マレイシア国熱帯病研究プロジェクト計画打合せ調査報告書

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平成５年11月

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国際協力事業団
医療協力部

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序　　文

マレイシア国政府は、日本政府に対し熱帯病研究分野における分子生物学的手法の導入を目的として、平成２年10月に保健省医学研究所(IMR)を拠点としたプロジェクト方式技術協力を要請越した。日本政府はかかる要請を受けて平成４年６月にR/Dを署名交換し、平成５年１月より３年間の技術協力を開始することとなった。国際協力事業団は平成５年11月に計画打合せ調査団を派遣し、現在までの協力内容をレビューすると共に今後の協力計画について協議を行い、その結果を本報告書として取纏めた。

終わりに本調査の任に当たられた団員のご協力に敬意を表するとともに、調査に際し多大のご協力を頂いたマレイシア国政府関係機関、在マレイシア国日本大使館、および外務省はじめ国内関係機関各位に対し、深甚なる謝意を表する次第である。

平成５年12月

国際協力事業団

医療協力部長　小早川隆敏

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1．計画打合せ調査団の派遣

1－1　派遣の経緯と目的

平成2年1月、中山外務大臣がマレイシアを訪問した際のマハティール首相との会談時に、日本側より『熱帯病に関連した両国間の医学協力の可能性について』提起した。これを受けて同年2月、JICAはプロジェクト方式技術協力の可能性を調査するためにプロジェクト形成調査団を派遣し、マレイシア側関係者と協議を行った。その後、同年10月要請書が提出されたが、協力要請分野は10項目にもわたるため、再度内容の絞り込みを行うことを目的として、平成3年4月に専門家チームを派遣した。その結果、要請分野の中でIMR(Institute of Medical Research)を拠点とした熱帯病に係る研究協力がJICAのスキームで実現の可能性が高いとの結論に至った。

上記の経緯を踏まえて平成4年2月に事前調査団、同年6月に実施協議調査団を派遣し、R/Dを署名交換した。平成5年1月1日より3年間の協力が開始され、今般協力計画について先方と詳細に検討するべく計画打合せ調査団を派遣することとなった。

1－2　調査団の構成

総　括	池田日出男	東京大学医科学研究所生物物理化学教授
研究協力	福原　俊一	東京大学医学部国際交流室講師
医学教育	三枝　広人	文部省高等教育局医学教育課主任
技術協力	穴田　浩一	国際協力事業団医療協力部医療協力第1課課長代理
協力計画	吉田　　弘	国際協力事業団医療協力部医療協力第1課職員

1－3　計画打合せ調査団派遣に係る日程

日順	月　日	曜日	時　間	ス　ケ　ジ　ュ　ー　ル
1	11月13日	土	10:30 16:25	成田→（ＭＨ０８９便） クアラルンプール着
2	11月14日	日		資料整理
3	11月15日	月		大使館表敬、ＪＩＣＡ事務所にて打ち合わせ 日本人専門家との打ち合わせ
4	11月16日	火	8:30 9:30 pm	ＩＭＲにて全体会議（所長出席） 各部門別個別会議（医昆虫学部門） 各部門別個別会議
5	11月17日	水	終日	各部門別個別会議（バイテオテクノロジーセンター、免疫学部門）
			13:15 19:35	穴田出発　成田→（ＪＬ７２３） クアラルンプール
6	11月18日	木	終日	各部門別個別会議（ウイルス学部門）
7	11月19日	金	11:00 pm	合同運営会議、ミニッツ署名 ＪＩＣＡ事務所へ報告
8	11月20日	土	09:30 17:10	クアラルンプール　→ＭＨ０９２ 成田（ＪＩＣＡ以外帰国）
9	11月21日	日	10:30 12:10	以後ＪＩＣＡ（穴田、吉田）のみ クアラルンプール→（ＭＨ０８０） クチン
１０	11月22日	月		サラワク総合病院にて打ち合わせ
１１	11月23日	火		クチン→シンガポール
１２	11月24日	水		シンガポール→成田

1－4　調査内容・項目

①　協力部門別活動状況

・協力部門別進捗状況

・専門家の業務活動

・カウンターパートとの連係（研究テーマについて双方の責任者を確認、R/Dミッション派遣以後の状況）

・マスタープランとの整合性（変更の必要性があるか）

②　専門家派遣

・長期専門家派遣、短期専門家派遣の妥当性

③ 研修員受入

・帰国研修員の状況(Mr. Ng Chong、Mr. Victor Chew Tong Kheong)

・研修内容の改善点

④ 資機材供与および利用状況

・通関状況（特に携行機材について）

・管理状況（管理責任者、管理台帳の有無）

・メインテナンス状況

⑤ ローカルコスト負担事業

・ローカルコスト支出状況（既に示達済み現地業務費の執行状況）

⑥ 詳細年次計画

・TSIの作成

⑦ 実施運営状況の問題点

⑧ 協力内容について日本側＆マ側のC/Pの修正

（実施協議調査団派遣時の状況）

テーマ	日本側責任者	マレイシア側責任者
1. malaria		
a. development and use of DNA probes for malaria diagnosis	DR. ARAI	DR. PATRISIA LIM DR. STEPHEN AMBU
b. identification and characterization of protective epitopes of malaria antigens	DR. TAKIGUCHI	DR. PATRISIA LIM DR. NOOR RAIN
c. analysis of mitochondrial genes	DR. KITA	DR. STEPHEN AMBU DR. NORMAZNAH
d. better understanding of the vectorial status of malaria vectors at the molecular level	DR. MORI	DR. G. L. CHIANG DR. V. INDRA
2. dengue and Japanese encephalitis (JE)		
a. strengthening of diagnostic capability using molecular biology and biotechnology	DR. MORITA	DR. VIJAYAMALAR. O
b. epidemiological studies on dengue and JE		DR. MANGALAM SINNAH DR. LYE
c. understanding of pathogenesis of dengue hemorrhagic fever (DHF) at the molecular level	DR. TANAKA, M	DR. MALAR/SARAS
d. Production of diagnotic reagents	PROF. IGARASHI	DR. ZAINAH
e. Vector studies	DR. MORI	DR. V. INDRA DR. G. L. CHIANG MR. LEE

1－5　主要面談者

① IMR (Institute of Medical Research)

Dato' Dr. M.Jegathesen	Director
Dr. Mak Joon Wah	Head, Biotechnology Center
Mr. Lee Han Lim	Head, Division of Entomology
Dr. Vijayamalar B.	Acting Head, Division of Virology
Dr. Nasuridin Nj.A.	Head, Division of Immunology
Dr. Patricia Lim	Biotechnology Center

② 在マレイシア日本大使館

小島　光昭	公使
片上　慶一	一等書記官

③ JICAマレイシア事務所

水田加代子	所長
小樋山　覚	次長
三角　幸子	所員

2．要　約

本調査団の派遣目的は、①実施協議調査団派遣時に策定したTSIの修正および②プロジェクトの全般的な活動をレビューすることであった。

①に関しては、調査団員のうち吉田職員が別件にて、93年7月にマレイシアを訪問した際に、IMRに立ち寄り、田中チーフアドバイザーとの間で打合せを行い、修正の方向性について、おおよその合意を得た。これを受け東京大学国際交流室福原講師、同医科学研究所北助教授らが中心になり、国内関係者と調整の上、修正TSIのドラフトができあがった。

②に関しては、プロジェクト関係者、すなわち日本人専門家とマレイシア側カウンターパートとのインタビューにて行った。

調査は順調に進められ、大きな問題点もなく終了し、11月19日にミニッツ署名をした。

以下、今般の調査の概略を示す。

2－1　TSIの変更

92年6月に行った実施協議調査時に策定した年次計画について専門家派遣後、下記の項目について修正が必要となってきた。

a. development and use of DNA peohes for malara diagnosis

b. identification and charactor, zation of protective epitops of malaria antigens

c. analysis of mito chondrial genes

d. better understanding of thevectorial status of malrial vectorsal molecular level

修正のポイントは第8章を参照、先方との協議の結果修正年次計画は双方で合意し、ミニッツにとりまとめた。

2－2　プロジェクトの全般的な活動状況

本プロジェクトは、93年1月1日開始後、6名の長期専門家および7名の短期専門家が派遣された。

また、研修員は開始前に2名のテクニシャン、開始後に1名の研究員が受入れられた。

機材供与は全て現地調達でまかなわれ、プロジェクト開始前にA4フォーム取りつけを行ったため、早急に必要機材の整備が行われた。93年11月現在で、その供与額は約73,000千円である。

当プロジェクトの協力期間は3年間のため、開始後の早急なるプロジェクト立ち上がりが課題であったが、専門家派遣研修員受け入れ、機材供与は適切に行われ順調に推移している。

IMRの協力対象部門は①バイオテクノロジーセンター、②ウイルス学部門、③医昆虫学部門である。また、免疫学部門も一部関与している。

バイオテクノロジーセンターでは、マラリアのDNA診断法の開発、ミトコンドリアDNAの研究が行われている。93年２月に派遣された古田長期専門家により、分子生物学的手法(DNAシーケンス、PCR etc)は、順調に技術移転されている。また北短期専門家が93年11月までに２度派遣され、本センターへ研究手法のアドバイスを行っている。今後は、１年目に不充分であった技術移転を含め指導が行われる予定である。

ウイルス学部門には、93年１月より小田長期専門家および五十嵐、森田、土江短期専門家が派遣され、デング熱、日本脳炎の疫学手法および分子生物学的手法を用いた診断技術の導入が計られている。当分野で現在（93年11月）迄に、日本脳炎ウイルスが動物、蚊に広範囲に分布していることが、マレイシア国で初めて明らかになった。今後は、ヒトへの感染の実態が調査される予定である。

医昆虫学部門には、93年５月より只野長期専門家、６月より森長期専門家が派遣された。他部門より専門家派遣が遅れたため、研究室の整備に時間を要している。なお、只野専門家が活動する研究室の整備はほぼ終わり、技術移転が開始されたところである。

２－３　合同運営会議

各部門のC/Pインタビューおよび日本人専門家のインタビューを通して、下記の点について調査団よりコメントを行った。

① マレイシア側C/Pと日本人専門家間のコミュニケーションの強化

② 効果的に技術移転を行うために大型汎用性機器の共用

③ これらを促進するために定期的なマ側、日側のミーティングの開催

これに対し、IMR側も日本側のコメントに理解を示し、③のミーティングについて、開催を検討してゆくことになった。

また、修正TSI案（年次計画のみ）は、双方で合意され、ミニッツとしてとりまとめた。

２－４　その他

ウイルス学部門への機材設置（培養案の整備）に伴うリノベーションは、本調査団派遣中にようやく開始し、マレイシア会計年度末である93年12月中に終了予定である。

医昆虫学部門の施設のリノベーションも行われたが、主に分子生物学的研究を行う部屋に関しては、水、電気といったインフラが不充分であり、調査団より改善を申し入れた。

3．進捗状況

3－1　日本人専門家の活動状況

(1) 古田隆久専門家（マラリア）

①DNAの塩基配列の決定。ミトコンドリアDNA断片を用いた35Sによる塩基配列決定に成功した。100～200bpぐらい。ケミルミネッセンスによるシーケンス法をpharmaciadキットを使ってうまく行った。また、ABIシーケンサーのtrainingを農業大学において受けた。これらは日本のレベルにくらべると遅れている（日本では300～400bp一度に決定できる）が、取りあえず、IMRにおいてシーケンス決定を行う基礎を作ったという点で評価できる。②現地マラリアサンプルisolate間の違いの検討。PCR productをrestriction enzymeでcutし、RFLPをしらべた。いくつかの株で違いが見つかった(Noor Rainと共同)。③Nested PCRのdiagnosisへの応用。double PCRを用いてうまく行った。falcipolunとvivaxを区別できる。また、ED-PCRやプレートPCRもうまく行った。投稿準備中(Lokmanとの共同)。プレートPCRはうまく行っているが、フィールドのサンプルで検出するところまで行ってない。高感度のPCR法を開発する努力は今後も必要（例えば、rDNAの代りにミトコンドリアDNA、lepeated sequence、RT-PCRの利用などが考えられる)。

(2) 森章夫専門家（医昆虫学）

実験室がset upされていない。Dr.Indraが帰ってきてから本格的なset upをする予定。Aedesのマラリアsusceptibility geneとリンクするDNAプローブを約30種類持っている。これをMaculatusに応用したい。このgeneのisolationはKafatosグループにおいて進んでおり、近い将来に成功すると思われる。AedesではこれらのDNAプローブの染色体マッピングが進んでいるが、Maculatusで同じmapになるかどうかはやって見ないとわからない。chromosome №の同定も必要と思われる。IMRでできるかどうか問題がある。他国に出張の可能性あり。実験室にはいくつか問題あり。freezerがない、水がでない。雨もりあり、実験台がせまい。オートクレーブが使いにくい。Mr.Lee、Dr.Makの協力を得て解決する必要がある。

以上のプロジェクトとは別に、Mr.Leeより蚊を殺す毒素を出す細菌の遺伝子のクローニングがプロポーズされているが、蛋白はまだ単離されていず、確実なアッセイ法もないので、できるかどうか不明。Mr, Leeの企画力に疑問がある。

(3) 只野長夫専門家（医昆虫学）

ハマダラカ Anopheles maculatusを野外から分離し、マラリア感受性についてしらべる。このマラリア感受性のgene mappingを行うために数種の遺伝子のisozyme変異株を分離し、これをマーカーとしてlikage analysisを行う。この計画は、現実的なものであり、

特に問題は少ないと思われるが、gene cloningを行うほど詳細な決定はむずかしいと思われる。只野氏自身もその点を心得ていると思われる。今後の地道な進展が期待される。

(4) 小田和正専門家（ウイルス学）

既存のJE診断法(serological method)によって動物および蚊よりウイルスを検出した。動物サンプルでは、ブタが100％で、carrierの主役であることがわかった。蚊よりの検出では、日本より検出率が高い。Cx. SitiensおよびCx. spbより検出されたのは新発見であり、投稿を準備している。今後、人のサンプルで検出を行うが、更に面白い事実がでてくる可能性がある。成果が上がっており、今後の展開にも期待ができる。

3－2　カウンターパートとの連係

プロジェクトにおけるカウンターパート（以下C/Pと略）と日本人専門家との連係状況については、以下の項目に沿って調査を行った。

① C/Pの当プロジェクトに対する理解：プロジェクト全体のレベルとそれぞれの部門別サブ・プロジェクトのレベルにおいて。

② 当プロジェクトに対するコミットメント：各部門全体としておよび個々のC/Pとして。

a. プロジェクトに対する興味および意欲。

b. 自分達の時間の何割位を当プロジェクトに割いているか。

c. IMR本来の仕事と当プロジェクトの関連。

③ C/Pと日本人専門家のコミュニケーション：

a. 個々の研究者同士ひいては各部門にいたるまで。

b. 定期的なresearch meetingやその他コミュニケーションをはかるための場の設定。

以下、各部門毎に、要約する。

3－2－1　バイオテクノロジーセンター

前回の実施協議調査団派遣の際は、マラリア・フィラリア部という名称であったが、上記の名称に変更している。これは、部長のDr. Makが、熱帯病研究においても他分野と同じく分子生物学・生体工学的なアプローチが必須になっている時代の流れを鋭敏に感じて行った積極的・発展的改称といえよう。

① 当プロジェクトに対する理解

部門全体として、当プロジェクトの意義をもっともよく認識していると思われる。個々のC/Pのレベルでは、個人差があるというものの、理解度は良いと感じた。

② 当プロジェクトに対するコミットメント

a. 前述したように、当プロジェクトの目的と改称したこの部門の目的とが合致しており、興味意欲は以前より非常に高くなったと感じた。当プロジェクトによりこの部門の研究レベルを飛躍的に向上させたいという期待を持っているようであった。Dr. Makはこの部門に限らず当プロジェクト全体の良き理解者であり、IMR側の中心的推進者である。

b. Ms. Noor Rainのようにほぼ100％コミットしている者もいれば、ほとんど時間をさいていない者もあるが、総じて見れば30％というところであろう。

c. IMR本来の業務（国内の診断検査サービス）やJICA以外のプロジェクトを兼任している者がほとんどである。それらと当プロジェクトの内容が必ずしも関連しているわけではない。これはC/Pがいる間は、一生懸命やるが、いなくなると継続性がとだえるおそれがあるひとつの理由である。

③ 日本人専門家とのコミュニケーションは、総じてうまくいっているようであるが、マレーシア特有の人種（マレー系、中国系、インド系）問題がある。日本人専門家は、この問題をよく理解して注意深く行動しているが、時に大きなストレスとなっているようである。定期的なresearch meetingは月に1回程もたれているようだが、さらに頻回に行うことを提言し、C/P側からも了解を得ている。

なおHLA関連の実質的なC/Pである免疫部門も面接した。部長のDr. Nasurudlinは、このプロジェクトに参加することにより、HLA部門のレベルが向上することを期待しており、協力的な姿勢を示した。長期のC/Pがいないため、まだ端緒についたばかりであるが、単なるサービス部門の性格が強いHLA室を研究面で強化するという最低目標は期待できよう。

3－2－2　ウィルス部門

部長のDr. Mangalamはサバティカルで英国におり、代理をDr. Vijayamalarがつとめている。

①② 当初は、C/Pの理解、意欲、そしてコミットメントが低いのではないかと心配されたが、プロジェクトが好調にすべり出し、着実な成果があがるにつれ、C/Pの姿勢が大きく変化を見せている。個々のC/Pのコミットメントは、個人差が多い。この部門も診断・検査サービスの義務が多く、当プロジェクトに多くの時間をさくのが望めないのがひとつの問題である。

③ コミュニケーションの点でも、3部門中最も良いのではないかと思われた。

定期的なミーティングも月一回程度行われている。

3－2－3　昆虫部門

前回訪問時部長であったDr. Indraが定年退職しており、変りにDr. LeeがActing Headを勤めている。

①②　総体的に、当プロジェクトに対する理解、意欲、協力度がもっとも低い部門と考える。

③　当部門におけるコミュニケーションは円滑とは言えず、そのためにお互いの意志が通じていないことから、かなり誤解しあっている部分もあるように見うけられた。

日本人研究者の側に、研究室の不備や理解度、協力度が低いと不満が高いが、これもコミュニケーションの改善に努めることで少しずつ解決できると希望する。Dr. Leeと調査団が話した範囲では関心意欲は充分あるように感じられた。

4．専門家派遣

平成5年11月現在、長期専門家6名、短期専門家7名を派遣した。（表1参照）またその他専門家派遣に関する詳細は以下のとおり。

・プロジェクト開始直後に田中、大田、小田専門家が派遣されたが、各専門家には2カ月程度の派遣前業務委嘱等のプロジェクト研究期間を設けることでプロジェクト立ち上がりに多いに貢献した。

・小田専門家には長崎大学熱帯医学研究所ウイルス部にて平成4年12月に1カ月弱の個別技術研修を行ったが、研修期間と合わせてIMRより最初のカウンターパート(Mr. Ng Chong Sing;Div. of virology)受け入れを行い共に研修を受けた。

・また田中チーフアドバイザーは平成4年6月に派遣した実施協議調査に参加したのち、今般の派遣に至っている。

・平成5年1月に五十嵐、小田専門家が派遣され、ウイルス部門の立ち上げを行い、その後、森田、土江専門家が技術指導を行っている。

・東京大学医科学研究所より北、古田専門家が平成5年2月に派遣されマラリア研究プログラムの計画を先方と詳細に検討した。北専門家は計画打ち合わせ調査団派遣直前の11月に再度派遣され、協力計画の調整を行った。

・医昆虫部門には只野、森専門家がそれぞれ平成5年5月、6月に派遣され、ラボのセッティング等の整備を行い業務を開始した。

・日本赤十字社中央血液センターより赤座、徳永専門家が、TSIに記述されているプロジェクトの活動内容中、1.1）b.『identification and characterization of protective epitopes of malaria antigens』プログラムについて詳細に検討するため、平成5年6月に派遣された。

