

5-3-3 Planning of middle class staff training

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1. Plan for 5- year training course
2. Training Course on Research Methodology

Tentative Planning for middle level staff training

Training course	man day	Budget (Baht) x 1000				
		1986	1987	1988	1989	1990
1. Research Methodology						
Phase I	40/5	77.4	-	77.4	-	77.4
Phase II	30/3	57.6	-	57.6	-	57.6
Phase III	40/3	60.5	-	60.5	-	60.5
2. Administration	50/5	-	59	59	-	-
3. Microcomputer Application	20/20	-	170	170	170	170
4. Instrumental Analysis Techniques and Practices	50/20	-	50	50	50	-
5. Electron Microscopy	20/10	-	100	100	100	100
6. Operation and Maintenance of Equipment	40/20	-	20	20	20	20
7. RI technique	15/10	-	150	-	150	-
8. Application of Biotechnology	20/10	-	100	-	100	-
9. Principle of Tissue Culture Technique	20/10	-	100	100	-	100
10. Virology	20/5	-	69	69	69	69
11. Clinical Pathology	40/5	-	114	114	114	114
12. Clinical Chemistry	40/10	-	183*	183*	183*	183*
13. Haematology	40/10	-	183	183*	183*	183*
14. Clinical Microbiology	40/10	-	183	183*	183*	183*
15. Clinical Microscopy	40/10	-	183	183	183*	183*
16. Clinical Immunology	40/5	-	109	109	109	109*

Training course	man day	Budget (Baht) x 1000				
		1986	1987	1988	1989	1990
17. Blood Bank	30/5	-	89	89	89*	89*
18. Analysis of Drinking Water	30/5	-	89	89	89	89*
19. Vector Control	40/5	-	116.6	116.6	116.6	116.6
20. Control of <u>Aedes</u> <u>aegypti</u> and Dengue Haemorrhagic Fever	50/2	-	86	86*	86	86*
21. Laboratory Management	20/5	-	69	69*	69	69*
22. Technical Aspect and Administration of Brovincial Health Laboratory	100/5	-	229*	229	229*	229*
* DMS		-	412.0	704.0	1,050.0	1,403.0
JICA		195.5	2,039.6	1,693.1	1,242.6	885.1
Total		195.5	2,451.6	2,397.1	2,292.6	2,288.1

Course Name	Justification
Administration	: Training course in administration will be emphasized on the policy and system of administration, filing, and personnel. This will strengthen the management system in NIH proceed efficiently.
Microcomputer applications	: Workshops for health services planner, manager, and researcher to remove the barriers in using the microcomputer effectively.
Instrumental Analysis Techniques and Practices	: Courses in NMR SPECTROMETRY, IR SPECTROPHOTOMETRY, UV-VIS SPECTROPHOTOMETRY, ATOMIC ABSORPTION SPECTROPHOTOMETRY, AND CHROMATOGRAPHIES will be conducted to enable the biomedical researcher and analyst in using the particular instrument efficiently.
Electron Microscopy	: Workshops on electron microscopic sample preparation, ultramicrotomy, observation under the electron microscope, micrographic processing, qualitative and quantitative interpretations of electronmicrograph will enable the researcher to use the electron microscopes and related instruments successfully.

Course Name	Justification
Operation and Maintenance of equipment	: Workshop on instrumentation will give the researcher provision for using instruments effectively, refraining from any hazard that may occur with lack of understanding. Proper maintenance program will ensure you the instrument is still honest to you.
RI technique	: Workshop in RI technique will be organized for those who work in RI Laboratory both in central area and regional medical center. The advanced knowledge and technology obtained from the training course will provide the capability of the regional medical center to improve their own RI laboratory and efficiently participate in the research work with the central laboratory.
Application of Biotechnology	: This training course will provide basic information and technical guidance on genetic engineering specifically its application on health research including vaccine development and biological control of infectious disease vectors.
Principle of cell biology and tissue culture technique	: Provision of fundamental knowledge on various aspects of cell biology including morphology, growth characteristics, metabolism, nutritional requirement, transformation as well as the tissue culture techniques will certainly be beneficial for researchers in microbiology and related areas.

Course Name	Justification
Virology Clinical Pathology Clinical Chemistry Haematology Clinical Microbiology Clinical Microscopy Clinical Immunology Blood Bank Laboratory management Technical aspect and and administration of provincial health laboratory	Workshop in these area will be organized for the scientists and technicians in the Provincial health laboratories. The objectives are to increase the knowledge, to discuss, and to exchange the experience and information among the scientists in the related field. The high and new technology will be modified and improved in their laboratories.
Analysis of drinking water	: Drinking water in the rural area has been doubted in quality. It has to be tested in order to ensure the quality. Knowledge and technology obtained from the training course will assist the trainees to efficiently perform the analysis of drinking water in the provincial area.
Vector Control Control of Aedes aegypti and Dengue Haemorrhagic fever	: Knowledge on vector control is necessary for efficient control and prevention of vector-borne diseases. Trainees will be able to apply the knowledge to improve provincial vector control program as well as stimulate the community to participate in the program.

## Training Course on Research Methodology

### 1. Background and justification

It is known that the National Institute of Health (NIH) has been established to serve as the national research center for public health research. To accomplish this objective, the technical cooperation including the provisions of fellowships for NIH staff, equipment and the dispatch of Japanese experts have been initiated to promote the research capabilities of the NIH researchers. It must be accepted that there are a large number of NIH staff who have enthusiasm and potential to be good and creative researchers. However, due to the lack of fundamental understanding of research methodology and experiences in research, these researchers are not capable of planning and performing research efficiently. It is, therefore, necessary that NIH researchers be properly informed about the concept of research methodology in the form of training courses so that they can apply the knowledge to improve their research abilities.

### 2. Main objective of the training course

To promote the research capabilities of the NIH researchers.

### 3. Specific objectives

This training will consist of 3 phases;

Phase I of this training course is for the trainees to

1. understand the concept of scientific research.
2. know how to prepare a research proposal including identification, justifying and defining research problems, and research planning as well as writing research proposal.
3. learn sampling techniques as well as collection, preparation and analysis of data.



