

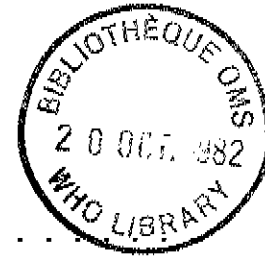


*Arboviral infections - 2 copies
 Rickettsial infections - 1 copy
 Dengue - 1 PC
 Encephalitis, Japanese - 1 PC
 Haemorrhagic fever, Japanese - 1 PC
 WHO/SEARO/WPRO/82.1
 ENGLISH ONLY
 Asia, S.E.
 W.P.*

REGIONAL OFFICE FOR SOUTH EAST ASIA ; REGIONAL OFFICE FOR THE WESTERN PACIFIC

JOINT CONSULTATIVE MEETING ON ARTHROPOD- AND RODENT-BORNE
 VIRAL AND RICKETTSIAL DISEASES

Bangkok 31 May-3 June 1982



| <u>CONTENTS</u> | <u>Page</u> |
|---------------------------------------------------------------------------------------------------------------------------|-------------|
| 1. INTRODUCTION | 3 |
| 2. OBJECTIVES OF THE MEETING | 4 |
| 3. ARTHROPOD- AND RODENT-BORNE VIRAL AND RICKETTSIAL DISEASES IN SOUTH EAST ASIA AND WESTERN PACIFIC REGIONS | 4 |
| 3.1 Dengue haemorrhagic fever (DHF) | 5 |
| 3.2 Japanese encephalitis (JE) | 5 |
| 3.3 Haemorrhagic fever with renal syndrome (HFRS) | 5 |
| 3.4 Rickettsial diseases | 6 |
| 4. DENGUE, DENGUE HAEMORRHAGIC FEVER, DENGUE SHOCK SYNDROME - A PLAN OF ACTION FOR PREVENTION AND CONTROL | 6 |
| 4.1 Situation analysis | 6 |
| 4.2 Objectives | 7 |
| 4.3 Targets | 7 |
| 4.4 Strategies and approaches | 7 |
| 4.5 Activities | 8 |
| 4.6 Programme monitoring | 11 |
| 5. JAPANESE ENCEPHALITIS - A PLAN OF ACTION FOR PREVENTION AND CONTROL | 11 |
| 5.1 Situation analysis | 11 |
| 5.2 Objective | 11 |
| 5.3 Targets | 12 |
| 5.4 Strategies and approaches | 12 |
| 5.5 Activities | 13 |
| 5.6 Programme monitoring | 14 |
| 6. HAEMORRHAGIC FEVER WITH RENAL SYNDROME (HANTAN VIRUS) - A PLAN OF ACTION FOR PREVENTION AND CONTROL | 14 |
| 6.1 Situation analysis | 14 |
| 6.2 Objectives | 14 |
| 6.3 Targets | 14 |
| 6.4 Strategies and approaches | 15 |
| 6.5 Activities | 15 |
| 6.6 Programme monitoring | 16 |

The issue of this document does not constitute formal publication. It should not be reviewed, abstracted or quoted without the agreement of the World Health Organization. Authors alone are responsible for views expressed in signed articles.

Ce document ne constitue pas une publication. Il ne doit faire l'objet d'aucun compte rendu ou résumé ni d'aucune citation sans l'autorisation de l'Organisation Mondiale de la Santé. Les opinions exprimées dans les articles signés n'engagent que leurs auteurs.

| | |
|------------------------------------------------------------------------|----|
| 7. OTHER ARTHROPOD- AND RODENT-BORNE VIRAL DISEASES | 16 |
| 7.1 Situation analysis | 16 |
| 8. RICKETTSIOSES - A PLAN OF ACTION FOR PREVENTION AND CONTROL | 16 |
| 8.1 Situation analysis | 16 |
| 8.2 Objectives | 17 |
| 8.3 Targets | 17 |
| 8.4 Strategies and approaches | 17 |
| 8.5 Activities | 18 |
| 8.6 Programme monitoring | 18 |
| 9. RECOMMENDATIONS TO WHO | 18 |

