</table>

(NOTE: The population consisted of those covered by surveillance (in millions); SPR = Slide Positivity Rate (%); ABER = Annual Blood Examination Rate (%)- the 1985 figure being calculated from blood collected in all activities; API = Annual Parasite Incidence (per thousand population.)
These data have been obtained from the most recent Malaria Division report.\textsuperscript{1} Control operations distinguish between two contrasting situations in the country as a whole, one being the Control Area (consisting of forested hills, border areas and insecure areas -- population 12 million) and the other the Eradication Area (most of the country centrally -- population 40 million). The present strategy is that of long-term malaria control in the Control Area, where the disease is endemic, and prevention of re-establishment of transmission in the Eradication Area. Actual measures depend on the local epidemiological situation, the main control measures being interior house spraying with DDT or fenitrothion once or twice a year, diagnostic and treatment centers (Malaria Clinics - see Annex 7), provision of anti-malaria drugs, and health education. Supplemental measures include larviciding,\textsuperscript{2} space spraying, case detection and treatment, and deployment of larvivorous fish. At the village level, Village Voluntary Malaria Collaborators (VVC) educate the public, assist in spraying operations, take blood smears, and give presumptive treatment (see Annex 8).

The objectives of the program, as indicated in the current National Health Development Plan (1982-1986), are to reduce malaria mortality to less than 8 per 100,000, reduce morbidity in control areas to less than 12 per thousand, prevent re-introduction in eradication areas by limiting cases to 1 or less per 10,000 population, and implement a primary health care approach to malaria control, involving villagers in personal protection measures. Achievement of these objectives is seen in the data, although there are fluctuations in the incidence; success is attributed largely to the numerous malaria clinics and the work of the VVC, resulting in earlier diagnosis and appropriate treatment. The clinics, numbering 454, are located strategically in high transmission areas, marketing centers, and on routes of migration.

In 1984 the parasite formula was \textit{P. falciparum} 70.7 percent, \textit{P. vivax} 29.0 percent, \textit{P. malariae} 0.02 percent, and the remainder mixed. This indicates a slight gain in \textit{P. falciparum} over \textit{P. vivax} in recent years, although during the past year actual numbers of \textit{P. vivax} cases have increased. \textit{P. falciparum} has been increasingly resistant to chloroquine since around 1957; now more than 95 percent of infections with this parasite show some degree of resistance to that drug and also, in high density resistance areas, to amodiaquine and quinine. A few cases showing primary resistance to mefloquine also have been identified. \textit{P. falciparum} strains resistant to the combination sulfadoxine-pyrimethamine started to appear in the south-east on
the Kampuchean border, and have spread at high levels to all parts of the country.

The vectors in Thailand are considered by the Anti-Malaria Program to include An. dirus, An. minimus and An. maculatus. An. minimus is thought to be the most important vector and is prevalent throughout Thailand in forested and cleared foothill areas with slow running streams.\(^1,3\) Formerly highly endophagic and endophilic, it has become in recent years strongly exophagic and exophilic. An. dirus, also outdoor resting, is thought to be another main vector, and its distribution coincides with the forested areas. In northern Thailand, 89 percent of infections are considered to be contracted in the forest, 3.3 percent to be contracted in villages, and 7.7 percent to be imported. An. maculatus was incriminated once as a vector in southern Thailand. Two species, An. sundaicus and An. aconitus, are considered to be secondary vectors, respectively in coastal areas and in the rice-growing plains areas. The mosquitoes appear to be sensitive to DDT, but following spraying, An. minimus shows a higher proportion of outdoor biting. This situation has been met by use of larvivorous fish, thermal fogging using fenitrothion in epidemic situations, and promotion of the use of bednets, repellents and similar items for personal protection.

C. Problems Encountered by the Program

The Thai Anti-Malaria Program has identified three main problems. These are (1) the rapid spread of P. falciparum strains resistant to 4-aminoquinoines (they are apparently biologically advantaged in the sporogonic stages by the continued use of chloroquine\(^4\)) and to the sulfadoxine-pyrimethamine combination, making it difficult to provide effective presumptive treatment; (2) the exophilic behavior of vectors which enables them to avoid DDT residual spray; and (3) occupational migration of large numbers of people for gem mining, farming, and woodcutting. Infected individuals bring malaria into areas freed of the disease, and uninfected, often non-immune individuals entering endemic areas contract the disease, but lack ready access to treatment and are beyond the reach of the program.\(^1\) The migrants cover long distances. For example, people from northeast and central Thailand move to work as laborers in sugarcane plantations in Kanchanaburi Province and encounter transmission said to be caused by An. minimus. Or they travel short distances within the Province into An. dirus-infested forest to mine ore and make charcoal. The latter developed higher rates of malaria.\(^5\)
These problems are being addressed to the extent possible by (1) continuing the presumptive use of sulfadoxine-pyrimethamine where feasible, while using the combination mefloquine-sulfadoxine-pyrimethamine curatively in P. falciparum-diagnosed cases (excluding pregnant women, children aged less than 6 months, and patients allergic to sulfa drugs) or prophylactically in highly select groups (e.g., field health personnel and entomologists); (2) deployment in exophilic vector areas of larvivorous fish or use in epidemic circumstances of thermal fogging with fenitrothion -- both of these methods obviously have very limited potential; and (3) education of occupational migrants in personal protection methods, notably bednets and repellents.

While these are the main problems specified by the Anti-Malaria Program, the consultants feel that another problem is fundamental to planning and implementing the program -- the identity of the principal vector. For many years the main vector has been said to be An. minimus. An. dirus is acknowledged as a lesser and more focal vector, and An. maculatus is viewed as a possible vector in the south. Other vectors of limited focal significance are thought to be An. sundaicus (at the coast) and An. aconitus. The consultants feel that the roles attributed to An. minimus and An. maculatus may be exaggerated (although the vectorial capacity of the former has been well-established in field and laboratory), while An. dirus may be of paramount importance, as has indeed been indicated before. The extent and impact of any of these problems are difficult to evaluate because the data base is inappropriately collected and inadequately analyzed in many of the Thai malaria control regions (although some malariometric work continues to provide useful information, for example slide microscopy checked against IFA in Chiangmai Province). In general, however, the methods for obtaining, storing, analyzing and utilizing essential epidemiological, parasitological, entomological, and sociological information are defective. These problems are addressed in the research proposals advanced later in this report.

D. Purpose and Terms of Reference of the Consultant Team

The three members of the Vector Biology & Control Project's consultant team visited Thailand in June and July 1986 primarily to advise on optimal anopheline mosquito control measures for the ensuing five years. These depend upon clarification of the targets to be attained by implementation of applied research projects. The terms of reference were as follows:
1. Assess the current control strategies of the Ministry of Public Health in each geographic area of the country and assist in updating them where appropriate. The assessment requires the consultants to pay particular attention to the value and effectiveness of spraying efforts.

2. Assess needs for operational research over the next five years and formulate a plan for implementation. The plan must address each proposed research topic in terms of the need it addresses and the manner in which the information will be applied to control efforts. Each topic must have a stated hypothesis, a projected schedule for completion, and a budget.

3. Train approximately 15 Ministry of Public Health, Malaria Division research workers in research design, implementation, and report writing. It is expected that protocols for the next year's program will be written with assistance from the consultants.

4. Advise on establishing appropriate laboratory techniques for mosquito identification and the separation of species complexes. Methodologies for identification of malaria parasites in mosquitoes will also be developed.

5. Recommend a plan and schedule for future short-term assistance to the Ministry of Public Health by the VBC Project.

6. Prepare a written draft report addressing all issues listed above in-country and present it to USAID and the Ministry of Public Health before departure from Thailand.

Dr. Andre, the team leader, arrived in Thailand on June 22, 1986 and Drs. Doberstyn and Clyde July 12 and 13, respectively.

The work was completed on August 1. Dr. Andre initially visited important vector control sites in various parts of Thailand (see his itinerary at Annex 3), and then worked in Bangkok with Drs. Doberstyn and Clyde for the remainder of the assignment period. The research design training course was held at the Malaria Division headquarters in Bangkok July 23-29 (see Section 6).
Throughout the visit, the greatest assistance was provided by Dr. Surin Pinichpongse, Director of the Malaria Division, and his staff, in particular Dr. Chusak Prasittisuk.

III. RECOMMENDATIONS BASED ON CURRENTLY AVAILABLE DATA

The consultants were struck by certain problems and needs faced by the antimalarial program. Some recommendations concerning these problems may be made immediately, even before the initiation of relevant research. These include (a) house spraying in a few selected areas should be stopped as a test to assess impact on malaria transmission, (b) a more rational policy of antimalarial chemotherapy is needed, (c) systematized collection of adverse reaction data for drugs and organophosphate insecticides should be required, and (d) advanced training is needed for the new generation of malaria scientists and managers.

A. Discontinuance of House Spraying in Selected Areas, and Assessment of Impact on Transmission

Residual insecticide spraying should be stopped in selected areas having readily accessible malaria clinics, and the impact on malaria transmission assessed. In order to assess this impact, it will be necessary to augment the measurement of entomological parameters and malaria incidence.

In the early years of the malaria control program in Thailand, indoor residual spraying of DDT reduced An. minimus populations and halted malaria transmission in many parts of the country. However, entomological data collected from the late 1960's until the present indicate that the two primary vectors, An. dirus and An. minimus, are exophilic and exophagic. These behavior patterns are not amenable to a control method based on the effects of insecticides against mosquitoes that rest on the interior surfaces of houses.

Spraying continues on the premise that the repellent effects of DDT (but not fenitrothion) force the mosquitoes to bite outdoors and to feed on animals, lessening their contact with man. In fact, there may be a sibling-species complex in An. minimus, and observations of two or more species are leading to misinterpretation of these insecticide effects.

More importantly, however, no well-designed study since 1970 in Thailand has shown the interruption of malaria transmission to be correlated directly with residual insecticide spraying. The consultants recommend that such a study be initiated immediately.
We recommend that selected areas with endemic malaria be studied to determine if insecticide spraying of interior walls reduces or stops malaria transmission. To do this, areas with readily accessible Malaria Clinics should be chosen. The standard baseline data should be collected and analyzed (if indicator village), spraying halted completely, and the impact on malaria transmission assessed. ELISA and IFAT techniques should be used to augment the measurement of entomological parameters and malaria incidence.

B. Rational Drug Use

The consultants noted that vast amounts of potentially toxic antimalarial drugs are distributed by the program. Of particular concern is the policy of distributing drugs to people without prior diagnosis of malaria. The use of "presumptive treatment" is addressed in the section of this report devoted to priority research areas (Section 5), but the consultants felt that the anti-malaria program must be urged to consider means of stopping the large-scale distribution of drugs, particularly those which may be associated with a predictable number of allergic and toxic reactions when used on a mass scale (it is noted that more than six million tablets of sulfadoxine-pyrimethamine were purchased by the program in 1985).

The anti-malaria program has received worldwide recognition for its successful implementation of the system of malaria clinics, in which malaria is diagnosed and treated appropriately (the clinic system was established with USAID assistance). With such a capability, the routine distribution of potentially dangerous drugs by malaria volunteers and survey teams is unnecessary and inconsistent with the otherwise largely reasonable approach to malaria control that characterizes the Thai program.

C. Systematized Collection of Adverse Reaction Data for Drugs and Insecticides

There is growing evidence of a significant incidence of allergic reactions to sulfonamide-containing antimalarial drugs, including sulfadoxine-pyrimethamine (SP), and mefloquine-sulfadoxine-pyrimethamine (MSP). These drugs constitute the major presumptive and radical treatments used in the Thai anti-malaria program.

This evidence has been obtained following the implementation of an adverse reactions monitoring system initiated at the time that MSP was introduced to the Thai program as the standard
therapy for *P. falciparum* infections (1984-1985). The monitoring system, which depends on the use of questionnaires distributed to peripheral treatment centers (malaria clinics and sector offices) has, to date, identified a number of possible adverse reactions to MSP, at least four of which were severe, and one of which was associated with permanent disability—blindness resulting from an acute Stevens-Johnson reaction in an 11-year old boy. The two most clear-cut cases will be reported in the medical literature (Bulletin of the World Health Organization, September 1986, in press).

Although the monitoring system has produced results, it is still implemented in a somewhat unsophisticated way, and requires refinement. The consultant team feels strongly that an experienced consultant in post-marketing surveillance of drug risks should be recruited immediately for the purpose of strengthening the adverse reactions monitoring and notification system.

The same consultant also could address another related problem which requires immediate attention, i.e., monitoring for side effects of organophosphate (OP) - containing insecticides. Since the initiation of the Japanese government's aid program (1982-1983), fenitrothion, in addition to DDT, has been used by the anti-malaria program on an expanding scale. Routine testing of spraymen for cholinesterase levels was planned as part of the spray program for fenitrothion, but this testing has been carried out somewhat haphazardly and has been associated with inconsistent application of guidelines for removal of spraymen from exposure. No fatalities or major instances of severe toxicity have been identified to date; however, it is recognized even within the program that precautions are inadequate and surveillance is incomplete. A new problem in this regard was explained to the consultant team — acetylcholine availability had been restricted by the Thai government. Since this compound is essential to the testing procedure for organophosphate toxicity, it may be expected that the toxicity testing routine will deteriorate further.

In its recommendations concerning spray operations, the 1983 USAID Evaluation Team strongly suggested that careful monitoring of OP toxicity be meticulously carried out.

The consultant in Adverse Reactions Monitoring Systems could be expected to help the Malaria Division improve its surveillance for OP toxicity in order to determine more clearly the risks associated with the use of these chemicals in Thailand. In association with studies recommended later in this report
concerning the wisdom of continuing large-scale spraying operations at the present level, clear toxicity information would result in rational determination of a spraying risk/benefit ratio, in the specific case of OP insecticide usage.

D. Advanced Training of Scientists and Managers

The consultant team also felt that a need exists for advanced training of mid-level administrative/technical Malaria Division staff. Several key retirements or promotional moves are pending, which will bring relatively young staff members to positions of considerably increased responsibility. In addition, in order to maintain a national corps of experts in malaria control, recruitment of capable young physicians/scientists will require some opportunity for specialized training abroad in malaria technology and public health administration. Funds for such training fellowships have not been available since the withdrawal of direct USAID assistance in 1983 and the reorientation of the WHO country program.

The consultant team recommends that, as a priority matter, funding support be identified for academic/technical training in U.S. institutions such as Tulane, Johns Hopkins, Harvard, and the Centers for Disease Control.

IV. NEEDS OF THE PROGRAM AS SEEN BY THE CONSULTANT TEAM

Among the needs of the program, three appeared to be outstanding. These were (a) identification of the vectors currently (as contrasted with formerly) responsible for the maintenance of transmission, (b) selection of methods most appropriate to control this transmission, and (c) improvement in the collection and interpretation of epidemiological and entomological data.

A. Identification of the Vectors Responsible for Transmission

It is thought that in the early years of the malaria control program, Anopheles minimus transmitted malaria parasites to more people than did any other anopheline species in Thailand. In the 1950's, this species was shown to be highly endophilic, anthropophilic, and endophagic. This behavior facilitated extremely successful control efforts by interior DDT spraying in the plains of Thailand, bringing a stop to malaria transmission in places like the Chiangmai Valley. During those early years, An. dirus (= balabacensis) was not considered a vector; this opinion changed only after extensive movement of the population
into forested areas.