以上の専門家によって、協力計画の調整を行った後、今般の計画打ち合わせ調査団にて協力計画の変更を先方と正式に合意した。この合意に基づく来年度以後の専門家派遣は平成6年2月に実施されるリーダー会議にて詳細を協議するものとするがおおよその方針は次のとおり。

・94年度は古田専門家の後任者を短期専門家で対応。95年度は長期専門家派遣予定

・五十嵐専門家を2月上旬から3週間程度派遣予定

・ウイルス学の小林専門家を94年度秋から長期派遣予定

表1　専門家派遣実績（氏名、所属先）

チーフアドバイザー		
1．田中寛（杏林大学）	93.01.13－95.01.12	(long term)
調整員		
2．大田泉（ＪＩＣＥ）	93.01.13－95.01.12	(long term)
Parasitology		
3．古田隆久（東大医科研）	93.02.24－94.02.23	(long term)
4．北潔　（東大医科研）	93.03.03－93.03.20	(short term)
5．北潔　（東大医科研）	93.10.18－93.11.02	(short term)
Entomology		
6．只野長夫（元聖マリアンナ大学）	93.05.12－95.05.11	(long term)
7．森章夫　（長崎大学）	93.06.16－95.06.15	(long term)
Virology		
8．小田和正（元神奈川衛研）	93.01.27－95.01.26	(long term)
9．五十嵐章（長崎熱研）	93.01.17－93.02.25	(short term)
10．森田公一（長崎熱研）	93.04.14－93.05.12	(short term)
11．土江秀明（阪大微研）	93.07.17－93.09.11	(short term)
Biotechnology		
12．赤座達也（日赤）	93.06.28－93.07.03	(short term)
13．徳永勝士（日赤）	93.06.28－93.07.03	(short term)

5．研修員受入

平成5年11月現在3名の研修員を受け入れ、平成5年度内であと2名受け入れる予定である。（表2参照）また、平成6年度は4名の受け入れ要望があった。

表2　研修員受け入れ実績（氏名、研修先）

Parasitology

1．Mr. Ng Chong Sing（東大医科研）　92.11.17－93.02.22

Virology

2．Mr. Victor Chew Tong Kheong（長崎熱研）　93.12.02－93.03.01

Entomology

3．Dr. Indra Vythilingam（長崎熱研）　93.09.20－93.12.21

今後の研修員受け入れ予定

Virology

・Mr. Ravindran Thayan　93.01.10－93.03.22

Biotecnology

・Ms. Normaznah Yahaya　93.03.14－93.06.14

6．ローカルコスト負担事業

平成4年度（平成5年1月から3月）は5,906千円支出され、プロジェクト立ち上げのための環境整備を行った。なお平成5年度は8,270千円支出予定であり11月5日現在の執行状況は76％である。（表3、4参照）本プロジェクト実施にあたり、当初から懸念されていた高価な試薬類（制限酵素等DNA研究用試薬）の先方負担が今後の課題である。

表3

平成５年11月５日現在

平成５年度　現地業務費執行状況

Ⅰ．第１及び第２四半期

（単位：リンギ）

	受入額			支払額			残額
	第１四半期	第２四半期	計	第１四半期	第２四半期	計	
一般現地業務費	35,828.59	27,200.00	63,028.59	17,661.17	44,226.74	61,887.91	1,140.68
現地研究費	4,494.86	6,800.00	11,294.86	2,750.70	1,644.97	4,395.67	6,899.19

第１及び第２四半期　一般現地業務費執行率　：　98%　－　①
現地研究費執行率　：　38%　－　②　☞　現地業務費執行率　：　68%　－　③

Ⅱ．第３四半期（支払額は11月５日現在）

（単位：リンギ）

受入額	支払額	残額
一般現地業務費	63,000.00	22,851.78	40,148.22
現地研究費	6,500.00	8,654.39	△2,154.39

※☞ 第２四半期末残額との残額計

	残額
一般現地業務費	41,288.90
現地研究費	4,744.80

第３四半期　一般現地業務費執行率　：　36%　－　④
現地研究費執行率　：　133%　－　⑤　☞　現地業務費執行率　：　84%　－　⑥

Ⅲ．平成５年度開始時より11月５日現在

一般現地業務費執行率　：　①　＋　④　＝　67%
現地研究費執行率　：　②　＋　⑤　＝　85%

☞

現地業務費執行率　：　③　＋　⑥　＝　76%

表4

マレイシア国熱帯病研究プロジェクト実績　1

予算費目	平成２年		平成３年		平成４年		平成５年	
	当年度	繰越	当年度	繰越	当年度	繰越	当年度	繰越
（事項）調査実施に必要な経費	0	0	2.264.077	0	130.880	3.626.480	0	0
（目）調査諸費	0	0	2.264.077	0	130.880	3.626.480	0	0
事前調査	0	0	2.264.077	0	57.680	0	0	0
（節）調査諸費	0	0	2.128.117	0	0	0	0	0
（節）現地調査費	0	0	0	0	0	0	0	0
（節）資機材購送費	0	0	135.960	0	57.680	0	0	0
（節）報告書作成費	0	0	0	0	0	0	0	0
実施協議	0	0	0	0	73.200	3.626.480	0	0
（節）調査諸費	0	0	0	0	0	2.745.212	0	0
（節）現地調査費	0	0	0	0	0	0	0	0
（節）資機材購送費	0	0	0	0	73.200	881.268	0	0
（節）報告書作成費	0	0	0	0	0	0	0	0
計画打合せ	0	0	0	0	0	0	0	0
（節）調査諸費	0	0	0	0	0	0	0	0
（節）現地調査費	0	0	0	0	0	0	0	0
（節）資機材購送費	0	0	0	0	0	0	0	0
（節）報告書作成費	0	0	0	0	0	0	0	0
巡回指導	0	0	0	0	0	0	0	0
（節）調査諸費	0	0	0	0	0	0	0	0
（節）現地調査費	0	0	0	0	0	0	0	0
（節）資機材購送費	0	0	0	0	0	0	0	0
（節）報告書作成費	0	0	0	0	0	0	0	0
（目）所属先補填経費	0	0	0	0	153.000	0	0	0
（事項）専門家派遣に必要な経費	0	0	0	0	30.236.270	0	33.234.410	0
（目）派遣諸費	0	0	0	0	18.513.870	0	20.740.410	0
専門家	0	0	0	0	18.513.870	0	20.740.410	0
（節）派遣費	0	0	0	0	12.513.383	0	19.909.648	0
（細節）赴任旅費	0	0	0	0	6.242.233	0	6.425.972	0
（細節）滞在費	0	0	0	0	4.425.934	0	10.126.829	0
（細節）住居手当	0	0	0	0	1.336.216	0	3.137.904	0
（細節）語学手当	0	0	0	0	0	0	218.943	0
（節）携行機材費	0	0	0	0	6.027.487	0	830.762	0
（細節）購入	0	0	0	0	5.463.124	0	258.324	0
（細節）輸送	0	0	0	0	564.363	0	572.438	0
（節）一時帰国旅費	0	0	0	0	0	0	0	0
（目）所属先補填経費	0	0	0	0	5.816.400	0	4.224.000	0
（節）国内俸	0	0	0	0	3.781.000	0	2.910.000	0
（節）所属先給与	0	0	0	0	2.035.400	0	1.314.000	0
（節）所属先諸経費	0	0	0	0	0	0	0	0
（目）技術費	0	0	0	0	0	0	0	0

予算費目	平成２年		平成３年		平成４年		平成５年	
	当年度	繰越	当年度	繰越	当年度	繰越	当年度	繰越
（目）現地業務費	0	0	0	0	5.906.000	0	8.270.000	0
（節）一般現地業務費	0	0	0	0	5.906.000	0	8.270.000	0
（細節）一般現地業務費	0	0	0	0	4.880.000	0	7.140.000	0
（細節）現地研究費	0	0	0	0	1.026.000	0	1.120.000	0
（事項）機材供与に必要な経費	0	0	0	0	21.423.000	39.998.000	0	11.575.000
（目）機材供与費	0	0	0	0	21.423.000	39.998.000	0	0
（節）一般機材供与	0	0	0	0	0	0	0	0
（細節）購入費	0	0	0	0	0	0	0	0
（細節）輸送費	0	0	0	0	0	0	0	0
（節）機材管理費	0	0	0	0	0	0	0	0
（節）機材仕様書等作成費	0	0	0	0	0	0	0	0
現地調達機材費	0	0	0	0	21.423.000	39.998.000	0	11.575.000
（事項）プロジェクト実施に必要な経費	0	0	9.000	0	252.720	0	118.420	0
（目）実施計画諸費	0	0	9.000	0	252.720	0	118.420	0
（節）調査団実施計画費	0	0	9.000	0	0	0	0	0
（細節）会議費	0	0	9.000	0	0	0	0	0
（節）プロジェクト運営費	0	0	0	0	247.720	0	118.420	0
（細節）プロジェクト運営費	0	0	0	0	5.000	0	118.420	0
（細節）プロジェクト会議費	0	0	0	0	0	0	0	0
年度小計	0	0	2.264.077	0	46.136.870	43.624.480	33.352.830	11.575.000
年度合計		0		2.264.077		89.761.350		44.927.830

合計 136.953.257

平成５年１０月１６日現在

7．資機材の活用状況

現地における資機材の活用状況は以下のとおりである。

① 供与機材には番号がふりあてられ、仕様、購入年月日、シリアル番号、purchase order №、ディーラー名（住所）、保管場所とともに記録されている。メインテナンスのための情報も記録されている。

② 機材の保証期間中に修理、交換が必要になった場合、購入したディーラーによる無償修理が行われている。

③ 定期メインテナンスが必要な機材は、マレイシア側において、メインテナンス契約が行われる。この場合、3社もしくはそれ以上の見積りをとりつけ、仕様にあうもっとも安い業者と契約する。交換部品を含めたメインテナンス契約も同様の入札を経て行われ、IMRより支払われる。

④ 定期的なメインテナンス契約に基づかない、機材修理も必要に応じ行われ同様の入札を経て契約される。

⑤ 機材を正しく使用するため、全ての研究室スタッフが利用できるようマニュアルが整備されている。操作の難しい機材の場合は、専用のスタッフが定められている。もっと難しい機材の場合には、ディーラーによる研修が行われる。

各研究者およびテクニシャンは、自分の研究室に置かれている機材に対し責任を負っている。

⑥ JICAにより93年11月までに総額約73,000千円（ミニッツ参照）の機材が供与されている。なお93年12月から94年3月までの今会計年度中に更に、約30,000千円供与される予定である。

供与された機材は全て現地調達によりまかなわれており、現在（93年11月）のところ調達に問題はない。

しかしながら分子生物学的手法を用いる研究活動には、精密機器が数多く使われており、操作法およびpreventive maintenanceを習得するには、今後も継続的に注意を払う必要がある。

⑦　空送による機材の通関状況

日本から購送される機材の空港での引取は、すべてIMRのストア室が行っている。現在までに、引取に何らかのトラブルがあったという話は一度もない。

⑧　専門家同時携行機材の通関状況

現在専門家の赴任時に同時携行しているのは、主に薬品類である。スバン国際空港では、ダンボール箱およびクーラーボックスは例外なく開封調査の対象となり、その場合課税や収賄を要求される。最悪の場合は、空港内に薬品を長く止めておかれることになる。税関審査の際、免税カウンター（『グリーンレーン』）はほとんど荷物の中身を調べないので、そのカウンターを通行するよう指導しているが、改装等でそのカウンターが閉鎖されている時もあるのが問題である。現在スバン国際空港内の一時通行パスは、まったくといってよいほど取得が不可能になっていることから、調整員が専門家の税関審査をサポートすることもできない状況であるが、現在まで荷物を調べられトラブルになりかけたのは一度だけである。

8．年次計画の修正

平成４年６月に派遣した実施協議調査時に作成したTSIの変更を正式に先方と確認するのが今般の計画打ち合せ調査団の目的のひとつであった。

なおプロジェクトは平成５年１月より開始し、同年11月までにTSI中の各プログラムの責任者が専門家として派遣され、協力計画について調整を行った。その結果、マラリアプログラムのうち４つのサブテーマの年次計画について修正することとなったが、日本脳炎・デング熱ウイルス側のプログラムに関してはオリジナルのまま修正を行わないこととなった。TSIの修正箇所を表５に示す。

また実施協議調査時とプロジェクト開始時ではマレイシア側、日本側双方のカウンターパートが人事異動あるいは退職等で変更を来しているため再度確認を行った。（表６参照）

表５

Revision of Tentative Echedule of Implementation.

Description of the item should not be changed.

1．1nd year, 1993
2．2nd year, 1994
3．3rd year, 1995

実施協議調査時のTSIより抜すい

TENTATIVE SCHEDULE OF IMPLEMENTATION

1．Activities for the items of technology transfer related to each objective of the Project

1）Strengthening the use of biotechnology in the diagnosis and management of malaria

a. development and use of DNA probes for malaria diagnosis

b. identification and characterization of protective epitopes of malaria antigens

c. analaysis of mitochondrial genes

d. better understanding of the vectorial status of malaria vectors at the molecular level

1) Strengthening the use of biotechnology in the diagnosis and management of malaria

Item a. development and use of DNA probes for malaria diagnosis

Existing schedule

1. Development and use of DNA probes.
   Selection of primer and use for PCR
2. Examination of DNA isolation method from patients'blood samples
3. Comparative analysis of new diagnosis methods to standard one.

Proposed revigion, draft 1

1. Laboratory set up and technical transfer of fundamental procedures in biotechnology for the purpose of malaria diagnosis.
2. Studies on development of diagnostic procedures, and selection and production of candidate DNA probes or primere.
3. Comparative evaluation of diagnostic procedures, and DNA probes or primers.

Item b. identification and characterization of protective epitopes of malaria antigens.

Existing schedule

1. Study on relationship between severity of malaria and HLA haplotypes
2. Search for protective epitopes of malaria antigens
3. Gene cloning of protective antigens

Proposed revision (draft by JW Mak, Nasarudin and Tanaka)

1. Typing of HLA class I in malaria patients and healthy controls.
2. Blood sample collection and typing of HLA class II.
3. HLA haplotypes in malaria patients.

Item c.analysis of mitochondrial genes

Existing schedule

1. Establishment of preparation techniques for mitochondrial fraction of Plasmodium and determination of nucleotide sequence of mitochondrial DNA
2. Analysis of gene expression of mitochondrial DNA at various developmental stages of Plasmodium
3. Typing of mitochondrial DNA of isolated straing of Plasmodium

Proposed revision, draft 1

1. Laboratory set up, isolation of mitochondrial DNA, and trials of DNA sequencing.
2. Characterisation of mitochondrial DNA in local malaria strains by analysing fixed and variable eequence structures.
3. Sequencing of mitochondrial DNA among locally available strains of Plasmodium faiciparum

Existing scheduleにあるマラリア原虫ミトコンドリア画分の単離が現状では非常に困

難な点（後述）、また1992年後半に米国のDr. Feaginにより 6 KbのP. falciparum（熱帯熱マラリア）のミトコンドリアDNAの配列が決定されたことからかなりの変更が加えられた。（資料 6 参照）

Item d. better understanding of the vectorial atates of malaria vectors at the molecular level.

Existing schedule

1. Determination of nucleotide sequence of DNA isolated from susceptible/refractory vector mosquitoes
2. Localization and analysis of susceptible genes of mosquito vectors
3. Production of refractory vector mosquitoes by point mutation and exploration of biological control of susceptible vector mosquitoes.

Proposed revision, draft 1

1. Laboratory set up and establishment of susceptibility bioassay method of Anopheles against malaria.
2. Isolation of susceptible and resistant strains of Anopheles, and chromosome mapping by ensyme markers and DNA fragment markers.
3. Determination of malaria susceptible locus on genes in relation to other enzyme and DNA markers.

表6

ANNEX IV. List of Japanese and IMR members responsible for each research field

Field of Research	Japanese Experts	Leader	Malaysian Counterparts
Malaria			
1. DNA Probes	Dr. 古田隆久(L)(IMSUT)	Head, Biotecnology Centre	Dr. Normaznah/Ms. Noor Rain Dr. Lokman/Dr. A.Khoo
2. Protection Epitopes	Prof. 田中 寛(L)(Chief Advisor)		Dr. Nasuruddin/Dr. A.Khoo
3. Mitochondrial Gene	Dr. 北 潔(IMSUT)/ Dr. 古田隆久(IMSUT)		Dr. Patricia/Ms. Tan/ Mr. Ng
4. Vector of Molecular Level	Dr. 只野長夫(L)/ Dr. 森 章夫(L)(Nagasaki Univ.)	Head,Medical Entomology	Dr. Indra/Ms. Rohani
Dengue/JE			
5. Rapid Diagnosis and Characterization of Dengue and J.E.by PCR, Seqencing and Igm−ELISA	Prof. 五十嵐章(Nagasaki U.)/ Dr. 土江秀明(Osaka Univ.)	Head, Virology	Dr. Vijayamalar/Ms. Halimah/ Mr. Ravindran
6. Epidemiological Study on Dengue and J.E.	Dr. 小田和正(L)		Dr. Vijayamalar/Mr. Chew
7. Pathogenesis of DHF Comparative Nucleotide Sequence of Viral Isolates	Dr. 森田公一(Nagasaki Univ.)		Dr. Zainah/Mr. Ravindran
8. Production of Diagnostic Reagents	Prof. 五十嵐章(Nagasaki Univ.)	Head,Medical Entomology	Dr. Zainah/Mr. Apandi Yusop
9. Vector Studies	Dr. 森 章夫(L)(Nagasaki Univ.)		Dr. Indra

(L)Long term experts, (IMSUT)Institute of Medical Science, the University of Tokyo

～～～～～～～～ は実施協議調査時より変更のあった箇所

9．実施運営状況の問題点

9－1　運営方法によって改良できる問題点

① 会議の間に、IMR C/Pと日本人専門家との間でコミュニケーションの悪さがしばしば問題にされた。合同会議の席でコミュニケーションを良くする努力を要請した。

② 部門間のセクショナリズムの傾向があり、技術移転がなされてもその技術が他の部に出て行かないという傾向が認められた。この問題を打破するために、プロジェクトの成果を発表するScientific meetingを部門を越えて行うことが提案された。

③ JICAで提供された機材、とくにIMRに1台しかないDNA合成機、DNAシーケンサーを共通の機材であると認識し、だれもが必要に応じて使用できる状態で維持管理されることが提案された。

9－2　その他問題点

① 田中チーフ・アドバイザー用の部室の改善

スペースが狭く、音がうるさい（機械の音）

② 森専門家の実験室の改善

雨もりの修理、水の供給、電気の配線の充実、実験台の構造の改良等はIMR側に要請すべきである。

③ 日本人専門家間の通信手段：無線電話の購入

④ シーケンス解析用にDNASIS soft（日立）が導入され、シーケンスの解析に効果を上げているが、DNAデータベース（CD1枚ぐらいの容量）が購入されてないため、得られたシーケンスも既存のシーケンスを比較できない状態である。これでは中途半端なので、DNAデータベースとそれを読むための器機を購入してシーケンス分野を充実させる必要がある。

資　料

1）ミニッツ

2）プロジェクトより提出された現況レポート

3）WHO/IMRの活動レポート

4）1992年IMR Annualレポートより抜すい
（予算、スタッフ表）

5）11月16日の議事録

6）11月19日の議事録

7）北潔専門家報告書より抜すい

1) ミニッツ

THE MINUTES OF DISCUSSIONS
BETWEEN THE JAPANESE PLANNING AND CONSULTATION TEAM
AND
THE AUTHORITIES CONCERNED OF THE GOVERNMENT OF MALAYSIA
ON JAPANESE TECHNICAL COOPERATION FOR
THE PROJECT FOR RESEARCH AND DEVELOPMENT ON DIAGNOSIS
OF SELECTED TROPICAL DISEASES

The Japanese Planning and Consultation Team (hereinafter referred to as "the Team") organized by Japan International Cooperation Agency (hereinafter referred to as "JICA") and headed by Dr. Hideo Ikeda, Professor of the University of Tokyo, visited Malaysia from 13 to 20 November 1993 for the purpose of studying the activities concerning the Project for research and development on diagnosis and management of selected tropical diseases (hereinafter referred to as "the Project"), and discussing the future implementation plan of the Project.