For phase II, the aims are for the trainees to

1. know the scope of health research needed to solve the current public health problems in Thailand.
2. understand the management and administration of research project.
3. learn the health information system for monitoring and evaluation.
4. understand the application of computer in research.

For phase III, the objectives are for the trainees to

1. understand various types and structures of scientific papers.
2. learn how to properly formulate the information (data) into interesting graphs, charts, tables, and etc.
3. learn how to prepare manuscript.
4. practice writing scientific paper.
5. learn and practice the proper way of presenting scientific paper.

#### 4. Curriculum

The training course will be divided into 3 phases:

Phase I : A five - day session comprising 24 hours of lectures and 9 hours of group discussion.

Phase I will focus on the concept of research methodology and the preparation of research proposal. In addition, various techniques of sampling and data collection will also be discussed. The tentative schedule is presented in annex I.

Phase II : A three - day session consisting of 10 hours of lectures and 8 hours of discussion.

Phase II will be primarily for those who already have basic knowledge about research methodology and have had experiences in performing research. The tentative schedule is presented in annex II.

Phase III : A three - day session comprising 10 hours of lectures and 10 hours of discussion and practice.

Phase III will focus on the proper way of writing and presenting scientific paper. The trainees will also learn how to arrange scientific data into more interesting and understandable data. They will also have chances to practice writing and presenting scientific paper. The tentative schedule of phase III is shown in annex III.

## 5. Trainees

5.1 Phase I : Approximately 40 trainees will be selected from the NIH young researchers who have never attended any training courses on research methodology before.

5.2 Phase II : Thirty trainees will be selected from NIH the researchers who already have experiences in conducting research and have had basic knowledge about research methodology.

5.3 Phase III : Approximately 40 trainees (they may or may not have attended phase I or phase II of this training course) will be selected from the NIH researchers.

## 6. Lecturers and instructors

Phase I and phase II : The lecturers and instructors will be invited from

- Institute of Health Research, Chulalongkorn University, Bangkok.
- Department of Medical Sciences, Bangkok.

Phase III : The instructors will be invited from

- National Research Council.
- Mahidol University.

## 7. Location

National Institute of Health, Department of Medical Sciences.

8. Date

8.1 Phase I February, 2, 1987 - February, 6, 1987

8.2 Phase II February, 23, 1987 - February, 25, 1987

8.3 Phase III March, 3, 1987 - March, 5, 1987

9. Budget

9.1 Phase I

Honorarium (30 hrs x 500)	15,000	Baht
Travel fees for instructors (18 persons x 600)	10,800	"
Teaching materials	15,000	"
Stationaries	24,000	"
Gasoline	5,000	"
Envelopes and papers	1,600	"
Xerox	6,000	"
Total	<u>77,400</u>	"

9.2 Phase II

Honorarium (18 hrs x 500)	9,000	Baht
Travel fees for instructors (18 persons x 500)	9,000	"
Teaching materials	15,000	"
Stationaries	20,000	"
Gasoline	1,000	"
Envelopes and papers	1,600	"
Xerox	2,000	"
Total	<u>57,600</u>	"

### 9.3 Phase III

Honorarium (24 hrs x 500)	12,000	Baht
Travel fees for instructors (15 persons x 600)	9,000	"
Stationaries	13,000	"
Teaching materials	13,500	"
Printing of documents and Xerox	10,000	
Gasoline	3,000	"
Total	<u>60,500</u>	"
<u>Grand total</u>	<u>195,500</u>	Baht

### 10. Expected Results

For phase I, the trainees will understand the concept of research methodology and have confidence and capabilities to prepare research proposal, as well as to select the appropriate methods to accomplish the objectives.

For phase II, the trainees will know the scope of health research needed to solve the current public health problems in Thailand. Trainees will also be able to manage, evaluate, and improve their research projects more efficiently.

For phase III, the trainees should be able to write scientific paper and have confidence to scientifically present their research work.

### 11. Evaluation

1. Questionnaires
2. Group discussion
3. Presentation of research proposals and scientific paper

Annex I

Tentative Schedule of Training Course on  
Research Methodology (Phase I)

February 2, 1987

9.00 - 10.30	What is research ?
10.30 - 10.45	Break
10.45 - 12.00	Scientific reasoning and scientific process
12.00 - 13.00	Lunch
13.00 - 14.15	Identification of problem, objective and hypothesis
14.15 - 14.30	Break
14.30 - 16.00	Research design

February 3, 1987

9.00 - 10.30	Role of laboratory in research
10.30 - 10.45	Break
10.45 - 12.00	Role of animals in research
12.00 - 13.00	Lunch
13.00 - 14.30	Population and sample
14.30 - 14.45	Break
14.45 - 16.00	National history and diagnostic test

February 4, 1987

9.00 - 10.30	Descriptive study
10.30 - 10.45	Break
10.45 - 12.00	Analytic study
12.00 - 13.00	Lunch
13.00 - 14.30	Experimental study and ethics
14.30 - 14.45	Break
14.45 - 16.00	Experimental study

February 5, 1987

9.00 - 10.30	Data preparation and analysis
10.30 - 10.45	Break
10.45 - 12.00	Research management
12.00 - 13.00	Lunch
13.00 - 16.00	Writing research proposal (group discussion)

February 6, 1987

9.00 - 12.00	Project presentation and discussion
12.00 - 13.00	Lunch
13.00 - 14.30	Presentation and discussion
14.30 - 14.45	Break
14.45 - 16.00	Writing research report and scientific paper

Annex II

Tentative Schedule of Training Course on  
Research Methodology (Phase II)

February 23, 1987

9.00 - 10.30	Priority and need for health research in Thailand
10.30 - 10.45	Break
10.45 - 12.00	Current epidemiological status of infectious diseases in Thailand
12.00 - 13.00	Lunch
13.00 - 14.15	Environmental health situation in Thailand
14.15 - 14.30	Break
14.30 - 16.00	Group discussion