Because *An. maculatus* was shown to be a vector in Malaysia and was once 20 years ago found positive for sporozoites in southern Thailand, this species is considered also to be a vector throughout the country. *An. sundaicus* is thought to be a vector in coastal areas; and again, based on one positive salivary gland dissection 20 years ago, *An. aconitus* is thought to be a potential vector in the Central Plains. Based on this information, the vector importance ranking scheme would be: *minimus > dirus > maculatus > sundaicus > aconitus*.

What changes have been noted since these early observations? *An. minimus* now is exophilic and exophagic. There appear to be two distinct populations — one zoophilic and the other anthropophilic. In recent years, few *An. minimus* have been found positive for sporozoites. Despite hundreds of dissections of *An. maculatus*, no salivary gland positives have been detected. Neither *An. sundaicus* nor *An. aconitus* have been examined to any extent in recent years. Only in *An. dirus* were sporozoite positive mosquitoes consistently detected during recent studies. So, based on recent information, the current vector ranking scheme would be: *dirus > minimus*.

The problems in vector determination are compounded by the occurrence of sibling species complexes. There are four species in the *dirus* complex in Thailand: *dirus A, dirus B, dirus C, and dirus D*. Both *A* and *D* occur in many parts of Thailand, *C* is found mostly in the western provinces, and *B* is found mostly in the south. There are at least six species in the *maculatus* complex in Thailand, and it is suggested (but not proven) that two species of *minimus* occur in the north and the west. The relative importance of these various members of the species complexes is unknown, except that *dirus A* has been proven to be a vector in the southeast. Methods for differentiating the members of the *maculatus* and *dirus* complexes should be available within six months to a year, facilitating accurate vector incrimination. Until extensive man-biting surveys are carried out with concomitant sporozoite detection methods, however, the Malaria Division will continue to be faced with the problem of not knowing the main malaria vector in Thailand.

B. **Control of Transmission by the Identified Vectors**

Control of malaria vectors in Thailand appeared to be very easy in the early days of the program. *An. minimus* came inside houses to feed on man and would rest on inside surfaces that had been sprayed with DDT, thereby reducing the vector's longevity.
However, in the 1960's studies showed that the majority of minimus and dirus did not rest on walls to any extent. This exophilic behavior precluded the effective use of DDT spraying, but nevertheless, it is still being used. One or two cycles of spraying with this insecticide continued in endemic malaria areas, based on the premise that biting by infective vectors would be prevented or reduced.

In 1982, fenitrothion (FNT) was introduced to enhance control by interior spraying. Despite numerous studies in various parts of Thailand using either FNT or DDT (1 or 2 cycles), no real proof of the reduction of infective man-bites in houses has been shown. In addition, problems in experimental design have prevented definitive conclusions on the spray effects on the vector population. The presence of several members of a species complex in a study area compounds the difficulties in these analyses of spraying effects.

In summary, the Malaria Division is really faced with two primary control problems:

- What is the vector to be controlled?
- Does interior residual spraying affect the vector population enough to reduce malaria transmission in an area?

Changes in the overall control program should be based on the answers to these two questions. Control strategies may very well be dependent upon different epidemiological situations.

C. Epidemiological/Entomological Data Collection and Interpretation

It has long been recognized by both national malaria control staff and international advisers and consultants that the present system of collecting and analyzing epidemiological data is extraordinarily cumbersome and provides very little information of operational utility. It is based on obsolete operational strata related to the early program of malaria eradication and currently produces little more than rough incidence figures related to broad geographical areas. As the data are currently collected and analyzed, it is impossible to obtain valid information of basic importance, such as age/sex ratios, origin of "imported" cases, occupation-related incidence, to say nothing of changes in incidence at the peripheral level.

This last consideration was addressed by Cullen et al., 18 when an attempt was made to devise an "early warning system" for
malaria outbreaks at the district level. This system represented a significant improvement over previous attempts to monitor incidence but has been somewhat difficult to maintain in practice, largely because of a dramatic decrease in malaria incidence nationwide beginning in 1983. This change in the baseline and the necessary reconstruction of the floating averages has caused some confusion and a loss of enthusiasm for the system at the district/sector level. The concept of the early warning system, however, must be viewed as a serious attempt to utilize incidence data for operational decision-making.

Sector office personnel are still saddled with the onerous task of completing six to ten monthly report forms aimed at relating incidence data to various, somewhat arbitrary operational strata. Data characteristically flow from clinic to sector to unit (zone) to region to Headquarters. At each step, they are recopied, reorganized, typed and inevitably, errors are introduced and compounded. Information reaching the central level has had much of the important data (e.g., age and sex) eliminated during its journey, resulting in the production of figures that are nearly useless for any reasonable epidemiological interpretation. Attempts to improve the system have characteristically resulted in the addition of one or more forms and there has been great reluctance to drop any previously devised forms.

The consultant team felt that there is a pressing need to revise the epidemiological reporting system in order to simplify the input required at the most peripheral level, to reduce or eliminate altogether the need for partial data reduction at the unit (zone) and regional levels, and to make optimal use of newer information technology at the Headquarters (or possibly regional) level.

A certain amount of data-processing sophistication exists at the Division Headquarters, where an Apple II and IBM-XT compatible are in use. Unfortunately, this equipment is largely used to generate traditional incidence data and attractive graphs, but is not put to any creative use.

The consultant team felt that it should be possible, with existing technology, to devise a one-page form, to be filled out at the periphery by the malaria staff member making contact with the positive case, which could then be automatically added to a data base (perhaps through the use of an optical scanner). Using a properly devised, simple form and appropriately developed software, it would be possible to obtain valid epidemiological
information of great importance to planning control operations. For this purpose a two-consultant team would be required -- a malarriologist/epidemiologist with practical knowledge of the sources and uses of malaria information and a computer expert, optimally one with experience in public health data handling.

It is likely that a microcomputer system (e.g., IBM-AT), possibly with an additional hard disk for data storage and several terminals, would suffice for this purpose, and that a minicomputer would not be required. That is important, since Ministry regulations would most likely not permit purchase and installation of a minicomputer in the Malaria Division.

It is also envisaged that, as newer information, such as the results of seroepidemiological surveys and entomological data (e.g., sporozoite rates as determined by the new ELISA or DNA probe technology) becomes available to the program, such information can be integrated into the data base, resulting in an optimally complete range of epidemiological information.

V. PRIORITY RESEARCH AREAS

A. Identification of Transmission Models

Background

Ecologically, Thailand has changed dramatically during the last 20 years. These ecological changes have been brought about by man’s activities, primarily extensive mining, logging, and modern farming. Gone is much of the forest that formerly covered foothills and mountains. Monocultures of rubber, fruit trees, corn, tapioca, and sugarcane are replacing the natural forests.

With extensive changes in flora, there can be extensive changes in fauna, including mosquitoes. How does this affect transmission of malaria? For example, does Anopheles dirus disappear from areas cleared of forest? Is it able to reestablish itself in mature fruit and rubber monocultures? Do mining and deforestation practices create better breeding situations for An. maculatus or do they bring man into closer contact with An. dirus? Do irrigation practices increase the breeding period of An. minimus? The data necessary to clearly answer these questions have not been collected, although a number of studies have been made.8,9,19-22
Need

The effectiveness of malaria control depends upon the degree of interruption of the transmission cycle. The transmission cycle can be interrupted by preventing man-vector contact, by killing gametocytes or preventing their formation, by killing the vector, or by preventing the completion of the sporogonic cycle in the mosquito. The accomplishment of one or more of these means of interruption in a particular area relies on a thorough understanding of the transmission dynamics. To gain this understanding of malaria transmission in Thailand, models of representative transmission situations need to be intensively studied. Specific examples of important models to be examined are as follows: tin mines in southern Thailand; rubber plantations in southeastern and southern Thailand; villages in fruit-growing areas; recently cleared foothills with farmhuts; sugarcane plantations; various activities of man in natural forests; and hilltribe villages in forested foothills.

Control Application

A thorough understanding of a particular transmission situation is necessary for proper control. By establishing transmission models for Thailand, control policies can be tailored to increase efficiency, and thereby, decrease needless expenditure. For example, in rubber plantations man-vector contact may only be during the tapping period from midnight to sunrise; therefore, residual spraying might be inappropriate, but use of repellents might be effective.

Hypotheses

There are eight major epidemiological situations in Thailand in which the majority of malaria transmission takes place.

Schedule of Completion

Each of eight transmission models should be studied in a particular area for a minimum of two years to account for seasonal and yearly variations. Dr. Chusak will determine transmission models for rubber plantations and forest activities in southeastern Thailand. He will begin work in January 1987 and carry on field collections for two years. For other models, consultants are needed to assist in protocol preparation, funding for data collection, and two years of field work. These projects could begin by mid-1987 but more likely would begin in 1988. Final models and delineation of proper control activities could be completed by 1991.
B. **Vector Incrimination**

**Background**

The Malaria Division lists as its principal malaria vectors, *Anopheles dirus* (= balabacensis), *An. minimus*, and *An. maculatus*. The secondary vectors are considered to be *An. sundalicus* and *An. aconitus*, and suspected vectors are *An. campestris*, *An. philippinensis* and *An. culicifacies*. In the last ten years, however, almost no salivary gland dissections have been made in connection with man-biting studies. Limited areas have been studied by investigators from other institutes who have looked for sporozoite-positive mosquitoes. From these dissections, only *An. dirus* complex mosquitoes were found to be infective, although several species (e.g., *An. maculatus*) were found with oocysts.

Much research has been conducted on sibling-species complexes in Thailand but mostly from a taxonomic viewpoint. Some basic malaria susceptibility trials also have been made. We know that at least four species of the *An. dirus* complex and six species of the *An. maculatus* complex occur in Thailand. These species are found in various regions and ecologically distinct situations. Their susceptibility to malaria parasites varies, as does their propensity to feed on man. *Anopheles minimus* shows two distinct behaviors in host feeding.
There has been rapid progress in the development of tools to identify members of species complexes and to detect infective mosquitoes. It is now possible to use an ELISA method to identify sporozoites in dried mosquitoes. This technology is available to investigators in the Malaria Division and could aid them in the determination of Thailand's primary vector.

Need

In the early years of the malaria control program in Thailand, *Anopheles minimus* was the most important vector, and control efforts were aimed specifically at this species. Due to its endophilic and endophagic behaviors, interior residual spraying with DDT controlled it in many areas. The situation now has changed, however, and *An. minimus* is no longer endophilic and endophagic, but rather is exophilic and zoophagic. Due to frequent incursions into the forest by man, the contact with the *An. dirus* complex has increased greatly. Does this mean that, overall, more people are being bitten by infective *dirus* than by infective *minimus*? There is an urgent need to answer this question because the interior residual DDT or FNT spray program has little effect on members of the *An. dirus* complex.

Control Application

Determination of the most important malaria vector in an area is the first step in designing an effective mosquito control program. Once the vector is identified, its biology and bionomics can be studied to focus on potential control points. Modifications in control efforts can be made then to reduce the risk of malaria transmission by this species (e.g., repellents or repellent-impregnated bednets).

Hypotheses

Members of the *Anopheles dirus* complex are the primary vectors of malaria in most endemic areas of Thailand.

Schedule of Completion

Dr. Chusak, with funding from BOSTID, will set up an ELISA lab to detect and identify sporozoites in mosquitoes starting in November 1986. He should have a working lab by January 1987. This lab should be able to support other projects within Malaria Division by 1988.
Taxonomic keys for members of the *An. maculatus* complex will be published in the next few months by AFRIMS. It is hoped that a taxonomic key to the *An. dirus* complex will be ready in six months at WRAIR. If not, there are more complex methods (i.e., electrophoresis and DNA probes) that are in the final stages of development. These could be used by the Malaria Division by mid-1988, if funding to support these costlier technologies were forthcoming.

Since mosquito specimens could be provided from the projects listed in V-A, scheduling would coincide with the schedule of completion listed in that section.

**Budget (per year)**

1. ELISA supplies and reagents $ 3,000
2. Additional ELISA equipment 2,000
3. Technician for ELISA 1,500
4. VBC consultant (for ELISA) 10 days 3,000
5. Local consultant per diem (14 days) 500
   (for taxonomy)
6. Mosquito collection costs
   (included in V-A.2 budget)

Total $10,000

For two years $20,000

**C. Value of Control Activities in Vector Reduction**

**Background**

During the past 30 years, the malaria control of vectors in Thailand has been based on the assumption that interior residual insecticide spraying reduces the infective vector population. The reduction is due to direct mortality of adult mosquitoes (i.e., FNT), shorter life span of the female mosquitoes, excito-repellency effects of the pesticide (i.e., DDT), and selection against man-biting populations of *Anopheles minimus*. At least this is what was (or is) thought. The reported data show several things:
1. *An. minimus* populations are no longer endophilic and endophagic.

2. There are both zoophilic and anthropophilic populations of *An. minimus*.

3. *An. minimus* is not resistant to DDT.

4. *An. minimus* may be repelled by DDT.

5. Parity rates in *An. minimus* caught on bovids are higher than those caught on humans.

6. Parity rates of *An. minimus* are higher (not lower) in sprayed villages.

7. Overall populations of *An. minimus* fluctuate seasonally in villages with little relationship to spraying cycles with either DDT or FNT.

Since malaria incidence does not necessarily decrease in villages that have been sprayed once or twice a year with DDT or FNT, alternative methods have been tried. The use of surface-feeding fish, like guppies, has been particularly popular as a way of possibly reducing *An. minimus* in streams. Larvicides like ABATE and Bti have been tested also. Thermal fogging against adult mosquitoes also has been tried to a limited extent. These alternative methods have not significantly reduced man-biting by *An. minimus* in the test villages.

Need

A great proportion of the budget of the Malaria Division goes into the house-spraying program to pay for insecticide, spraymen, sector personnel, and other pertinent staff. Yet, there has been little proof from recent studies that interior spraying reduces the number of infective bites (the only important aspect) that the house occupant receives, whether in a village house or in a farm hut. Definitive studies in the major control areas in Thailand should be carried out in the next 2-3 years to prove or disprove the usefulness of residual spraying in Thailand with the current epidemiological situation. Farm huts need to be addressed as a separate item since there has been a major shift in spraying policy, (i.e., spray farm huts, not village houses) in certain areas of Thailand.
A lot of effort has gone into production and distribution of larvivorous fish into small streams to control larvae of An. minimus. The aim is to reduce the number of An. minimus biting man; the assessment usually is based on point-prevalence surveys or passive-case detection. Of course, the research has shown nothing since results depend upon many things other than the actual consumption of larvae. There is an immediate need for a definitive study just to prove or disprove that released fish in a stream reduce significantly the number of An. minimus larvae in a defined area. Any other considerations of adult densities, malaria transmission, and fish survival are premature until this one point is proven.

There is a need to look at alternative measures to reduce the density of man-biting vectors and the number of bites received each night. Impregnated bednets may prove to be effective and should be evaluated.

Control Application

The impact of interior residual spraying of insecticide will determine if this type of program has a control application in Thailand at present. If well-designed studies show no significant effect on primary vector populations and man-vector contact, then consideration should be given to changing control strategies. In limited ecological and epidemiological situations, anti-larval measures may be considered (ABATE, Bti, fish?, stream clearance?), but these are generally expensive and have only short-term effects. Impregnated bednets may hold better promise for control of malaria in Thailand. These nets offer protection from biting and may kill mosquitoes that land on the impregnated fabric, potentially reducing the vector population.

Hypotheses

Spraying of interior house walls with a residual insecticide will reduce significantly the number of infective vectors biting man.

A high number of larvivorous fish released into a stream will reduce significantly the number of larval anophelines.

Impregnated bednets will reduce significantly the number of infective vectors biting man.
Schedule of Completion

Projects to prove or disprove the significant impact of residual insecticides need a minimum of two years to complete following funding. These projects should start in early 1987 and should be finished by mid-1989.