ANNEX I: LIST OF PARTICIPANTS, OBSERVERS AND SECRETARIAT

ANNEX II: A SUGGESTED OUTLINE FOR A PLAN OF ACTION

INTRODUCTION

Since 1974, several joint meetings and consultations between the South East Asia and Western Pacific Regions on dengue haemorrhagic fever have taken place. However, with the growing concern for other viral and rickettsial diseases in countries in the two regions, a joint consultative meeting with a widened scope was convened from 31 May to 3 June 1982 in Bangkok, to consider arthropod- and rodent-borne viral and rickettsial diseases which are of public health importance in the two regions.

The Regional Directors of both regions attended the meeting.

Welcoming addresses were given by the Dean of the Faculty of Medicine, Dr Thavi Boonchoti, followed by the Rector of the Mahidol University, Professor Natth Bhamarapravati, Dr Prakorb Tuchinda, Under-Secretary of State for Public Health and Dr Nadda Sriyabhaya, Director-General, Department of Communicable Diseases Control addressing the meeting mentioned that dengue haemorrhagic fever (DHF) and Japanese Encephalitis (JE) are major public health problems in Thailand. Extensive research has been carried out in particular by the Virus Research Institute and the Medical Entomology Division, Department of Medical Sciences, Bangkok. Effective measures for prevention and control of both diseases have yet to evolve within the country's resources. There has been a marked reduction in dengue haemorrhagic fever (DHF)/dengue shock syndrome (DSS) case fatality thanks to better case management but there has been no impact on attack rates. He stressed the timeliness of the present meeting to review the prevailing disease problems caused by arthropod- and rodent-borne viruses and rickettsiae in South East Asia and Western Pacific areas and the need to come up with concrete proposals for a plan of action.

Dr U Ko Ko, Regional Director of the WHO Regional Office for South East Asia after welcoming the participants invited Dr H. Nakajima, Regional Director of the WHO Regional Office for the Western Pacific to inaugurate the meeting.

Dr H. Nakajima outlined the objectives of the meeting (see page ..) and mentioned that both Dr U Ko Ko and himself will consider ways and means of putting the recommendations and advice of the Joint Consultative Meeting into action.

He stressed that the Western Pacific region's awareness and concern about the importance of arbovirus infections dates back to 1962 when the First Seminar on Japanese Encephalitis and Arbovirus Infections was held in Tokyo. A Second Seminar on Mosquito-borne Virus Diseases was held in Manila in 1969. In 1973, reported outbreaks of dengue fever/dengue haemorrhagic fever reached alarming proportions and were a cause of grave concern not only to the health authorities in countries of the Western Pacific but in South East Asia as well. This prompted the Regional Directors of the South-East Asia and Western Pacific regions to form a Technical Advisory Committee on Dengue Haemorrhagic Fever for South-East Asia and the Western Pacific regions with membership from both regions, in order to prepare a rational and practical guide for the prevention and control of dengue fever/dengue haemorrhagic fever. The Committee met three times, in 1974, 1975 and again in 1978 when representatives from the American and Eastern Mediterranean regions joined in the meeting.

The Committee produced the "Guide for Diagnosis, Treatment and Control of Dengue Haemorrhagic Fever", the latest edition of which was published in 1980. The Committee also stimulated the publication of the "Dengue Newsletter", which provides up-to-date information on various aspects of dengue, particularly in both regions. Another good example of inter-regional cooperation was the meeting in New Delhi in 1980 of experts, from the East Mediterranean, South-East Asian and Western Pacific regions on viral haemorrhagic fevers in Africa, Asia and the Western Pacific.

Attention should also be given to rickettsial infections. However these did not seem to be a major problem at the moment for the simple reason that clinical manifestations are not well defined and laboratory diagnostic support is lacking in areas where these infections are expected to be common.

Dr Natth Bhamaraprevati was elected Chairman, Dr Jacinto Dizon Vice-Chairman and Dr John Miles and Dr Suchitra Nimmanyita, rapporteurs. A list of participants is given in Annex 1.