February 24, 1987

9.00 - 10.30	Management and administration of research project
10.30 - 10.45	Break
10.45 - 12.00	Group discussion
12.00 - 13.00	Lunch
13.00 - 14.30	Role of computer in research
14.30 - 14.45	Break
14.45 - 16.00	Group discussion

February 25, 1987

9.00 - 10.30	Health information system for monitoring and evaluation
10.30 - 10.45	Break
10.45 - 12.00	Group discussion
12.00 - 13.00	Lunch
13.00 - 14.30	Writing research proposal for international fund
14.30 - 14.45	Break
14.45 - 16.00	Group discussion

Annex III

Tentative Schedule of Training Course on  
Research Methodology (Phase III)

March 3, 1987

08.30 - 09.30	Registration
09.30 - 10.00	Opening Ceremony
10.00 - 10.15	Break
10.15 - 12.00	Type and Standard of Scientific Journal Type and Structure of Scientific Paper
12.00 - 13.00	Lunch
13.00 - 16.30	Scientific Paper Writing Scientific Article Review Article General Article

March 4, 1987

08.30 - 10.00	How to formulate information Graphs, Charts, Tables etc. Reference
10.00 - 10.15	Break
10.15 - 12.00	Problems in Scientific Writing
12.00 - 13.00	Lunch
13.00 - 16.30	Preparing Good Manuscript How to present Scientific Paper Homework



March 5, 1987

08.30 - 12.00	Presentation of Scientific Paper by Workshop Participants and Discussion
12.00 - 13.00	Lunch
13.00 - 15.00	Presentation and Discussion (continued)
15.00 - 15.15	Break
15.15 - 16.30	Conclusion and Remarks
16.30	Closing Ceremony

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5 -- 3 -- 4 Anticipative problems on administration at NIH

Anticipative problems on administration at NIH

Anticipative Problems on Administration of NIH

Field	Problems	Countermeasures
<p>1. Personnel</p> <p>2. Budget</p>	<ul style="list-style-type: none"> <li>- How to recruit promising young staff.</li> <li>- Sectionalism among Division and staff.</li> <li>- Shortage of budget for research work.</li> </ul>	<ul style="list-style-type: none"> <li>- Hiring temporary research assistant.</li> <li>- A few more young scientists will be recruited after FY 1987.</li> <li>- Development of collaborative research work and use of equipment.</li> <li>- Project of self-supporting of glassware and chemicals.</li> </ul> <p><u>For glassware</u> - There are some private sectors produce simple laboratory glasswares but the quality is not satisfied.</p> <p><u>For chemicals</u></p> <ul style="list-style-type: none"> <li>- Pure chemical material; it is not possible to produce within NIH.</li> <li>- Ready to use laboratory reagent/mixture eg. media can be self-producing but the cost of self-producing and commercial should be compared.</li> </ul>

Field	Problems	Countermeasures
<p>2. Budget (continued)</p>	<p>- Increase of utilities expenses (Electricity, oil, gas, telephone).</p>	<p>- Policy of economizing in Electricity, air conditioner, telephone etc. will be formulated including;</p> <p>a) guideline/rule for proper use of electricity, air conditioner and water.</p> <p>b) telephone system.</p> <p>c) others.</p>
<p>3. Research activity</p>	<p>- Supply of appropriate themes to scientist.</p> <p>- Tactics for promoting their research activity.</p>	<p>- DMS has already organised the activities concerning the promotion of research project as follows:</p> <p>a) Monthly presentation of research work by scientists from various divisions since January 1986.</p> <p>b) Famous lecturers from other institutes were invited to present their experiences to DMS staff.</p> <p>c) Research Abstracts (1982-1984) from all divisions have been published</p>

Field	Problems	Countermeasures
<p>3. Research Activity (continued)</p>	<ul style="list-style-type: none"> <li>- Establishment of research moral (es. no dining in lab, washing glassware and cleaning each room by scientist).</li> <li>- Safety direction for biohazard lab. RI lab., Virus lab. etc.</li> </ul>	<p>in August 1985 and for those in 1985-1986 have now being collected.</p> <ul style="list-style-type: none"> <li>- Group discussion among the researchers in the same laboratory to exchange views and problems.</li> <li>- Encourage young scientists to initiate their own projects and have confidence to present their research work.</li> <li>- Senior scientists should act as good examples for younger scientists in regard to the research moral.</li> </ul>
<p>4. Security</p>	<ul style="list-style-type: none"> <li>- Prevention of Crimes</li> </ul>	<ul style="list-style-type: none"> <li>- Regulations for biohazard lab. and RI lab. have already been set up by each committee.</li> <li>- Contact Department of Central of the Intelligence for the advise on the arrangement of security system.</li> </ul>
<p>5. Maintenance</p>	<ul style="list-style-type: none"> <li>- Main building, laboratories, Utilities.</li> <li>- Control of electricity, water, gas, drain, ventilation, steam, garbage, including dangerous waste.</li> </ul>	<ul style="list-style-type: none"> <li>- At the beginning, the experienced technicians will be temporarily selected from each division. After October, 1987, permanent technicians will be recruited.</li> <li>- There will be training courses for all staff in NIH which are now under planning.</li> </ul>

Field	Problems	Countermeasures
	<ul style="list-style-type: none"> <li>- Common machine and equipment.</li> <li>- Medical machine and equipment.</li> <li>- Cleaning</li> </ul>	<ul style="list-style-type: none"> <li>- Scientific instrument center will conduct the activities concerning the maintenance of the mentioned equipment.</li> <li>-- There will be a training course for workers in the area of biohazard and RI Lab to guide them how to work properly and safely.</li> </ul>



### 5 – 3 – 5 Research Activities

1. Virology
2. Bacteriology
3. Parasitology
4. Mycology
5. Immunology
6. Development and Control of Biological Products
7. Medicinal Plant
8. Medical Entomology
9. Environmental Health Science Research
10. Biomedical Research on Food
11. Pharmaceutical Sciences
12. Radioisotope Laboratory
13. Animal Center
14. Biohazard Laboratory