A simple larvivorous fish project could start this year with very few funds but may have to wait until peak An. minimus breeding in early to mid-1987. Only a few months would be needed to complete the study.

The impregnated bednet project will require external funding for a two-year period. Therefore, project start-up could be mid-1987 and completion mid-1989.

Budget (per year)

Impact of spraying (four sites)

1. Equipment and supplies for budget insecticide application
   Operational

2. ELISA supplies and reagents
   Budget (V-B)

3. Mosquito collection costs
   $ 3,000

4. Per diem for PI
   1,000

5. Transportation
   1,000

6. VBC consultant (two weeks/year) two times per year
   8,000

Total one site $13,000
Total four sites (6)+(3),(4),(5)x4 28,000
Total two years $56,000

Larvivorous fish (one year)

1. Supplies and equipment
   $ 500

2. Mosquito collection costs
   500

3. Per diem for PI
   500
4. Transportation  
Total cost $2,000

Impregnated bednets (two years)
1. Supplies and equipment $1,000
2. Mosquito collection costs 1,000
3. Per diem for PI 1,000
4. Transportation 1,000
5. VEC consultant (two weeks) 4,000

Total cost $8,000
Total cost (two years) $16,000

D. Alternative Methods for Anopheles dirus Control

Background

Anopheles dirus A may very well be the most important vector in Thailand in terms of malaria transmission (total cases caused by its bite). Certainly, the members of the dirus complex play an extremely important role in forest malaria transmission. Species in this complex are thought to be exophilic and exophagic, and therefore, do not lend themselves to easy control by interior residual insecticides. Resistant species in this complex have not been noted and excito-repellency effects from DDT have not been seen. These are not unexpected findings since members of this complex do not rest on inside walls but on outside vegetation. Unfortunately, the immature stages of this complex are very difficult to locate, making anti-larval measures useless in most situations.

Since standard control measures are ineffective against the An. dirus complex, alternative measures have been considered and tried. Smoke coils and repellents have been used with some positive results. Bednets can prevent biting, and permethrin impregnated bednets could cause mortality of mosquitoes. That land on the net; impregnated clothing also may be effective. Extensive vegetation clearance may exert a negative effect on members of the dirus complex seeking a resting site or a host. Although there has been extensive vegetation clearance in
Thailand, no one has examined the effects on dirus populations.

Need

Because the An. dirus complex is of primary concern and because standard control procedures are ineffective against these mosquitoes, there is a great need to determine alternative methods to reduce dirus biting. Methods are available, but they must be carefully tested before conclusions on their usefulness against these species can be reached.

Control Application

The use of repellents or smoke coils may reduce biting by infective An. dirus but probably will not reduce the population. Impregnated (permethrin) bednets and clothing should reduce biting by members of the An. dirus complex and may reduce actual numbers. Extensive vegetation clearance may impact on populations of dirus and may reduce biting.

Hypotheses

The use of skin repellents and/or smoke coils will reduce the number of man-bites per hour by members of the Anopheles dirus complex.

Permethrin impregnated bednets and/or permethrin impregnated clothing will reduce the number of man-bites per hour and will reduce the actual numbers of members of the Anopheles dirus complex.

Extensive vegetation clearance will reduce the numbers of members of the An. dirus complex attempting to bite man in an area.

Schedule of Completion

The members of the An. dirus complex are found in low numbers in general, making them hard to sample and data interpretation difficult. To overcome these problems, samples should be collected frequently over one or two years. Repellent effects on dirus biting could start immediately and should be conducted over a year. Impregnated bednets and clothing tests will need to be funded and probably could not start before mid-1987. The same is true of the vegetation clearance study. These studies would require two years and could be finished by mid-1989.
## Budget

### Repellent study (one year)

1. Supplies and equipment $500
2. Mosquito collection costs 500
3. Per diem for PI 500
4. Transportation 500

Total cost $2,000

### Impregnated bednets/clothing (two years)

1. Supplies and equipment $1,000
2. Mosquito collection costs 1,000
3. Per diem for PI 1,000
4. Transportation 1,000
5. VBC consultant (two weeks) 4,000

Total cost $8,000

Total cost (two years) $16,000

### Vegetation clearance (two years)

1. Supplies and equipment $1,000
2. Mosquito collection costs 1,000
3. Per diem for PI 1,000
4. Transportation 1,000

Total cost $4,000

Total cost (two years) $8,000
E. Collection and Interpretation of Data

Background

Since the initiation of the malaria program in Thailand approximately 30 years ago, a system of reporting data of interest to the program has developed in response to changing orientation and priorities. Particularly during the "eradication" era, reporting forms were used which are inappropriate to the current strategy. Using the current system, it is difficult or impossible to obtain information of crucial importance to a control program which will respond principally to local epidemiological situations including occupation-related exposure, migration patterns, and changing patterns of infection. In order to use resources and personnel most efficiently, the program needs a more useful way to monitor malaria incidence. If it is determined, for example, by age and sex analysis and source of infection data that an increasing incidence of malaria from a certain village is the result of labor circulation to the forest (as would be suggested by the majority of cases occurring in adult males) there will be less pressure to make a major effort to increase spray coverage within the village.

A parallel data collection system would be set up in a pilot area (e.g., one unit or zone) in order to compare the old and new systems. Data would be manually entered into a database (e.g., using dBase III) and analyzed weekly. At the end of a six-month trial period, the parallel systems would be compared with regard to sensitivity, speed of feedback, and provision of information useful for making operational decisions.

Hypotheses

A single, properly-designed form filled in by peripheral malaria staff for each positive use and computer-analyzed using simple database software can provide more information than all of the other data currently collected on the epidemiology forms used by the program.

Schedule of Pilot Project

January 1 - December 31, 1987

Budget

IBM-AT - compatible microcomputer $ 5,000
### Salary for Data Entry Personnel

- **Two people at $7,000/year**
  - **Total:** $14,000

### Salary for Field-Level Supervisor

- **One person at $7,000/year**
  - **Total:** $7,000

### Overtime Pay for Sector Personnel

- **Ten people at $50/month x 12 months**
  - **Total:** $6,000

**Total:** $32,000

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**F. Policy for Management of Fever Cases**

Thailand has the most difficult problem with drug-resistant *P. falciparum* currently faced by any malarious country. The national program's policy (a remnant of the malaria eradication strategy) of giving a presumptive dose of antimalarial drug to villagers visiting malaria volunteers has become even more problematic with the incrimination of commonly-used sulfonamide-containing antimalarials in the production of severe allergic reactions. Since resistance to 4-aminoquinolines is so prevalent, these drugs are the only ones available which are sufficiently active. Of the people receiving presumptive doses of medication, only 5-10 percent subsequently prove to have malaria. The remainder receive a potentially toxic drug with no therapeutic indication.

A nationwide network of malaria volunteers (Village Voluntary Collaborators) was established with major USAID assistance in the years 1978-81 and now numbers 40,619 (see Annex 8). These volunteers function as passive case detection posts; they take blood slides from fever cases and dispense "presumptive" antimalarial drugs which are intended to reduce parasitemia and relieve symptoms while the slides are being examined. When a positive result is obtained, sector personnel return to give the patient radical treatment.

The Malaria Clinic system, one of the most important innovations of the Thai malaria program, has obviated the need for presumptive treatment in many areas where the clinics are easily accessible to at-risk populations. Many areas, remain, however, where remote villages are not in easy reach of clinics, and there is a real risk of infections getting out of control. The best way to reach these remote populations and prevent death and severe illness needs to be determined. A properly developed alternative system could result in eliminating the need to use presumptive treatment in such areas.
At the Malaria Division, researchers are already studying some alternative techniques, including mobile microscopists on motorcycles who drive to villages to read slides collected by volunteers, and fixed-schedule mobile clinics.

Areas where presumptive treatment is considered indispensible must be better characterized. A research project designed to examine such areas and to evaluate and compare various approaches would provide valuable information for planning purposes. Such approaches include "autonomous" malaria clinics established to require less outside supervision, volunteers, perhaps paid, who could be trained to read malaria slides using monocular and natural light microscopes.

Hypotheses

Alternative systems for case detection and treatment will reduce demand for presumptive treatment and will increase protection of at-risk populations in remote areas.

Schedule of Completion

A two-year project could begin in early 1987.

Budget (two years)

Salaries (two field investigators x two years) $24,000
Travel and per diem 12,000
Consultant (two person months) 10,000
Total $46,000

G. Collection of Background Data Leading to Rational Development of Alternative Policies

Background

In recent years there has been a decentralization of some aspects of the anti-malaria program, with an increasing degree of integration with primary health care. In a review of the program (see Addendum 1), it was indicated that "the steady decrease in mortality and morbidity in the last few years is attributed to the expansion of primary health care delivery and the establishment of malaria clinics providing prompt diagnosis and treatment... a country-wide service of village volunteers has
been established and a great deal of emphasis is being given to personal protection." The Village Voluntary Collaborator (VVC) assists in taking blood smears and giving presumptive treatment to people suspected of having malaria (see Section V(F)), and assists in spraying operations, being controlled at the first level by malaria field workers who collect blood slides, replenish drug supplies and provide health education materials for use in community instruction. Large amounts of such materials, including posters, radio/cassette tape recorders, and movies (such as a Malaria Program film made in 1981), have been supplied by the U.S. Agency for International Development and have proved valuable.\(^{11}\)

The VVCs also collaborate closely with the Malaria Clinics, established in 1979 and now numbering 454 (432 a year ago). The clinics are located strategically in high transmission areas, marketing centers, and on migration routes (see Annex 7). The program now has 40,619 VVCs working in the Control Area and the Eradication Area (see Annex 8); this compares with 41,048 a year ago.

Expansion of the VVC system has been a major advance towards integration of the malaria program and primary health care. Approaches to such integration have in general been the subject of a number of WHO documents.\(^{12,13}\) Stress has been laid on the need to investigate social and economic as well as technical and operational constraints to integration. In rural Thailand, awareness of the disease is greater among villagers in the Control Area than in the less afflicted Eradication Area, and this influences the use of available services. It has been stated that "illness behavior of malaria was found similar to the general pattern of care-seeking behavior of rural villagers the main feature of which is the sequential use of alternative treatment resorts, starting from the more to the less geographically and socially accessible treatment resorts."\(^{14}\) These investigators point out that new approaches and methods are needed in Thailand for implementation of malaria control in the context of primary health care at the community level, and that support is particularly necessary from the health education sections of the malaria control program. Community participation in malaria control should start with treatment activities, and subsequently extend to aspects of the program such as personal protection and vector control. This was, in fact, one of the secondary objectives of the Health Development Plan No. 5 covering the period 1982-1986, while establishment and support of Village Voluntary Collaborators was a main objective.
Trials have recently been undertaken, commencing in Region II, to define the duties and coverage of individual malaria field workers in the context of the village malaria volunteer program and the clinics. These duties include (1) regular visits to PCD posts, (2) investigation of slide positive cases and administration of radical treatment, (3) follow-up of these cases, (4) supervision of spraying operations, (5) special case detection in silent or suspect areas, which are mostly outside villages, and (6) motivating and supporting community participation in malaria control.

Further integration with primary health care will require amalgamation of the Village Voluntary Collaborators with general-purpose Village Health Volunteers, although the malaria situation and particularly the pervasive problem of drug resistance make it unlikely that the specialized work of the malaria clinic can be modified in the foreseeable future in the control areas. It has already been suggested that demonstration projects should be undertaken for the gradual conversion of malaria workers to multi-purpose health workers, initially in Region II and then in each of the other regions. There should be no illusions concerning the difficulties that will confront these health workers, however, particularly in diagnosing cases and administering radical treatment to the extent necessary. In Chanthaburi province, for example, it has been ascertained that 57 percent of patients went to the local drug seller for self-treatment when they became ill.

House spraying with DDT has been studied with reference to community understanding of its purpose, based on health education, and acceptance; these two were found to be closely related in all but a few instances where individuals in superior quality houses understood the purpose but rejected spraying on grounds of inconvenience or damage.

Need

In view of these considerations as well as for budgetary reasons, there is clearly a need to examine the feasibility of developing alternative policies to the mainly mono-disease oriented program against malaria now in operation. Preliminary work along these lines is in progress, both in respect to integration of malaria personnel and primary health care personnel (VVCs and VHVs), and identification of those control methodologies, such as personal protection and simple vector control that may be used by villagers and communities under expert guidance. Care should be taken, however, to ensure that the present specialized input of the anti-malaria program in its
many aspects is not discarded in favor of inadequately planned, supervised and implemented community-level efforts.

Control Application

The several approaches to further integration of the anti-malaria program and primary health care involve interaction between PHC multi-purpose workers, the Village Health Volunteers, and members of the community. Expertise would be provided by a cadre of specialists (malarialogists and entomologists). Special units at central and regional levels would be required for statistical (computerization) purposes and for monitoring of drug or insecticide resistance. It is not envisaged that the Malaria Clinics will be integrated in the foreseeable future.

Measures that might be further integrated included diagnosis and radical treatment; presumptive treatment (allowing for the prevalent constraint of multi-drug resistance), personal protection by use of repellents, coils and bednets, and simple vector control directed against larval or adult stages. In addition, reporting systems and inter-sectoral liaison will need development. All of these are subject to scientific study, but the first questions to be asked are (1) to what extent (in terms of ability and time involved) can multi-purpose PHC workers reliably incorporate anti-malaria activities in their workload and (2) how effectively can different types of communities, allied in future with the VHVs who will assume the functions of the VVCs, utilize the measures indicated.

Hypotheses

Any study must distinguish between the various levels of participants in an integrated program (PHC level and below), isolating for study as few variables as possible. There are two aspects: the time and enthusiasm to undertake integrated duties, and the ability to do it well. In terms of output, the latter may be improved progressively by experience and practice, or may deteriorate. The three hypotheses that follow relate simply to ability to learn and do the basic job, and not to quality of achievement which would have to be measured against a baseline.

Hypotheses 1

Multi-purpose PHC workers have the time and can be trained to undertake the duties of malaria field workers, including (1) case detection, microscopic diagnosis, radical treatment, and follow-up; (2) supervision of spraying operations; (3) special case detection in silent or suspect areas; and (4) motivating and
supporting community participation in malaria control (health education).

Hypotheses 2

Village Health Volunteers have the time and ability to be trained to undertake the duties of Village Malaria Voluntary Collaborators, including (1) fever recognition, presumptive treatment where feasible (allowing for drug resistance), and taking blood films; (2) assistance with control activities such as spraying; and (3) educating of the villagers to recognize the disease and employ measures for its control or avoidance, such as use of repellents, coils, bednets, or chemoprophylaxis.

Hypotheses 3

Communities with different social, economic, occupational, and educational backgrounds are capable of learning and implementing anti-malaria measures such as fever treatment, personal protection, and vector control in simple form.

Schedule of Completion

Each hypothesis will require testing in the two main situations of Control Area and Eradication Area, preferably under socio-economically contrasting situations within each of the five regions. Since a considerable body of retrospective information should be available, the studies may be limited to one year.

Budget

Much of the work in this investigation involves obtaining information at PHC centers and at the community level, and is of a sociological rather than a malarialogical nature. It may be undertaken by administrative staff at the regional malaria offices, the detailed design having been drawn up by a national principal investigator assisted by one international and one or two national consultants. The latter individuals with some experience in the subject may be found at national universities, while an international consultant experienced in the problems in other countries would be available in the United States. At the community level, it will be necessary to employ information-gatherers acceptable and trusted within each community, to work with the local VVCs.