During its stay, the Team exchanged views and had a series of discussions with Malaysian authorities concerned in respect of the desirable measures to be taken by both Governments for the successful implementation of the above-mentioned Project.

As a result of the discussions, both sides agreed upon the matters referred to in the document attached hereto.

Kuala Lumpur, 19 November 1993

Dr. Hideo Ikeda

Leader,
Planning and Consultation Team,
Japan International Cooperation Agency,
Japan

Dato' Dr. M. Jegathesan

Director,
Institute for Medical Research,
Ministry of Health,
Malaysia

1. GENERAL REVIEW

The Project has started from 1 January 1993 for three years for the purpose of contributing to the control of selected tropical diseases in Malaysia; malaria, dengue and Japanese encephalitis (JE) by strengthening research activities in the field of parasitology, entomology and virology at IMR, thus enhancing the health of Malaysian people.

In accordance with the Record of Discussions signed on 22nd of June 1992 by both sides, JICA has dispatched 6 long-term experts and 7 short-term experts to Malaysia and has accepted 3 counterparts for training in Japan, and also has taken necessary measures to provide equipments necessary for smooth implementation of the Project.

Both sides reviewed the activities of the achievement made so far with regard to the implementation of the Project. Thus, based on the common recognition of the present state of the Project, both sides confirmed the continuous cooperation between the Japanese and Malaysian governments for the further progress of the Project.

II. SUMMARY OF DISCUSSIONS

Both sides agreed upon the matters as follows;

1. After long term experts started working in IMR, and as a result of their discussions with IMR counterparts on research plans, tentative schedule of implementation was revised as described in Chapter IV.

2. It is noted that research fields indicated in Chapter IV have been implemented together with Japanese experts and IMR counterparts as shown in Annex IV.

3. Scientific and technical progress having been made in each division is studied and summarized in Annex V.

4. A review team for FY 1994 will be sent at the next time by JICA to IMR around August 1994.

III. ACHIEVEMENT OF TENTATIVE SCHEDULE OF IMPLEMENTATION

The technical cooperation activities under the Project which have been carried out in Japanese fiscal year (hereinafter referred to as "FY") 1992 and 1993 are presented in ANNEX I, II and III.

IV. REVISED SCHEDULE OF IMPLEMENTATION

According to the present state of progress and other conditions of the Project, both sides jointly formulated workable Annual Implementation Plan of the Project.

The outline of the Annual Implementation Plan for FY 1993, 1994 and FY 1995 is as follows:

1. Outline of activities of the Project

1) 1st year

a. Malaria

- Laboratory set up and technical transfer of fundamental procedures in biotechnology for the purpose of malaria diagnosis.
- strengthening of laboratory procedures for HLA class I typing. establishment of method for separating lymphocytes in the field condition.
- laboratory set up, isolation of mitochondrial DNA and trials of DNA sequencing.
- laboratory set up and establishment of susceptibility bioassay of Anopheles against malaria.

b. Dengue and JE

- preparation of reagents for dengue IgM ELISA including antigens and monoclonal antibodies
- virus isolation in tissue culture and mosquito inoculation
- PCR detection of viral genome
- seroepidemiology and entomological study on Dengue and JE
- serodiagnosis on encephalitis

2) 2nd year

a. Malaria

- studies on development of diagnostic procedures, and selection and production of candidate DNA probes or primers.
- strengthening of laboratory procedures for HLA class II typing. Blood sampling and HLA typing of malaria resistant and susceptible patients.
- characterization of mitochondrial DNA in local malaria strains by analyzing fixed and variable sequence structures.
- isolation of susceptible and resistant strains of Anopheles, and chromosome mapping by enzyme markers and DNA fragment markers.

b. Dengue and JE

- routine method for serodiagnosis using the procedures established in the 1st year
- seroepidemiology of JE
- nucleotide sequence analysis of virus isolates
- year-round surveillance on the activity of Dengue and JE virus

3) 3rd year

a. Malaria

- comparative evaluation of diagnostic procedures, and DNA probes or primers.
- studies on HLA types associated with severity of malaria in Malaysia.
- sequencing of mitochondrial DNA among locally available strains of Plasmodium falciparum
- determination of malaria susceptible locus on genes in relation to other enzyme and DNA markers.

b. Dengue and JE

- comparative study on specificity and sensitivity among detection methods by virus isolation, PCR of viral genome, serodiagnosis and clinical diagnosis
- comparative sequence analysis of viral isolates to deduce pathogenic gene sequences
- prevalence of Dengue and JE virus in Malaysia

2. Plan of dispatching Japanese experts to the Project

FY 1993

a. Short-term experts

1) Parasitologist

Dr. Kiyoshi Kita Feb. 1994 (a few weeks)

2) Virologist

Dr. Futoshi Hasebe Dec. 1993 (1 month)

Dr. Akira Igarashi Feb. 1994 (a few weeks)

b. other relevant fields mutually agreed upon as necessary

FY 1994

a. Long-term experts

1) Virologist

Dr. Nobuyoshi Kobayashi

b. Short-term experts

Several specialists will be dispatched as necessary.

3. Plan of training of Malaysian counterparts in Japan

FY 1993

1) Virology

Mr. Ravindran Thayan

2) Biotechnology Center

Dr. Normaznah Bt. Yahaya

FY 1994

3 - 4 persons

4. Provision of the Equipment

Equipment necessary for the Project will be provided within the limit of allocated budget of the Japanese side.

ANNEX I

LIST OF JAPANESE EXPERTS DISPATCHED BY JICA

Chief Advisor		
1. Dr. Hiroshi Tanaka	93.01.13 - 95.01.12	(long term)
Coordinator		
2. Ms. Izumi Ohta	93.01.13 - 95.01.12	(long term)
Parasitology		
3. Dr. Takahisa Furuta	93.02.24 - 94.02.23	(long term)
4. Dr. Kiyoshi Kita	93.03.03 - 93.03.20	(short term)
5. Dr. Kiyoshi Kita	93.10.18 - 93.11.02	(short term)
Entomology		
6. Dr. Takeo Tadano	93.05.12 - 95.05.11	(long term)
7. Dr. Akio Mori	93.06.16 - 95.06.15	(long term)
Virology		
8. Dr. Kazumasa Oda	93.01.27 - 95.01.26	(long term)
9. Dr. Akira Igarashi	93.01.27 - 93.02.21	(short term)
10. Dr. Koichi Morita	93.04.14 - 93.05.12	(short term)
11. Dr. Hideaki Tsuchie	93.07.17 - 93.09.11	(short term)
Biotechnology		
12. Mr. Tatsuya Akaza	93.06.28 - 93.07.03	(short term)
13. Dr. Katsushi Tokunaga	93.06.28 - 93.07.03	(short term)

ANNEX II

LIST OF MALAYSIAN COUNTERPART PERSONNEL SENT TO JAPAN

Parasitology

1.	Mr. Ng. Chong Sing	92.11.17 - 93.02.22

Virology

2.	Mr. Victor Chew Tong Kheong	92.12.02 - 93.03.01

Entomology

3.	Dr. Indra Vythilingam	93.09.20 - 93.12.21

ANNEX III

PROVISION OF MACHINERY AND EQUIPMENT

Machineries, equipments and other materials (hereinafter referred to as "the Equipment") necessary for the implementation of the Project have been approved in FY 1992 and FY 1993.

The total amount of equipment is 73 million yens approximately on CIF basis.

The following is the list of main Equipment provided to the Institute for Medical Research.

In FY 1992 (by the budget of FY 1991 and 1992a)

Equipment	Q'ty	Divisions installed
1. Fume cupboard	2	Biot Ent
2. Autoclave	2	Biot Ent
3. Ultrafiltration System	2	Biot Vir
4. Ultrapure water	2	Ent Vir
5. Ice Machine	1	Biot
6. Deep Freezer -80 C	1	Ent
7. Deep Freezer -20 C	1	Vir
8. Chromatography	1	Biot
9. Refrigerated Centrifuge Eppendorf	3	Biot Ent Vir
10. Refrigerated high speed centrifuge	2	Biot Vir
11. Electronic balance	1	Biot
12. Shaking incubator	2	Biot Vir
13. CO 2 incubator	2	Ent Vir
14. Microplate reader	1	Vir
15. Microplate reader UV	1	Biot
16. HPLC Waters System	1	Biot
17. DNA Sequencing System with GS Automated Gel Loading System and GS Gene Reader	1	Biot
18. Safety Cabinet Class 2	1	Vir
19. PCR Thermal Cycler Model 9600	2	Biot Vir
20. PCR Thermal Cycler Model 480	1	Ent

21. PCR Thermal Cycler Iwaki TRS-300	1			Vir	
22. Microplate Washer	1			Vir	
23. SpeedVac Centrifuge	1	Biot			
24. Vacuum Blotter	1	Biot			
25. Hybridization Oven	1	Biot			
26. Dot Blot Apparatus	1			Vir	
27. Electroporator	1	Biot			
28. Pulse Field Electrophoresis	1	Biot			
29. Multichannel Pipette (8)	2	Biot		Vir	
30. Gilson Pipettes (Micro)	1	Biot			
31. Holten Laminair HV 2448 Clean Bench	1			Vir	
32. Photodocumentation System	1	Biot			
33. Mitsubishi Pajero 4WD	1				Proj
34. Sharp Plain Paper Copier	1				Proj
35. WYSE Decision Computer with Laser Printer	1	Biot			
36. Bellco Pipette Aid	10	Biot	Ent		
37. Vacuum pump, Oil-Less Diaphragm. DDA-P104-BN	1	Biot			
38. Air-Conditioner Split Unit 2HP	4	Biot			
39. Tissue Homogenizer with 6 5ml and 6 10ml pestles	1	Biot			
40. UV Cross Linker	1	Biot			
41. Millipore Ball Valve	2	Biot			
42. Submarine Gel System,Minicell	1	Biot			

In FY 1993 (by the budget of FY 1992b)

Equipment	Q'ty	Divisions installed			
1. Overhead stirrer with stand, Heidolph, RZR 2025	2			Vir	
2. Autoclave top loading, Hirayama HA-300M	1			Vir	
3. Compact Table-top centrifuge Kubota with 3 buckets, 24X10 ml, 16X15 ml, 4x50 ml,	2	Biot		Vir	
4. Ice making machine	2		Ent	Vir	
5. Peptide Synthesizer Ecosyn P300	1	Biot			
6. Refrigerator, Sharp 225 litres, SM 25 TAL	1		Ent		
7. Incubator, ASTELL/UK JBH 800, -10 to +50 C	1		Ent		
8. Ultrasonic cell disruptor with a tip (Sonics, USA)	1	Biot			
9. Genesphere UV-100	1	Biot			

10. Waters HPLC columns, 3 units Delta-pak C18, RCM, Gen-pak Part No. 15490	1	Biot	
11. ELISA Reader	1		Ent
12. Rotors for Kubota Centrifuge 2 sets, RA 155 R and RS-1400	1	Biot	
13. Fireboy burner	2	Biot	
14. Microwave oven, Sharp Model R 4A53	1	Biot	
15. 8-channel pipette, 200 ul	2	Biot	
16. Eppendorf micropipettors		Biot	
0.5 - 10 ul	5		
10 - 100 ul	5		
100 - 1000 ul	4		
17. Eppendorf micropipettors Autoclavable		Biot	
0.5 - 10 ul	2		
10 - 100 ul	1		
100 - 1000 ul	1		

ANNEX IV. List of Japanese and IMR members responsible for each research field

Field of Research	Japanese Experts	Leader	Malaysian Counterparts
Malaria			
1. DNA Probes	Dr. T. Furuta(L) (IMSUT)	Head, Biotechnology Centre	Dr. Normaznah/Ms. Noor Rain Dr. Lokman/Dr. A. Khoo
2. Protection Epitopes	Prof. H. Tanaka(L) (Chief Advisor)		Dr. Nasuruddin/Dr. A. Khoo
3. Mitochondrial Gene	Dr. K. Kita (IMSUT)/ Dr. T. Furuta (IMSUT)		Dr. Patricia/Ms. Tan/ Mr. Ng
4. Vector of Molecular Level	Dr. T. Tadano (L)/ Dr. A. Mori (L) (Nagasaki Univ.)	Head, Medical Entomology	Dr. Indra/Ms. Rohani
Dengue/JE			
5. Rapid Diagnosis and Characterization of Dengue and J.E. by PCR, Seqencing and Igm-ELISA	Prof. A. Igarashi (Nagasaki U.)/ Dr. H. Tsuchie (Osaka Univ.)	Head, Virology	Dr. Vijayamalar/Ms. Halimah/ Mr. Ravindran
6. Epidemiological Study on Dengue and J.E.	Dr. K. Oda (L)		Dr. Vijayamalar/Mr. Chew
7. Pathogenesis of DHF Comparative Nucleotide Sequence of Viral Isolates	Dr. K. Morita (Nagasaki Univ.)		Dr. Zainah/Mr. Ravindran
8. Production of Diagnostic Reagents	Prof. A. Igarashi (Nagasaki Univ.)		Dr. Zainah/Mr. Apandi Yusop
9. Vector Studies	Dr. A. Mori (L) (Nakasaki Univ.)	Head, Medical Entomology	Dr. Indra

(L) Long term experts, (IMSUT) Institute of Medical Science, the University of Tokyo

ANNEX V.

Scientific and technical progress
Period; January to September 1993

1. Biotechnology Centre

1.1. Development of Technology.

An intensive course in 'Basic Molecular Biology' was held for 9 weeks by Dr. K. Kita and Dr. T. Furuta, and Head and all officers attended.

1.1.1. Lecture sessions

Introduction to biotechnology
Preparations of glassware, plastic ware and reagents
Extraction of plasmid DNA
Use of restriction enzymes

1.1.2. Practical sessions

Preparation of medium and agar plates
Extraction of mitochondrial DNA from Plasmodium falciparum
Extraction of RNA from P. falciparum
Determination of bacterial cell count
Extraction of plasmid DNA using mini-prep
Restriction enzyme digestion and agarose gel electrophoresis
Preparation of insert fragment for ligation
Vector DNA for ligation
Ligation
preparation of competent cells, and transformation
polymerase chain reaction, including double PCR, enzyme detection PCR and plate hybridization PCR
DNA sequencing
Thermal cycle DNA sequencing with chemiluminescence

1.2. Research Activities.

1.2.1. DNA probes for malaria diagnosis

1.2.1.1. Blood sample collection: About 40 blood samples were collected from patients at the Orang Asli Hospital in Gombak, Selangor and Kuala Lumpur General Hospital. About 500 samples were collected during a field survey in an Orang Asli Settlement, Betau in the State of Pahang by Dr. Lokman Hakim, Dr. Alan Khoo and Dr. Furuta.

1.2.1.2. Restriction enzymatic analysis: Genomic DNA from Plasmodium falciparum was extracted from 27 isolates. The digestion of the genomic DNA was carried out using 10 restriction enzymes: Pst-1, EcoR1, HindIII, SalI, SacI, BamHI, HaeIII, HhaI and AluI. Preliminary analysis of the digestion pattern did not show any marked difference between the isolates. PCR amplification was also carried out on genomic DNA and their amplified products were compared after digestion with restriction enzymes to examine the difference between isolates. By this, different banding patterns were recognized among isolates when PCR amplified products were cut by Hind III.

1.2.1.3. Polymerase chain reaction

a. Nested PCR: The test results of 23 positive and 12 negative blood samples indicated that 3 sets of primers out of 4 gave good results of 100% sensitivity and specificity. A remaining set did not work well.

b. Enzyme detection-Polymerase chain reaction (ED-PCR); ED-PCR were carried out on 12 samples. In this preliminary test, the sensitivity and specificity were 100%.

c. Plate hybridization-Polymerase chain reaction (PH-PCR); By PH-PCR, 47 blood samples were examined. The probes gave specific results that differentiate between P. falciparum and P. vivax infections. In this preliminary test, the sensitivity and specificity were 94%.

1.2.2. Mitochondrial DNA

Project on mitochondrial DNA extraction was carried out. As researchers are encountered difficulties due to the incomplete function of an upright type of homogenizer, DNA sequencer and DNA sequence film reader, the project was hampered much. These problems have been solved. The sequence of mitochondrial genes in P. vivax will be studied first.

1.2.3. HLA studies and malaria resistance

The main objective of this plan is to study the relationship of any between HLA and resistance to P. falciparum infection.

Two Japanese experts made a plan to strengthen the HLA testing. The recommendation for the serological test design for HLA class I which is analyzed in Tokyo will be sent to the laboratory. The human blood samples collected will be examined for class I by the recommended procedures and DNA isolated from the sample will be preserved in a freezer.

In 1994, a technologist in the division will be sent to Japanese Red Cross with these preserved samples to learn the biotechnological test method of class II and to examine the samples for class II.

2. Division of Medical Entomology

a. Biotechnology: Since Dr. Akio Mori arrived at IMR in June 1993, a room in the insectary was completely renovated into a laboratory for biotechnological works. The revision of research protocol was completed and the plan of study is defined to determine the malaria susceptible or resistant genes of chromosomes of Anopheles maculatus. Trials are being made to isolate resistant and susceptible strains of An. maculatus against Plasmodium. Since the completion of all laboratory facilities will take 6 months more, his laboratory activities will be conducted in the Biotechnology Centre for the time being. For this study, special strains of P. falciparum producing a lot of gametocytes are necessary, and efforts are being made to obtain such strains.

b. Genetics of Anopheles: Another room in the insectary was renovated for a genetics laboratory for Dr. T. Tadano at his arrival in May 1993, and laboratory set up was almost completed. The main objectives are to

detect the malaria susceptible site on An. maculatus chromosomes using enzyme markers. An artificial anopheline blood feeding technique was established by modifying the method using moistened "Baudruche" membrane.

Out of 3 peninsular Malaysian strains and 1 Sabah strain of An. maculatus tested for isozyme variants, the Jeram Kedah (JK) and Kuala Milot (KM) have been selected for the fast allele(F) and slow allele(S), respectively, for 3 generations in order to purify each of the two alleles (F and S).

c. Mosquito transmission of JE: collaborated with Division of Virology. Refer 3.2.2.b.

3. Division of Virology

3.1. Development of Technology

Laboratory set up and technical transfer were performed by Prof. Igarashi, Dr. Morita and Dr. Tsuchie, and subjects improved were as follows;

Set up of PCR facilities
Technical transfer of PCR procedures for Dengue and JE diagnosis
Molecular cloning and direct sequencing of the JE virus isolates
Direct sequencing of the JE isolate
A modified protocol for the PCR technique

3.2. Scientific Activities

3.2.1. Biotechnological studies

Arrangements were made with General Hospital Kuala Lumpur to obtain fresh serum samples from suspected Dengue cases to increase the chances of isolating Dengue virus and to facilitate for the plans to sequence the Malaysian Dengue & JE virus strain.

PCR was attempted on 16 clinical human samples, and Dengue type 3 virus was detected in 3 out of those samples. The presence of Dengue virus was detected in 8 of the tissue culture samples by PCR and none from the serum samples.

PCR was also conducted on the 26 JE isolates obtained by PAP staining. JE virus was detected in 19 of them.

3.2.2. Epidemiology

a. Antibody detection from animal sera

By the agreement with Dr. Jane Cardosa from USM, Penang and Dr. Sharifah from Veterinary Research Institute (VRI), Ipoh to collaborate with the JICA-IMR project, serum samples were submitted.