The participants in meeting formed four discussion groups to consider the following:

- Group 1 - Dengue haemorrhagic fever/Dengue shock syndrome (DHF/DSS);
- Group 2 - Japanese Encephalitis (JE);
- Group 3 - Haemorrhagic Fever with Renal Syndrome (Hantaan virus); Other arthropod- and rodent-borne viruses
- Group 4 - Rickettsiosis.

2. OBJECTIVES OF THE MEETING

The Joint Consultative meeting had the following objectives:

- (1) to review the developments with regard to arboviral diseases which constitute major health problems in South East Asia and Western Pacific regions. Emphasis will be on dengue haemorrhagic fever.
- (2) To carry out a preliminary review of the rodent-borne viral and rickettsial diseases relevant to both regions.
- (3) To identify priority areas for future plans of action; and
- (4) To formulate general and specific recommendations to the Regional Directors of the South East Asia and Western Pacific regions.

3. ARTHROPOD- AND RODENT-BORNE VIRAL AND RICKETTSIAL DISEASES IN SOUTH EAST ASIA AND WESTERN PACIFIC REGIONS - AN OVERVIEW

Arthropod-borne viral diseases continue to be a public health problem in both regions and the most important of these are dengue haemorrhagic fever (DHF) and Japanese encephalitis (JE) but since 1979 the sudden spread of Ross River virus from its endemic home in Australia and Papua New Guinea to the islands of the Pacific has provided a new problem. In their own areas Kyasanur Forest disease and Australian encephalitis due to Murray Valley encephalitis virus provide significant although less important public health problems. The other arboviruses endemic in the regions are of limited public health significance. The significance of Crimean-Congo haemorrhagic fever has not yet been fully assessed.

The rodent-borne viral disease, haemorrhagic fever with renal syndrome (HFRS) has been found to be much more widespread than previously recognized, since the isolation of Hantaan virus has enabled serological studies to be carried out. It is now clear that in any obscure epidemic of glomerulonephritis not post-streptococcal in nature, infection with this virus should always be suspected.

All the main groups of human rickettsial diseases have been recorded from some countries in the regions. Louse-borne typhus has not been recorded since 1978, but murine typhus occurs in many countries in both regions. Various forms of tick-borne rickettsioses have been recognized and probably more would be found if they were sought. Scrub typhus is widespread in both regions and extends from Japan in the north to tropical Queensland in the south and from India in the west to the eastern Solomon Islands and northern Vanuatu to the east. Q fever is also widespread and is a significant occupational hazard throughout Australia.

3.1 Dengue haemorrhagic fever (DHF)

Dengue infection has occurred throughout both regions except in areas climatically unsuited to the vectors. The areas in which DHF/DSS is endemic or epidemo-endemic are more limited and, in some cases the reasons for this are obscure. DHF provides an important public health problem in Burma, Malaysia, Thailand, Indonesia and Viet Nam. The disease has decreased in importance in the Philippines and, with very good vector control, in Singapore. In other countries severe cases with the dengue shock syndrome (DSS) are not common. Studies have been initiated under WHO auspices attempting to elucidate why DHF is rare in some countries where dengue viruses are endemic and to clarify the immunopathology of the diseases. In view of its public health and economic importance considerable emphasis is being given to finding methods of control.

3.2 Japanese Encephalitis (JE)

JE has been well controlled in Japan by vaccination with inactivated mouse brain vaccine, and altering rice growing practices so that paddies are drained at the time when the maximum breeding of the main vector (Culex tritaeniorhynchus) is expected and by altering swine husbandry so that pigs are no longer normally kept in close association with humans in living quarters. There has also been a considerable reduction in incidences in Korea and the province of China. In some countries the disease has increased in importance and epidemics have occurred in areas where the disease was previously rare or absent. In equatorial areas the

virus remains endemic throughout the year with sporadic clinical cases occurring. In other tropical countries epidemics have occurred at the end of the wet season. In the subtropical and temperate zones epidemics and epizootics occur in the summer and autumn when mosquito populations are maximal. In many countries the cost of the vaccine is thought to make large-scale immunization impossible, but cost-benefit analyses have not been made.¹