A tentative budget for a one-year study is as follows:
Salaries: National principal investigator
(15 percent of time) $1,000

Equipment/material: Data collecting and recording 500

Travel: (1) Malaria personnel within each of the five Thai malaria regions 1,500
(2) National consultants (seven days x ten) 2,000
(3) VBC international consultant (three weeks) 6,000

For one year $11,000

H. Migration Patterns

Background

Movement of people provides one of the major constraints to successful malaria control in Thailand. Three levels of "migration" can be identified:

a. Labor circulation, e.g., from the village to a nearby forest for logging or hunting

b. Within-country, long-distance migration of temporary labor, e.g., northeastern peasants moving to Kanchanaburi sugar cane plantations during the dry season or northern farmers travelling to Chanthaburi for rubber-tapping or gem-mining

c. International migration, e.g., labor teams to the middle east, which entails little malaria risk, or people crossing illegally into Kampuchean border areas for gem-mining, which carries a near-certain risk of malaria.

It is essential to understand these different types of population movement and to appreciate their impact on the local situation (e.g., if the source of the migrants is an area from which the parasite reservoir has been eliminated but vectors persist, reintroduction of convalescent gametocyte carriers may re-establish the transmission cycle). Also, introduction of large numbers of non-immune migrants into an area of intense falciparum transmission may result in epidemics of severe and even fatal infections, overwhelming local diagnostic and therapeutic facilities.
The motivation of migrants should be understood. Does the financial return resulting from migration really justify the social displacement and risk of disease? This information could then be used in health education programs.

The average duration of stay, and in the case of long-distance migration, the organization of the laborers should be documented in order to determine whether special approaches, e.g., the identification and training of malaria workers from among the migrants, are feasible.

A small study concerned with local labor circulation is about to begin in the northern province Chiangmai. On a larger scale, further work needs to be done covering other important sources and destinations of migrants. Any such work should, however, be planned in consultation with the northern group, headed by Dr. Anchalee Singhanetra of Chiangmai University.

It would seem most appropriate to recruit an experienced consultant to be based for several months at the headquarters of the Malaria Division in Bangkok. The consultant would, in collaboration with a Thai investigator from the Malaria Division, perform a feasibility study of the situation based on field investigations of representative field sites.

Hypotheses (for the feasibility study)

Labor circulation and labor migration are the most important and least understood human factors contributing to malaria incidence in Thailand.

Schedule

After a suitable consultant is recruited, the feasibility study must be expected to take at least 4-6 months, e.g., Jan.-June 1987.

Budget

<table>
<thead>
<tr>
<th>Description</th>
<th>Cost</th>
</tr>
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<td>Consultant for six months</td>
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<tr>
<td>Local travel</td>
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</tr>
<tr>
<td>Local travel expenses for national counterpart</td>
<td>3,000</td>
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<tr>
<td><strong>Total</strong></td>
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</table>
VI. MEANS OF APPROACHING THE RESEARCH NEEDS

A. Workshop on Proposal Preparation, July 23-29, 1986

A principal task assigned to the Team was to train national workers in the several steps of designing research proposals. A workshop on Proposal Preparation was organized by the Malaria Division of the Ministry of Public Health, and occurred July 23-29, 1986 at Division headquarters in Bangkok (see Annex 4 for the schedule). The participants, Malaria Division personnel (see Annex 5 for list), were organized into four groups. Each group dealt with a general researchable topic, within which were a number of subtopics. The participants were assigned to the general category of topic most compatible with their area of expertise, and were requested to select among the subtopics.

The researchable topics selected by the instructors for the training workshop related to principal problems being encountered by the anti-malaria program, as follows:

Group 1: Control of malaria outside the village

1. Optimal control measures in farm huts
   a. Use of residual insecticides?
   b. Use of bednets?
   c. Use of impregnated bednets for personal protection and/or vector reduction?

2. Measures for personal protection of forest workers
   a. Repellents?
   b. Smoke coils?
   c. Impregnated clothing?
   d. Bednets (impregnated or not)?
   e. Chemoprophylaxis?

3. Measures for protection of rubber tappers
   a. Repellents?
   b. Smoke coils?
   c. Impregnated clothing?
   d. Bednets (impregnated or not)?
   e. Chemoprophylaxis?
Group 2: Vector bionomics

1. Forest ecology of vectors
   a. Is the vector ecology in "created forests" (fruit orchards, rubber plantations, etc.) the same as in natural forests?
   b. In settlements situated in deforested and forest fringe areas - (i) What is the anopheline fauna? (ii) Which vectors are most important for malaria transmission?

2. Control of An. dirus
   a. Does vegetation clearance interfere with An. dirus feeding?
   b. Do insecticide impregnation techniques (e.g., in bednets or in clothing) have a place in control of An. dirus?

3. Control of vectors other than An. dirus
   a. Other than An. dirus, do any Thai anophelines contribute significantly to malaria transmission?
   b. Do larvivorous fish have any place in malaria control in Thailand?
   c. Is stream clearance useful for control of An. minimus?

Group 3: Data collection and interpretation

1. How might essential basic parasitological and entomological data collection be standardized and reported?

2. How should data be summarized, analyzed and interpreted (computerization) in organizing and directing the control program?
   a. With reference to the routine program (e.g., cost-effectiveness of spraying)
   b. With reference to special programs (e.g., vaccine trials, or monitoring of drug or insecticide side-effects)

3. Do passive case detection data reflect, in any way, the status of malaria transmissions in an area?
Group 4: Strategy

1. What is the relevance of new technology for insecticide susceptibility testing?

2. What is the desirable make-up of spray teams in terms of use of community personnel?

3. Since presumptive treatment is no longer generally recommended, what is the most effective role of malaria volunteers in areas of multi-drug resistance?

4. What is desirable in terms of antimalarial drug usage?
   a. Do any new compounds have a place in treatment of resistant *P. falciparum*?
   b. Does chloroquine have any use as presumptive treatment?

5. What is the role of serum antibody levels (blood stage, sporozoite) in operational decision-making?

The members of each group selected what they considered to be the more important researchable problems from among these subtopics. Then in plenary session, they were instructed in the sequences of producing a research protocol, under each of the following steps:

1. Hypotheses
2. Objectives (general and specific)
3. Introduction
4. Experimental Design (materials and methods)
5. Budget and Justification

After presentation of each of these steps, the participants separated into their groups to apply it to their selected topics. They then presented the results in plenary for criticism. The amended versions were used for further development in the next step.

The research proposals emerging from this training exercise are considered in the ensuing section.
B. Specific Research Proposals Emanating from the Workshop "The Hypotheses" Exercise

Group 1: Control of malaria outside the village

a. "DDT spraying will reduce the number of vectors biting man in farm huts."

Comment: A good hypothesis. Selected for further development in the Workshop.

b. "Skin repellent, impregnated clothing, and bednet (non-impregnated) can be used for reducing man-vector contact."

Comment: Too many variables. Better as "Non-impregnated bednets will reduce man-vector contact in farm huts."

c. "The optimum control in farm huts can use chemoprophylaxis and bednet for self-protection during harvest season."

Comment: Better wording would be "Use of chemoprophylaxis and bednets for self-protection in farm huts during the harvest season will prevent malaria infection." Two protocols will be required to evaluate the two measures properly, or else the project will require four study groups (chemoprophylaxis, bednets, both, neither).

d. "CT Stop-Fly repellent can reduce man-biting contact about 4-6 hours during tapping."

Comment: Change "can" to "will." Otherwise, a good hypothesis. Selected for further development in the Workshop.

e. "Doxycycline can be used as chemoprophylaxis for malaria control among forest workers."

Comment: Imprecise statement. Better wording would be "Doxycycline prophylaxis will reduce malaria incidence in forest workers."
Group 2: Vector ecology

a. "Release of *Poecilia reticulata* in slow-running stream will decrease anopheline larval density."

Comment: Should specify anopheline species. "Release" is not sufficiently precise. "Introduction of large numbers of *Poecilia reticulata* every month in slow-running streams will decrease larval density of *An. minimus*" is more informative. This study was selected for further development in the Workshop.

b. "*Poecilia reticulata* will survive and increase their population in slow-running streams."

Comment: Delete the word "survive."

c. "*An. maculatus* are vectors of malaria transmission in Khon Kaen province."

Comment: Straightforward and clear. Delete "transmission." This study was selected for further development in the Workshop.

d. "Stream clearance will decrease *An. minimus* larval density."

Comment: Specify "stream clearance," e.g., "The removal of marginal stream vegetation will decrease..." 

e. "*An. aconitus* is a vector of malaria in Ubon."

Comment: Good.

f. "*Poecilia reticulata* in nature in northern Thailand feed on larvae."

Comment: This is an introduced fish, but some have been maintained in streams in Thailand for some years. Better wording: "Dissection of fish proves that *Poecilia reticulata* feeds on mosquito larvae in nature."

g. "Permethrin-impregnated bednets in non-sprayed houses will change the behavior of *Anopheles* vectors to exophagic."

Comment: Specify the vector, i.e., *An. minimus*. 
Group 3: Epidemiology

a. "Malaria Clinic data do not reflect the status of malaria transmission in endemic areas."

Comment: Specify what data will be examined. Re-word to "Malaria Clinic data alone do not reflect..." This study was selected for further development in the Workshop.

b. "Malaria infection data from children under nine years old is the parameter for malaria transmission."

Comment: Specify village transmission.

c. "IFAT and ELISA could be a tool for malaria vigilance in the partial integration areas."

Comment: Change "could be a tool" to "are useful tools." This study was selected for further development in the Workshop.

d. "Parasite rate from the village volunteer can reflect the status of malaria transmission in eradication areas."

Comment: Change "can" to "will."

e. "Analysis of EP3 form from every zone shows the pattern of labor migration."

Comment: Change "analysis" to "the data from."

f. "The resurgence of P. vivax in Songkhla province is related to sub-microscopic threshold."

Comment: "Missed diagnoses of P. vivax cases, due to low parasitemias not detectible by microscope, have contributed to an increasing pool of this parasite" might be better wording but is still not clear. It would be preferable to begin with a comparison of light microscopy and ELISA in vivax diagnosis.

g. "There is a relationship between Anopheles species and parasite species in southern Thailand."
Comment: Need to specify anophelines and plasmodia, and restate and focus - (i) "Change in ecology results in change in vectors," (ii) "the newly predominant vector is more efficient for transmission of \textit{P. vivax} than \textit{P. falciparum};" and (iii) "this explains the resurgence of \textit{P. vivax}.

Group 4: Strategy

a. "The use of 10 percent sucrose solution instead of human blood is effective for insecticide susceptibility testing of \textit{An. minimus} in the northern part of Thailand."

Comment: Change "is effective for" to "will support female anophelines for."

b. "The use of local woman spray teams instead of man to increase spray coverage in malaria region 3, Khon Kaen."

Comment: Change "to" to "will."

c. "Weekly fixed-schedule mobile Malaria Clinics will reduce use of presumptive treatment in high-risk areas."

Comment: Preferable as "Weekly fixed-schedule mobile clinics will reduce the demand for presumptive treatment by villagers." This study was selected for further development in the Workshop.

d. "Malaria volunteers can be responsible for the follow-up of malaria patients in control areas in eastern Thailand properly."

Comment: Better phrasing would be "Malaria volunteers are capable of accepting greater responsibility for malaria control activities..." This study was selected for further development in the Workshop.

e. "Chloroquine can prevent death in the low endemic area in Thailand."
Comment: Better phrasing would be "Response to chloroquine in Kanchanaburi is generally S, RI or RII, and therefore, this drug is still useful for presumptive treatment in that area. Must be done in hospital, on ethical grounds."

f. "The use of IFAT to indicate local epidemic in non-transmission area."

Comment: Change "non-transmission" to "low-risk," and make it a statement, i.e., "IFAT use will document the occurrence of recent transmission in an area considered to be low risk."

"The Objectives" Exercise

Each group continued the training exercise by developing the objectives (general and specific) for the two studies selected from the several submitted as hypotheses.

Group 1

Proposal (a)

General objective: "To determine the usefulness of DDT spraying in farm huts for the malaria control program."

Specific objective: "To compare the number of man bites indoors by An. minimus in DDT-sprayed and unsprayed farm huts."

Comment: If man-biting inside the huts is to be the specific objective of this study, then the title (hypothesis) needs to be changed to reflect this further focusing.

Proposal (d)

General objective: "To determine whether CT Stop-Fly repellent can be used as a supplementary measure in rubber plantation areas."

Specific objectives: (1) "To compare numbers of An. maculatus biting man before and after using CT Stop-Fly" and (2) "To determine the side-effects of CT Stop-Fly use in rubber tappers."

Comment: The stated objectives have been reorganized to reflect the priority better.
Group 2

Proposal (a)

General objective: "To know the role of An. maculatus in malaria transmission in northeastern Thailand."

Specific objectives: (1) "To determine which members of the An. maculatus complex are present in northeastern Thailand," (2) "to determine whether they are vectors through use of the ELISA technique for presence and species identification of sporozoites;" and (3) "to characterize the feeding behavior and seasonal prevalence of sibling species of An. maculatus."

Proposal (c)

General objective: "To determine the usefulness of Poecilia reticulata as a supplemental measure for malaria control."

Specific objectives: (1) "To determine An. minimus larval density in slow-running streams in northern Thailand," (2) "to determine An. minimus adult density in the same area;" (3) "to determine the survival of Poecilia reticulata in slow-running streams;" and (4) "to relate the distribution of fish to numbers of indigenous malaria cases."

Comments: The consultants felt that the objectives in proposals (a) and (c) should be more limited in their scope. Study (c) would be ambitious enough if it concentrated on An. minimus larval and adult density. Should an attempt be made to relate fish application to malaria incidence, a great number of additional variables would have to be considered, e.g., the possible presence of another vector, the efficiency of case detection techniques, and other matters.

Group 3

Proposal (a)

General objective: "To determine whether Malaria Clinic data reflect actual incidence of malaria."

Specific objectives: (1) "To determine the actual incidence of malaria in the study area," (2) "to identify biases of clinic data;" and (3) "to evaluate whether data collected by other surveillance measures reflect malaria incidence more accurately."
Proposal (c)

General objectives: (1) "To determine the reliability and feasibility of IFAT and ELISA in the detection of continuing transmission in an area from which anti-malaria activity has been recently withdrawn;" and (2) "to formulate a standard protocol for the use of these two techniques for this purpose."

Specific objectives: (1) "To compare various available sporozoite antigens and blood safe antigens with respect to their utility in documenting recent malaria infections;" and (2) "to determine a specific vigilance standard."

Group 4

Proposal (c)

General objective: "To reduce the presumptive demand by villagers and prevent parasite resistance to antimalarial drugs."

Specific objectives: (1) "To reduce the rate of presumptive treatment consumption by villagers to less than 20 percent of the current level;" (2) "to minimize the rate of presumptive treatment so that it is used in less than 5 percent of all cases detected by active case detection in the study area;" (3) "to reduce time lag and the transmission rate in the study area;" and (4) "to prevent parasite resistance to drugs used presumptively."

Comment: It was pointed out that these "objectives" were in fact operational targets, not research objectives. It was suggested that the general objective be worded as "To determine to what extent, if any, the use of presumptive treatment can be reduced by introduction of fixed-schedule mobile Malaria Clinics." The specific objectives then would need to be re-formulated also.

Proposal (d)

General objective: "To formulate a more suitable role for malaria village volunteers in an area of multiple drug resistance."