## A. RESEARCH ACTIVITIES IN THE NATIONAL INSTITUTE OF HEALTH

The Department of Medical Sciences (DMS) was established with the main objectives of promoting health laboratory services and conducting medical research. It is generally accepted that both laboratory services and health research activities are essential for efficient medical care and effective control and prevention of infectious diseases. The DMS has been successfully serving as the national service center for diagnosis of various infectious diseases, identification of health problems in community, detection of health hazard, and quality control of food and drugs for consumer protection. Despite the activities accomplished, public health authorities are now recognizing the importance of the health research activities which are also essential for solving public health problems prevailing in the country. Introduction of advanced technology, and development of new chemicals or biological products urgently needed can be achieved through the promotion of basic and applied health science researches. Therefore, the National Institute of Health (NIH) has been established within the DMS with the cooperation of the government of Japan to primarily serve as the national center for intensive health research. It will also function as a national reference and training center for local and provincial researchers and will promote the extension of the results and application of researches conducted throughout the country.

### Objectives

The NIH will perform health sciences research to support health promotion of the whole nation. Fundamental and applied research in various fields of microbiology and environmental health are to be conducted to solve public health problems, consumer protection, diseases prevention, and support the Primary Health Care Project.

### Specific objectives

The objectives of the Health Sciences Research Project are as follows:

1. To conduct research in the fields of virology, bacteriology, mycology, parasitology, immunology, medical entomology, environmental health biology and chemistry, toxicology, pharmacology and pharmaceutical sciences, vaccine and serum production and standardization, biomedical research on foods, medicinal plants and other relevant fields.

2. To extend health research activities to areas outside Bangkok through the Regional Medical Sciences Centers.

3. To expand and strengthen health laboratory monitors with special emphasis on food analysis, drug analysis and toxicological analysis in the provinces.

4. To support the diagnosis, treatment, and prevention of diseases through laboratory interventions at the central, regional, provincial and local levels.

5. To coordinate and cooperate with medical scientists in Japan in carrying out joint research projects in various health fields, particularly tropical medicine and environmental health.

6. To serve as the national and international training center for medical scientists, analysts and laboratory technicians.

There will be 11 main activities and 5 supportive activities. The main activities are: Virology, Bacteriology, Mycology, Parasitology, Immunology, Biological Products, Medical Entomology, Medicinal Plants, Environmental Health Sciences, Biomedical Research in Food, Pharmaceutical Sciences.

The supportive activities are: Administrative office, Animal Experiment Center, Biohazard Laboratory, Radioisotope Laboratory and Scientific Instrument Center.

## VIROLOGY

The virological activities are fundamental and applied researches on viral diseases prevailing in Thailand which will bring progress in the elucidation of occurrence, prevention, control and treatment of the diseases. The research activities are primarily concerned with various viruses namely, arboviruses, respiratory viruses, enteroviruses, rabies, hepatitis and oncogenic viruses as well as rickettsia and chlamydia. It also serves as national reference center and provides consultation services and training for local and regional medical scientists.

### Research activities

#### *Research to support*

1. Epidemiological surveillance of viral diseases prevailing in Thailand.
2. Research, development and improvement of rapid diagnosis of viral diseases.
3. Research and development of viral vaccine production either by conventional methods or biotechnology.
4. Production and supply of diagnostic reagents to regional laboratories.
5. Establishment of new laboratories for chlamydia, rickettsia and oncogenic viruses.

### Specific objectives and activities

Public health authorities are now becoming more and more concerned about the diseases caused by Japanese encephalitis (JE), hepatitis and rabies viruses due to their prevalence among Thai population. Therefore, the aim of virus research activities to be conducted in the next 3 years (1987-1989) is to solve the problems in regard to the diseases caused by these 3 viruses namely JE, hepatitis and rabies viruses.

1. Viral hepatitis

*Research to support*  
A. Epidemiological surveillance

- Epidemiological studies of sporadic acute viral hepatitis.
- Studies on immune status to hepatitis B virus among Thai population including pregnant women, newborn babies, soldiers and hospital personnel.

B. Diagnosis

- Development of diagnostic techniques for hepatitis A, and Non A non B.

C. Vaccine

- Pilot project of plasma-derived hepatitis B vaccine production (in progress).
- Quality control of the vaccine produced (Biological Product Activity).
- Clinical trial of hepatitis vaccines.

D. Reagent production

- Production of reagents used in reversed passive hemagglutination (RPHA) and passive hemagglutination (PHA) assays for the detection of anti hepatitis virus antibody.

2. Japanese encephalitis (JE)

*Research to support*  
A. Epidemiological surveillance

- Survey of immune status to JE virus in Thai population and amplifier (swine) in different areas in Thailand (joint-research with Division of Epidemiology).

B. Vaccine

- Production of JE virus from suckling mice (Biological Product Activity).
- Quality control of JE vaccine produced (Biological Product Activity).
- Vaccine Trial.

C. Diagnosis

- Development of new and more efficient diagnostic technique for JE virus.

### 3. Rabies

- Pilot production of rabies vaccine from chick embryo fibroblast.
  - Quality control of rabies vaccines produced from vero cells, chick embryo and etc. (Biological Product Activity).
- development of new diagnostic technique for rabies.

4. Besides the research activities mentioned above, the following research projects will also be conducted;

#### Development of new diagnostic techniques

- Oligonucleotide finger printing (influenza, dengue and JE viruses).
- RNA electrophoretotyping (rota virus).
- Monoclonal antibody for the diagnosis of dengue virus and cytomegalovirus.

Finally, the diagnosis of other viruses including adenovirus, RSV, polio virus, measles, rubella, arboviruses, herpes viruses will also be conducted.

VIROLOGY

RESEARCH PLAN FOR RABIES VACCINE PRODUCTION

1987	1988	1989	1990
Expert [ ]			
	Fellowship [ ]		
	Expert [ ]		
		field trial [ ]	
			large scale production of vaccine?