As part of the epidemiological studies on Japanese encephalitis, a total of 1699 samples have been examined. Serum samples showing positive haemagglutination inhibition (HI), reactive at serum dilution at 1:10 or more, were defined as positive. The positive rates were 95/95 (100%) in pigs, 55/96 (57.3%) in buffaloes, 237/576 (41.5%) in

cattle, 70/347 (20.7%) in sheep, 63/449 (14.0%) in goats, and 1/96 (1.0%) in birds.

b. Isolation of JE virus from mosquitoes

The cell culture system using C6/63 cell line for isolation of Japanese encephalitis and dengue viruses were set up.

A total of 77 pools of field-collected Culex mosquitoes were assayed for the presence of JE virus by using 3 methods. No JE virus was detected in these mosquitoes using larval inoculation method and PCR amplification.

For isolation of JE virus, of 123 mosquito pools tested, 26 isolates were obtained. There were 8 isolates from Culex tritaeniorhynchus, 7 from Cx. vishnui, 3 from Cx. sp. B, 2 from Cx. sitiens, 1 from Cx. pseudovishnui, 1 from Cx. gelidius, 2 from Culex mixtures and 1 from an Aedes mixture. Cx. sitiens and Cx. sp. B would be new mosquitoes as the transmitter of JE.

4. List of Publications

Vythilingam, I., Oda, K., Tsuchie, H., Mahadevan, H. S. and Vijayamalar, B. Research Note: Isolation of Japanese encephalitis virus from Culex sitiens in Selangor, Malaysia. submitted to Journal of American Mosquito Control Association on 11 Sept. 1993

Lee, H. L. & Tadano, T. Monitoring resistance gene frequencies in Malaysian Culex quinquefasciatus Say adults using rapid non-specific esterase enzyme microassay. Submitted to Southeast Asian J. Trop. Med. Pub. Hlth.

2）プロジェクトから提出された現況レポート

INSTITUTE FOR MEDICAL RESEARCH AND
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プロジェクト名； マレーシア国　熱帯病研究プロジェクト

Institute for Medical Research と日本の技術協力プロジェクトの概況

1993 年 10 月 15 日
Chief Advisor 田中 寛
調整員 大田 泉

本プロジェクトの設立

1990 年 1 月　中山外務大臣とマレイシア首相 DR. MAHATHIR の両 MD 間の会談で熱帯医学分野の研究協力について留意された。
1990 年 3 月　第１次調査団を派遣　各省と東大
1990 年 4 月　第２次調査団を派遣　国際協力事業団と長崎大
｜　協力対象をＩＭＲとして課題の検討
1992 年 6 月　ＲＤ が結ばれる
1993 年 1 月　技術協力プロジェクト方式を開始。期間３年の予定

Institute for Medical Research（ＩＭＲ）の概況

創立　1901 年　英国により創立　東大医科研（1892 年創立）
1957 年　独立以前は英国人部長による
戦時中の所長に日本人２名が任命されている。
1967 年以来　全部長がマレー国民で占められる。
数年前まで Hooper Foundation, US Army Medical Research Unit.が所内に研究所をもっており、近年も SEAMEO-TROPMED, WHO, SEAMIC など国際機関との連携も多い。

所長名　Dato Dr. M. Jegathesan
Project 部長名　Dr. Mak Joon Wah, MBBS, Head, Biotechnology Centre
Mr. Lee Han Lim, MSc, Head, Medical Entomology
Dr. Vijayamalar B., MBBS, Acting Head, Virology

職員概数　研究者、講師　１３１名
技術職員　４４３名
管理系職員　６０名

予算規模　(million Ringgit, m RM)　1992 年　　RM = JY 43

政府予算（管理費、人頭割当）	m RM 15.0
検査技術学校奨学金	2.2
科学研究費	3.0
受託予算　TRUST ACCOUNTS SEAMEO-TROPMED/WHO	0.3
改築営繕	1.0
総計	21.5

組織　　所長、副所長
ADMINISTRATIONS
DIVISIONS　　＊ JICA Project 関連部

	ACAROLOGY	ダニ学
	BACTERIOLOGY	細菌学
	BEHAVIOURAL RESEARCH	人類生態学
	BIOCHEMISTRY	生化学
＊	BIOTECHNOLOGY CENTRE	生物技術センター
	CYTOLOGY	細胞学
	EPIDEMIOLOGY AND BIOSTATISTICS	疫学・生物統計
	HAEMATOLOGY	血液学
	HUMAN NUTRITION	栄養学
	IMMUNOLOGY　＊ HLA laboratory	免疫学
	LABORATORY ANIMAL RESOURCES	実験動物管理
	LIBRARY, INFORMATION OAND PUBLICATION	図書情報
	MEDICAL ECOLOGY (MUSEUM)	医学生態系
＊	MEDICAL ENTOMOLOGY	医用昆虫学
	PARASITOLOGY (ELECTRON MICROSCOPY)	寄生虫学
	PATHOLOGY	病理学
	RADIOCHEMISTRY	放射線化学
	STOMATOLOGY	口腔学
＊	VIROLOGY	ウイルス学
	CLINICAL RESEARCH CENTRE	臨床検査センター
	COMPUTER UNIT	コンピューター室
	SNAKE FARM	蛇飼育場
	SCHOOL OF MEDICAL AND HEALTH LABORATORY TECHNOLOGY	医学検査学校

国際機関
SEAMEO-TROPMED
  DIPLOMA COURSE IN APPLIED PARASITOLOGY AND ENTOMOLOGY (6 months)
  DIPLOMA COURSE IN MEDICAL MICROBIOLOGY (6 months)
WHO REGIONAL CENTRE FOR RESEARCH AND TRAINING IN TROPICAL DISEASES AND NUTRITION
WHO REGIONAL ANTI-MALARIA TEAM
IMR-JICA RESEARCH PROJECT ON TROPICAL DISEASES　＊

技術協力の概要
R／D；　1992 年 6 月 22 日
協力期間；　1993 年 1 月 ～ 1995 年 12 月、 3年間

主要目標　生物技術（バイテク）手法の熱帯病研究への導入；
－－ マラリア、デング、日本脳炎の診断と管理方法の強化

日本側の技術諮問機関　(TOKYO TAC)　東大医学部国際交流室
開原 成允 教授　東大医学部医療情報
福原俊一 助教授　東大医学部国際交流室
五十嵐 章 教授　長崎大学熱研ウイルス学
小島 荘明 教授　東大医科研寄生虫部
森田公一 助教授、 北 潔 助教授

具体的な課題
マラリア　遺伝子診断用のＤＮＡ探索子の開発
長期専門家 古田隆久 博士
原虫内のミトコンドリアＤＮＡ配列の読み取りと分析
北 助教授 担当
人のマラリア抵抗性を支配するリンパ球型（HLA）の検索
田中 寛 担当
昆虫学　マラリア媒介蚊 Anopheles のマラリア感受性遺伝子の酵素マーカーを用いた検索
長期専門家 只野長夫 博士
同上遺伝子の核酸マーカーを用いた検索
長期専門家 森 章夫 博士
ウイルス学　日本脳炎の疫学的研究（動物、媒介蚊、人）
デング熱の疫学研究
長期専門家 小田和正 博士
日本脳炎イウルスの遺伝子診断（ＰＣＲ）
デング熱の診断
ウイルスの遺伝子診断と型分け（ＰＣＲ）
ＩｇＭ抗体の検出法の改良
デング熱ウイルスの病原性遺伝子の探索
土江秀明 教官（阪大微研）短期滞在
森田 助教授 担当

プロジェクトの進行と成果の概要

１９９３年１０月２０日　現在

プロジェクト開始の平成５年１月より１０月までの、進行状況と主要な成果は以下の通りである。本プロジェクトは長期専門家が早期に赴任して充実し、機材が早く設置され、本研究所の既存の設備とともに、仕事が早期に開始された。

チーフアドバイザーの田中と調整員の大田が１月１３日に赴任し、現在までに長期専門家（１年以上の任期）６名、短期専門家６名を受け入れている。

１９９２年より、研修員の受入を開始し、現在まで３名（各人３カ月）を日本に受け入れている。

機材は現地調達で行い、１９９３年２月末までに、６千万円（平成３年度と４年度の一部の予算）の機材の発注を終了し、３月末に納入され、研究室に設置された。現在１３００万円（１９９２年度予算）の機材が納入されつつある。１９９３年度の日本への機材要請が、当国政府に提出されている。

日本脳炎の研究では、動物の血清で抗体検査を行い、陽性率はブタ１００％、水牛５７．３％、牛４１．５％、鳥１．０％で、当地が日本脳炎の流行地であることを初めて明らかにした。当所に冷凍保存されたイエカの類から、細胞培養でウイルスが続々と検出され、従来知られていた４種類の蚊の他に、２種類以上の日本脳炎媒介蚊が見つかっている。

蚊から分離されたウイルスは、すぐに分子生物学的に日本脳炎ウイルスと決定できた。　また、今年のデングの患者からウイルスは分子生物学的にデング３型であることも判明した。

マラリアではＰＣＲによるＤＮＡ診断で、熱帯熱マラリアの診断が行われ、予備的な小数の調査では鋭敏度、特異性ともに１００％という好成績を得、熱帯熱と三日熱の鑑別も出来た。

生物技術部、ウイルス部では、日本の専門家による、部内講習を終了した。生物技術部は研究所の中心になるので、併せて８週間も講習が行われ、部長以下研究者全員が出席し、必要な生物技術は全て行えるようになった。

ハマダラカのマラリア感受性の遺伝子の検索も開始され、染色体上の目印になる酵素産生の有無の株分けを開始し、基本的な実験系を組立てつつある。

プロジェクト関連３研究部主要人物

Biotechnology Centre

Head	Mak Joon Wah, MBBS
Research Officers	Patricia Lim Kim Chooi, PhD
	Noor Rain binti Abdullah, MSc
Medical Officers	Normaznah binti Yahaya, MD
	Lokman Hakim, MD
	Alan Khoo, MD
	古田隆久　博士 長期専門家
	北　助教授

HLA Laboratory in Immunology Head: Nasuruddin Hj. Abdulla, MD
Experimental Officer: Mohd. Zaidi bin Abu Samah, Dip. Microb.
Senior Medical Laboratory Technologist: Ong Kian Joo
Medical Laboratory Technologist: Maimelanah binti Lisut

Medical Entomology

Head	Lee Han Lim, M.Sc
Research Officers	Indra Vythilingam, PhD
	Rohani binti Ahmad, MPH
Senior Medical Laboratory Technologist	Patrick R. Nonis, AIMHLT
	只野長夫　博士　長期専門家
	森　章夫　博士　長期専門家

Virology

Head (long leave)	Mangalam Sinniah, MBBS
Acting Head	Vijayamalar Balasubramaniam, MBBS
Medical Officer	Zainah Sa'at, MBBS
Research Officers	Haliman Mohamed, BSc
	Rabindran Thayan, BSc
Senior Medical Laboratory Technologist	Arthur Jebaratnam, AIMLT

小田和正　博士　長期専門家　　五十嵐　章　教授　長崎大熱研
森田公一　助教授　長崎大学　　土江秀明　博士　阪大微研

協力部門別進捗状況　　生物技術中心（バイテクセンター）

1。部内研修

当所北、古田で部内研修をスタートさせ、後半は古田が担当し、総計して9週間行った。講義と実習が含まれている。行った内容は以下の通りである。

DNA フェノール抽出法
アガロース電気泳動法
制限酵素の使用法
プラスミド DNA の調整
DNA クローニング法
ＰＣＲ法　NESTED PCR
　　ENZYMATIC DETECTIVE PCR
　　PLATE HYBRIDIZATION PCR
ＤＮＡ SEQUENCE 法　M13mp 系ファージ　PUC 系プラスミドからの
　　TEMPLATE DNA の調整
CHEMILUMINESCENCE による CYCLE DNA SEQUENCING 法

2。研究課題の進展

a. マラリア診断用 PROBE および PRIMER の開発

a-1. 部内で 61 株のマラリア原虫株が培養維持されており、世界的にもこれだけ保持している研究室は希である。そのマラリア原虫 30 株から DNA の抽出を行った。それぞれの RFLP を調べている。その結果ほとんどのものが同じ様な切断パターンを示したが、一部に異なったパターンがみられ。さらに検討を進めている。

a-2. 熱帯熱マラリアに対する PRIMER 4 種に付いて NESTED PCR を行い、そのうち３種類は予備試験で特異性、鋭敏度ともにすぐれていた。

a-3. 他の PRIMER でビオチン標識されているものを用い、酵素抗体法で発色反応させる方式も試みて、良い精度が得られた。

a-4. 現在 DNA 解析、PRIMER 設計用のコンピュータシステムがないが、設置されれば、PRIMER 設計が可能になる。DNA SYNTHESIZER はあるが、PRIMER 設計がしにくいのと、一度に多数の PRIMER を作らないと、経済効率が悪い。当地で外注の方法も調べたので、これの利用も考慮すべきである。目下のところ、PRIMER 設計は日本で行う方が効率的である。

b. ミトコンドリア DNA の解析。

培養マラリア原虫から Mt DNA を分離、解析後、マラリア診断に有用なプローブや PRIMER を得ようとするものである。現在まで3度 Mt DNA の分離精製を試みたが成功していない。研究の遅れに関して、C／Pの研究意欲に問題があるようにも思える。研究が促進されなければ、C／Pの変更も考慮する必要が生じよう。

c. マラリアとＨＬＡの関連研究

マラリア感染における防御機構の一端をＨＬＡが担っていると思われる。7月初旬に短期専門家によって計画が企画された。TYPE 1 はＨＬＡ室で行い、実験室の行程の整理と強化が必要である。TYPE 2 については、日本に試料を持って研修員を送り、技術を修得するとともに、試験をすませる予定である。

専門家の業務活動　　古田隆久

当部には北助教授が２度短期で指導にこられているのみである。その他当部の進捗が殆ど長期専門家の活動を示すものである。主要な項目をあげると以下のようになる。

１。分子生物学の基礎的な技術講習会を通して技術移転を行った。

２。血液サンプルの収集のために７月５日－７月９日の間、マラリア流行地である PAHANG 州 BUTAU のジャングルへ原住民のマラリア患者材料の収集のために、研究部のスタッフと共に出張した。

３。各種研究の指導を行った。

４。Ａ４ FORM による機器の運転と、職員の管理を見守り、指導しているが、業者からの納入上の問題もなく、順調に行われている。

５。研究成果の公表。

１２月４日にマレイシア政府、科学技術庁主催の NATIONAL BIOTECHNOLOGY SEMINAR で研究の一部を発表する予定である。また、学術誌への投稿も準備中である。

協力部門別進捗状況　　医昆虫学

医昆虫部には只野専門家が５月に、森専門家が６月に着任して活動を開始した。また、５月末に部長の DR INDER SINGH が定年退職し、MR LEE が ACTING HEAD に任命された。

当部の本来の研究室は改造中で暫定的に所内に分散されているので、昆虫飼育棟に２室を改装し、只野、森　用の研究室とすることにし、プロジェクト中は２室は移動しないことになった。２室とも水道、電気の設備が不十分で、ＪＩＣＡの供与機器が活用できない恐れが生じ、早急な改善を申し出ている。当部の設備、備品の使用および保管状態は悪く、専門家の必要とするレベルに保たれた機器は少ない。多少とも最新の機器もあるが、概して貴重な機器は研究者各自の手元にしまわれていて、自由な使用はしにくい。

実験室の環境は分子生物学的に必要な環境の清浄度が低く、分子生物学的な手技の定着のためには、現状の SCIENTIST, TECHNICIAN, WORKER の手技および研究室での動作、行動を改める必要があり、仕事の進行につれて、教育する必要があり、そのつもりでいる。

目下、只野専門家はマレーシア半島部でのマラリアの主要媒介蚊である Anopheles maculatus のマラリア感受性遺伝子の検索のため、この蚊の酵素多型の発見に務め、この手技を Ｃ／Ｐ の MRS. ROHANI binti AHMAD に修得させつつある。

森専門家は Ｃ／Ｐ である DR INDRA が９月１９日より長崎大学で研修中であるので、この間に Anopheles maculatus のマラリア感受性系統と抵抗性系統の淘汰分離を進めている。またＱＴＬ(QUANTITATIVE TRAIT LOCI) MAPPING に用いるのに適する熱帯熱マラリア培養株を入手し培養保存している。飼育棟の中の研究室の機器が揃わず、その室で分子生物学的な仕事は出来ないので、当分の間、 BIOTECHNOLOGY CENTRE の第１室で仕事をすることにした。

専門家の業務活動　　只野長夫

1. 研究環境の改善

赴任以来５カ月で、暫定的に必要な化学薬品やガラス器具の購入、搬入はほぼ終了した。

現在のところ、IMR の MEDICAL ENTOMOLOGY の旧来の方法で、一部の電気泳動実験を行なっているが、二つの部屋でこの種の実験が出来るように改善を行なっている。そのために、MINOR な機材、用具（電源伸長用コード、飼育用器具など）を直接、百貨店で購入することが多い。また、コンセントの位置の関係などで器具の配置替えも必要であった。

2. 実験材料の作成

マレー半島の4系統とサバ系統のハマダラカ Anopheles maculatus から ISOZYME 変異株の分離を STARCH GEL 法で行なっている。AGAR GEL 法の準備が出来次第、この分離は、AGAR GEL 法で行なう予定である。今後、新しい系統を野外から採集して蚊材料を補充する予定であり、これらの実験は Ｃ／Ｐ との共同作業で行なっている。

3. COUNTERPART との研究計画連絡

Ｃ／Ｐ との計画連絡は随時行ない、確認のため紙面でも行なっている。また、その計画理解のために、MINOR な機材の購入をも Ｃ／Ｐ に説明している。

専門家の業務活動　　森　章夫

ＴＳＩでの研究課題はマラリア媒介蚊のマラリア感受性遺伝子の核酸構造の解析であるが、赴任以来計画書をまとめる段階で、当初計画の大幅な変更が必要となった。遺伝子の核酸構造の研究には、まず当該遺伝子の染色体上の正確な位置の決定が必要である。関連する研究で、マラリア感受性遺伝子の位置は Anopheles gambiae や Aedes aegypti で２カ所にあるとされている。当課題の Anopheles maculatus では全く不明である。この位置の決定には、cDNA probe をマーカーとして、関連する遺伝子の数と位置を正確に推定することを中心に、詳細な計画書作成から始めた。

当初ＩＭＲの中で、熱帯熱マラリア患者の血液でアノフェレス感受性、および抵抗性系統の淘汰と純粋株の作成ができると聞いていたが、実験に必要な量と頻度、治療剤混入のない適切な材料のが入手できないことも判明した。そのために蚊のなかで、卵嚢子をつくるための GAMETOCYTE を産製する熱帯熱マラリアの培養株を大阪工業大学田辺和裕博士より分与をうけて、当所に定着させようとしている。

一方 Anopheles maculatus のマラリア感受性、抵抗性株の作成を Plasmodium gallinaceum を用いて行いつつある。

与えられた実験室は古い昆虫飼育室の一部を改装したもので、電源、水道の整備を行いつつある。なお、必要機器の購入が十分行われていないため、不足のものが多々ある。一方では機器が全部設置された場合の電気容量にも問題があり、その改善も行ないつつある。現在、純水製造装置、製氷機を設置しつつある。また、Ｃ／Ｐ　DR. INDRA が日本で研修中であり、有能な代替者もいない。この室の完成を無為に待つ事もないので、田中 CHIEF ADVISOR, DR. MAK JOON WAH の勧めで、実験室が完成するまで、BIOTECHNOLOGY CENTRE で仕事をすることにした。