Specific objectives: "In order to determine the suitable activities of malaria village volunteers in eastern Thailand, several aspects of their work and approach would have to be investigated, such as: (1) Can they take and send malaria slides to the Malaria Clinic properly; (2) can they investigate malaria cases in the area; (3) can they be responsible for giving radical
treatment; (4) can they select and transfer cases correctly; (5) can they follow up vivax cases for relapse; (6) are they able to determine the malaria status in their area; (7) are they able to coordinate effectively with malaria personnel; (8) are they capable of leading the community in undertaking vector control and spraying operations; and (9) can they be taught to use monocular microscopes for malaria diagnosis. In addition, specific geographical, epidemiological, and sociological situations would invoke other activities and attributes of the village volunteers."

Comment: The consultants felt that an additional objective would be to evaluate the current productivity of malaria volunteers. The specific objectives indicated above were felt to be far too numerous, and should be limited to no more than three for the purposes of the investigation.

Following presentation and constructive criticism by their colleagues and by the consultants of their "Hypotheses" and "Objectives," the groups were then instructed in and prepared the subsequent parts of their research proposals, namely "The Introduction," where overall aims, rationale, and use of the literature were taught, "The Experimental Design," and "The Budget and Justification." These were presented to colleagues and consultants, and criticized and improved. It was felt by all participants, faculty and students alike, that the training course had been most useful although (on account of limited time) too condensed. Similar courses in future should allow at least seven if not ten full working days for full elaboration and drilling in the subject.

C. Identification of Funding Sources

The consultants recognized from the start of their mission that most research proposed to the Malaria Division would require external funding. If the projects do not meet funding criteria, then the Malaria Division will not be able to conduct needed operational research. Therefore, we spent much time trying to identify appropriate funding agencies or funding programs. We discussed the Malaria Division's research funding needs with a number of key personnel in USAID, WHO, and the Thai scientific community. Unfortunately, no one was optimistic about any substantial support of operational research by the Malaria Division, with the possible exception of WHO/TDR.
The following agencies or programs were considered:

(1) National Academy of Sciences
   - BOSTID Research Grants Program

(2) USAID
   - U.S. - Israel Cooperative Development Research Program
   - Program in Science and Technology Cooperation
   - Project Development and Support Funds
   - Emerging Problems of Development 2 Project
   - Science and Technology for Development Project

(3) World Health Organization
   - WHO/TDR program
   - WHO/SEARO Regional research funds
   - Research funds from the WHO country budget for Thailand

(4) Thai Sources
   - National Medical Research Council

D. Requirements for Consultants

It is recognized that consultants will be needed to assist the Malaria Division in detailed planning of research projects outlined in Section V - Priority Research Areas. As indicated in the telegram at Annex 6, the Mission and the Ministry of Public Health have requested the following:

- On or about December 1986. One consultant is requested for two weeks to assess and recommend possibilities for biological control of malaria vectors.

- On or about March 1987. One or two consultants are requested for one week to train entomology staff of the Malaria Division in ELISA techniques for identification of malaria parasites in mosquitoes and in the identification of new species. The consultants should be recruited from Armed Forces Research Institute for Medical Science (AFRIMS) in Bangkok.
On or about September 1987. One consultant is requested to follow up on the research activities to be carried out by the Mission. The consultant is expected to make recommendations on modification or improvement of research strategies originally developed.

This request may be considered by VBC in respect of recommendations for consultant assistance contained in the various items of Section V of this report. A list of potential consultants follows:

(1) **Entomology (projects V.A. - V.D.)**

**USA**

T. Burkot (IMR Papua New Guinea)  
F. Collins (CDC)  
G. Georghiou (U. of CA - Riverside)  
N. Gratz (retired WHO)  
B. Harrison (WRAIR)  
J. Hobbs (CDC)  
G. Jeffery (CDC - retired)  
D. Roberts (USUHS)  
R. Rosenberg (WRAIR)  
L. Self (WHO - Manila)  
A. Spielman (Harvard)  
R. Tonn (WHO - Geneva)

**Other Countries**

J. Cullen UK (former WHO)  
C. Curtis UK (London School)  
J. Hemingway UK (London School)  
J. Hii Malaysia (Malaysian Govern.)  
A. Ismail Egypt (WHO - Geneva)  
W. MacDonald UK (Liverpool)  
S. Meek UK (UNBRO - Bangkok)  
D. Muir UK (WHO - Geneva)  
C. Pant India (WHO - Geneva)  
R. Slooff Netherlands (WHO - Geneva)

(2) **Chemotherapy (projects V.F. - V.G.)**

**USA**

E. F. Boudreau (Washington, DC)  
C. C. Campbell (CDC)  
W. Chin (CDC)
Other Countries

C. Draper UK (London School)
W. H. Wernsdorfer West Germany (WHO - Geneva)

(3) Epidemiology (projects V.E. V.G. V.H.)

USA

D. Brandling-Bennett (CDC - Nairobi)
C. C. Campbell (CDC)
D. T. Dennis (New Hampshire State Health Dept.)
R. Desowitz (Hawaii)
T. Dondero (CDC)
T. Mack (Univ. of Southern CA)
L. Pang (WRAIR - BKK)
P. E. Winter (AIBS - Washington, DC)

Other Countries

P. F. Beales UK (WHO - Geneva)
L. Molineaux Belgium (WHO - Geneva)
J. A. Najera Spain (WHO - Geneva)
J. Pull France (retired - WHO)
H. J. Vanderkaay Netherlands (Leiden)

(4) Other Areas of Research

USA

S. Bjorge (Univ. Hawaii)
M. Ettling (Harvard - BKK)
B. Jacobs (Univ. Hawaii)
L. Miller (NIH)
M. Warren (CDC)

Other Countries

G. Gramiccia Italy
VII. LIST OF REFERENCES CITED


### ANNEX 1

**PROGRAM FOR VBC/USAID EVALUATION CONSULTANT TEAM**

Dr. R. G. Andre, Dr. E. B. Doberstyn, Dr. D. F. Clyde

<table>
<thead>
<tr>
<th>Date</th>
<th>Time</th>
<th>Activity</th>
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<tbody>
<tr>
<td>June 22, 1986</td>
<td>-</td>
<td>Dr. R. G. Andre arrives Bangkok</td>
</tr>
<tr>
<td>June 23, 1986</td>
<td>-</td>
<td>Visit USAID/Thailand</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>Courtesy call Dr. Surin Pinichpongse, Director of Malaria Division</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>Discuss terms of reference with Dr. Chusak Prasittisuk, Mr. Amnat Charoenkul, Mr. Samart Wongprayoon, Mr. Suthas Nudsathapana</td>
</tr>
<tr>
<td></td>
<td>a.m.</td>
<td>Prepare tentative program with Dr. Chusak Prasittisuk and Mr. Suthas Nudsathapana</td>
</tr>
<tr>
<td></td>
<td>p.m.</td>
<td>Proposal evaluation</td>
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<td>June 24, 1986</td>
<td>a.m.</td>
<td>Collect entomological information</td>
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<td></td>
<td>p.m.</td>
<td>Collect information about vector control operations</td>
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<td>June 25, 1986</td>
<td>a.m.</td>
<td>Meet director or USAID/Thailand Malaria Division</td>
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<td></td>
<td>p.m.</td>
<td>Collect data on entomology and epidemiology</td>
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<td>June 27, 1986</td>
<td>-</td>
<td>Meet Dr. Visut Baimai, Dr. C. A. Green, Dr. R. Harbach, Dr. Somsak Panthuwattana, Dr. Sakol Panyim, Mahidol University</td>
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<tr>
<td></td>
<td></td>
<td>Vector identification and biological control</td>
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<tr>
<td>June 28-29, 1986</td>
<td>-</td>
<td>Weekend</td>
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June 30 - July 3, 1986 - Travel to Chiangmai and Phrae
- Observe spray and insecticide resistance testing

July 4, 1986 - Malaria Division, Bangkok
- Analyze data
- Meet Dr. Supat, Faculty of TROP MED

July 5-6, 1986 - Weekend

July 7, 1986 - Malaria Division, Bangkok
- Analyze data
- Meet Dr. Sodetz, AFRIMS

July 8-11, 1986 - Travel to Rayong, Chantaburi, Trad
- Select study village

July 12-13, 1986 - Weekend
- Arrival of Dr. D. F. Clyde and Dr. E. B. Doberstyn

- and R. G. Andre at Malaria Division

July 16-18, 1986 - To be arranged

July 21-22, 1986 - Prepare report

July 23-29, 1986 - Conduct training
- (July 26-27 -- weekend)

July 30-31, 1986 - Prepare report

July 31, 1986 - Exit briefing with Dr. J. Eriksson, USAID

August 1, 1986 a.m. - Presentation of report to MOPH
p.m. - Depart Bangkok
ANNEX 2

LIST OF PEOPLE MET DURING THE EVALUATION

1. Dr. John Eriksson, Dir., USAID/Thailand
2. Mr. Narintr Tim, USAID/Thailand
4. Dr. Supat Sucharit, Head, Entomology, Trop. Med., Mahidol
5. Mr. Suthas Nutsathapana, Ento. Br., HQ., MOPH
6. Dr. Surin Pinichpongse, Dir., Malaria Div., MOPH
7. Dr. Chusak Prasittisuk, Head, App. Res. Branch
8. Mr. Amnat Charoenkul, Chief, Educ. & Trn. Branch
11. Dr. Sunchai Ketrangsee, Dir. Reg. V., MOPH
12. Mr. Kasem Nimtrakul, Chief, Ento. Branch, HQ., MOPH
13. Dr. Kondrachin, Malarialogist, Reg. WHO Office, New Delhi
14. Ms. Valaikanya Plasai, Sect. Dr. Surin
16. Dr. Sombat Chaiyapet, Consultant, Malaria Div., MOPH
17. Dr. Ralph Harbach, Ento., AFRIMS
18. Ms. Rinthong Suphachartwong, Epid. Branch, HQ., MOPH
22. Dr. Somsak Pantuwatana, Microbio., Dept. of Micro., Mahidol
23. Ms. Rampa Ramnatikul, Tech., AFRIMS
24. Dr. Sakol Panyim, Head, Biochem., Fact. of Sci., Mahidol
25. Dr. Kyle Webster, Chief, Immun., AFRIMS
26. Dr. Udom Chitprarop, Dir. Reg. 2, MOPH
27. Dr. Somsak Prajakwongse, Dep. Dir. Reg. 2
28. Mr. Phorn Sawadvongpron, Ent. Reg. 2
29. Mr. Boonserm Aumaung, Ent. Reg. 2
30. Ms. -Wannapa Suwonkerd, Ent. Reg. 2
31. Mr. Boonyong Panichpanth, Vec. Cont. Reg. 2
32. Mr. Thairat Banjongaksorn, Dept. Dir. Reg. 2
33. Mr. Trong Suwan, Driver, Reg. 2
34. Mr. Prateep Klepmek, Chief, Zone 2, Lampang
35. Mr. Amek Montienmanil, Ento., Zone 2, Lampang
36. Mr. Skol Promsil, Chief, Zone, Phrae
37. Mr. Prasong Chuaosomboon, Asst. Chief, Zone, Phrae
38. Mr. Boonyong Nanta, Chief, Ento., Zone, Phrae
40. Dr. Frank Sodetz, Dir., AFRIMS
41. Dr. Janet Hemingway, Ento., London School
42. Dr. Jack Gingrich, Chief, Ento., AFRIMS
43. Mr. Somsak Krachaiklin, App. Res. Br., MOPH
44. Mr. Nukul Suthinat, Asst. Zone Chief, Zone 5, Rayong
45. Mr. Chuchart Klangdit, Asst. Zone Chief, Zone 5, Rayong
46. Mr. Noo Hengli, Chief, Zone 5, Rayong
47. Mr. Songkram Ngampatom, Zone Chief, Zone 7, Chantaburi
48. Mr. W. Rooney, WHO Laboratory Specialist, MOPH
49. Ms. Laksami Suebsaeng, Epid. Branch, HQ., MOPH
50. Mr. Richard Kalina, Sci. & Tech., Project, USAID
51. Dr. Jaroon Kumnuanta, Sci. Affairs Specialist, USAID
52. Dr. Santasiri Sornmani, Dean, Fact. Trop. Med., Mahidol
53. Dr. Natth Bhamarapravati, Dir., Sci. & Tech., Dev., Bd., USAID
ANNEX 3

LIST OF PLACES VISITED DURING THE EVALUATION

1. USAID Mission, Bangkok
2. Malaria Division, Ministry of Public Health, Bangkok
3. Faculty of Science, Mahidol University, Bangkok
4. Faculty of Tropical Medicine, Mahidol University, Bangkok
5. Armed Forces Research Institute for Medical Sciences, Bangkok
6. Division of General Communicable Disease Control, Bangkok
7. HQ, Region 2, Malaria Division, Chiangmai
8. Village 3, Ban Pang Mae Tang, Mae Tang, Chiangmai
9. Village 7, Mae Luang Nasal, Mae Mao, Lampang
10. Tung Hua Suang, Lampun, Chiangmai
11. Sector Office, Li, Chiangmai
12. Village 10, Tung Hua Suang, Puong, Lampun, Chiangmai
13. Village 1, Tung Hua Suang, Puong, Lampun, Chiangmai
14. Zone 2 Office, Lampang
15. Village 4, Phaitom, Rongkwang, Phrae
16. Village 6, Phaitom, Rongkwang, Phrae
17. Village 11, Phaitom, Rongkwang, Phrae
18. Zone Office, Phrae
19. Zone 5 Office, Rayong
20. Zone 7 Office, Chantaburi
21. Village 7, Pat Thieu, Makaam, Chantaburi
22. Village 8, Pat Thieu, Makaam, Chantaburi
23. Village 5, Tamai, Chantaburi
24. Khao Ta Nuk Wat, Tamai, Chantaburi
25. Village 8, Dan Chumporn, Borai, Trad
26. Wat Phluang, Makaam, Chantaburi
## ANNEX 4

### SCHEDULE FOR THE WORKSHOP ON PROPOSAL PREPARATION

<table>
<thead>
<tr>
<th>Date</th>
<th>Time</th>
<th>Speaker</th>
<th>Subject</th>
</tr>
</thead>
<tbody>
<tr>
<td>July 23</td>
<td>9:30 a.m.</td>
<td>Dr. Surin</td>
<td>Problems facing the Malaria Control Program</td>
</tr>
<tr>
<td></td>
<td>10:30 a.m.</td>
<td>Coffee Break</td>
<td>(Each day)</td>
</tr>
<tr>
<td></td>
<td>11:00 a.m.</td>
<td>Dr. Chusak</td>
<td>Applied Entomological Research</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dr. Andre</td>
<td>New Entomological Technologies</td>
</tr>
<tr>
<td></td>
<td>12:00 noon</td>
<td>Lunch Break</td>
<td>(Each day)</td>
</tr>
<tr>
<td></td>
<td>1:30 p.m.</td>
<td>Dr. Doberstyn</td>
<td>Chemotherapy of Malaria</td>
</tr>
<tr>
<td></td>
<td>2:30 p.m.</td>
<td>Coffee Break</td>
<td>(Each day)</td>
</tr>
<tr>
<td></td>
<td>3:00 p.m.</td>
<td>Dr. Clyde</td>
<td>Prospects of Vaccination in Malaria</td>
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<tr>
<td>July 24</td>
<td>9:00 a.m.</td>
<td>Panel-Groups</td>
<td>Subjects assigned proposal</td>
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<tr>
<td></td>
<td>9:30 a.m.</td>
<td>Panel</td>
<td>The Hypothesis</td>
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<tr>
<td></td>
<td></td>
<td>Groups</td>
<td>Explanatory talk</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Prepare draft</td>
</tr>
<tr>
<td></td>
<td>11:00 a.m.</td>
<td>Panel</td>
<td>Specific Objectives</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Groups</td>
<td>Explanatory talk</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Prepare draft</td>
</tr>
<tr>
<td></td>
<td>1:30 p.m.</td>
<td>(In plenary)</td>
<td>Presentation and Critique of Hypotheses and Objectives</td>
</tr>
<tr>
<td>Date</td>
<td>Time</td>
<td>Event Description</td>
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<td>-----------------------------------------------------------------------------------</td>
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<tr>
<td>July 25</td>
<td>9:00 a.m.</td>
<td>The Introduction (General Purpose and Background)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Panel Explanatory talk</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Groups Prepare draft</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1:30 p.m.</td>
<td>(In plenary) Presentation and Critique of Introductions</td>
<td></td>
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<tr>
<td>July 26-27</td>
<td>Weekend</td>
<td></td>
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</tr>
<tr>
<td>July 28</td>
<td>9:00 a.m.</td>
<td>Experimental Design (Materials and Methods)</td>
<td></td>
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<td></td>
<td></td>
<td>Panel Explanatory talk</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Groups Prepare draft</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1:30 p.m.</td>
<td>(In plenary) Presentation and Critique of Materials and Methods</td>
<td></td>
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<tr>
<td>July 29</td>
<td>9:00 a.m.</td>
<td>Budget and Justification</td>
<td></td>
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<td></td>
<td></td>
<td>Panel Explanatory talk</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Groups Prepare draft</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1:30 p.m.</td>
<td>(In plenary) Presentation and Critique of Budgets and Justifications</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3:00 p.m.</td>
<td>(In plenary) Final Appraisal of Proposals</td>
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</table>
ANNEX 5