1. In January, 1987, the expert will be dispatched for preliminary survey of facilities and technical guidance needed for rabies vaccine production.
2. A 12-month fellowship will be granted to NIH staff for production of rabies vaccine from chick embryo fibroblast.
3. After completion of training in Japan, the fellow, accompanied by the expert, will return and start the production of rabies vaccine under the supervision of the expert.
4. Field trial of the vaccine produced will be conducted.



PROGRESS REPORT AND RESEARCH PLAN OF  
JE VACCINE PRODUCTION PROJECT

Project    Production of JE vaccine from                    mouse brain

Activities accomplished

The production of JE vaccine from                    mouse brain follows the method conformed to Kanonji Institute's method. Briefly, JE virus-infected mouse brain was treated with protamine sulfate to precipitate brain proteins. Following the inactivation of the virus, the concentration and purification steps were accomplished through series of ultracentrifugation. Quality control was conducted parallelly to evaluate the quality of purified viruses obtained.

So far, 8 batches of purified JE virus were achieved. However, only the last 2 batches gave satisfactory titers for vaccine production. To improve the performance, several measures have been suggested:

1. Infected mouse brain should be frozen only once before the viruses were harvested otherwise the titers will drop.
2. The volume of inactivated protamine sulfate treated solution should be properly adjusted for ultrafiltration apparatus.
3. Appropriate time and speed for sucrose gradient centrifugation should be determined.

It also has been suggested that there should be improvement on techniques for quality control, potency and sterility tests. In addition, the NIH should plan appropriate measures to solve the possible problem encountered regarding the shortage of mouse supplies.

Additional equipment needed

1. cold room (4°c) or refrigerator (20 cu. ft)
2. freezer (-20°c)
3. deep freezer (-70°c)

4. N<sub>2</sub> tank
5. microdilutor (25 ul) 36 pieces
6. microdropper (50 ul) 18 pieces  
(25 ul) 12 pieces
7. microtiterplate mixer

Research activities

	1986	1987	1988	1989	1990
1.	8,000 doses				
2.	field trial				
3.	expert (Q.C.)				
4.	20,000 doses				
5.	50,000 doses/year				
6.	fellowship (biotech.)				
7.	expert				

1. Small scale production of JE vaccine (8,000 doses) will be accomplished by the beginning of 1987.
2. Field trial of vaccine produced will be conducted.
3. One Japanese expert will be dispatched to provide advice and technical guidance in regard to the improvement of quality control, potency and sterility tests of JE vaccine.
4. In 1987, it is expected that 20,000 doses of JE vaccine will be produced.

5. From 1987, GPO is expected to produce 50,000 doses of vaccines annually.

6. One fellowship will be granted for the study of molecular approach to the development of JE vaccine production.

7. After the completion of the training, the fellow accompanied by Japanese expert, will return and start JE vaccine production employing biotechnology under the supervision of the expert.

RESEARCH PLAN FOR RABIES VACCINE PRODUCTION

1987	1988	1989	1990
1. <u>fellowship</u>	2. <u>expert</u>	3. <u>field trial</u>	large scale production of vaccine ?
4. <u>field trial of Japanese vaccine</u>			

1. A 12-month fellowship will be granted to the NIH staff to learn
  - A. production of rabies vaccine from chick embryo fibroblast.
  - B. new techniques for quality control, potency test and efficacy test of rabies vaccine.
  
2. Following the completion of the training in Japan, the fellow, accompanied by the Japanese expert on rabies vaccine production, will return and start the rabies vaccine production project (small scale) at the NIH under the supervision of the expert. The quality control, potency test and other necessary tests will be undertaken to evaluate the safety and efficacy of the vaccine produced.
  
3. Field trial of the vaccine will be conducted on the condition that the quality control and other tests on the vaccine are satisfactory.
  
4. Field trial of Japanese rabies vaccine (chick embryo fibroblast rabies vaccine) will be conducted (1987/1988) for post exposure treatment to evaluate the immunity in the vaccinees and efficacy of the vaccine

## BACTERIOLOGY

Bacteriology activity serves as central and reference laboratory for the country and carry out research work on etiology, epidemiology and immunology of infectious diseases especially gastrointestinal and respiratory infections. Technical guidance and support will be provided to regional and provincial public health laboratories. Bacteriology laboratory will also produce antisera, antigen and reagents for diagnosis of bacterial diseases especially gastrointestinal infections.

### Research activities

1. Epidemiological and etiological studies of gastrointestinal and respiratory infections by improving bacteriological techniques and introduction of modern technology of medical sciences and taxonomical method.

2. Establishment of National Reference System in

- 1) Clinical Microbiology
- 2) Public Health Microbiology

3. Study of mode of infection and immunity concerning pathogenicity in term of molecular biology in some bacterial diseases e.g. those caused by gram negative bacilli and anaerobic bacteria.

4. Study on toxicity and therapeutic evaluation of new antimicrobial drugs and drug resistance of microorganisms employing new technique in genetics.

### Specific activities

1. Mycoplasma - related acute respiratory tract infection in children.

2. Epidemiology of streptococcus infections.

3. Epidemiological study of Legionnaires' disease.

4. Develop and improve the techniques of isolation and characterization of pathogenic bacteria by biological and genetical character, serology, toxin detection. (ETEC, Campylobacter jejuni, Bdellovibrio, Clostridium difficile, Clostridium tetani, etc.)

5. Detection of enteric bacterial toxins. (e.g. C. difficile, ETEC, etc.)

6. Isolation and purification of bacterial toxins and prepare antibodies against toxins for confirming those toxins.

7. Biological activities of purified enteric bacterial toxins and role of toxins in pathogenesis.

8. Plasmid characterization of drug - resistance of enteric bacteria.

9. Production and development of serodiagnostic reagents for enteropathogenic bacteria e.g. - enterotoxigenic E. Coli.

## PARASITOLOGY

Parasitology laboratory serves as central and reference laboratory for the country and will carry out epidemiological researches on parasitic infestations and application of monoclonal antibodies in the study of malarial parasites.

### Research activities

1. Application of monoclonal antibody in the study of epidemiology of parasitic infectious diseases.
2. Research in parasitology with special reference to in vitro cultivation of parasites and test of efficacy of medicinal plants.
3. Epidemiological researches on parasitic infestations.