協力部門別進捗状況　　ウイルス学

実行計画書に示されているように、当部の課題は日本脳炎とデングの疫学とウイルスの分子生物学的解析に大別される。

1．疫学

1．1．日本脳炎

a．蚊からウイルスの分離；当所の昆虫学部との共同により、昆虫学部で採集同定した野外蚊から C6/36細胞により日本脳炎ウイルスを分離している。現在までに 143 グループが供試され、26 株（18.2%）からウイルスが分離され、酵素抗体法で陽性を示しそのうち 19 株がＰＣＲで陽性を示している。ウイルスを保有する蚊の種類が多い、しかも陽性率が高いことが、熱帯地マレイシアの特徴と考えられる。

b．日本脳炎の血清疫学；

VETERINARY RESEARCH INSTITUTE (VRI, Dr. Sharifah) との共同研究により、マレイシア VRI の８支所で、ブタ、野牛、水牛、山羊、羊、野鳥から採血された動物血清について、血球凝集阻抗体を測定し、ウイルスの分布を調査した。現在までに、1,699 検体を調べ、陽性率は 33.0%，抗体価は 10 倍から 640 倍に分布し、専門家の業務活動で述べるように、動物間に反応の有意な差を認めた。

1．2．デング熱およびデング出血熱

隣接する総合病院との共同により、提供されたデング熱患者の血液からデングウイルスを分離し、さらにその型別を行い、患者診断に資するとともに疫学的要因の解析に努めている。現在患者血液 80 例から 19 例（23.8%）が陽性であり、本年は３型の流行と思われる。

2．分子生物学的解析

日本脳炎、デング熱ともに分離ウイルスおよび供試材料（蚊、血液）からのウイルス遺伝子検索に PCR を適用し、その実用化による迅速診断法の検討が行われた。さらに基礎的研究として、日本脳炎ウイルスについては PCR によるウイルス遺伝子の検出とクローニング、および化学発光による DNA SEQUENCING と SOUTHERN HYBRIDIZATION による遺伝子解析が試みられた。

デング熱についても患者血液から RT-PCR によりデング遺伝子を検出し、ウイルスの型別まで可能になった。

これらの分子生物学的原理と手技はＣ／Ｐへ積極的に技術移転され、所定の目的が得られた。今後これらの技術の定着と実用化により多くの研究成果が得られるものと期待される。

専門家の業務活動　　小田和正

日本脳炎の人の分布の調査には手続きを要するので、手早くできる動物の血清の提供をうけて、マレーシアにおける日脳の有無、分布、流行の度合いの概要をつかむために、血清の抗体価を調べた。一方では、日脳ウイルス分離の為に冷凍保存してあったイエカよりのウイルス分離も行い、疫学相をあきらかにした。

1。動物血清の検査結果

動物血清の抗体を凝集阻止反応 (HI) で測定した。現在までに 1,699 検体を調べ、ブタ 100% (陽性数 95/被検数 95)、野牛 41.5% (239/576)、水牛57.3 % (55/96)、羊 20.2% (70/347)、山羊 14.0% (64/449)、および野鳥 (ｽｽﾞﾒ､ｳｽﾞﾗ) 1.0% (1/96) の各陽性率を示し、全体の陽性率は 33.0% (561/1,699)であった。これらの成績からマレイシアにおける日脳ウイルスの増幅動物の主役はブタであり、野鳥の関与は小さく、羊、山羊も低率であると考えられる。

2。蚊からのウイルス分離

SELANGOR 州で 1992 年に野外で採集され、種類別に保存された蚊について、C6/36 細胞により日本脳炎ウイルスの分離を行った。最終時に吸血している蚊を除外し、５０個体を１プールにしてある。１０月中旬までに 143 プールを調べ、26 プールが PAP (酵素抗体法) でウイルス陽性であり、このうち 19 株が PCR で日脳と同定された。蚊の種別による陽性株数は Culex tritaeniorhynchus 8 (PCR 陽性 6), Cx. sp. B 3 (3), Cx. vishnui 7 (4), Cx. pseudovishnui 1 (0), Cx. citiens 2 (2), Cx. gelidus 1 (0), Cx. spp 3 (3), Aedes spp 1 (1), の 8 (6) 種類、26 プール (19) がウイルス陽性を示し、Cx. tritaeniorhynchus ほか、多数の蚊からウイルスが検出された。
Cx. sitiens, Cx. sp B からの日脳ウイルスの分離されたのは始めてのことであり、さらにその他の種類からも分離される可能性がある。

3。当国の日脳の流行状況

以上を総合して、日脳は当国で広く蔓延している事が初めて明らかにされ、その媒介蚊の種類も多数にのぼり、新しい媒介蚊もさらに追加されるであろう。人の感染の様相などを探るのが次の課題で、病院からの材料、地域的な調査を計画中である。

3）WHO/IMRの活動レポート

14th. WHO/IMR Coordination Meeting of the WHO Regional Centre for Research and Training in Tropical Diseases

IMR, Kuala Lumpur, Malaysia 25th. October 1993

1992 IMR PROGRESS REPORT IN ITS ROLE AS THE REGIONAL CENTRE FOR RESEARCH AND TRAINING IN TROPICAL DISEASES AND NUTRITION

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Director

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Kuala Lumpur
Malaysia

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1. GENERAL INFORMATION

1.1 Organization of the IMR

The IMR comes directly under the jurisdiction of the Ministry of Health, Malaysia, and is therefore a Government institution. The Institute provides considerable inputs to the health programmes of the country by way of research, diagnostic services, training and consultative services.

1.1.1 Scientific Departments

The divisions in the IMR are grouped into departments. These are as follows:

Department	Division
TROPICAL MEDICINE & INFECTIOUS DISEASES Dr. Mak Joon Wah	Parasitology Entomology Medical Ecology Acarology Bacteriology Virology
CLINICAL & EXPERIMENTAL PATHOLOGY Dr. Khalid Hassan	Histopathology Cytopathology Stomatopathology Haematology Biochemistry Immunology Endocrinology
COMMUNITY MEDICINE Dr. Lye Munn Sann	Epidemiology & Biostatistics Behavioural Research Human Nutrition
SUPPORT SERVICES Dr. Ismail	Biotechnology Centre Clinical Research Centre Library Medical Illustration Electron Microscopy Lab Animal Centre Computer Engineering

1.1.2 Other Sections of the IMR
1.1.2.1. Training facilities (permanent courses)
i. School of Medical Laboratory Technology
- Basic Course
- Advanced Course
ii. Diploma in Applied Parasitology and Entomology (DAP&E) (SEAMEO-TROPMED)
iii. Diploma in Applied Microbiology (DMM) (SEAMEO-TROPMED)

1.1.2.2. Administrative sections
i. Service
ii. Finance
iii. Stores

1.1.2.3. International affiliations
i. WHO Regional Centre for Research and Training in Tropical Diseases and Nutrition
ii. WHO Regional Anti-Malarial Team
iii. National Centre for Tropical Medicine, SEAMEO (SEAMEO-TROPMED)
iv. Secretariat for the Inter-Islamic Network on Tropical Medicine (IFSTAD)

1.2 Staff

The professional, laboratory and other categories of staff of the IMR as at 15 Aug 1993 are as listed below:

Staff Category	Posts		
	No. filled	Vacancies	Total on the Establishment
A. Professional Staf			
Director	1	-	1
Deputy Director	1	-	1
Medical Officers	41	16	57
Research Officers	56	8	64
Dental Officers	3	-	3
Veterinarian	1	-	1
Librarian	2	-	2
Pharmacist	0	1	1
Administrators	1	-	1
SUB-TOTAL	106	24	131
B. Supporting Staff			
MLT Tutors	22	5	27
MLT	147	11	158
Asst. MLT	41	5	46
Other Categories	220	52	22
TOTAL	430	73	503

1.3 Funding

The following were the IMR's sources of funding in 1992:

SOURCE	AMOUNT (RM)
1. Malaysian Government:	
i. For personnel emoluments and operating expenditure	14 988 414.00
ii. Training and scholarship allowances (for trainees attending IMR's senior and junior MLT courses)	2 165 460.00
iii. Research & development grants (Ministry of Science, Technology & Environment)	2 955 180.00
2. Trust Accounts (SEAMEO-TROPMED & WHO)	332 935.00
3. Development (heritage building)	1 030 000.00
TOTAL	21 471 989.00

US$ 1.00 = MR 2.50 (approx.)

1.4 Diagnostic Services

The divisions in the Institute continued to perform various routine and specialised tests, totalling close to 500 000 in the year. There were no major changes in the types of tests carried out by the Divisions. However, compared with figures in 1991, there were significant changes in the number of tests. Six Divisions reported increases in the total number of tests carried out in the year compared to the ffigures for 1991. The increase was less than 15% for 4 of these Divisions, while the Division of Entomology reported an increase of over 60%. On the other hand, 9 Divisions reported decreases in the number of tests carried out, with decreases ranging from 5 to 41%. Overall, the total number of tests carried out in 1992 showed an increase of 7% over the 1991 figure.

1.5 IMR 90th. Anniversary Celebrations

The IMR commemorated its 90th. Anniversary in the year. Among the activities held were a scientific seminar and a Family Day.

The scientific seminar was held on 23-25 June. The main objectives of the seminar were to review the achievements of medical research carried out by researchers in Malaysia during the last 15 years and to determine the future direction and emphasis of activities in the Institute in relation to health care needs of the country. Invited speakers included the Director-General of Health, prominent scientists from local institutions and abroad, as well as international organizations.

1.6 External Evaluation of the WHO Regional Centre for Research and Training in Tropical Diseases and Nutrition by WHO Task Force

Following the recommendation of the 13th. session of the Western Pacific Advisory Committee on Health Research (WPACHR) in July 1990, a task force was convened to undertake an external evaluation of the WHO Regional Centre for Research and Training in Tropical Diseases and Nutrition, IMR.

The Task Force visited the IMR from 29 June to 6th. July 1992. In its report, it stated that the efforts made by the IMR in developing and carrying out research and training programmes were impressive. Most of the short-term and medium-term goals had been achieved, while the long-term goals, especially in regional collaboration, are being actively pursued. It congratulated the IMR on its long history of excellence and contributions to medical sciences and for the training of biomedical scientists and technicians from Malaysia, countries of the Western Pacific and South-East Asia Regions as well as other parts of the world. The Task Force recommended that the terms of the original agreement be retained except for the addition of "non-communicable diseases" and "nutrition" in the objectives and plan of action. The report also contained recommendations with regard to personnel, training, linkages, the diagnostic services performed by the IMR, and specific recommendations about individual divisions and facilities of the IMR.

The Task Force also recommended that future thrust of IMR activities should be in the areas of clinical epidemiology, clinical nutrition, molecular biology and biotechnology, behavioural sciences, clinical research, occupational medicine, environmental health and non-communicable diseases. It suggested that full use be made of the programmes initiated by the IMR and of future collaborative efforts with the Japanese International Coorporation Agency (JICA) to enhance the Regional Centre.

2. RESEARCH

2.1 Research Projects and Funds, 1992

A total of 55 research projects were funded by the Research and Development Grants from the Ministry of Science, Technology and Environment under the programme for the Intensification of Research in Priority Areas, IRPA). Another 29 projects were funded by the regular budget of the divisions of the IMR and another 2 were funded by the World Health Organization. The number of projects funded, by division, is as follows.

Table 1

IMR Research Projects, 1992, funded by R&D Grants from the NCSRD

Division of the IMR	No. of Projects
Acarology	6
Bacteriology	2
Behavioural Research	1
Biochemistry	7
Biotechnology	6
Clinical Research	1
Entomology	10
Epidemiology	1
Haematology	4
Immunology	2
Medical Ecology	2
Nutrition	5
Parasitology	2
Radiochemistry	3
Stomatology	1
Virology	2
Total	55
RM 2.6 Million	

Table 2
IMR Funded Research Projects, funded by Division Funds of the IMR

Division of the IMR	No. of Projects
Acarology	1
Animal House	1
Bacteriology	7
Behavioural Research	1
Biochemistry	1
Biotechnology	1
Cytology	2
Epidemiology	3
Nutrition	1
Parasitology	6
Radiochemistry	1
Virology	4
Total	29

Projects funded by WHO Research Grants, 1991/92

The IMR Research projects funded by the WHO in 1992 were as follows:

Source	Principle Investigator	Project	Amount (US$)
TDR	Dr. Mak Joon Wah	Screening potential filaricides against *B. malayi* infection in *Presbytis* spp.	47 450
TDR	Mr. Lee Han Lim	Entomological and parasitological evaluation of the effect of *B. thuringiensis* on malaria in Malaysia	29 050
		TOTAL	76 590

2.2 Publications, 1992

138 scientific papers were published by research workers of the Institute. 84 of these were published in either international or local journals while an additional 54 had been accepted for publication. In addition, there were 2 Ph.D. theses and 17 reports.

2.3 Highlights of Research projects in Tropical Diseases and Nutrition, 1992

In keeping with the Ministry of Health's priorities, research efforts are directed at the characterization of health problems, and, more importantly, at their solution. Health research at the IMR attempts, wherever possible, to achieve this goal through

i. the provision of leads in decision-making for programme managers and administrators,

ii. assistance to health administrators and communities for the utilization and application of available technology for the control of important diseases, and

iii. contribution to the increase of basic knowledge related to disease control and prevention.

The following are some highlights of the research undertakings at the IMR at various disciplines of tropical diseases and nutrition in 1992.

2.4.1 Malaria

B-cell epitopes of Plasmodium vivax Circumsporozoite proteins: Scanning of B-cell epitopes of Plasmodium vivax circumsporozoite protein (CSP) using the multiple peptide synthesis technique was carried out. A total of 189 octapeptides was synthesized by F-moc chemistry using the multiple pin technique. Enzyme-linked immunosorbent assay was used to identify octapeptides in the P. vivax CSP that reacted strongly with anti-sporozoite antibodies present in sera of 30 P. vivax infected patients from the Gombak Hospital. The highest O.D. readings was against peptides at residues ranging from 351 - 371 located at the C-terminal region of the sequence.

Plasmodium vivax DNA probes: 600 colonies obtained from transformation experiments using the pUC18-DH5a E. coli system was screened with biotin-labelled probes of various Plasmodium and hlst DNA to identify specific colonies. 100 colonies did not cross-react with P. falciparum, P. cynomolgi, P. inui, monkey and human DNA probes indicating specificity. For P. inui, 20 out of 900 colonies did not cross-react.

Permethrin-impregnated bednets: The study, started in 1990, was completed this year. Monitoring of malaria cases, vector density and sporozoite rate were carried out. There was a significantly greater reduction in malaria parasite rates when permethrin-impregnated, rather than placebo-treated, nets were provided. The treated nets also caused a reduction in the sporozoite rate in the An. maculatus vector population.

Drug sensitivity of Plasmodium falciparum isolates: 27 hospital specimens from the General Hospital, Kuala Lumpur and Gombak Hospital as well as 11 field specimens from the Orang Asli Settlement, Betau were subjected to in vitro drug sensitivity studies using the WHO microtest kits. Of 7 hospital strains, 6 were resistant to chloroquine, 1 to mefloquine, 2 to quinine and 2 to amodiaquine. Of the field specimens, 6 were resistant to chloroquine, none to mefloquine, none to quinine and 2 to amodiaquine.

2.4.2 Filariasis

The filariasis research programme continued to be in experimental chemotherapy, epidemiological studies and the production of reagents using molecular biology techniques for the development of diagnostic assays.

Production of cDNA and fused polypeptides of B. malayi: cDNA colonies were screened using B. malayi infected monkey sera. Polyacrylamide gel electrophoresis was carried out to confirm that positive colonies contained parasite proteins. Immunoscreening using the western blot technique was used to isolate species specific fusion proteins.

Single-dose diethylcarbamazine-citrate (DEC): The effectiveness of single-dose DEC was to be compared to the standard six-day

regime in the control of Brugian filariasis. A preliminary survey showed that the prevalence rates of Brugian filariasis were 25.5% for Pos Air Banun and 12.6% for Pos Dala. The parasite densities were more than 25 mf per 60 ul in both places. Anopheles donaldi was shown to be the vector. Mansonia sp. mosquitoes were found in the areas but were not infected.

Entomological investigations in filariasis endemic areas: 298 mosquitoes from 12 species belonging to 4 genera were caught by bare leg catch in RPS Air Banun while 239 mosquitoes from 6 species belonging to 3 genera were caught in RPS Dala. In both areas Culex gelidus was the main species (62%). In RPS Air Banun, 57 Anopheles donaldi were obtained comprising 19.1% of the catch. 1.8% of these were infected with Brugia malayi. In RPS Dala, 27 An. donaldi were obtained comprising 11.3% of the total catch. 4.1% of these were infected with Brugia malayi.

UMF 289: The filaricidal effects of UMF 289 which is a hydrochloride salt of of a benzimidazole carbamate, UMF 078 given as a single oral dose of 129 mg/kg was tested in the treatment of subperiodic Brugia malayi in Presbytis cristata. There was a gradual reduction in microfilarial counts in the treated animals, probably due to slight adulticidal activity. The geometric mean count at 6 weeks post-treatment was 74.2% of the initial counts compared to the control group which was 2165.0% of the initial count. The mean adult worm recovery in the treated animals was 5.0% compared to 16.0% in the treated animals. No significant changes in biochemical parametres other than a slight rise in AST and ALT was observed.

2.4.3 Human nutrition

Nutritional status of the major functional groups: A large scale nutritional assessment of the extent of nutritionally related problems in various occupational/functional groups, i.e. the rural poor (mainly agricultural workers), urban poor and urban affluent is being carried out on a 4-year nation-wide study with the Department of Nutrition and Community Health of Universiti Pertanian Malaysia and the Health Division of the Ministry of Health beginning in 1992. By the end of 1992, 1120 households representing rice, rubber and coconut small holders in Kedah, Penang and Perak were sutdied. Clinical data, anthropometric measurements and biochemical data from about 4200 villagers were collected.

Effect of riboflavin supplementation on susceptibility to malaria: 32 riboflavin-deficient subjects aged 2 - 10 years were given 18 mg riboflavin daily. 32 riboflavin-deficient subjects matched for age and sex but not given riboflavin were chosen as controls. Malaria infections was 15.0 per 100 person-months at risk in the riboflavin-supplemented group compared to 17.5 per 100 person-months in the controls. None of those in the riboflavin-supplemented group and three in the control group had parasite counts in excess of 1000 parasites/mm^3 blood. The observations did not indicate any significant difference in susceptibil-

ity associated with riboflavin supplementation of riboflavin-deficient individuals.

Determination of B-vitamins in foods using HPLC: Experiments were carried out to determine the appropriate chromatographic conditions for the separation of six B-vitamins (thiamine, riboflavin, niacin/niacinamide, pyridoxine, folic acid and cyanocobalamin) and ascorbic acid. A suitable eluent was found to be a mixture of methanol, glacial acetic acid and water (26.5:0.5:0.73) with 10 mM sodium pentanesulfonic acid and 0.09% triethylamine. The effect of pH on thiamine and riboflavin, heat on riboflavin and pyridoxine, fluorescent light on riboflavin, sunlight on pyridoxine, alkaline hydrolysis on niacinamide, and oxidation of ascorbic acid with activated charcoal was studied. Methods of extraction of the vitamins from pure standard solutions and vitamin tablets were studied. Acid hydrolysis was found to be satisfactory for most water soluble vitamins in multivitamin preparations except for folic acid and cyanocobalamine. The inability of folic acid to dissolve in the acid extract could be overcome by diluting the extract in 0.01N sodium hydroxide before filtration.

Ion-liquid chromatographic analysis of trace elements: Sodium borate gluconate eluant was found to be a suitable eluent/buffer for the separation of nitrate, nitrite, iodide, fluoride, chloride and sulphate in a Waters IC-Pak A column. Detection was carried out using a UV detector (at 210 nm for nitrate and 230nm for nitrite and iodide) and a conductivity detector for fluoride, chloride and sulphate. Studies on sensitvity range, cell temperature, concentration of mobile phase, calibrations of standards and reproducibility were carried out. Tests were carried out using water samples and vegetables. It was found that the anion concentration in the water samples was low and required concentration. Aqueous extraction of blended vegetables followed by boiling resulted in good recovery of all anions tested. Large carbonate peaks, cations and pH differences were found to cause baseline problems and interfere with early eluating peak.