LIST OF PARTICIPANTS IN THE WORKSHOP ON PROPOSAL PREPARATION

Coordinators (no group assignment)

Dr. Chusak Prasittisuk, Headquarters
Dr. Krongthong Timasarn, Headquarters

Group 1: Topic -- Control of Malaria Outside the Village

Mr. Suthas Nudsathapan, Headquarters (Group Leader)
Mr. Suchart Thatipongse, Headquarters
Mr. Siriporn Chatapatama, Region 3
Mr. Chira Boonyang, Region 4
Mr. Pongwit Bualombai, Region 1

Group 2: Topic -- Vector Biology and Control

Dr. Somsak Prajakwongse, Region 2 (Group Leader)
Ms. Nilobon Theerasilp, Headquarters
Mr. Virapon Pothichitti, Region 1
Ms. Amporn Imvitya, Region 1
Mr. Boonserm Uamong, Region 2
Mr. Vuthipong Sae-lim, Region 3
Ms. Laksana Pratumsuwan, Region 3

Group 3: Topic -- Data Collection and Interpretation

Ms. Supranee Molichat, Region 5 (Group Leader)
Ms. Malinee Prasittisuk, Headquarters
Ms. Rinrong Suphachartwong, Headquarters
Ms. Saowanit Chanchio, Headquarters
Ms. Arporn Laomapol, Region 1
Ms. Pornpimol Wejwit, Region 4
Mr. Virat Sae-uid, Region 4

Group 4: Topic -- Strategy of Malaria Control

Dr. Pinan Daengharn, Region 3 (Group Leader)
Mr. Somsak Krachaiklin, Headquarters
Dr. Chirapt Sirichaisinthop, Region 1
Ms. Wanapa Suwannakird, Region 2
Ms. Somjai Thongfeua, Region 3
Ms. Suwanna Tansophalak, Region 1
Ms. Pornthip Nopharat, Headquarters
TELEGRAM REQUESTING CONSULTANTS FOR RESEARCH ACTIVITIES

VZCZCBK1
RR RUEHC
DE RUEHDX #6263 161
ZNR UUUU ZZH
R 100952Z JUN 86
FM AMBASSADY BANGKOK
TO SECSTATE WASHDC 2239
ET
UNCLAS BANGKOK 26283

AIEAC

FOR ST/H-BABIEO

E.C. 123566: N/A
SUBJECT: FY 87 REQUEST FOR RA FROM VEC PROJECT

REF: STATE 144677

1. MISSION AND THE MCPH REQUEST THE FOLLOWING ASSISTANCE:

A. SUBSCRIPTION OF JOURNALS/PERIODICALS ON ENTOMOLOGY THROUGHOUT CY 87.

B. O/A DECEMBER 1986; ONE CONSULTANT IS REQUESTED FOR TWO WEEKS TO ASSESS AND RECOMMEND POSSIBILITIES FOR BIOLOGICAL CONTROL OF MALARIA VECTORS.

C. O/A MARCH 1987; ONE OR TWO CONSULTANTS ARE REQUESTED FOR ONE WEEK TO TRAIN ENTOMOLOGY STAFF OF THE MALARIA DIVISION IN ELISA TECHNIQUES FOR IDENTIFICATION OF MALARIA PARASITES IN MOSQUITOES AND IN THE IDENTIFICATION OF NEW SPECIES. THE CONSULTANTS SHOULD BE RECRUITED FROM ARMED FORCES RESEARCH INSTITUTE FOR MEDICAL SCIENCE (AFRIMS) IN BANGKOK.

D. O/A SEPTEMBER 1987; ONE CONSULTANT IS REQUESTED FOR FOLLOW-UP ON THE RESEARCH ACTIVITIES TO BE CARRIED OUT. THE CONSULTANT IS EXPECTED TO MAKE RECOMMENDATIONS ON MODIFICATION OR IMPROVEMENT OF RESEARCH STRATEGIES ORIGINALLY DEVELOPED.

2. PLEASE ADVISE POSSIBILITY OF AFOREMENTIONED ASSISTANCE. REGRET NO MISSION BUY-INS AVAILABLE.

THANK YCU. BROWN

BT
#E283

NNNN
### ANNEX 7

#### NUMBER AND DISTRIBUTION OF MALARIA CLINICS
(As of December 1985)

<table>
<thead>
<tr>
<th>Antimalaria Program Division or Region</th>
<th>Division HQ</th>
<th>Regional HQ</th>
<th>Zone Office</th>
<th>Sector Office</th>
<th>Out-Post</th>
<th>Total</th>
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<tbody>
<tr>
<td>Division</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Region 1</td>
<td></td>
<td>7</td>
<td>51</td>
<td>46</td>
<td></td>
<td>104</td>
</tr>
<tr>
<td>Region 2</td>
<td></td>
<td>6</td>
<td>50</td>
<td>21</td>
<td></td>
<td>77</td>
</tr>
<tr>
<td>Region 3</td>
<td></td>
<td>6</td>
<td>54</td>
<td>51</td>
<td></td>
<td>111</td>
</tr>
<tr>
<td>Region 4</td>
<td></td>
<td>1</td>
<td>7</td>
<td>54</td>
<td>18</td>
<td>80</td>
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<tr>
<td>Region 5</td>
<td></td>
<td>7</td>
<td>54</td>
<td>20</td>
<td></td>
<td>81</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
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<td><strong>1</strong></td>
<td><strong>33</strong></td>
<td><strong>263</strong></td>
<td><strong>156</strong></td>
<td><strong>454</strong></td>
</tr>
</tbody>
</table>

**Antimalaria Program Division or Region:**

- Division
- Region 1
- Region 2
- Region 3
- Region 4
- Region 5
ANNEX 8

NUMBER AND DISTRIBUTION OF VILLAGE VOLUNTARY MALARIA COLLABORATORS
(As of May 1986)

<table>
<thead>
<tr>
<th>Antimalaria Program Region</th>
<th>Control Area</th>
<th>Eradication Area</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of Volunteers</td>
<td>Number of Villages</td>
<td>Number of Volunteers</td>
</tr>
<tr>
<td>1</td>
<td>3,113</td>
<td>1,750</td>
<td>6,606</td>
</tr>
<tr>
<td>2</td>
<td>5,619</td>
<td>5,690</td>
<td>4,205</td>
</tr>
<tr>
<td>3</td>
<td>4,363</td>
<td>3,986</td>
<td>6,399</td>
</tr>
<tr>
<td>4</td>
<td>3,804</td>
<td>2,912</td>
<td>1,983</td>
</tr>
<tr>
<td>5</td>
<td>3,790</td>
<td>1,524</td>
<td>734</td>
</tr>
<tr>
<td>TOTAL</td>
<td>20,692</td>
<td>15,862</td>
<td>19,927</td>
</tr>
</tbody>
</table>
Addendum (1) Unpublished document

The Current Situation of the Anti-Malaria Programme in Thailand

Surin Pinichpongse

Director, Malaria Division, Department of Communicable Disease Control, Ministry of Public Health, Bangkok, Thailand

August, 1985
ABSTRACT

The activities of the Malaria Control Programme in Thailand have reduced the mortality rate of 351 per 100,000 population in 1947 to 4.4 per 100,000 population in 1984. Over the same period the morbidity rate showed a reduction from 286 per 1,000 population to 6.3 per 1,000 population. The steady decrease in mortality and morbidity in the last few years is attributed to the expansion of primary health care delivery and the establishment of malaria clinics providing prompt diagnosis and treatment.

Difficulties are being experienced in maintaining and improving the malaria situation. These include multi-drug resistance in *Plasmodium falciparum*, exophilic tendencies of major anopheline vectors and continual population migration. A country-wide service of village volunteers has been established and a great deal of emphasis is being given to personal protection. The combination drug mefloquine-sulfadoxine-pyrimethamine was introduced into the country as first line drug for the treatment of falciparum malaria.
INTRODUCTION

The Malaria Control Division was established in 1943 with drug distribution as its chief function. At that time malaria was the leading cause of death with a mortality rate of 351 per 100,000 population. Following the encouraging results of a Pilot Project for Malaria Control with DDT residual spraying in 1949, the Government developed a country-wide malaria control programme in 1951. In 1964, a country-wide eradication programme was established, with an eight year plan of action. Although complete coverage by DDT spraying had not yet been achieved, vast areas were cleared of endemic malaria, and the death rate was reduced to 22.8 per 100,000 population. By 1970, this rate had been further reduced to 10.1 per 100,000. In 1971 a new policy was developed, as a result of the WHO revised global strategy of malaria eradication, for maintaining the gains already made and for the prevention of the rise of new problem areas.

At present the Anti-Malaria Programme provides services to all the population with operations being divided into two areas as follows:

a) Control Area, consisting of forested hills and mountains, border areas, and insecure areas with a population of approximately 10.5 million.

b) Eradication Area, consisting of the major part of the country with a population of approximately 38.5 million.

The strategy implemented is that of long-term malaria control in the forested and hilly areas of the country (Control Area), and prevention of the re-establishment of malaria transmission in the remaining areas (Eradication Area).
The country has been appropriately stratified according to different levels of receptivity in association with major variations in the terrain. The main control measures are residual insecticide (DDT/Fenitrothion) house spraying once or twice a year, radical treatment centres (malaria clinics), provision of anti-malaria drugs, and health education. Other measures are supplemented as appropriate including larviciding, space spraying, case detection and treatment, and the use of larvivorous fish. In order to establish appropriate health care delivery to all individuals in all villages, the programme has developed the Village Voluntary Malaria Collaborator (VVC) to assist in taking blood smears from and giving presumptive treatment to any person who is suspected of having malaria, and to assist in spraying operations.

PRESENT SITUATION

1. MORBIDITY The incidence of malaria throughout the country has been greatly reduced during the past 35 years. In 1947 the morbidity rate was 286 per 1,000 population. This rate was reduced until the period of 1966-1972 when the incidence appeared to stabilize, varying from 2.2 to 3.6 per 1,000 population. Since that time it has risen annually, to 7.1 in 1979, and 10.6 in 1981 (Table 1). The increase in 1979-1981 in malaria incidence is attributed mainly to population movements, and problems of parasite resistance to drugs. However, the increasing trend in malaria morbidity which reached a peak in 1981, had shown a downward trend in early 1982 and has persisted through 1983. The reasons for this improvement are not completely clear, but the most plausible explanation may be the striking increase in the numbers of malaria clinics and productive malaria village volunteers, resulting in earlier diagnosis and appropriate therapy. In 1979, the Malaria Division had established 174 malaria clinics located at various malaria offices and field sites. Based upon results and epidemiological data accumulated, it was determined that the effectiveness...
of malaria clinics could be increased by extending the services outside the malaria offices to strategic locations in high transmission areas, marketing centres and on migratory routes. At present there are 454 malaria clinics. The annual parasite incidence for fiscal year 1983 is the lowest in the last 10 years (Figure 1).

2. MORTALITY. In 1947 malaria claimed some 40,000-50,000 lives annually with the death rate of approximately 300 per 100,000 population. Now it is the seventh ranking cause of death nationwide, preceded by accidents, heart disease, malignant neoplasms, respiratory tuberculosis, pneumonia, and diarrhoeal diseases. The mortality rate from malaria in 1974 was 15.8 per 100,000 population, decreasing to 4.4 in 1984, which is the lowest mortality rate from malaria ever recorded in Thailand (Figure 2). The steady decrease in the mortality rate since 1974 is due to the expansion of peripheral health care delivery and the establishment of malaria clinics providing prompt diagnosis and treatment in areas of high transmission.

3. PARASITOLOGY. The three species of Plasmodium found in Thailand are *falciparum*, *vivax*, and *malariae*. The parasite formular in 1984 showed 70.7% *P. falciparum*, 29.0% *P. vivax* and 0.02% *P. malariae*.

*P. falciparum* started showing poor response to chloroquine in 1962, and at the present time it is found that more than 95% demonstrate resistance, mainly at R II and R III level. Furthermore, resistance to sulfadoxine-pyrimethamine occurred and spread throughout the country during the last few years.

4. ENTOMOLOGY. To date three species of anopheline mosquitoes have been proven responsible for malaria transmission in Thailand, namely *Anopheles balabacensis* (An. dirus), *An. minimus*, and *An. maculatus*. *An. minimus*, considered to be the most important
vector, is prevalent in forested and cleared forested foothill areas with slow-running streams throughout the country. *An. balabacensis* (*An. dirus*) is the other main malaria vector and its area of prevalence can be taken to coincide with the distribution of forest. *An. maculatus* has been incriminated as a vector in southern Thailand. *An. sundalicus* and *An. aconitus* are considered as secondary vectors in some particular areas. The result of DDT susceptibility tests carried on the principal and secondary vectors have shown that they respond favourably to the insecticide. However, in the presence of DDT residual spray, the vectors show a higher density of outdoor biting.

PROBLEMS

At present there are three major problems confronting the Anti-Malaria Programme in Thailand. These include the rapid dissemination of *P. falciparum* strains highly resistant to both 4-aminoquinolines and sulfadoxine/pyrimethamine drugs, the exophilic behaviour of malaria vectors, and occupational migration of the people.

For many years, chloroquine was the mainstay of anti-malarial chemotherapy and it is still an effective treatment for *P. vivax* infections. However, in the late 1950's *P. falciparum* clinical treatment failures with chloroquine were noted. Studies in twenty provinces applying the *in vitro* macro technique, in 1977-1981, showed chloroquine resistance in 97% of isolates tested.¹

The combination of sulfadoxine/pyrimethamine was an effective replacement until the mid 1970's when resistance was first noted along the Kampuchean border. Resistance to this combination is now widespread but is strongest in the Thai-Kampuchean border provinces and in areas involved in the migration to and from these areas.²
The regimen which has replaced sulfadoxine/pyrimethamine in areas of high resistance is a combination of quinine and tetracycline. This combined course, while generally effective, is difficult to supervise and because of the side effects of quinine, compliance in outpatients is poor over the necessary seven days of treatment.