### Specific activities

1. The effect of monoclonal antibody on Plasmodium falciparum in continuous culture.
2. Study on the effect of medicinal plant on Plasmodium falciparum.
3. In vitro cultivation of Plasmodium vivax.
4. A survey of prevalence and severity of helminthic infections in school aged children.

## MYCOLOGY

The main responsibility of mycology activity is to serve as central and reference laboratory and to give technical guidance and support to regional and provincial public health laboratories.

Development and improvement of the technique of handling mycological work in those laboratories.

### Research activities

1. Study of various deep seated and systemic fungi (pathogenic & opportunistic) and methods of their isolation and identification.
2. Histopathological study of fungi in human tissue and in experimental animals.
3. Study of various toxic fungi and their mycotoxins.

### Specific activities

1. Study on the saprophytic stage of Histoplasma capsulatum from soil and bats guano and the occurrence of Histoplasmosis.
2. Histopathologic study of opportunistic and dimorphic fungi in experimental animals.
3. A study on the identification of Nocardia sp. and streptomycetes sp. by electrophoresis.
4. Isolation and identification of toxin - producing fungi and their toxins.



BACTERIOLOGY  
REFERENCE SYSTEM

Research Activities

Establishment of National Reference System in

1. Clinical Microbiology
2. Public Health Microbiology

Specific Activities

1. Strengthening the bacteriology and mycology laboratories at NIH to become as the reference laboratory centers.

- Quality control, standardization and diagnostic method of bacteria and fungi.

- Characterization of pathogenic bacteria by biological and genetical character (G:C ratio, DNA hybridization) serology, toxicity and pathogenicity test.

- Phage typing of some pathogenic bacteria.

- Type culture collection.

- Characterization of pathogenic yeast and fungi by biochemical and serological technique.

2. Establishment of laboratory for Mycoplasma.

3. Establishment of laboratory for Rickettsia and Chlamydia.

4. Transfer the following technology to the regional medical sciences center laboratories (6 labs) to become as the regional reference laboratories.

- Isolation and identification of infectious bacteria (enteric and miscellaneous bacteria including anaerobic bacteria) by biochemical and serological character.

- Cultivation of yeast & fungi and identification by their morphological characters.

## Rickettsia

Until now, laboratory investigations of Rickettsia have not been developed in Thailand because of lacking in instruments, expenditure, and technology. Only Weil Felix Test is performed in large hospitals. In 1984, 104 cases of scrub typhus were reported by the Division of Epidemiology, Ministry of Public Health : 40.4 % in the north - eastern, 36.5 % in the northern, 16.4 % in the central and 6.7 % in the southern part of Thailand. High incidence (200,000) of PUO (Pyrexia of Unknown Origin) was also reported and some cases were confirmed as scrub typhus and murine typhus. From two studies in southern Thailand in 1985, scrub typhus cases were reported among PUO cases at 28 % (71/253) whereas murine typhus cases were 7 % (11/160) and 37 % (61/65). Further study by culture and seroepidemiology should be carried out.

### Training activity

1. Rickettsial isolation by animal and chick embryo.
2. Serological diagnosis : Fluorescent antibody technique, Immune peroxidase, Agglutination test and Neutralization test etc.
3. Rickettsial isolation from insect vectors.
4. Rickettsial antigens and conjugate preparation.

### Research activity

1. Seroepidemiology of rickettsial infection in Thailand.
2. Isolation and identification of rickettsia from insect vectors (joint project with the Division of Medical Entomology).

## Chlamydia

In Thailand, the problems of chlamydial infections are conjunctivitis and pneumonitis in newborn, and sexually transmitted disease. In STD, non-gonococcal urethritis is the second important disease and chlamydial infection is included in this category.

Chlamydia trachomatis was isolated from neonatal conjunctivitis cases at 20-40 % (7/36 - 35/89) (Chulalongkorn and Siriraj hospital, 1985). Chlamydia was transmitted from mother to newborn during pregnancy. It could also be isolated from pregnant women at 15 % (21/140) (Chulalongkorn, 1985)

In case of venereal disease, C.trachomatis was isolated at 18.7% (9/48) in male with non-gonococcal urethritis, 9.5 % (6/69) in male with gonococcal urethritis and 5.2 % (2/38) in male without urethritis (carrier) (Armforces Research Institute of Medical Sciences, 1985). In women with vaginal discharge symptom, C.trachomatis could be found at 8 % (31/379) (Siriraj hospital, 1985). In other study, 24 % (321/1,363) were found from socially handicapped women (The Division of Epidemiology and Division of Venereal Disease Control, 1985)

## Training activity

1. Immunotyping (15 types) of C.trachomatis.
2. Differentiate C.trachomatis and C.psittaci.
3. Chlamydial antigens and conjugate preparation.
4. ELISA of Chlamydia

## Research activity

1. Epidemiology of chlamydial infection in various groups: conjunctivitis, sexually transmitted disease, respiratory infection and etc.
2. Differentiate species and types of Chlamydia isolated in Thailand.
3. Collect data and join project with the Division of Epidemiology, Division of Venereal Disease Control and etc.

Present status of Laboratory for Chlamydia in Thailand

The followings are performed in some institutions:

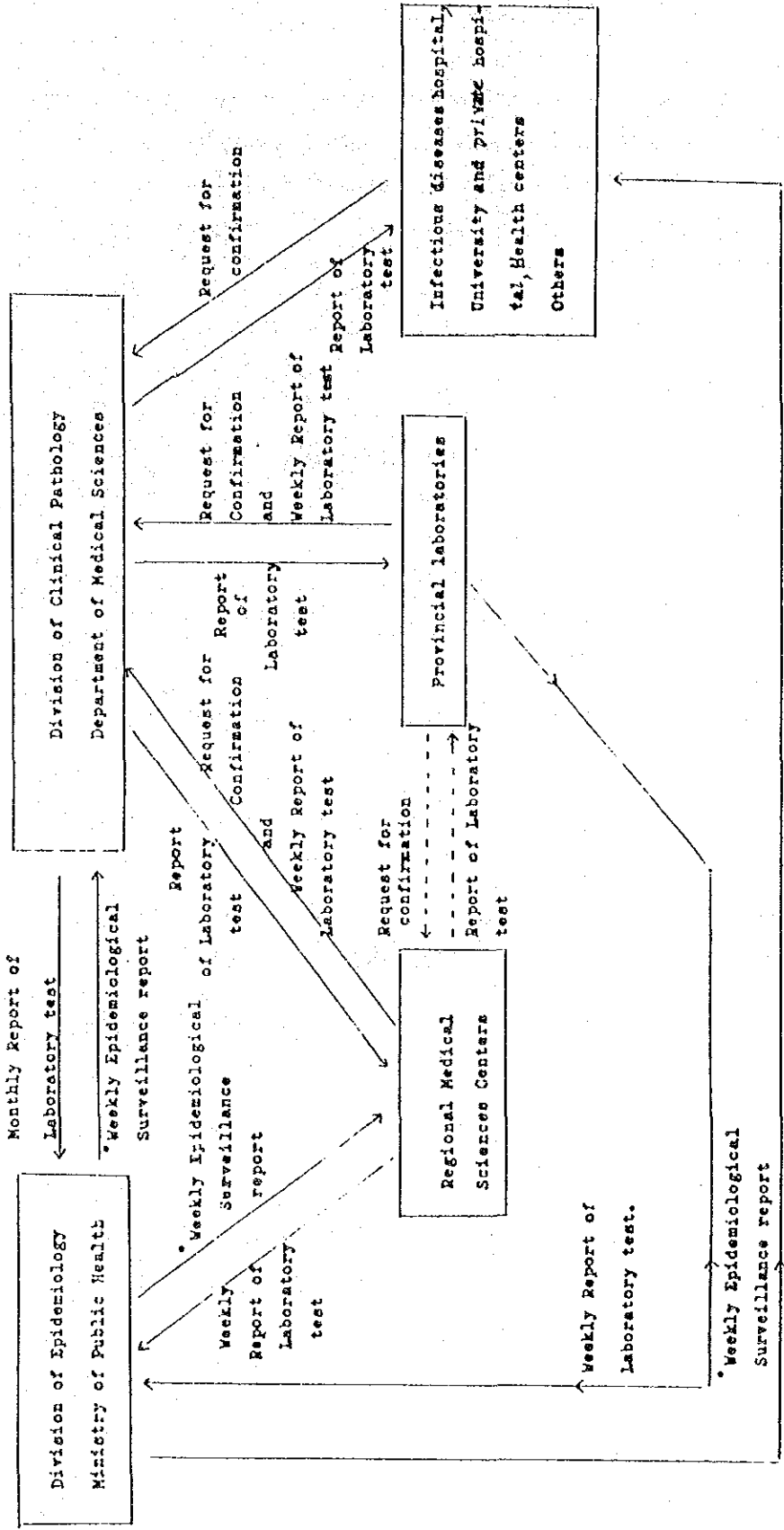
1. Isolation (culture by MacCoy cell)
2. Iodine and Giemsa stain
3. Direct FA
4. MIF (Indirect FA)

No. 1 & 2 are performed by 4 institutions : Department of Microbiology, Faculty of Medicine, Chulalongkorn University; Department of Microbiology, Faculty of Medicine, Siriraj Hospital; AFRIMS, and Division of Venereal Diseases Control.

No. 3 is performed by Department of Microbiology, Faculty of Medicine, Siriraj Hospital.

No. 4 is performed by Department of Microbiology, Faculty of Medicine, Chulalongkorn University.

Present Condition of Reference Activities in Bacteriology



- Summary - Identifications of specified bacterial and viral pathogens.
- Monitoring susceptibility of bacterial pathogens to commonly used antimicrobials

----- Future Plan

## IMMUNOLOGY

The Immunology activities emphasize on the basic and applied researches on the immunity to infectious diseases caused by viruses, bacteria or parasites. The research to be conducted will be inter-division projects with the cooperation between the Immunology and other divisions concerned.

### Objectives

To conduct the immunological researches which will bring about effective measures for prevention, control and treatment of infectious diseases.

### Research activities

1. Development and production of biological reagents utilized in the immunological research.
2. Development of new rapid diagnostic techniques for viral and bacterial diseases.
3. Studies on immunological properties of viruses, bacteria, and toxins.
4. Research on the immune mechanisms responsible for the prevention, control and recovery of various infectious diseases.
5. Utilization of biotechnology for the diagnosis of viruses and bacteria as well as the development of new vaccines.

The activities planned for the next 3 years (1987-1989) are as follows:

1. Production, purification and identification of class specific immunoglobulin and anti-class-specific immunoglobulin.

\*  
2. Development of new diagnostic techniques:

-- production and characterization of monoclonal antibodies for the diagnosis of cytomegalovirus, JE and **dengue viruses**.

-- Oligonucleotide finger-printing for the detection and analysis of polio and influenza **JE and dengue viruses**.

\*  
3. Development of in vitro assay of cell-mediated immune responses including lymphocyte proliferation and cytotoxic assays for the studies of immune status in individuals infected with viruses such as herpes simplex virus.

\* joint-research with Virology

## DEVELOPMENT AND CONTROL OF BIOLOGICAL PRODUCTS

Section of Development and Control of Biological Products conducts the research on the biological products in the aspect of quality, safety and efficacy. Development of vaccine is another activity to achieve in producing efficient new biological products.

### Research activities

1. To produce the national standards and preparations calibrated against the International Standards and reference preparations of biological products.

2. To carry out and cooperate on the development of new biological products.

3. To develop and improve the biological control technology for the existing and new biological products.

4. Research and evaluation of the cold chain system immunologic effects and efficacy of EPI programme.

### Specific activities

1. Small and large scale productions of JE vaccine from mouse brain.

2. Development of Pertussis Vaccine (acellular).

3. Development of technology for quality control of Hepatitis B vaccine, Vero cell rabies vaccine. Hepatitis B Immunoglobulin.