3.3 Haemorrhagic fever with renal syndrome (HFRS)

Although HFRS has only been widely recognized quite recently, Chinese records indicate that it has been occurring for more than 1,000 years. Before the isolation of Hantaan virus it was uncertain whether the clinically similar syndromes of varying severity existing from Western Europe to East Asia were due to the same agent, but it has not been possible to show that closely related or identical agents are responsible throughout the previously recognized range and to demonstrate that closely related agents are present in South Asia, Africa and the Americas. In the past the disease has been regarded as rural and the main reservoir host in the Far East (Korea) is the field mouse Apodemus agrarius corea while in the West the bank vole Clethrionomys glareolus is important.

During the 1960s urban cases were recognized in Osaka in Japan and it has now been shown that urban cases in both Japan and Korea are associated with infection in the commensal rats Rattus norvegicus and R. Rattus. Further it has been shown that in both countries many strains of laboratory rats are infected and a high percentage of animal handlers have become infected in the affected institutions.

¹ See Guide for Diagnosis, Treatment and Control of Dengue Haemorrhagic Fever, 2nd Edition). Report of the Technical Advisory Committee on Dengue Haemorrhagic Fever for the South East Asian and Western Pacific Regions, World Health Organization, 1980.

Studies are required in other countries to determine the full distribution of this virus and its overall public health importance.¹

3.4 Rickettsial diseases

Studies on the distribution and importance of rickettsial diseases in the two regions have been very limited.

3.4.1 There is evidence that in certain areas Rickettsia tsutsugamushi is responsible for a high proportion of undiagnosed fevers and further studies of the geographical limits, public health importance and serological characteristics of this group of closely related agents is required to determine the need for an eventual development of a vaccine. Further studies are required of the serotypes dominant in various areas.

3.4.2 Murine typhus is endemic in most countries in the two regions and in some is certainly a significant urban disease associated with commensal rodents and the house shrew (Suncus murinus). In Australia it is a rural infection. This rickettsia requires further study to define its full distribution and public health importance.

3.4.3 Q fever is of moderate public health importance but of considerable economic impact in Australia. It is known to be present in India and is absent from those Pacific Islands which have been studied. The rickettsia is almost certainly widespread in the two regions but it is probably not of great public health significance in most countries.

3.4.4 The other rickettsial diseases are apparently not of great importance at present, but the possibility of a reappearance of epidemic typhus always exists. The significance of tick-borne agents has received some attention in Australia and India, but little elsewhere.²

4. DENGUE, DENGUE HAEMORRHAGIC FEVER AND DENGUE SHOCK SYNDROME A PLAN OF ACTION FOR PREVENTION AND CONTROL³

4.1 Situation analysis

Dengue haemorrhagic fever/dengue shock syndrome (DHF/DSS) is widespread in the South East Asia and Western Pacific regions. DHF/DSS ranks among the major causes of childhood morbidity and mortality in Viet Nam, Malaysia, Thailand, Burma, Indonesia, while milder dengue syndromes are common in China, India, Bangladesh and Sri Lanka. From its discovery 25 years ago, over 600,000 children have been hospitalized with a clinical diagnosis of DHF and 20,000 died. More than 200,000 of the cases have occurred since 1978. There is considerable evidence that Aedes aegypti is extending its geographical domain. Because DHF might spread to any dengue, or dengue-receptive area of the world, it has been estimated that the disease could occur in 61 countries inhabited by 1,500 million people. As an example, a sharp outbreak of DHF/DSS occurred in Cuba in 1981 with thousands of reported cases and over 150 deaths.

¹ World Health Organization, Regional Office for the Western Pacific. Report of a Working Group on Haemorrhagic Fever with Renal Syndrome, Tokyo, 22-24 February 1982.

² See a Report of a Working Group on Rickettsial Diseases, Geneva, 28-30 October 1981.

³ Sections 4 to 8 are presented in the format outlined in Annex 2.