Mefloquine promises to be both an effective and an operationally feasible substitute for quinine-tetracycline. The Anti-Malaria Programme has been involved in a number of field clinical trials of both mefloquine and the triple combination mefloquine-sulfadoxine-pyrimethamine. A large scale field trial of the triple combination has been carried out in selected border areas. The results showed that this drug has a potent blood schizontocidal activity against strains of *P. falciparum* resistant to other anti-malarial drugs, it gives a cure rate of greater than 95% and is very well tolerated. Following this large scale trial involving some 60,000 falciparum malaria cases the combination drug has been introduced into malaria programme from January 1985, to be used as the first line drug for the treatment of falciparum malaria.

Regarding the exophilic behaviour of the vectors, the principal techniques employed to overcome this problem are the use of larvivorous fish, thermal fogging with Fenitrothion in epidemic situation and encouraging the use of personal protection measures.

The third problem is that of occupational migration of Thai people to the Kampuchean border area for gem mining and farm labour as well as local migration from villages to forests for wood cutting and expanded cultivation in foothill forest fringe areas. This problem has been addressed through increased health education by stressing the importance of personal protection measures such as mosquito nets and repellent.
Table 1. Results of Surveillance Activities (1980-1985)

<table>
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<tr>
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<tr>
<td>Population covered by surveillance</td>
<td>44,230,292</td>
<td>44,515,133</td>
<td>46,026,197</td>
<td>46,924,325</td>
<td>48,595,751</td>
<td>48,914,780</td>
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<tr>
<td>Blood smears examined</td>
<td>4,852,919</td>
<td>5,583,689</td>
<td>6,094,665</td>
<td>5,365,960</td>
<td>6,666,441</td>
<td>6,627,815</td>
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<td>Positives</td>
<td>395,442</td>
<td>473,210</td>
<td>420,799</td>
<td>243,910</td>
<td>306,569</td>
<td>273,360</td>
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<td>SPR&lt;sup&gt;2&lt;/sup&gt;</td>
<td>8.1</td>
<td>8.5</td>
<td>7.0</td>
<td>4.5</td>
<td>4.6</td>
<td>4.1</td>
</tr>
<tr>
<td>ABER&lt;sup&gt;3&lt;/sup&gt;</td>
<td>8.1</td>
<td>8.9</td>
<td>9.1</td>
<td>8.2</td>
<td>8.2</td>
<td>13.6*</td>
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<tr>
<td>API&lt;sup&gt;4&lt;/sup&gt;</td>
<td>8.9</td>
<td>10.6</td>
<td>9.1</td>
<td>5.2</td>
<td>6.3</td>
<td>5.6</td>
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</table>

1) Blood smears taken by Active and Passive Case Detection and Mass Blood Surveys

2) SPR = Slide Positivity Rate (%)

3) ABER = Annual Blood Examination Rate (%)

4) API = Annual Parasite Incidence per thousand population

*ABER was calculated from blood collected from all activities
REFERENCES


FIGURE 1: MALARIA MORBIDITY IN THAILAND
FROM 1965-1983
Figure 2: Mortality due to malaria in Thailand 1944 - 1984

Mortality rate per 100,000 population

Year

1944 1954 1964 1974 1984
Addendum (2) Unpublished document

The Practice of Anti-malarial Drug Usage
In the Field and In a Large Scale Trial with Mefloquine
and its combination in Thailand

Surin Pinichpangse*

A country wide Anti-malaria Programme in Thailand was established in 1951. At that time malaria was the leading cause of death, claiming some 40,000 - 50,000 lives annually; malaria morbidity rate was 300/1,000 population approximately. Following establishment of the malaria control programme including activities both DDT residual house spray and treatment of suspected and positive cases, malaria mortality and morbidity have been greatly reduced. In 1964 the mortality rate was 4.4/100,000 population. The numbers of detected malaria cases in that year were 306,567 with the incidence rate (API) of 4.3/1,000 population. P. falciparum continues to be dominant species showing 70.7 %, P. vivax 29.0 % and P. malariae 0.02 %. The malaria control measures are applied depending upon the local epidemiological situation. The country has been stratified according to different levels of receptivity and terrain variations. The main activities are insecticide (mainly DDT) residual house spraying, once or twice a year in the transmission areas, provision of anti-malaria drugs for "Presumptive" and "Radical" treatment, and health education. Since 1979, Malaria Division has established "Malaria Clinic" or "Radical Treatment Centre" located at various field sites in highly malaria transmission areas, resulting in earlier diagnosis and appropriate treatment of the malaria cases. PHC workers e.g. Village Malaria Voluntary Collaborators at the village level are trained to assist in taking blood smears from and giving "Presumptive" treatment to persons suspected of malaria and to assist in other control activities.

At present there are 3 major factors hampering the anti-malaria

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programme, which are: the drug resistance of malaria parasites to anti-malarial drugs, the wide spread of population movements, and the changing in patterns of vector biocycles.

Chloroquine for Radical Treatment

Resistances of P. falciparum to chloroquine, the most widely used drug in malaria chemotherapy, was documented in Thailand in 1962. During the last two decades chloroquine resistance had spread rapidly through out Thailand. Current in-vitro studies indicate that over 90 % of the isolates are resistant to chloroquine. The clinical responses most often demonstrate failures at the level of R11 and RIII. The use of chloroquine for radical treatment of P. falciparum in malaria control programme has been discontinued since 1972. At present chloroquine (1,500 mg. base) given together with antirelapse drug (primaquine 15 mg / 14 days) are being used only for radical treatment of P. vivax and P. malariae.

Radical treatment of P. falciparum

1. S/P and Quinine/Tetracycline

The combination of sulfadoxine and pyrimethamine had been used as a standard radical treatment regimen for P. falciparum since the early 1970s. At that time S/P could produce cure rates between 80 and 90 %. Beginning in 1972 reports were received that failure rate of some 50 % were being seen in areas near Kampuchea border. Infections resistant to S/P were seen regularly in malaria clinics in widely separate parts of the country. In 1980, the in-vivo drug response of P. falciparum has been performed in the various regions of the country, it was apparent that the efficacy of S/P was low in three regions namely Kampuchea border (cure rate 32 %), the northeast (cure rate 50 %) and at a point on the Burmese border (cure rate 42 %). In the south and the north at that time, S/P was still found to be effective with the cure rates
of 82% and 90% respectively. However, the resistance of S/P has been spread rapidly, with increasing in resistance level. Studies in 1964 indicated that the response of P. falciparum to S/P in many parts of Thailand was very poor, with high percentage of RI and RIII responses.

Studies in 1980 showed that 7 day course of Quinine provided an overall cure rate of 90% among uncomplicated out-patients. However, the disadvantages of administering long course, if given to out-patients, are obvious, including problems with compliance and side effects. A three day course of Quinine (600 mg x 3 x 1) administered simultaneously with a 7 day course of tetracycline (500 mg x 2 x 7) has been tested and found to be highly effective to P. falciparum. This regimen was used as standard treatment in areas where P. falciparum is resistant to S/P and is still being used for treating of recrudescence cases since 1982.

2. Mefloquine and its combination

Quinine, even if used for 3 days, produces annoying side effects: tinnitus, light-headedness, nausea, and blurred vision. It also has a rapid effect on reducing parasitaemia and controlling fever, resulting in quick recovery and a tendency to discontinue taking medication. Monitoring studies in many parts of Thailand using both in-vivo and in-vitro techniques indicated the diminishing trend of P. falciparum sensitivity to Quinine. Due to difficulties in the administration of a long course medication and evidence of changing in sensitivity of Quinine, the Anti-malaria Programme of Thailand recognized that it must encourage the completion of studies required for speedy released of mefloquine. The WHO, on the advice of the Steering Committee of the SWG/CHENAL, has recommended that, in an attempt to delay the emergence of mefloquine - resistant
parasites for as long as possible, mefloquine should be used in combination with S/P. Trials in large numbers of infected patients were required to show the efficacy and the tolerance of this drug and its combination.

Operationally, not only schizontocidal drugs will be given to individual patients but also a gametocidal dose of primaquine should be used in order to reduce transmission. Field trials of this drug combination were also required.

Beginning 1981 adult male outpatients without clinical complications who attended the malaria clinics at Kuchinarai, North eastern Thailand (3 trials) and at Ratburai, Western Thailand, (1 trial) were admitted to the studies done by the Malaria Division. The results of studies are shown in Table 1.

Table 1
Field Trials of Mefloquine and its Combination, Thailand, 1981 - 1983

<table>
<thead>
<tr>
<th>Trial No.</th>
<th>Treatment Group</th>
<th>Cure Rate</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Group 1: M 750 mg + 3 tab. Placebo</td>
<td>97.87</td>
<td>Drug tolerance</td>
</tr>
<tr>
<td></td>
<td>M = 47</td>
<td></td>
<td>Life wise similar in two groups. No severe adverse effects found.</td>
</tr>
<tr>
<td></td>
<td>Group 2: M 750 mg + 3 tab S/P</td>
<td>97.95</td>
<td></td>
</tr>
<tr>
<td></td>
<td>M = 39</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trial No.</td>
<td>Treatment Group</td>
<td>Cure Rate</td>
<td>Conclusions</td>
</tr>
<tr>
<td>-----------</td>
<td>-----------------</td>
<td>-----------</td>
<td>-------------</td>
</tr>
<tr>
<td>2</td>
<td>Group 1: M 1,000 mg + 45 mg Primaquine on Day 0, N = 72</td>
<td>98.31</td>
<td>1) Drug tolerance like wise similar in all groups. No severe adverse effects found.</td>
</tr>
<tr>
<td></td>
<td>Group 2: M 1,000 mg + 45 mg Primaquine on Day 3, N = 72</td>
<td>100</td>
<td>2) Group 3,4 showed better tolerance than Group 1,2.</td>
</tr>
<tr>
<td></td>
<td>Group 3: M 750 mg + 45 mg Primaquine on Day 0, N = 63</td>
<td>100</td>
<td>3) Primaquine on Day 0 has better gametocidal effect.</td>
</tr>
<tr>
<td></td>
<td>Group 4: M 750 mg + 45 mg Primaquine on Day 3, N = 75</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Group 1: N + S/F = MSP</td>
<td>100</td>
<td>1) Both showed well tolerance. No severe adverse effects found</td>
</tr>
<tr>
<td>(Kuchinarai)</td>
<td>3 tab., N = 50</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Group 2: M + S/F = MSP</td>
<td>97.95</td>
<td>2) Group 2 effectively produces a complete cure with marked decrease in gameto-cytelmin.</td>
</tr>
<tr>
<td></td>
<td>3 tab + Primaquine 45 mg on Day 0, N = 47</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trial No.</td>
<td>Treatment Group</td>
<td>Cure Rate %</td>
<td>Conclusions</td>
</tr>
<tr>
<td>----------</td>
<td>--------------------------------------</td>
<td>-------------</td>
<td>-------------------------------------------------------</td>
</tr>
<tr>
<td>4</td>
<td>Group 1 = MSP 3 tab. N = 55</td>
<td>94.54</td>
<td>1) High failure rate occurred in Group 1, 2 due to vomiting in 6 out of 8 failure cases.</td>
</tr>
<tr>
<td></td>
<td>Group 2 + Primaquine 45 mg on day 0 N = 52</td>
<td>90.38</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Group 3 = S/P + Primaquine 45 mg on day 0 N = 52</td>
<td>19.23</td>
<td>2) 1 case of severe skin reaction found from Group 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3) Efficacy of S/P was very low</td>
</tr>
</tbody>
</table>

**Note**
- M = Mefloquine, 1 tab. = 250 mg.
- MSP = Mefloquine + Sulfadoxine + Pyrimethamine (1 tab. = M 250 mg, S 500 mg, P 25 mg)
- N = No of patient with complete follow-up at least 28 days
- Cure rate in Trial 4 determined by slide negativity for 42 days

From the studies described in Table 1 several conclusions may be drawn as follows:

1) Mefloquine is extremely potent anti-malaria agent with cure rate over 97%
2) The drug is well tolerated particularly at the 750 mg dose, even if given together with the S/P or with a gametocidal dose of Primaquine.

3) In comparison with currently used regimen QT, mefloquine has the obvious advantage of a single dose formulation and is better tolerated.

Continuing from the conclusions, beginning in June 1983 to April 1985, a large scale field trial of Mefloquine/Sulfadoxine/Pyrimethamine (MSP) had been established corresponded to phase 5 clinical screening of a new anti-malarial drug. The study was phased, beginning in 2 sectors and proceeding to two zones, where MSP was compared with QT, then proceeding further to full scale trial of MSP treating as many as over 60,000 *P. falciparum* patients. The MSP for the trial had been made available through the WHO assistance. 2,520 patients receiving medication from the full scale trial were followed up and the results are analyzed and shown in Table 2.
<table>
<thead>
<tr>
<th>Phase/Date</th>
<th>Treatment Group</th>
<th>Areas</th>
<th>Cure Rate within 24 hrs</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 June 83 to</td>
<td>1) MSP 3 tab.</td>
<td>Chantaburi, East</td>
<td>97%</td>
<td>1) MSP is more effective than QT</td>
</tr>
<tr>
<td>Feb 84</td>
<td></td>
<td>Thailand</td>
<td>24.3%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2) Q3 T7 (Quinine 600 mg x 3 x 3 + Tetracycline 500 mg x 2 x 7)</td>
<td>Trad, East Thailand</td>
<td>72%</td>
<td>2) Vomiting is more common with MSP than QT</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>6.7%</td>
<td>3) No severe adverse effect is found</td>
</tr>
<tr>
<td>2 June 83 to</td>
<td>MSP to all falciparum cases except pregnancy</td>
<td>10 provinces (Chantaburi, Trad, Prachinburi, Chonburi Rayong, Nakornnayok, Chachoengsao, Sakol nakorn, Mahasarakaa, Kalasin)</td>
<td>96.7%</td>
<td>1) MSP is safe effective and well-tolerated</td>
</tr>
<tr>
<td>April 85</td>
<td></td>
<td></td>
<td>19.25%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2) Acceptability to patients is high</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3) Resulting in better confidence to Malaria staff to use MSP</td>
</tr>
</tbody>
</table>

**Table 2**

Large Scale Field Trial of MSP
Thailand, 1983 - 1985
3. **Current Standard regimen for Radical Treatment of P. falciparum cases**

Following the large scale field trial involving some 60,000 falciparum malaria cases, the combination of Mefloquine/Sulfadoxine/Pyrimethamine (MSP) has been introduced into the malaria control programme from January 1985, to be used as the standard regimen for Radical Treatment of P. falciparum.

For reducing the malaria transmission, a gametocidal dose of Primaquine is given together with the MSP on day 0.

**Presumptive Treatment**

In order to establish appropriate health care delivery to all individuals in all villages, Village Malaria Voluntary Collaborators, and Village Health Volunteers are assisting the programme in taking blood smears from and giving presumptive treatment to the suspected cases. S/P is still continued to be the drug of choices to use as presumptive treatment, even it was apparent that the efficacy of this drug was low. Many studies are now performed by the Malaria Division staff to establish more appropriate drug regimen for presumptive treatment.
Abstract

Abate 500 E was tried against Anopheles minimus larvae in flowing streams using a Hudson X-Pert spray can with an 8002 nozzle tip. Spraying was done in one swath on both sides of a stream bank at a maximum dosage of 1 PPM. Results obtained indicated that with this application method and dosage, Abate larvicide is very effective against Anopheles minimus larvae.