## MEDICINAL PLANT

Medicinal Plant activities conduct the research studies on medicinal plants and plant-derived products. The medicinal plant is involved in cultivation, physico-chemical analysis of active constituents, structure elucidation, pharmacological, toxicological studies and utilization of the products.

The specific activities to be implemented in 1987-1989 are:

1. Phytochemical study on Thai medicinal plants and determination of their effect on in vitro development of *Plasmodium falciparum*.

2. Preparation of crude extracts from selected medicinal plants for preliminary in vitro screening test.

## MEDICAL ENTOMOLOGY

The main activities of Medical Entomology are fundamental and applied research on vector surveillance, vector control, and insecticide susceptibility of vectors to support the epidemiology, prevention and control of vector-borne diseases such as DHF, JE, malaria, filariasis and typhus.

### Research Activities

1. Survey and development of local pathogenic bacteria for controlling mosquito vector of DHF and Malaria.
2. Studies on biology and ecology of mosquitoes and insect vectors carrying diseases. Surveillance systems of DHF and JE vectors will be established.
3. To monitor the susceptibility status of DHF/JE vectors and other insects of medical importance throughout Thailand.
4. Study the suitable ways to prevent and control vector-borne diseases focused on community participation.
5. Study on the control measures which consist of biological, chemical, environmental management etc. in order to search for the most appropriate means with minimum cost.
6. To establish museum of Medical Entomology.
7. Research on rodent and related diseases.

### Specific activities

The aims of Medical Entomology research in the next 3 years (1987-1989) are to prevent and control vector-borne diseases including

1. Research and development of biological control of mosquitoes.
2. The study of JE and DHF vector density at different season from 5 regions.

3. Research on biology and ecology of JE and malaria vectors in reference to their epidemiology and control.

4. Community participation in the control and prevention of vectors of DHF.

5. Study on residual effectiveness of house hold aerosols against cockroach.

6. Research on urban rodent study in relation to

6.1 house dust mites as the causative of asthma.

6.2 HFRS (joint-project with Virology).

## ENVIRONMENTAL HEALTH SCIENCE RESEARCH

The research in this area is responsible for conducting biological and chemical analysis, evaluating the hazards of environmental toxic substances for public safety and health promotion.

### Research activities

1. Toxicological evaluation of human environments caused by chemical poisons and other natural sources.
2. Mutagenicity and carcinogenicity of chemical hazards, toxins and pollutants in Bioassay using bacteria.
3. Histopathology of experimental animals obtaining the environmental toxic substances.

The specific activities to be implemented in 1987-1989 are:

1. Relationship between red blood cells and serum cholinesterase values, blood organophosphates and their metabolites with the insecticide clinical symptoms.
2. Toxicity evaluation of detergent pollutant to water animal and their influence on human, animals and plants.
3. Trichothecines in feedstuffs and the environment.

## BIOMEDICAL RESEARCH ON FOOD

Biomedical Research on Food conducts the studies on toxic substances in local food, food additives, chemical and microbiological contaminants and also other related fields such as pathogenic bacteriology, mycology, parasitology, virology and toxicology.

### Research activities

1. Conducting a nation wide survey on food contaminants caused by environmental pollution and also actual intake of those contaminants.

2. Methodology development for qualitative analysis of certain kinds of compounds in food.

3. Food microbiology and toxicology.

The specific activities to be implemented in 1987-1989 are:

1. Pilot study on production of X. perfringens type A antiserum for routine laboratory investigation.

2. Analysis of critical control point of hazardous compounds in food prepared in village household in different geographical areas in Thailand.

3. Investigation on toxins produced by food poisoning microorganisms (*S. aureus*, *Campylobacter*, *E. Coli* etc.)

## PHARMACEUTICAL SCIENCES

Pharmaceutical Sciences activity is mainly responsible for the improvement of the quality assessment of drug. Research activities are concerned with radioimmunoassay, physico-chemical, microbiological and biological assay. The objective is to promote the better control of the quality of pharmaceutical preparations.

### Research activities

1. Initiation of radioimmunoassay (RIA) technique for the quality control of pharmaceuticals and production of antisera and tracer used in RIA laboratories.
2. Quality control of radiopharmaceutical products.
3. Study on stability and bioavailability of pharmaceutical preparations.
4. Animal test and assay of pharmaceutical products.
5. Testing and method development for determining the drug substances.

The specific activities to be implemented in 1987-1989 are:

1. Continuation of research on Digoxin treatment of heart disease patients in Thailand.
2. Bioavailability study of DMPA as contraceptive by RIA technique.
3. Continuation on RIA kit production project.
4. Antisera production for RIA assay of steroid hormones.
5. Establishment of RIA assay of antisera production in (4).
6. Establishment of radiopharmaceutical section.
7. Quality control of radiopharmaceuticals used in the country.

8. Animal assay of insulin.
9. Survey of bacterial endotoxin in parenteral preparation by LAL method in comparison with rabbit pyrogen test.
10. Fermentation Pilot plan of Penicillin
  - Strain improvement of Penicillin-producing microgenism.
  - Microbial transformation of Penicillin G to 6-APA.

## RADIOISOTOPE LABORATORY

Radioisotope laboratory serves as the supportive activity for other laboratories. The major responsibilities are involved with all experiments employing radioisotopes.

### Research activities

1. Radioimmunoassay in microbiology and chemical substances.
2. Radioisotope technique in virology, microbiology, toxicology and pharmacology.
3. Production of antisera and tracers used in RIA laboratory.
4. Quality assessment of radiopharmaceutical products.



## Research Activities at Animal Experiment Center

### Bacteriology

1. Study on pathogenicity and toxicity of pathogenic bacteria by using animal experiments.
2. Research on biological activities of purified enteric bacterial toxins and role of toxin in pathogenesis.
3. Antitoxin production (for confirming bacterial toxins in laboratory).

### Mycology

1. Study on the histopathology of fungi in human tissue and in experimental animals.

BIOHAZARD LABORATORY

Infectious and genetic research in Virology, Bacteriology, Mycology and unknown infectious agents that call for biological safety.



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