2.4.4 Medical entomology

Isolation of mosquitocidal fungus: An isolate of larvicidal fungus identified as *Aspergillus niger* was first isolated from larval carcass of *Aedes albopictus* collected from ovitrap. This isolate was highly pathogenic to larvae of *Culex quinquefasciatus*, *Aedes aegypti* and *Anopheles maculatus* due to production of toxin(s).

Isolation of protozoa from mosquito larvae: 924 collections of immature mosquitoes were carried out in various parts of the country to determine the incidence of ciliates and other parasites in the natural populations of mosquito larvae. Of these, 41 collections were positive for *Lambornella* sp. while 62 were positive for *Coelomyces* sp. Out of 3835 *Armigeres* examined, 50 were positive for *Lambornella* sp., most of them were from rubber

cups. In vivo cultures were maintained in Aedes albopictus. Susceptibility studies showed that Ae. albopictus and Ae. aegypti were both susceptible to Lambornella sp.

Cloning of mosquitocidal gene of Clostridium bifermentans malaysia (Cbm): Cbm chromosomal DNA was digested with Sau3AI and ligated onto pUC18 was used to transform E. coli JM109. 1 colony (among the 150 clones) caused more than 50% mortality of Anopheles maculatus larvae. This clone was confirmed to contain the Cbm insert by agarose gel electrophoresis.

Fermentation of Bacillus thuringiensis: Studies on the Production of a Malaysian isolate of mosquitocidal Bacillus thuringiensis H-14 (IMR-BT-8) utilizing coconut water, corn and chicken feed showed that these were not suitable for production.

Evaluation of the impact of Bacillus thuringiensis against malaria vectors: Control of An. maculatus was attempted by slow dripping of B. thuringiensis into the stream. A mass blood survey four months after the initiation of the control measure showed a slide positivity rate of about 1% which was maintained at 2 subsequent surveys. This indicate that B. thuringiensis may exert some effect on the malaria vectors and incidence.

Laboratory and field evaluation of insecticides: i) The LC 50 value of permetrin against Ae. aegypti and Ae. albopictus was 0.0015 mg/L and 0.0023 mg/L respectively. Larvicidal activity of permetrine at 0.07 mg/L compared with temephos at 1 mg/L showed that both larvicides were effective in causing complete larval mortality up to 49 days post-treatment. Rain did not affect the effectiveness of permetrine. The effective dosage of permetrine was 14 fold lower than that of temephos.

ii) The effectiveness of Trebon sprayed on various materials against certain species of mosquitoes were studied. Based on the mean percentage mortality, the order of susceptibility of the mosquitoes was An. dirus > An. maculatus > Ae. aegypti > Culex quinquefasciatus. The order of effectiveness based on wall material sprayed was bamboo > wood > cement.

Resistance studies: i) A strain of Culex quinquefasciatus adults were selected for resistance against DDT, malathion and permethrin. Assay of glutathion S-transferase level in this strain showed that the level was not significantly different from that in a susceptible laboratory strain. This indicate taht DDT resistance might not be due to elevated glutathion S-transferase.

ii) Selection of a strain of Ae. aegypti resistant to temephos showed that development of resistance was slow. Attempts to select a strain of An. maculatus resistant to DDT was initiated.

Field evaluation: i) The evaluation of cyfluthrin against Ae. aegypti and Cx. quinquefasciatus adults and larvae using ULV fogging at dosages 1:67 and 1:19 and discharge rate of 35 ml/min showed that mosquito mortality was low both indoors and outdoors

when compared with malathion.

ii) The residual effectiveness of cyhalothrin applied to cattle against , An. dirus, Ma. uniformis and An. maculatus showed a 24-hour post exposure mortality of 92-94% for the first two species and 79% for the last species. The day 7 post exposure mortality was 18%, 31% and 10% respectively. On day 21 post exposure, the mortality rate was 2 - 3% for all species tested. This suggest that Ma. uniformis may be controlled if cattle can be sprayed with cyhalothrin or other suitable insecticides.

Forensic entomology: Studies on the succession of arthropods and decomposition of monkey carrions in Ulu Gombak was continued. Decomposition occured rapidly on exposure to grass and was completed by the 6th. day. Most of the maggots were those of Chrysomya velleneuvi. The rate of decomposition was about the same as carcasses exposed on rocky floor or partially buried. The dominant larvae appeared to be those of Calliphoridae. Decomposition in water-submerged carcass was the slowest. No larvae of Ch. villeneuvi or Ch. rufifacis were recovered. These data are useful for forensic work.

Dengue outbreak predictive model: Retrospective analysis of Aedes aegypti mosquitoes collected in 1985 - 1991 in sentinel traps around Kuala Lumpur city using sequential sampling techniques was conducted. The mosquitoes exhibited a contagious distribution fitted to a negative binomial model without a common K value (except in 1988). The critical Aedes adult threshold required fro dengue transmission for each year was computed. The population density of Aedes vectors exceeded the calculated threshold value in all the years.

Bionomics of Japanese encephalitis vectors: Longitudinal studies of vectors of Japanese Encephalitis was commenced at Sungai Pelek, Sepang, Selangor. 32706 mosquitoes were caught. 88% were of the Culex spp, many of which vectors of Japanese encephalitis. Mosquitos belonging to 9 genera and 44 species were obtained. Culex tritaeniorhynchus formed 62.5%, Cx. gelidus 16.5% and Cx. fuscocephala 3.2%. The mosquitoes were pooled according to species into 555 pools for virus isolation.

"Redtop Fly Catcher": The effectiveness of Redtop Fly Catcher was assessed and compared with the blue light trap and sticky trap. The sticky trap was most effective (98.9%) compared to the light trap (0.3%) and the Redtop Fly Catcher (0.9%).

Diethyl Methylbenzamide (DEET): DEET was evaluated as an attractant of local medically important species of mosquitoes under field conditions. CDC light traps were set up with carbon dioxide (CO_2), DEET and DEET with CO_2. In one study site (a pig farming area), DEET attracted more mosquitoes than other traps. In another site (an open swamp area with water plants), DEET attracted less mosquitoes than the trap with CO_2 and CO_2 + DEET.

2.4.5 Dengue

Dengue IgM Elisa Technique: The aim of this project was to determine the effectiveness of the Dengue IgM Elisa technique as a first line screening for dengue. 14486 serum samples from patients were tested using the IgM Elisa technique and 930 serum samples have been tested using the haemagglutination inhibition test. The data are being analysed.

2.4.6 Febrile illnesses

This programme covers viral diseases other than dengue.

Hepatitis B: A randomised placebo-controlled double blind clinical trial was started in mid-1989 to evaluate a recombinant interferon preparation in the treatment of chronic hepatitis B. 13 patients were admitted to the trial. They were primed with prednisolone for 6 weeks followed by a two-week rest period. Interferon alpha-2b (Intron A) was administered subcutaneously at 5 m.i.u daily for 1 week then 5 m.i.u. three times weekly for another 15 weeks. Patients who did not show seroconversion after 1 month of discontinuation of the therapy were given a 2nd. phase of treatment. This consisted of 5 m.i.u. of Intron A three times a week for a month, every alternate month, until the completion of 3 courses of treatment. Patients were followed up until week 56. The results showed that Intron A treatment normalised ALT values in 10 cases at week 24. 30.8% achieved seroconversion while 69.2% did not. Side effects were mild, transient and well tolerated.

HIV-2 infection in Malaysia: More than 2404 individuals from varius high risk groups for HIV were screened for antibodies to HIV-1 and HIV-2 between mid 1990 and December 1992. 10% of these were positive for HIV antibodies. Further thests to differentiate HIV-1 and HIV-2 showed that HIV-2 has not yet been introduced into Malaysia.

Hepatitis C: The presence of HCV in renal transplant patients and in renal donors in Malaysia were studied. 30 (27.3%) out of 110 post renal transplant patients and 1 (2.33%) out of 43 donors were positive for HCV antibodies.

TORCHES study: The objective of this study was to determine the effectiveness of the Rubella mass immunization programme in controlling rubella in Malaysia. Since 1987, 5776 infants aged 0 - 4 months with various congenital abnormalities were screened. Preliminary results indicate that there is a gradual decline in the occurrence of congenital Rubella and the emergence of congenital CMV infection as the main cause of congenital disease in the TORCHES group of congenital diseases.

2.4.7 Other parasitic diseases

Seasonal variation of soil-transmitted helminthiases: This study, started in 1991, was continued to obtain epidemiological

data which could be used for planning of control strategies. Two villages in Selangor and two villages in Kelantan were surveyed monthly to study the prevalence of soil-transmitted helminthiases. The prevalence of ascariasis and trichuriasis was the lowest 2 months after the dry months. The wet season did not appear to affect the prevalence of both helminthic infestations.

Finger and nail dirt as possible sources of infections of Ascaris and Trichuris: A study was carried out to determine the sources of these infections among children below 12 years of age in an agricultural community which had indoor water supply and outdoor pour flush toilets. Helminth ova were recovered from 26.9% of hand washings, 17.8% of nail dirt, 65% of stool specimens. Ascariasis and trichuriasis were more common among the children from whom ova were recovered from the hands. Ascaris and Trichuris ova were found in the soil samples from almost all houses which the children lived.

Cryptosporidiosis in HIV positive iv drug users: Stool specimens from 100 inmates from Pusat Serenti, Tampin, Negeri Sembilan who were HIV positive and another 68 who were HIV negative were collected. Cryptosporidium were found in 25% of the HIV positive iv drug users. A higher percentage of positivity for cryptosporidiasis was found among those who had been iv drug users for 6 - 10 years (33.3%) than those who had been iv drug users for 1 - 5 years (26.4%). The infection was not observed in any of the HIV negative iv drug users. Therefore, HIV positives without AIDS were found to be significant carriers of Cryptosporidium.

Epidemiology of giardiasis: The objective of this joint project with the Queensland Institute of Medical Research is to isolate strains of Giardia duodenalis and study the strain variations responsible for symptomatic and non-symptomatic infections as well as to determine whether domestic animals act as reservoirs. Cysts from stools of positive cases among the Orang Asli in Kampung Bukit Kemandul were passaged through mice and cultured in vitro. Restriction of the DNA extract with HaeIII, HinfI and RsaI was done. M13 phage genome used to detect polymorphic DNA mini-satellites was found to be a specific method for strain detection. The isolation of Giardia from animals has not been suscessful.

2.4.8 Scrub typhus

The activities were continuations from 1991.

Tissue cultures of R. tsutsugamushi: Tissue cultures have proven to be a reliable alternative to cultures using yolk sacs. The partial purification of rickettsiae had been improved through the introduction of percoll gradient centrifugation.

Dot-immunobinding Assay (DIBA): Cellulose acetate discs coated with exudates of infected and noninfected chiggers, which had been stored at 4oC for a period of 1 year were found to retain their activity.

Monoclonal antibodies against R. tsutsugamushi: The fusion rates had been extremely low. Mycoplasma contamination is one of the main caused of failure of fusions.

Genomic library of R. tsutsugamushi: A genomic library was produced last year. A total of 2050 clones had been screened since 1991. 3 clones had been identified as potential probes - Rtkp1, 3 and 6. These probes had been extensively characterized.

Evaluation of pesticides against chiggers: 6 pesticides (fenvalerate, amitraz, pirimiphosmethyl, fenthion, S-bioallethrin and alpha-allethrin) were tested against Leptotrombidium fletcheri and L. arenicola. The LC50 and LC99 were determined.

2.4.9 Behavioural Research

Compliance in leprosy treatment: Leprosy patients, followed up at the Federal Territory, Negeri Sembilan and Pahang, who have commenced treatment between July 1990 and August 1992 and those who had defaulted more than a month at any time during the period were studied. Skin clinics in the general hospitals of the states were visited to obtain their lists of patients.

Socio-behavioural study of cancer patients: Patients in the General Hospital Kuala Lumpur and a private hospital were studied to gather data on the background of patients relating to their disease and to determine their coping behaviour. Preliminary discussions were held with the hospital specialists and officers of the National Cancer Society of Malaysia.

3. RESEARCH MANAGEMENT

3.1 IMR Research Committees

Three committees based at the IMR are involved in the review of research proposals from the IMR and other agencies of the Ministry of Health (MoH). The IMR Research Review Committee (IMR-RRC) undertakes the internal peer review of project proposals; in addition, there are two ethical committees which review research proposals that involve the use of humans or animals respectively, if this is deemed necessary by the IMR-RRC. The director of the IMR is the Director of Research for the Ministry of Health. Membership of these committees consists of IMR officers and others invited to serve in the committees by the Director of IMR.

3.2 Secretariat for MoH Standing Committee for Research

Since 1990, the IMR has been assigned the role of the Secretariat for the MoH's Standing Committee for Research, of which the Director-General of Health, Malaysia, is the Chairman. The Secretariat is entrusted with the responsibility of processing all research proposals involving MoH staff. The types of re-

search proposals received include:

a) projects funded by the programme for Intensification of Research in Priority Areas (IRPA);

b) clinical trials, usually funded by private pharmaceutical firms;

c) other projects, besides clinical trials, conducted by MoH staff or studies by undergraduate medical students from local universities; and

d) health related projects by foreign scientists; such projects are submitted via the Socio-Economic Research Unit of the Prime Minister's Department.

Upon receiving the research proposals and ensuring that the submissions are in order, the Secretariat directs the proposals to the relevant committee(s) of the MoH such as the Drug Control Authority, the IMR-RRC and the relevant ethical review committee (human/animal use) for their evaluation and comments. The research protocol and the comments from the various committees are then collated and forwarded to the Director-General of Health for final approval.

The Secretariat is also responsible for circularizing to all MoH agencies, invitations for submission of research project proposals for R&D funding from the government. The Secretariat compiles all the submissions and schedules a vetting session by the IMR-RRC, and where appropriate, the relevant ethical committee. All that are approved are then forwarded to the Ministry of Science, Technology and Environment for further action. The Secretariat then prepares a defence team for presentation of the projects from the MoH to the IRPA panel, the body responsible for the approval of funding under the national R&D budget.

The Secretariat is also involved in the monitoring and compilation of the progress reports of all R&D research projects conducted in the MoH.

3.3 Research Priorities

The IMR, through various mechanisms, ensures that its research activities are consonant with the national health research priorities. There are 7 major priority areas of health research which have been identified.

HEALTH RESEARCH PRIORITIES

Problem Areas	Disease/Condition
i. Research to facilitate application	Food and water-borne diseases,

of available technology to control food/water-borne diseases, nutritional deficiencies, inappropriate infertility and and immunizable diseases	nutritional deficiencies, inappropriate fertility, immunizable diseases
ii. Research in local diseases for which basic knowledge regarding control is still lacking	Vector-borne diseases, viral diseases, bacterial diseases, parasitic non-vector borne diseases, behavioual disorders, neoplasms (geographic/ethnic)
iii. Research in non-communicable diseases:	
a. Hazardous factors are known eg. smoking, alcohol	i. Cardiovascular diseases - acquired non-infective; ii. Respiratory diseases iii. Accidents iv. Substance abuse (glue, drugs, alcohol) v. Metabolic disorders vi. Occupational diseases
b. Hazardous factors are not known	Psychotic disorders, neoplasms (cosmopoliton)
iv. Research to reduce morbidity, mortality and to limit disability for conditions for which prevention is not known	Endocrine disorders, congenital and genetic diseases, degenerative diseases, metabolic disorders
v. Research to meet needs of policy makers and planners	Transmigration, alternative systems of health (traditional medicine) Resources: - availability and deficiency, management of health services; - community involvement; - evaluation of health services.
vi. Research for technology development	Biotechnology: - pharmaceuticals - biologicals - reagents Computerization in health care medical equipment and

		instrumentation (including design, production and maintenance) Appropriate technology for health
vii.	Research in toxicology	Poisoning by chemicals, natural toxins (e.g. from plants, animals or microbial sources) To ensure safety to the population and the maintenance of health standards

4. **STAFF DEVELOPMENT**

4.1 Completed Higher Degree/Diploma

i. Dr. Mirnalini Kandiah successfully completed her PhD. at Universiti Malaya in August 1992.

ii. Dr. Wan Nazaimoon successfully completed her PhD. at Universiti Kebangsaan Malaysia in August 1992.

iii. Dr. Normaznah Yahaya successfully completed his MSc (MM) at the London School of Tropical Medicine and Hygiene, United Kingdom in October 1992.

iv. Dr. Mohd. Kamel successfully completed his MSc (MM) at the London School of Tropical Medicine and Hygiene, United Kingdom in October 1992.

v. En. Badrul Amini Abd Rashid successfully completed his MSc at University Malaya, Kuala Lumpur.

vi. Mr. N. Manokaran successfully passed the Cytotechnogist, International Academy of Cytology (CTIAC) Examination held in Melbourne in May 1992.

4.2 Registered for Higher Degree

	Name	Degree	University	Sponsor
i.	Dr. Norazah Ahmad	MSc (MM)	London Sch Trp Med Hyg	M'sian Govt
ii.	Dr. Amal Nasir	MSc (Epid&Biostat)	Uni Ottawa Canada	SEAMEO-TROPMED
iii.	Dr. Azizah Md Radzi	MSc (MM)	London STMH	M'sian Gov
iv.	Pn. Haliza Mohd Riji	PhD	UM	IMR
v.	En. J.B. Lopez	MSc	UM	IMR
vi.	En. Lee Han Lim	MSc	USM	IMR
vii.	Dr. Noor Aziah Abidin	M. Path.	UKM	M'sian Govt
viii.	Pn. Zawiah bt Ahmad	MSc	UKM	IMR

ix. Dr. Ganeswrie a/p Rajasekaran	M.Path	UM	M'sian Govt
x. Dr. Zabedah Md. Yunus	M.Path	UM	M'sian Govt.
xi. Dr. Zubaidah Zakaria	Dip. Clin. Path.	London	-
xii. Dr. Kumari Manju a/p Jaganath	MPH	UM	M'sian Govt.
xiii. Dr. Fairuz Amran	M.Path.	UKM	M'sian Govt.
xiv. Dr. Nurahan Moming	M.Path	UKM	M'sian Govt.

4.3 Long Term Training

i. Dr. Henry R. Gudum	MRCPath attachment	St. George's Hosp, London	M'sian Govt
ii. Dr. Ng Kok Han	MRCPath attachment	Glasgow	M'sian Govt
iii. Dr. M.Sinniah	MRCPath attachment	United Kingdom	M'sian Govt

4.4.1 Short Term Training - Overseas

Name	Subject	Location	Sponsor
i. Dr. Ismail Mohd. Noor	Health Sector Management	Inst. Publ. Hlth. Dublin	ADB LoanIII
ii. Mr. Mohd. Zainuldin Taib	Technical training in plasmid analysis	Publ. Hlth. Lab, Colindale, London	WHO
iii. Ms. Tee Guat Hiong	MLT Tutor course	Royal Free Hosp. London	M'sian Govt
iv. Ms. Norsiah Md. Desa	Environmental Toxicology	NUS, Singapore	SEAMEO-TROPMED
v. Mr. Ng Chong Sing	Tropical Dis. Res.	Uni Tokyo,	JICA
vi. Dr. Hanjeet Kaur	Course in epidemiology	Mahidol Uni Bangkok	SEAMEO-TROPMED
vii. Ms. Chin Yeut Ming	Immunophenotyping & Flow Cytometry	Singapore	Min. Health
viii. Dr. Mirnalini	Nutritional epidemiology	Jakarta	SEAMEO-TROPMED
ix. Dr. Azriman	Cert course clin nutr	Natl Inst Nutr Hyderabad, India	WHO
x. Dr. Shanaz Murad	Serogical Tests for Syphilis	Yonsei Uni, Korea	KOICA
xi. Dr. Harvinder Kaur	Comm. dis. diagnosis	Mahidol Uni Bangkok	IAEA
xii. Dr. Jasbir S Dhaliwal	Immunology of of Inf Dis	Semarang,	WHO
xiii. Dr. M. Sinniah	HIV Virology	CDC, Atlanta	WHO
xiv. Dr. Zainah Saat	PCR in HIV Diagnosis	Japan	JFAP
xv. Dr. Stephen Ambu	In vitro culti-vation of filarids	Jakarta	WHO
xvi. Dr. Vijayamalar	HIV testing and QC	Bangkok	WHO

Many other officers and technologists also attended short training programmes held locally, including Mr. Yeoh Chee Weng, who received a WHO/IMR Research Training Grant to attend courses in programming techniques in Kuala Lumpur.