4.2 Objectives

4.2.1 To prevent death from DHF/DSS and eventually

4.2.2 to control the disease.

4.3 Targets

4.3.1 To improve clinical diagnosis and patient management.

4.3.2 To establish the epidemiological knowledge of dengue virus syndromes.

4.3.3 To expand and improve vector control.

4.3.4 To develop, test and produce a live attenuated dengue vaccine.

4.3.5 To secure regional self-reliance in scientific and technical manpower for research and disease control.

4.3.6 To foster and coordinate research on dengue in the two regions.

4.4 Strategies and approaches

Clinical 4.4.1 The use of the Technical Guide on Diagnosis, Treatment and Control of DHF should be encouraged to the widest possible extent.

4.4.2 Proper and reliable serology is the most valuable tool available to assist physicians to define the clinical features of dengue fever, DHF and DSS, they should be widely used.

4.4.3 Definition and reporting of DHF and DSS should be improved

Epidemiology- 4.4.4 Special efforts should be made to identify shock syndrome cases and report these separately from DHF without shock.

4.4.5 Identification of the risk factors in DHF/DSS. In 1980 an inter-country epidemiological study on DHF/DSS was initiated in endemic and silent areas: Rayong, Thailand, Jogjakarta and Medan, Indonesia and Colombo, Sri Lanka. The study is based upon a common protocol:¹

- to monitor specific dengue virus infection rates in a cohort of young children bled at one or two intervals per year;
- to monitor dengue diseases in residents of the study area, including serological confirmation of cases and virus isolation attempts;
- comparison of such attributes as dengue infection rates, dengue virus types in circulation, predicted total primary and secondary dengue infection in areas in which DHF/DSS is endemic (Rayong, Jogjakarta) versus epidemiologically "silent" areas (Medan and Colombo).

¹ (Research Study Group on Dengue Haemorrhagic Fever Epidemiology, 26-29 March, 1979, New Delhi).

Analysis of early results suggest that DSS occurs most frequently with secondary dengue infections in the infection sequences, dengue 1 followed by dengue 2, 3 then 2 or 4 then 2. It is important to test in as many countries as possible the hypothesis that most DHF/DSS cases follow a secondary/sequential infection with dengue virus type 2 as suggested by the Rayong Study.

Vector control 4.4.6 The vectors of dengue viruses breed in close proximity to man and can be controlled by simple environmental measures; the strategy for vector control should, therefore, rest on:

- promotion of community activities in vector control;
- control of adult mosquitos during outbreaks of DHF/DSS;
- fostering intercountry cooperation for preventing the introduction and spread of mosquitos including control of mosquitos at international airports and seaports;
- encouraging research on improved vector control methods.

Vaccine development 4.4.7 To continue to support the WHO dengue vaccine development programme, the technical approach to the development of the vaccine is appropriate and critical evaluation should await clinical trials. The current programme should be strengthened by the application of new techniques for monitoring genetic stability and virulence of candidate vaccine strains. The strategies for the development of a live attenuated vaccine entail:

- a planned developmental effort will be undertaken to attenuate the relevant dengue virus types utilizing procedures and methods leading to internationally acceptable vaccine virus seeds;
- a system of vaccine testing methodologies will be developed for control of each of the vaccine types;
- following the production and testing of primary and secondary seed lots, a pilot lot of each of the required vaccine types will be produced and tested;
- a phased, incremental plan for human testing will be developed and carried out for each of the vaccine types.

Manpower development 4.4.8 The long-term input of recognized regional and international experts on dengue research are necessary to promote and facilitate inter-regional research on dengue.

Coordination of research 4.4.9 An effort should be made to further improve the dissemination of scientific information on dengue.

4.4.10 A number of problems related to improved treatment, to an understanding of the pathophysiology and to pathogenesis mechanisms in DHF/DSS remains unsolved. Intercountry research should, therefore, be encouraged.