* This study was supported by the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases.
1. Introduction

*Anopheles minimus* breeds mainly in slow-moving streams and seepages in foothill mountainous areas. This species is considered to be a primary vector which is distributed widely and plays a major role in transmitting malaria in Thailand. It was originally thought to be largely endophilic and endophagic (Sambasivan et al., 1953). Sporozoites in the salivary glands of this species could be found throughout the year (Howard et al., 1963). Later in 1984, it was found that a proportion of the *An. minimus* population showed DDT avoidance behaviour (Nutsathapana et al., 1984). Therefore, DDT residual insecticide spraying has apparently decreased in its effectiveness for controlling this species.

DDT residual insecticide spraying has been widely used in Thailand for more than 30 years. Spraying refusal rates by house owners and the wiping off of newly sprayed walls have been increasing year after year. 50% completed spray became the normal rate of achievement, especially in areas where the number of malaria cases are decreasing. Currently, malaria vector control in Thailand emphasizes integrated control measures, combining such techniques as residual insecticide spraying, larviciding, larvivorous fish, environmental control, etc. Abate was shown to be a very effective larvicide for *An. maculatus* in Malaysia (Thevasagayam et al., 1979) and for *An. minimus flavirostris* in the Philippines (Catarigui et al., 1973). It is known to be an insecticide of low toxicity to non-target organisms and is safe to use. In streams, no apparent accumulation of Abate occurred in water or mud samples from the site of application or at sampling station downstream (Bowman and Orléski, 1966).
The objective of this study is to find out the effectiveness of Abate 500 E larvicide in flowing streams in foothill areas, the typical breeding place of An. minimus. This study was started in May 1985 and completed in August, 1985.

2. Description of study area

2.1 Treatment village. (Village number 4, Khun Yom Canton, Phrae Province). DDT spraying at a target dosage of 2 gm/m², twice per year, had been in progress for at least 20 years. Last spray was in March, 1984. This village is situated in a forested foothill area with one stream running through it. There were 102 houses with 460 inhabitants.

2.2 Comparison village. (Village number 3, Khun Yom Canton, Phrae Province). The history of DDT spraying and the topography of this village were similar to those of the treatment village which is located about 4 kilometers away.

2.3 Breeding places

The stream originated from a distant mountain, providing ideal breeding places for An. minimus in both villages. Water is present in the stream year-round at varying depths and at a width of ½ - 10 m., depending on the season. An. minimus larvae were mainly found at the edge of the stream, especially where there were accumulations of debris and aquatic plants. Water in the stream is used only for washing purposes.

2.4 Malaria situation

Entomological data obtained during 1981-84, revealed high density of An. minimus. Susceptibility test results indicated that this species is still susceptible to DDT. During 1980-84, there were
8 reported cases from the treatment village and 5 reported cases from the comparison village. Most of the cases were contracted outside the villages.

3. Materials and methods

This study was carried out from May to August 1985, comprising pre-treatment (May) and treatment periods (June-August).

3.1 Abate 500 E (50% emulsion concentrate).

Fresh sample of Abate 500 E (0,0,0,1,01-Tetramethyl 0,01-thiodi-p-phenylene phosphorothioate) was provided by the T.J.C. Chemical Co., LTD. Bangkok, Thailand. It is an organophosphate compound and is claimed to be a superior mosquito larvicide. Abate larvicide, when use in flowing stream, generally involved complicated measurement and calculation, e.g. drip application (Suchart Phatipongse, 1983), making it impractical for routine field work. In this study, Abate was to be sprayed along the edge of the stream at the approximate dosage of 1 PPM active ingredient.

3.2 Larviciding operation

Application of the larvicide was began early in the morning in the treatment village by three spraymen with one supervisor. At the bank of the stream, the workers poured 68 ml. of Abate 500 E into his spray can (Hudson X-Pert spraycrvith an 8002 nozzle) and added water to give a final volume of 7.5 litres. Each worker was assigned to cover a fixed distance of one kilometer of stream per application. Application was made in one swath (75 cm.) along each bank. Frequently, when the stream narrowed; one swath was adequate to cover the whole width. With average stream depth of 10 cm. and an average walking speed of 5 /minute by the worker
an approximate dosage of 1 PPM can be achieved by our calculation.

3.3 Frequency of application

Re-application was made on a weekly basis.

3.4 Method of Assessment

Assessment was based on the results of larval collections. This was done on a weekly basis, one day after Abate application. One team comprised of three larval collectors with one supervisor was assigned to carry out the larval survey in the treatment village and another team in the comparison village. They were rotated each week. Larval collectors were instructed to search for third and fourth stage An. minimus larvae from both sides of the stream. The number of first and second stages of anopheline larvae, culicine larvae and mosquito pupae were also recorded.

3.5 Feasibility study

Before starting the study, a feasibility study was carried out to determine if the larviciding operation by this method could work well. Four larval cages with 25 third stage anopheline larvae, were placed at different sites along the edge of the stream without informing the larviciders. Two hours after larviciding operation, 100% mortality was observed in all cages.

4. Results

Results are shown in Table 1 and Figure 1. Five surveys pre-treatment and nine surveys post-treatment were carried out in the comparison and treatment villages, giving a total of fourteen surveys. Surveys were carried out on a weekly basis, except one on 13 June, 1985 which was not done. Nine applications of Abate were made at a target dosage of 1 PPM, during the entire study period.
Before treatment (May, 1985), average densities of *An. minimus* larvae, first and second instar larvae and pupae were numerous in both comparison and treatment villages (Table 1 and Figure 1.). It was observed that low larval densities in the comparison villages during the period of June-August, 1985 were mainly due to heavy rainfall. After treatment, 8 out of 9 surveys yielded no *An. minimus* larvae, and 4 out of 9 surveys were positive for pupae at low densities. In the second application (20 June, 1985), 12 *An. minimus*, 23 first and second instar larvae and 7 pupae were collected. This was considered to be due to rainfall which occurred during the application period rather than to some problem with the Abate. Results indicated that nearly 100% control could be achieved per application, depending on the quality of spraying.

It is important to note that the fish and other forms of aquatic life which were found in the stream were not affected by this application.

5. Discussion

5.1 Effectiveness

It is obvious from this study that Abate 500 E, when applied at a maximum dosage of 1 PPM using this application method; results in nearly a 100% kill rate. When Abate 500 E is sprayed on flowing stream, only the first to fourth instar larvae were affected with no effects on eggs and pupae (Catangui et al., 1973). Therefore, it is necessary to re-treat the stream on a weekly basis.
5.2 **Application method**

The application method, tried in this study was very simple and can be easily used by field workers. It does not involve sophisticated equipment (e.g. dripping equipment), or measurement (e.g. water velocity), or complicated calculation which are not suitable for field practice. Emphasis was made on controlling a majority of *An. minimus* larvae at the edge of the stream, by applying Abate within 52 centimeters of the stream bank. With this type of application, little or no larvicide is wasted.

5.3 **Toxicity and hazards**

Among the know larvicides, Abate has been shown to have very low toxicity to warm-blooded animals. It is widely used in drinking water at a dosage rate of 1 PPM for *Aedes spp.* control. Observations made during this study gave no indication of any toxicity at the dosage used to workers, fish or other forms of aquatic life.

6. **Summary**

In Thailand, there are about 300,000 malaria cases reported each year. Most of the cases are found in the forested foothill areas, where *An. minimus* is prevalent. Due to ecological changes which favour the breeding of *An. minimus*, this species plays an increasingly important role in transmitting malaria. DDT spraying in houses, has been used as the main vector control measure for more than 30 years. However an ever increasing spray refusal rate and a reduced effectiveness of DDT against *An. minimus* (Nutsathapana et al., 1991), make it necessary to explore other possible vector control measures. Abate 500 E at a maximum dosage of 1 PPM proved to be very effective against *An. minimus* larvae, when spraying to flowing-stream on a weekly basis. This method of applying larvicide, does not involve special
equipment or complicated measurement and calculation and it is convenient for the field worker to carry out the work in remote areas.

Abate larviciding, can be used as a supplementary measure in an area where An. minimus density is consistently high. The use of Abate 500 E is safe for the field worker and it had no adverse effects on aquatic life in the stream.

Acknowledgements

The authors wish to thank Dr. Surin Pinichpongse, the Director of the Malaria Division, for his technical advice and general support; Mr. Boonyong Nanta, Assistant Chief of Entomological Team of Malaria Unit 3, Phrae Province; and Mr. Somchai Sanrucksa, Insect collector of Malaria Division for their constant help in this study; thanks also to T.J.C. Chemical Company Limited, Bangkok for supplying Abate 500 E for this study.

Finally, thanks also to the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases for financial support.

References


Suchart Phatipongse. 1983. Preliminary studies on the control of Anopheles minimus (Theobald, 1901) larvae in natural running streams by drip application of Temephos (OAS-786). M.Sc. Thesis. Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand.

Suthas Natsathapana, Phorn Sawasdi Wongphorn, Udom Chitprarop and J.R. Cullen. 1984. A study in northern Thailand on the behavioural response of Anopheles minimus subjected to differing levels of DDT selection pressure (in prep.).

Table 1 Results of larval and pupal surveys, third and fourth instar larvae of An. minimus from comparison and larvicide treated areas.

<table>
<thead>
<tr>
<th>Date</th>
<th>Comparison</th>
<th>Abate 500 E treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3+4 instar</td>
<td>1+2 instar</td>
</tr>
<tr>
<td></td>
<td>An.minimus</td>
<td>Anopheine</td>
</tr>
<tr>
<td></td>
<td>1 May,85</td>
<td>113.5</td>
</tr>
<tr>
<td></td>
<td>8 May,85</td>
<td>203.7</td>
</tr>
<tr>
<td></td>
<td>15 May,85</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>29 May,85</td>
<td>58.2</td>
</tr>
<tr>
<td>Total</td>
<td>531(4.19)</td>
<td>2184(17.23)</td>
</tr>
<tr>
<td></td>
<td>6 June,85</td>
<td>40(1.16)</td>
</tr>
<tr>
<td></td>
<td>20 June,85</td>
<td>49(1.58)</td>
</tr>
<tr>
<td></td>
<td>27 June,85</td>
<td>27(0.94)</td>
</tr>
<tr>
<td></td>
<td>5 July,85</td>
<td>28(1.12)</td>
</tr>
<tr>
<td></td>
<td>12 July,85</td>
<td>14(0.67)</td>
</tr>
<tr>
<td></td>
<td>19 July,85</td>
<td>21(1.08)</td>
</tr>
<tr>
<td></td>
<td>26 July,85</td>
<td>7(0.31)</td>
</tr>
<tr>
<td></td>
<td>1 Aug.,85</td>
<td>10(0.56)</td>
</tr>
<tr>
<td></td>
<td>8 Aug.,85</td>
<td>5(0.32)</td>
</tr>
<tr>
<td>Total</td>
<td>201(0.93)</td>
<td>641(2.97)</td>
</tr>
</tbody>
</table>

1 Actual number collected.
2 Number collected per 100 dips (density).
3 Larval and pupal surveys were carried out one day after larvicide treatment.
Fig. 1 Pre- and post-treatment larval surveys of *An. minimus* in the larviciding and in the comparison areas.

Comparison

Treatment.
Fig. 2 Map showing the stream in the comparison and treatment villages in Phrae Province, Northern Thailand.
Addendum (4)  COMMENTS CONCERNING A REQUEST FOR A LEISHMANIASIS CONSULTANT IN THAILAND

1. Term of Reference

(See copy of telegram appended)

Look into Leishmaniasis problem. Specifically, talk with personnel at the Faculty of Tropical Medicine, Mahidol University, as to why they feel that leishmaniasis is a problem, where they think it is a problem, what supporting data do they have, and to what extent is their proposal for consultant assistance valid.

2. Background

(Notes from conversation with Dr. Supat Sucharit, Head, Entomology, Faculty of Tropical Medicine, Mahidol University, on July 4, 1986)

About 100,000 laborers from Thailand have gone to the Middle East; however, it is unknown how many return each year, but it is believed to be "a lot." Twenty cases of cutaneous leishmaniasis have been diagnosed on the basis of symptomatology only. Two cases of visceral leishmaniasis have been diagnosed and treated (and reported in the Weekly Epidemiological Surveillance Report, Vol. 17, No. 8, February 28, 1986).

Dr. Supat is worried about the possible establishment of leishmaniasis in rodents and sandflies. He collected flies of various sorts by setting out CDC light traps for one night (June 1, 1984) at Bang Pha In, Village 3, Banghen. He then sent 100 specimens to Dr. D. J. Lewis (now deceased) at the British Museum (Natural History), London. One sandfly was present in this collection, and was identified as Sergentomyia indica. Subsequently Dr. Supat asked Dr. Lewis for assistance in writing up a key to the sandflies of Thailand. Dr. Lewis suggested he correspond with Dr. R. P. Lane of the London School of Hygiene and Tropical Medicine about assistance. Dr. Supat stated that he had been urged by Professor Tongchai Papasarthorn, Faculty of Public Health, Mahidol University, to submit a grant proposal.
The concern about leishmaniasis seems premature because of the following reasons:

1. No evidence of any man-biting behavior of Thai species of sandflies.
2. No evidence that man can act as a reservoir of Middle Eastern strains of leishmaniasis.
3. No evidence of leishmaniasis in Thai animals.
4. No current concern of leishmaniasis outbreak potential by the Division Director, General Communicable Disease Control, Dr. Sumporn Prugsarat.

The following recommendations were made to Dr. Supat for the collection of data to validate or invalidate the need for a leishmaniasis research proposal and/or for a consultant on leishmaniasis.

1. Follow up positive cutaneous and visceral leishmaniasis cases. Determine village locations that cases returned to for residence following diagnosis.
2. Collect sandflies in these villages. Set out CDC light traps and Shannon traps for at least four nights in each village.
3. Slide mount all sandflies and send to Dr. R. P. Lane, London School, or Dr. Dave Young, University of Florida, for confirmation of identification.
4. If high populations of sandflies occur in a village, then conduct seven nights of all night manbiting collections.
5. Identify manbiting (not just landing) species and send voucher specimens to Drs. Lane or Young.
6. If a village with man biting sandflies is found, then write up a proposed research project and ask for consultant assistance. Proposal could be submitted to WHO, BOSTID or USAID. Consultant request could go to VBC.

No consultant or research support to the Faculty of Tropical Medicine, Mahidol University, for leishmaniasis projects is recommended at the present time.
The following references were supplied to Dr. Supat for information concerning sandflies occurring in Thailand:


FOR S&T/H - VIC BARBIERO

SUBJECT: VBC - TA ON PHLEBOTOMINE TAXONOMY

REF: LENNOX/TIFFANY LETTER DATED MAY 5, 1986

PLEASE PASS THE FOLLOWING MESSAGE TO DR. ROBERT LENNOX, VBC PROJECT DIRECTOR:

MISSION SUGGESTS THE VBC TEAM, TO BE VISITING THAILAND FROM JUNE-JULY 1986, HAVE A LOOK AT POTENTIAL LEISHMANIASIS VECTOR PROBLEM. NO NEED FOR INDEPENDENT, SEPARATE CONSULTANT ON THIS ISSUE AS WE DO NOT FEEL IT'S MUCH OF A PROBLEM HERE. THE TEAM'S ADDITIONAL SCOPE OF WORK WOULD DESCRIBE THE EXTENT OF THE LEISHMANIASIS PROBLEM IN THAILAND, POSSIBLE EXISTENCE OF A PHLEBOTOMINE VECTOR AND TYPE AND RECOMMENDATIONS FOR FURTHER JTA IF NEEDED. BROWN

NOTE BY OC/T: (*) OMISSION. CORRECTION TO FOLLOW.