5. TRAINING PROVIDED

IMR continued to be actively involved in the training of doctors, scientists and other health workers from Malaysia and abroad, especially from within the region. Much of the training was in tropical diseases.

5.1 WHO Fellows

The IMR received a total of 19 WHO fellowship holders from 6 countries during 1992. They were from:

Indonesia	-	4
Vietnam	-	5
P.R. China	-	5
Myanmar	-	1
Sri Lanka	-	2
Philippines	-	1
Total	-	19

5.2 Diploma in Medical Microbiology (DMM)

The DMM course was held for a period of six months in IMR from 8 October 1991 to 28 March 1992. The SEAMEO-TROPMED candidates were from Malaysia (4), Philippines (2), Indonesia (2), Thailand (3) and one private candidate from Malaysia. The MTCP candidates were from Bangladesh (1), Tanzania (1) and Malawi (1).

Another 10 candidates was admitted in October 1992. The candidates were from India (1), Indonesia (1), Iraq (1), Philippines (2), Thailand (2), Papua New Guinea (1), Sri Lanka (1) and Malaysia (1).

5.3 Diploma in Applied Parasitology and Entomology (DAP&E)

The 23rd. DAP&E course was conducted from 8 April to 25 September 1992. There were 15 candidates - Cambodia (2), Lao PDR (3), Indonesia (2), Nigeria (1), Philippines (2), Solomon Islands (1), Tanzania (1), Thailand (2) and Malaysia (1).

5.4 School of Medical Laboratory Technology

135 trainees were admitted for the 3-year Diploma Course in Medical Laboratory Technology. 107 trainees admitted for the diploma course last year were following their Semester III at various training centres throughout the country, while 12 were terminated for failure to pass clear the earlier Semesters. 74 trainees sat for the final Certificate examination in Medical Laboratory Technology. Of these, 5 obtained credits and 53 passed.

The 2-year Advanced Certificate Course for Medical Laboratory Technologists commenced in September 1990 was completed during the year.

The number of successful candidates were 14 for Blood Transfusion, 18 for Haematology, 10 for Anatomical Pathology and 2 for Cytology. 60 students registered in 1991 for the Advanced Course in Chemical Pathology, Medical Microbiology and Medical Parasitology and were undergoing their posting at various clinical centres in the country.

Examinations for the Medical Assistants in the Ministry of Health and the Estate Hospital Assistants were also conducted.

5.5 Ad hoc training programmes and attachment training

The institute carried out ad hoc training programmes and attachment for 80 medical doctors, scientists and allied personnel from other departments and institutions from within the country and elsewhere. 35 undergraduate university students from the local institutions of higher learning were also attached to the Institute for practical training in various disciplines.

5.6 Courses/workshops/meetings

5.6.1 The 90th. Anniversary Scientific Seminar was held from 23 - 25th. June 1992.

5.6.2 The 34th. SEAMEO-TROPMED Seminar on Current Status of Filariasis in South-east Asia was held in IMR from 26 to 27th. June 1992.

5.6.3 A workshop on the biological and control of Vectors of Scrub Typhus was organized by the Division of Acarology and was attended by 11 state entomologist from the Vector-Borne Diseases Control Programme.

5.6.4 The Division of Virology conducted an In-House Training for HIV Screening from 17 February to 9 March. This was attended by 10 MLTs and 1 microbiologist.

5.6.5 The Division also conducted a HIV Screening Training Workshop Using ELISA-ABBOT HIV-1 and 2 Test from 4 to 6 October for 36 participants from 30 HIV screening centres in Malaysia.

5.6.6 The Snake Farm gave training to 11 staff from the Kedah Wildlife Department from 21 to 23 September on snakes of Malaysia, their identification and methods of catching.

5.6.7 A course on Transmission Electron Microscopy for the staff of the IMR was held at the Electron Microscopy Unit from 12 to 28 October. The consultant, Ms. Deborah J. Stenzel from Queensland University of Technology conducted the course which was sponsored by the WHO.

6. CONSULTANCIES

6.1 Officers of the IMR

Officers of the IMR provided consultative services to other departments of the Ministry of Health and various national and international bodies.

6.1.1. Dato' Dr. M. Jegathesan, Director

i. Attended the joint meeting of the WHO Western Pacific Regional Advisory Committee for Health Research and Heads of Medical Research Councils and Analogous Bodies, Manila, 10 - 19 August
ii. Attended the 31st. SEAMEO-TROPMED Governing Board Meeting, Port Dickson, 1 - 3 September
iii. Was appointed as Chairman of the Accreditation of Food Laboratory Committee of the Ministry of Health Malaysia
iv. Was appointed as the Head of the National Quality Assurance Programme on Laboratory Services
v. Attended the 13th. WHO/IMR Coordination meeting, IMR, Kuala Lumpur

6.1.2 Dr Mak Joon Wah of the Biotechnology Centre:
i. continued to serve as Member of WHO Expert Advisory Panel on Filariasis (since 1981);
ii. served as Editor, Southeast Asian Journal of Tropical Medicine and Public Health, since 1988; and
iii. served as Member of the Editorial Board of Tropical Biomedicine since 1985.

6.1.3 Dr Lye Munn Sann of the Division of Epidemiology and Biostatistics served as:
i.Member, Steering Committee, Advanced Asian Course in Tropical Epidemiology, SEAMEO-TROPMED;
ii.Member, Editorial Board, South East Asia Journal of Tropical Medicine and Hygiene

6.1.4 Dr Tee E Siong of the Division of Human Nutrition served as:
i. Secretary, Coordinating Committee for the Preparation of the FAO/WHO International Conference on Nutrition
ii. Attended "ICN Preparatory Committee Meeting" held in Geneva, 18 - 24 August 1992
iii. Attended FAO/WHO International Conference on Nutrition, Rome, 5 - 11 December 1992

6.1.5 Dr. G L Chiang of the Division of Medical Entomology
i. Attended "Inter-regional Meeting on Malaria for Asia and the Western Pacific" held in New Delhi, 3 - 7 February, 1992

6.2 Referral Diagnostic Services

The Divisions of the Institute provide specialised diagnostic tests and serve as referral centres for laboratories in the

Ministry of Health, other government agencies, and the private sector. Several laboratories served as National Reference Centres in various specialised fields.

6.3 WHO Collaboration

Four Divisions of the Institute continued to serve as WHO collaborating centres:

6.3.1. The Biotechnology Centre (formerly Division of Malaria and Filariasis) as a WHO Collaborating Centre for Taxonomy and Immunology of Filariasis and Screening and Clinical Trials of Drugs Against Brugian Filariasis, headed since 1981 by Dr Mak Joon Wah. The Centre continues to provide arthropod blood meal identification facilities to researchers in countries from the Western Pacific and Southeast Asian Regions, since 1985;

6.3.2. The Division of Medical Entomology as a WHO Collaborating Centre for Ecology, Taxonomy and Control of Vectors of Malaria, Filariasis and Dengue, headed by Dr K Inder Singh;

6.3.3. The Division of Bacteriology as the national focal point for the WHO Collaborative surveillance programme on antibiotic resistance in the Western Pacific Region; and

6.3.4. The Division of Virology as the WHO National Influenza Centre and the WHO National Reference Laboratory for the Eradication of Polio.

6.4 Other consultancies

6.4.1 The IMR has been providing consultancy services on the medico-ecological aspect of environment impact assessment (EIA) to other local agencies. The EIA team consists of staff from the Divisions of Parasitology, Malaria and Filariasis, Medical Entomology and Medical Ecology.

In September-October, the team conducted a study for Tenaga Nasional Berhad (TNB) on the medico-ecological changes in the Pergau Hydroelectric Project area in Kelantan during the construction phase of the dam. A preliminary report on the findings and recommendations on mitigating measures to remedy adverse medico-ecological situations and improve the health status of the construction workers had been submitted to TNB.

6.4.2 Several departments within the Ministry of Health and other agencies sought advice from the Division of Library, Information and Publications on online information retrieval from international databases and the use of CD-ROM databases.

6.4.3 Besides the activities listed above, officers of the IMR continued to provide advisory and consultative services through their presence in various committees of the Ministry of Health and other governmental and professional bodies. Their expertise contributed to the formulation, implementation and

evaluation of various health-related programmes and activities. Staff members also served as faculty members and experts in various courses, seminars and workshops in their respective specialities.

7. FACILITIES

7.1 Computer Unit

The computer facilities were utilised by the various Divisions of the IMR mainly for storage and retrieval of laboratory records and textual information, statistical analysis of research data and graphical presentations.

7.1.1 **Programmes Written and Maintained:** Computer programme development continued to be one of the major functions of the Computer Unit and for the year the following programming activities were undertaken :

i. New programmes written for the following projects/studies :

Antibiotic study
SCC Antigen Study
Health Survey Research
Parasitology's Soil Test
M.I.C. of antibiotics for different strains of N. Gonorrheae In Malaysia
Community Acquired Infection Project.

ii. Programmes modified and maintained for the following projects/studies :

Cytology Database
Oral Pathology Information Database
Haematology Database
Acute respiratory infections :
(a) Surveillance
(b) Case management
National Surveillance on antibiotic resistance

The Unit also provided assistance in the analysis of systems requirements and specifications for the various application packages, especially for the Histopathology Cancer Registry and Community Acquired Infections packages. Technical support services for usage of microcomputers as well as softwares were also provided.

7.1.2 **Computerized Vote-book** : The Unit reviewed the needs of the Administration Division and took measures to adopt the Accountant General's computerised vote-book system. Preparations for customised personnel information and store management systems were initiated.

7.1.3 **Future Needs** : In collaboration with the Information Technology Centre of the Ministry of Health, a study on the IMR's present and future computing environments and needs was conducted with the view to 'down-sizing' the existing system and to be in line with the open systems concept.

7.2 Division of Library, Information & Publications

7.2.1 **Library Hours:** From April, the Library has been kept open till 5.45 pm on week days, till 4.00 p.m. on Saturdays and from 10.00 am to 2.00 pm on Sundays.

7.2.2 **Collection:** During the year 310 books were purchased. The Library subscribed to 126 journals, received another 220 journals free or on exchange. There were many requests for additional journals, however these could not be met owing to lack of funds.

7.2.3 **Services:** The MEDLINE database on CD-ROM (1983-1991) was well utilized throughout the year both by IMR officers as well as officers from other departments of the Ministry of Health. For information other than that available in MEDLINE (1983-1992), online searches were carried out on databases offered by the National Library of Australia, the National Library of Medicine in USA and the DIALOG Information Services in USA. In order to keep researchers up-to-date with the latest information, the Library purchased Current Contents (Life Sciences) on Diskette. Photocopies of articles not available in Malaysia were obtained mainly from the Southeast Asian Medical Information Centre (SEAMIC), Tokyo.

7.2.4 **Activities at National/International Level:** The Division continued to serve as the National Focal Point for the WHO Regional Biomedical Information Programme and as the Co-ordinating Library for the SEAMIC Health Documentation and Publication activities in Malaysia. The National Library of Australia (through the WHO Biomedical Information Programme) and Kyushu University in Japan (through SEAMIC) provided, on request, photocopies of journal articles free-of-charge. The Division participated in the Mosquito-borne Diseases Information Network of the SEAMEO-TROPMED. Documentation of Malaysian medical and health literature, using the software CDS/ISIS, began as a joint project between the IMR and the local university medical libraries. The Ministry of Health made the IMR Library the central depository for all Ministry of Health publications.

7.2.5 **Computerization:** Computerization of the Library holdings, using an integrated library program, the Columbia Library System, is progressing and more than 50% of the books have been computerized.

7.2.6 **Publications:** The proceedings for the "National Seminar to Evaluate the Research Achievements of the Medical Section of IRPA during the Fifth Malaysia Plan" was published.

8. LINKAGES

8.1 Local Linkages

8.1.1 **Ministry of Health:** The activities of the IMR are closely associated with the overall objectives of the Ministry of Health (MoH). The Director of the IMR is the Programme Director of Research of the MoH. As the research arm of the MoH, the IMR conducts research relevant to the country's health problems. It also acts as the central reference laboratory of the MoH, providing diagnostic testing and consultative services. It is involved in the training of the health personnel of the MoH.

8.1.2 **Local Universities:** IMR has linkages with the University of Malaya, the National University of Malaysia, the Science University of Malaysia and the Agriculture University of Malaysia. Links are formed through collaborative projects, registration of IMR workers for higher degrees at the universities as well as provision of laboratory and training facilities.

8.1.3 **Government Hospitals and State Health Authorities:** The IMR has been collaborating with the health and hospital personnel in the country. It has a long-standing association with the Orang Asli Hospital, the National Leprosy Control Centre and the Kuala Lumpur General Hospital.

8.1.4 **Other Research Institutions:** The IMR has strong linkages with the Palm Oil Research Institute of Malaysia and the Malaysian Agricultural Research and Development Institute in the area of nutrition.

8.1.5 **The National Council for Scientific Research and Development (NCSRD):** The NCSRD provides grants for health research projects which are approved for funding by its Medical Sciences Sub-Committee.

8.1.6 **Other Government Agencies and Private Organizations:** The IMR has links with the Standards and Industrial Research Institute of Malaysia (SIRIM), various ministries and the Tenaga National.

8.2 International Linkages

8.2.1 **World Health Organization:** The IMR has been the WHO Regional Centre for Research and Training in Tropical Disease and nutrition since 1978. It also retains links with the WHO/TDR from which it has received funding for research and institutional strengthening. In addition, the Regional Anti-Malaria Team is based at the IMR.

8.2.2 **SEAMEO-TROPMED:** The IMR has been the National (Malaysian) Centre for Tropical Medicine and Public Health in the SEAMEO-TROPMED network. As part of this role, it conducts the DAP&E and DMM courses for participants from member countries and elsewhere.

8.2.3 **Canadian International Development Agency:** IMR continues to maintain its link with the University of Ottawa through the training of IMR personnel in identified priority areas such as epidemiology, biostatistics and behavioural sciences and in research where both institutions will explore common areas where they can collaborate profitably.

8.2.4 **Japan International Cooperation Agency:** The IMR began collaboration with JICA in malaria, Japanese encephalitis and dengue haemorrhagic fever.

8.2.5 **Islamic Foundation for Science and Technology Development:** The Inter-Islamic Network on Tropical Medicine was established in 1987 by the IFSTAD and its secretariat is based at the IMR. The participation of IMR in IFSTAD, among others, involves the provision of places for participants from member countries in the DMM and DAP&E courses.

4）1992年IMR Annualレポートより抜すい（予算．スタッフ表）

BUDGET FOR 1992

The Institute's total budget for 1992 is as follows:

(i)	From the Malaysian Government: for personal emoluments and operating expenditure	RM14,988,414.00
(ii)	Training and scholarship allowances: for trainees attending the IMR's courses in Medical Laboratory Technology	RM 2,165,460.00
(iii)	Research and Development Fund	RM 2,955,180.00
(iv)	Trust Accounts: (SEAMEO-TROPMED & WHO)	RM 332,935.00
(v)	Development (heritage building)	RM 1,030,000.00
	Total	RM21,471,989.00

DIVISION OF MEDICAL ENTOMOLOGY

Head of Division		K. Inder Singh., B.Sc.Hons., M.Sc. (Punjab), Ph.D. (Durham), F.R.E.S. (Lond.)
Research Officers	*	Lee Han Lim, B.Sc.Hons. (U.S.M.), D.A.P. & E. (Mal.) (退職) 93年現在
		Chiang Geok Lian, B.Sc.Hons., Ph.D. (USM), D.A.P. & E. (Mal.), C.Biol., M.I.Biol. (Lond.) (退職) 93年現在
	*	Indra Vythilingam, B.Sc.Hons. (Madras), M.Sc. (N.Z.), Ph.D. (Mal.)
	*	Rohani binti Ahmad, B.Sc.Hons. (Mal.), M.Phil. (Mal.)
Experimental Officer		1 vacant
Senior Medical Laboratory Technologist		Patrick R. Nonis, A.I.M.H.L.T. (Mal.)

DIVISION OF VIROLOGY

Head of Division	*	Mangalam Sinniah, M.B.B.S. (Madras), M.Sc. Med. Micro. (Lond.), Dip. G.U.Medicine (Lond.)
Medical Officers	*	Vijayamalar Balasubramaniam, M.B.B.S. (Mysore), M.Sc. Med. Micro. (Lond.)
	*	Zainah Saat, M.B.B.S. (Mal.), M.Sc. Med. Micro. (Lond.)
Research Officers		T.S. Saraswarthy, B.Sc. Hons. (Mal.), D.M.M. (Mal.)
	*	Halimah Mohamed, B.Sc. Hons. Microbiology (Wales) (from 8/6/92)
	*	Ravindran Thayan, B.Sc. Hons. Microbiology (UKM) (from 13/6/92)
Senior Medical Laboratory Technologist		Arthur Jebaratnam

プロジェクト関連部門（＊は日本人専門家のカウンターパート），92年9月30日現在

BIOTECHNOLOGY CENTRE

(Fomerly Division of Malaria and Filariasis until 30.9.92)

Head of Division	＊Mak Joon Wah, K.M.N., M.B.B.S., M.D. (S'pore), M.P.H. (Mal.), D.A.P.& E. (Mal.), M.R.C.Path. (Lond.), A.M. (Mal.)
Research Officers	Chong Hen Kee, B.Sc. Hons. (Mal.)
	Stephen Ambu, B.Sc. (Madras), M.Sc. (Wales), Ph.D. (Mal.)
	＊Patricia Lim Kim Chooi, B.Sc. Hons. (Mal.), M.Sc. (Mal.), Ph.D. (Mal.), Dip.Ed.(Mal.)
	＊Noor Rain Abdullah, B.Sc. Hons. (USM), M.Sc. (Lond.)
Medical Officers	＊Normaznah Yahaya, M.D. (UKM), M.Sc. Med. Micro. (Lond.), D.A.P.& E. (M'sia)
	＊Lokman Hakim S., M.D. (UKM), M.Sc. (PH) (S'pore), D.A.P.& E (M'sia)
Senior Medical Laboratory Technologist	Ismail bin Saat

DIVISION OF IMMUNOLOGY

Head of Division	＊Nasuruddin Hj. Abdullah, M.D. (UNAIR), M.Sc. (London)
Medical Officers	Shahnaz Tan Sri Murad, M.B.B.Ch. (Dublin), M.Sc. (Lond.)
	Azizah Mohd. Radzi, M.B.B.S. (Cairo)
	Dr Ho Wai Fuen, M.D. (UKM)
Research Officers	Harvindar Kaur Gill, B.Sc.Hons. (Adel.), M.Sc. (Mal.), Ph.D. (Oslo)
	Gan Seng Chiew, B.Sc. Hons. (Mal.), Dip.Ed. (Lond.), M.Sc. (Mal.), Ph.D. (Mal.)
	Haniza Mohd Anuar, B.Sc.Hons. (Central Lond. Poly.)
	Jasbir Singh Dhaliwal, B.Sc.Hons. (Mal.), M.Sc. (Mal.), Ph.D. (Lond.)
Experimental Officer	＊Mohd. Zaidi Abu Samah, Dip. in Microbiology (ITM)
Senior Medical Laboratory Technologist	＊Ong Kian Joo

5）11月16日の議事録

Minutes of Meeting between IMR and the Planning and Consultation Team, JICA.

Date : 16 November 1993

Time : 8.35 - 9.20 am

Venue : Conference Room, the IMR Director's Office.