4.5 Activities

Clinical 4.5.1 A sustained effort should be made to publish and distribute the Guide for Diagnosis Treatment and Control of Dengue Haemorrhagic Fever (Second Edition), 1980, so that it is a part of the library collection in all hospitals in every country of both regions. The Guide should also be widely available in dengue permissive countries. The present distribution system should be critically evaluated by member governments and WHO.

- Epidemiology 4.5.2 It is essential to adopt a reporting system which makes available data on syndromes with a strong probability of dengue etiology. Shock syndrome as defined in the Guide is often proven to be of dengue etiology. "Haemorrhagic Fever" without shock may be associated with a variety of agents and the diagnosis of this syndrome is subject to error. Reporting of shock syndrome will give a relatively objective assessment of total cases and will allow comparison of frequency of disease from year to year and country to country and largely excludes the over-diagnosis problem.
- 4.5.3 National epidemiological services and hospital staff should devise a reporting form based upon discharge diagnosis. In many instances this will reduce over-diagnosis of DHF without shock and increase the diagnosis of DSS.
- 4.5.4 Serological tests for dengue antibody and supplementary tests which can discriminate between primary and secondary dengue infections and which can distinguish dengue from Japanese encephalitis infections should be available in all teaching hospitals and in all provincial and regional public health laboratories. Results of serological tests should be returned promptly to the originating physician and hospital.
- 4.5.5 A wide variety of simple and reliable serological tests are now available for a large group of viral diseases. One or more of these techniques may be suitable for large-scale application in countries in the two regions. The calling of a Technical Committee is recommended for the evaluation of different methods.
- 4.5.6 It is important that the intercountry epidemiological studies be sustained for a period of five years. WHO should organize a meeting as soon as feasible of all participants in the intercountry epidemiology study for the purpose of data sharing, standardizing research methodology and adjusting research protocols. In countries with DHF/DSS, it may be helpful to solicit the cooperation of national DHF committees to assist in the conduct of the study and to solve any logistical or financial problems.
- 4.5.7 To determine secondary/sequential infections the following scheme is proposed:
- a large number of filter paper blood samples are collected from kindergartens, first and second grade children (age for DHF/DSS in areas endemic for DHF/DSS), and
 - all children hospitalized for DHF/DSS following collection of pre-illness blood should be identified. Acute and convalescent sera are collected from such children to provide serological diagnosis. Cases which meet the clinical criteria for DSS with confirmed dengue infection are matched with pre-illness blood specimens.
- Vector control 4.5.8 It is necessary to clearly identify vector control activities which the community can carry out and to promote health education especially in schools. Legislation also should be considered, whenever possible, to discourage breeding of Aedes mosquitos.¹

¹ A WHO inter-regional workshop is scheduled in 1983 which would cover the subjects of epidemiological vigilance and vector control at international airports.

4.5.9 Greater use of appropriate technology in vector control including biological methods where appropriate should be promoted and water storage containers covered to prevent larval breeding.

4.5.10 Insecticides are needed to kill adult mosquitos during DHF/DSS outbreaks. To respond rapidly and effectively to these outbreaks, government should be encouraged to obtain and maintain an adequate stock of emergency vector control equipment and insecticides.

4.5.11 Vector control activities fall within the concepts of primary health care and should be in cooperation with the over-all health service activities. Further training of health inspectors, laboratory technicians, entomologists and senior health officials responsible for vector control should be carried out to facilitate the introduction of new vector control strategies within the health services.

Vaccine
develop-
ment

4.5.12 Attenuation of candidate vaccine viruses. The general approach to the development of individual live attenuated vaccines will be to serially passage each of the four virus types in an acceptable, non-primate cell type in the expectation of selection for pools of attenuated candidate vaccine viruses.

Following passaging to an appropriate level, the viruses will be evaluated for attenuation by immunogenicity and other biological markers.

4.5.13 Control of attenuated live vaccine. A system of testing methodologies appropriate to each vaccine type is essential. This test system must address the control of all relevant aspects of seed lot and vaccine production.

4.5.14 Production of attenuated live vaccine. A seed lot system will be developed. An appropriate fraction of these seeds will be stored by WHO in more than one laboratory.