Attendence :

Dr. Mak Joon Wah (Head, Biotechnology Centre, IMR - Chairman)
Prof. Hiroshi Tanaka (Chief Advisor, IMR-JICA Project)
Dr. Nasuruddin Abdullah (Head, Immunology Division,IMR)
Dr. B.Vijayamalar (Acting Head, Virology Division, IMR)
Mr. Lee Han Lim (Head, Medical Entomology, IMR)
Professor Hideo Ikeda (Institute of Medical Science, the University of Tokyo - Team Leader)
Assistant Professor Shunichi Fukuhara (Division of International Health, Faculty of Medicine, UT)
Mr. Hirohito Saigusa (Ministry of Education, Science and Culture)
Mr. Hiromu Yoshida (First Medical Cooperation Division, JICA, Staff in charge of IMR-JICA Project, JICA/HDQ)
Miss Izumi Ota (Coordinator, IMR-JICA Office)
Dr. Normaznah Yahaya (Medical Officer, Biotechnology Centre, IMR)

The chairman welcomed everybody to the meeting on behalf of the Director of IMR. He also appologised on behalf of the Director for not being able to attend and chair the meeting due to some urgent matters that he had to attend to. Anyway, the chairman ensured that he will definitely be present for the signing of the Minutes of Discussions scheduled to be on 19 November 1993.

The chairman said that he was very happy and grateful with the decision made between the government of Malaysia and Japanese government in 1990 to start this collaborative research in the medical sector. The implementation of collaborative project was started in early 1993 and aws mainly centred in three diseases namely malaria, dengue and Japanese encephalitis. He personally felt that a lot of progress had been made in terms of acquisition and utilization of equipments, consultation and training for the local counterparts and also the results obtained during a relatively short period of time, about 10 months since the starting of the project. The IMR greatly appreciated the contributions of both the long and short term JICA consultants besides the provision of substantial

equipments by JICA for the projects.

In response to the Chairman's remarks, Prof. Ikeda, the Team Leader said that he was glad to hear that and hoped that the progress will continue in future.

Prof. Tanaka added that the purpose of the team this time is mainly to have a general review of the activities of the project this year and to plan for the next year's activities.

1. The tentative agenda prepared by Mr. Hiromu Yoshida was discussed and agreed to be adopted by the meeting.

The agenda is as follows:

16 (Tue) Nov 1993	8.30 am	- Plenary meeting at IMR Discussion and adoption of agenda
	9.30 am	- Meeting with officers in Entomology Division
17 (Wed) Nov 1993	8.30 am	- Meeting with officers in Biotechnology Centre
18 (Thu) Nov 1993	8.30 am	- Meeting with officers in the Division of Virology
	1.00 pm	- Lunch invitation by Prof. Ikeda
	2.00 pm	- A short lecture by Prof. Ikeda in Biotechnology Centre
19 (Fri) Nov 1993	11.00 am	- Joint Coordinating Meeting Signing for the Minutes of Discussions

Assistant Professor S.Fukuhara requested all the Heads to arrange for the Team to see the Malaysian counterparts individually for individual discussion during the visit to the laboratories. This was agreed to by all the Heads. Venues for meeting with the counterparts are as follows:

Biotechnology Centre - Conference Room (Biotechnology Centre).
Immunology Division - Conference Room (Biotechnology Centre)
Entomology Division - the IMR-JICA Office
Virology Division - the IMR-JICA Office

The names of the Malaysian counterparts are as on the page 12 of the hand- outs.

2. Minutes of Discussion on the Revised Schedule of Implementation.
The Chairman went through the outline of the annual implementation plan for FY 1993, 1994 and 1995 i.e. for the first,second and the third year. For the details of the schedule, please refer to page 3-5 of the hand-out.

Prof. Tanaka commented again that the main objective of the team is to modify and make a proposal to the Revised Scheduled of Implementation where necessary to a workable plan, and evaluation is of less priority.

Assistant Prof. Fukuhara said that the revised schedule of implementation had been discussed by the Technical Advisory Committee (TAC) in Tokyo.

Prof Ikeda added that each division has a chance to discuss and modify the revised schedule before it is signed by the Director of IMR and the Team Leader.

The Chairman reminded that any suggestion for modification of the revised schedule need to be communicated to him immediately.

Prof. Tanaka said that any correction pertaining to plan of despatching Japanese experts and typing error will be taken care by the JICA side. He also welcome all the Heads to correct or to add anything that he missed in the summary of the progress report.

The Chairman also agreed with Prof Tanaka that all the Heads should look carefully the matters on page 12 of the hand-outs and to make appropriate changes if necessary.

All the members of the team were each given a copy of 1992 IMR Annual Report. Finally the Chairman welcomed constructive suggestions from all members of the team which he believed can improve the project in future.

The meeting was adjourned at 9.20 am.

c.c. Director
Institute for Medical Research
Kuala Lumpur

NY/Biotek 1993.

6）11月19日の議事録

The Minutes of Meeting between the IMR and the Japanese Planning and Consultation Team on Japanese Technical Cooperation for the Project for Research and Development on Diagnosis of Selected Tropical Diseases.

Date : 19 November 1993

Time : 11.00 -11.40 am

Venue : Conference Room, the IMR Director's Office

Attendence :

Yang Bhg. Dato' Dr. M.Jegathesan	- Director, IMR (Chairman)
Dr. Mak Joon Wah	- Head, Biotechnology Centre, IMR
Prof. Hiroshi Tanaka	- Chief Advisor, IMR-JICA Project
Dr. Nasuruddin Abdullah	- Head, Immunology Division, IMR
Dr. B.Vijayamalar	- Acting Head, Virology Division, IMR
Mr. Lee Han Lim	- Head, Entomology Division, IMR
Prof. Hideo Ikeda	- Institute of Medical Science, the Univ. of Tokyo (Team Leader)
Assist. Prof. S.Fukuhara	- Division of International Health, Faculty of Medicine, UT

Mr. Hirohito Saigusa	- Ministry of Education, Science and Culture
Mr. Hirokazu Anada	- Deputy Director, First Medical Cooperation Division, JICA
Mr. Hiromu Yoshida	- First Medical Cooperation Division,JICA, Staff in charge of IMR-JICA Project, JICA/HDQ
Ms. Sachiko Misumi	- Assist. Resident Representative in charge of IMR-JICA Project, JICA Malaysia Office
Mr. Kok Chong Fatt	- Assist. Officer, JICA Malaysia Office
Dr. Kasumasa Oda	- Long term Japanese Expert (Virology Division)
Dr. Takahisa Furuta	- Long term Japanese Expert (Biotechnology Center)
Dr. Takeo Tadano	- Long term Japanese Expert (Entomology Division)
Dr. Akeo Mori	- Long term Japanese Expert (Entomology Division)
Ms. Izumi Ota	- Coordinator, IMR-JICA Project Office
Dr. Normaznah Yahaya	- Medical Officer, Biotechnology Centre

1. Dato' Chairman welcomed those present to the meeting. He introduced the officers from the IMR, and invited Prof. Tanaka to introduce the Japanese Experts present at the meeting. Mr. Yoshida from the JICA/HDQ introduced himself and the two officials from JICA Malaysia Office followed by the introduction of the members from the Planning and Consultation Team by Prof. H. Ikeda, the Team Leader.

2. Dato' Chairman expressed his appreciation to JICA and the Japanese Government for chosing the IMR as the counterpart for the collaborative research in the medical sector. He believed that Dr. Nakayama, who initiated the idea to start this collaborative research (he was then the Minister of Foreign Affairs of Japan) together with Dato' Seri Dr. Mahathir Mohammad, the Prime Minister of Malaysia in 1990, must be very impressed and happy with what he observed on the achievement made so far during his short visit to the Institute recently. Dato' Chairman was also happy with the good cooperation between both counterparts.

3. Remarks and feedback from the Japanese Planning and Consultation Team.

3.1 Prof. H.Ikeda appreciated the cooperation given to the Team during the conduct of their task that he felt had achieved the objectives. He made a few comments that he believed will further improve the projects, namely:

a. The importance of communication between the IMR and the Ja-

panese counterparts especially between the Heads and the Japanese counterparts.

b. The importance of having a common technology for the project. He suggested that a scientific meeting should be held between the IMR and the Japanese counterparts not only within the division but also inter-division or departments.

c. Machines and equipments provided by JICA irrespective of which division that they are allocated to should be of common use by all involved in the project.

3.2 Assist. Prof. S. Fukuhara who was representing the Technical Advisory Committee (TAC) said that the Committee is responsible as the headquarter for technical coordination between the IMR, Institute of Medical Science, University of Tokyo and Nagasaki University. He was impressed with the understanding of the IMR on the importance of the project as well as on the rapid progress made. He was concerned with the safety of some laboratories that they visited. He also stressed that it is their responsibility to identify the highly qualified Japanese counterparts to work on the project and to ensure continuity and progress of the project. It is also important for the Japanese Experts to understand this goal.

3.3 Mr. Hirokazu Anada, Deputy Director, First Medical Cooperation Division, JICA, appologized for his late coming due to some engagement in Tokyo. He was also impressed with the cooperation between those involved in the project. He was concerned with arrangement for their JICA personnel arriving in Malaysia and requested for indirect support from the IMR so that the Malaysian

Government can facilitate the job of JICA personnel in carrying this out. However he realized that this was not under the purview of the IMR.

In response to the matter raised by Mr. Anada, Dato' Chairman said that the IMR was aware about the problem and had in the post tried to solve the problem. He said that the IMR will repeat the request. However, we need to be patient since this is not within our jurisdiction.

With regards to the laboratory safety, Dato' Chairman ensured that necessary steps will be taken to improve the situation.

3.4 Mr. Yoshida said that he was involved with the discussion of the project about two years ago. He was satisfied with the present condition, and he felt that technology transfer among other objectives of the projects had been achieved.

3.5 Ms. S. Misumi from JICA Malaysia Office, thanked both the IMR and the Japanese Experts for the good job done for the project. JICA Malaysia was satisfied with the project and will continue to do their best for the project.

4. On behalf of the IMR and the Malaysian counterparts, Dr. Mak Joon Wah commented on a few matters:

a. He fully agreed that communication between the Japanese and Malaysian counterparts is very important. He believed that although language barrier and cultural differences may affect the communication, with patience and understanding this can be overcomed.

b. He also agreed with the suggestion to have a joint Scientific Meeting not only between the divisions involved with the JICA projects but also to share the knowledge with other divisions.

c. He stressed that it is the policy of the IMR and also the Ministry of Health that all equipments in IMR are for common use for all.

d. In line with the directives from the Ministry of Health, all laboratories are trying to comply with safe laboratory practice. In IMR we are doing our best to achieve this.

e. Due to some constraint, not all of the Japanese experts can serve as the long term consultants. This problem can be partly solved through the use of modern communication facilities such as the fax machine etc. that can facilitate communication between the counterparts.

5. Prof. Tanaka, the Chief Advisor for the IMR-JICA Project stressed a few points for consideration namely :

a. He would like to have a periodic meeting between the Heads of the divisions involved with the project with him to solve any problem encountered by the project.

b. Inter department/ division communication should be encouraged.

Scientific presentation by the IMR counterparts should be arranged such as once in every two months as to facilitate the progress of the project.

c. He fully agreed with the policy of common use of equipments purchased. Although it is quite difficult in practice, be believed that the matter can be solved.

d. He had discussed a problem of laboratory safety with Dr. Mak particularly on the electricity consumption and the safety of certain buildings such as the newly renovated building to function as a laboratory, that he felt need to be considered.

e. He will try his best together with the IMR authority to facilitate the entry of JICA personnel at the airport.

6. Dato' Chairman suggested that joint scientific meetings as recommended by the meeting to be integrated into our on going scientific presentations of research projects which are carried out monthly.

7. Dato' Chairman went through each page of the Minutes of Discussins between the Japanese Planning and Consultation Team and the Authorities Concerned of the Government of Malaysia on Japanese Technical Cooperation for the Project for Research and Development on Diagnosis of Selected Tropical Diseases.

The Minutes of Discussions were then signed by the Director of IMR and the Team Leader of the Planning and Consultation Team. Dato' Chairman thanked everybody present in the meeting and adjourned the meeting at 11.40 am.

7）北潔専門家報告書よりの抜すい

Analysis of mitochondrial genesについて

P. falciparum（以下P. fと略す）のintactなミトコンドリア画分やpureなミトコンドリアDNAの分離は基本的にかなり高い技術と経験を必要とし、また実際にこれを行っている欧米の研究者自身、再現性にはまだ多くの問題が残っていると報告している。

また本プロジェクトの立案が終了した昨年の後半にDr. FeaginによりP. fの6 Kbミトコンドリア DNAの全塩基配列が行われた。

CPであるDr. Patriciaも独自にミトコンドリアの調製を数回試みたが、高速のグラス－テフロンのホモジナイザーが利用できなかった事、ミトコンドリア研究の経験が無い点などから目的を達していない。

以上の現状を踏まえ、Dr. Feaginより配列の情報を得、P. fミトコンドリアDNA（以下、mito DNAと略す）に対する3種のprimer setsを携行機材として持参した。primerの位置、予想されるサイズを参考のため記す。

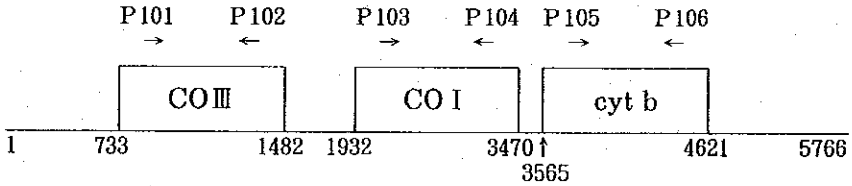

表1

Primer	5´ 3´	gene
P101	1070 – 1092	cytochrome oxidase subunit Ⅲ (COⅢ)
P102	1443 – 1421	〃
P103	2718 – 2739	cytochrome oxidase subunit Ⅰ (CO Ⅰ)
P104	3150 – 3129	〃
P105	3629 – 3650	cytochrome b (cyt b)
P106	3980 – 3959	〃

表2

Primer set	gene	予想されるPCR Productのサイズ(bp)
1. P101 – 102	COⅢ	373
2. P103 – 104	CO Ⅰ	432
3. P105 – 106	cytb	351
4. P101 – 104	COⅢ–CO Ⅰ	2080
5. P101 – 106	COⅢ–CO Ⅰ–cytb	2910
6. P103 – 106	CO Ⅰ–cytb	1262

以上のPrimer setsを用い、P. f, P. vivax (以下P. vと略す)、Humanのtotal DNAをtemplateとして実験を行った。

1) P. f total DNA (Dr. Normaznah, Noor Rain)

CPのNoor Rainによりすでに32株のisolateよりtotal DNAが調製され、rRNA遺伝子のPCRによる解析が古田専門家の指導のもとに開始されている。多くの生物種で通常の方法で調製したTotal DNA中にはmito DNAが含まれている事からP. fについても今回携行したPrimerを用いてPCRを行った。

株としてはIMRで最もよく用いられているGombak A株を用いた。その結果表2. 1~6の全ての組み合わせで予想通りのサイズのPCR productが得られた。

2) 患者血液から調製したDNAを用いたP. fのPCR (Dr. Harmaznah, Noor Rain)

病院において患者より採取した血液より調製したTotal DNAをtemplateとし、表2. 1~3のprimer setsでPCRを行った結果COⅢ、COⅠ、sytb全てのPCR productが得られたが、phencl処理を行ったsampleの方が増巾率が良かった。

3) P. v Total DNA (Dr. Patricia, Miss Tan, Mr. Ng)

マラリアの診断においてP. fによる熱帯熱マラリアとP. vによる三日熱マラリアを見分ける事は前者が治療しない場合、致死的になる可能性が高い点から極めて重要である。そこで患者血液より調製したP. vのTotal DNAをtemplateとして表2. 1~3のprimer setsでPCRを行った結果、COⅢ、COⅠのみ増巾されcytbのバンドは検出されなかった。

このことは、前2者を用いればP. f, P. vにかかわらず血中のマラリア原虫が検出でき、また後者を用いてP. fとP. vを区別する事ができる点を示している。

なお、negative controlとして行ったヒトのtotal DNAではこれらのバンドに相当する明瞭なPCR productは観察されず、今回作成したprimerの特異性の高さが証明された。mito DNAは1個のミトコンドリアの中にP. fの場合100分子以上存在するcopy数の高いDNAであり、DNA診断において高い感度も期待できる。

以上まとめると

a. マラリア原虫ミトコンドリアDNAを単離しなくてもtotal DNAからPCRにより増巾し必要な部分のDNA断片を得る事ができる。

b. この増巾断片を用いてマレイシアで患者より分離されたP. fのタイピングが可能であり、さらに薬剤耐性、地域差などとの相関性について解析を進める事ができる。

c. 今回作成したPrimerの組み合わせで患者血液を用いたマラリアのDNA診断が可能であり、またP. fとP. vの区別を行う事ができる。

この結果を踏まえ、次の様な研究計画を立案した。なお( )内は計画を実際に進行するマレイシア側研究者である。

A. PCRを用いたP. vivax ミトコンドリアDNAの解析(Dr. Patricia)

A−1　COⅢ、CO ⅠのPCR products、それぞれ373、432bpのcloningを行い、塩基配列の決定を行う。このPCR productのcloningには今回携行機材として持参したTA cloning kitを用いる。また1994年にABI自動DNA シーケンサーが設置された場合にはdivect sequeneにより配列決定を行う。

A−2　今回P. vでPCR productの得られなかったcytochrome b遺伝子はP. fと相当塩基配列が異なると考えられ両者の区別に有効と思われる。そこでネズミやトリのマラリア原虫との配列の比較から保存性の高い領域を選んでprimer (mixed primer)を作成しこれを増巾する。このPCR productをA−1同様配列決定して、その結果からP. fとP. vを確実に区別できるprimerをデザインする。

P. vのmito DNAの塩基配列の報告はなされておらず、この計画が順調に進行すれば欧文誌への投稿（国際的なレベル）も夢ではない。

B. マレイシアにおけるD. falciparum分離株からのtotal DNAの調製と制限酵素による切断パターンの解析(Noor Rain)。

B−1　現在までに行った32株の解析のうち、3種の制限酵素でその切断パターンに株間の差異が見出されている。(rRNA遺伝子のPCRによる増巾断片)。この再現性についてcheckする。

B−2　また解析を行っていない約30株について、培養を試み、total DNA調製後、B−1同様にPCR、制限酵素による解析を行う。

ここで株間における差異が明確になった場合、A−1に準じ配列決定を行う。

C. P. falciparum mito DNAの株間変異について(Dr. Normaznah)

Noor Rainが単離したマレイシアのP. f株について（計〜60株となる予定）

P101−106によるPCR product、2−9Kbの各種制限酵素による切断パターンを解析し、株間変異を見出す。さらにA−1に準じ配列決定を行い、薬剤耐性などとの相関性について調べる。

D. RT (cDNA)−PCRの指導 (Dr. Normaznah, Noor Rain)

RT−PCRは、total（あるいはmessenger）RNAをtemplateとしてReverse Transcriptase(RT)によりcDNAを合成し、このhetero duplexを用いてPCRを行うもので、組織や血液中のRNAウイルスの検出や一般の遺伝子の発現の解析に用いられている。今回はrRNAなどcopy数の多いRNAを分子診断の標的とする目的で培養したP. fよりtotal RNAを抽出し、古田専門家の作成したrRNAに対するprimer (R1, R2) とその内部primer (R3, R4) の系を用いてRT−PCRを行った。

サポニンで溶血して得たP. fの細胞よりISOGEN（ニッポンジーン）を用いてtotal

RNAを抽出し、R−2 primerでcDNA合成、R−3とR−4でPCRを行った。その結果、約400bpの予想されたサイズのPCR productが得られた。

この様にしてマレイシア側研究者のみでRT−PCRを行う事ができる様になったが、ウイルスの様に血清を用いる場合と異なり、赤血球中のマラリア原虫のRNAの抽出を行うので、逆転写、DNAの増巾などの各ステップに対する阻害物質の影響が大きい。今後感度、再現性をどの様に改善して行くかが課題と考えられる。

JICA