Vaccine pilot lot production will be carried out at Mahidol University. The quantity of vaccine should be adequate for all of the testing in man.

4.5.15 Testing of live attenuated vaccine in humans. A phased programme of testing in humans will be carried out. Phase I will be to assess vaccine safety in volunteers, and a phase II plan will be to assess vaccine efficacy in man. This may also include safety considerations in persons with pre-existing immunity to heterologous dengue virus types.

Finally, a phase III or field testing plan will be developed to test the ability of the type-specific vaccine viruses to prevent dengue haemorrhagic fever.

Manpower
develop-
ment

4.5.16 There is a serious shortage in the two regions, of scientists and technicians in the various disciplines which are necessary for research to find solutions to problems inherent in the control of the disease as well as to the implementation of different tasks in the whole procedure of disease control. Governments, in cooperation with WHO, should secure a rational balance between basic and applied research on one hand and health service research on the other. Immediate and recognizable objectives for manpower development in the control of dengue haemorrhagic fever appear to be essential to reach goal of Health for All by the Year 2000.

Coordina-
tion of
research

4.5.17 The Inter-regional Dengue Newsletter provides a valuable communication service, it should be expanded to include:

- publication of titles of new scientific articles on dengue including address of senior authors;

- Member countries should be asked to review and up-date the circulation list for the Dengue Newsletter, to include as a minimum, all academic paediatric departments and children's hospitals. Information concerning the availability of the Dengue Newsletter should be published in a number of medical journals with wide circulation

4.6 Programme monitoring

4.6.1 WHO should continue to sponsor specialized meetings on DHF/DSS, in the past these meetings have served as a powerful stimulus to productive research.

4.6.2 A scientific working group on dengue vaccine development should be constituted to periodically review and monitor the progress of the programme.

5. JAPANESE ENCEPHALITIS (JE) - A PLAN OF ACTION FOR PREVENTION AND CONTROL

5.1 Situation analysis

In South East Asia, Japanese encephalitis is a general and growing public health problem. The problem was reviewed at an interregional meeting in New Delhi in 1979.¹ JE appears to be subsiding in recent years in Japan, Korea, Taiwan Province and China, probably influenced by changing social conditions, more modern agricultural methods and animal husbandry and in some areas by immunization of vulnerable human populations. Currently, it is not possible to determine the precise relative contribution of the different factors causing this trend.

On the other hand, in the tropical areas, JE virus has been shown to be continually prevalent and indeed antibody studies show that a high proportion of children have immunity by the age of five years so that the case rate is low and dramatic outbreaks do not occur. In India, Thailand, Viet Nam and continental China and probably other parts of Asia, JE in the past decade has caused outbreaks involving thousands of cases with apparently increasing expansion into previously unrecognized areas.

The case fatality rate is high, at times exceeding 30% and the post encephalitic paralysis is permanent in a proportion of the patients entailing severe human suffering and financial burdens.

In the two regions the laboratory methods lack uniformity, and the available laboratory techniques do not favour a rapid diagnosis. Countries need competent laboratories to act as national reference centres.

5.2 Objective

To institute and maintain control of Japanese encephalitis infection in humans in the two regions.

¹WHO Technical Information on Japanese Encephalitis and Guidelines for Treatment, Regional Office for South-East Asia, New Delhi, September 1979.

The morbidity rates differ in some regions. In tropical areas the subclinical to apparent infection ratio is very high and may exceed 300 to 1, in India it may be as low as 30 to 1.

5.3 Targets

It is foreseen that the following measures can be established in the two regions by 1989:

1. Strengthen public health infrastructure to facilitate accurate recognition of the disease and effective intervention.
2. Define the epidemiological factors prevailing in different localities which favour the spread of infection.
3. Determine the host/environmental risk factors responsible for the disease.
4. Determine factors which may facilitate the prediction of epidemics.
5. Define the geographic distribution of the infection and delimit the epidemiologically priority areas of the disease.
6. Identify the main vectors in the various areas.
7. Develop interdisciplinary involvement of health, agriculture and vector control agencies to plan for prevention and epidemic action.
8. Develop early diagnosis and institute it at the peripheral level.
9. Increase vaccination coverage.
10. Institute research and appropriate technology development especially for diagnosis, treatment and control of JE.

5.4 Strategies and approaches

The public health infrastructure will be strengthened through manpower development. Training will be provided for the medical laboratory and other paramedical personnel. Community participation and the support of lay persons in the community to case detection and control activities will be secured. This will facilitate accurate recognition of disease, adequate recording of cases and effective intervention.

Training and information programmes instituted through the Collaborating Centres will aid in accumulating epidemiological data locally which in turn will define the factors favouring spread of infection, determine risk factors responsible for disease and facilitate prediction of epidemics.

On the national level, serological surveys will define geographical distribution, and vector surveillance will identify the main vectors in each JE endemic and epidemic area.

Laboratory diagnostic techniques will be developed utilizing (a) collaborative studies, (b) standardization of methods, and (c) tests of uniformity of results in national reference laboratories.

The control of vectors requires interdisciplinary involvement of public health agencies and other agencies concerned in the control of vectors. This interaction can reduce man-vector contact. Agricultural agencies will be consulted in the matter of land use methods, including drainage of rice fields and the use of agricultural pesticides. They will also advise on animal husbandry developments including movement of pigs away from houses.

These agencies should develop regional and national plans for prevention of disease and for action in the case of epidemics.

Vaccination is the single most promising strategy for control of JE. Effective inactivated vaccines are available and the technology should be transferred to countries needing such vaccines. The vaccine is presently too costly to produce and apply in the volumes needed for multiple dose coverage of the large population groups at risk in some of the areas. Experimental live attenuated vaccines have been developed. This approach in time is more likely to result in a single dose vaccine which would be cost effective and within current available resources.

5.5 Activities

5.5.1 Manpower development. Appropriate information for different levels of medical and health personnel should be provided about the epidemiology of the disease, the management of patients and current treatment practices.

Instruction on the subject of the required specimens for diagnosis, their collection, storage and transport should also be provided.

5.5.2 Community participation. Information on the programme should be provided through the mass media to avoid misconceptions.

Motivation programmes through posters and other vehicles in relevant matters such as protection against mosquitos and other personal hygiene measures should be provided.

5.5.3 Surveillance. Serosurveys and case finding with adequate reporting and diagnosis should be instituted. Vector densities should be monitored along with the tests for susceptibility to insecticides.

5.5.4 Standardization of diagnostic techniques. The following should be implemented: workshops for training of laboratory personnel, preparation of practical laboratory manuals, development of reagents programmes and provision of reference services. WHO should encourage links between the national laboratories and WHO Collaborating Centres.

5.5.5 Research and development. The following research and development should be implemented:

- (a) Development of attenuated live virus vaccines for eventual use in humans.
- (b) Transfer of technology for the further development and production of the currently available inactivated vaccines for JE.
- (c) Investigation of biological control of JE vectors.
- (d) Identification of the amplifying host (hosts) in endemic areas.
- (e) Investigation of the effect of agricultural herbicides and pesticides in relation to the population of JE vectors.
- (f) Comparison of the antigenic and biochemical composition of the local isolates of JE virus in the various areas.
- (g) Development and research application of monoclonal antibodies of JE virus.
- (h) Application of new developments in clinical research in the treatment of cases, especially in the use of antiviral agents.

5.6 Programme monitoring

It is considered that diagnostic methods should be refined and in routine use in peripheral hospitals in endemics within three years. A review of the progress in prevention and control and of new epidemiological information would be profitable in three years time

6. HAEMORRHAGIC FEVER WITH RENAL SYNDROME (HANTAN VIRUS) -
A PLAN OF ACTION FOR PREVENTION AND CONTROL6.1 Situation analysis

The current status of HFRS was recently reviewed in a WHO meeting and details are given in the Report of the Working Group on HFRS, WHO Meeting, Tokyo, Japan, 22-24 February 1982.

Although the disease impact may be analyzed for a few countries in HFRS endemic areas, very little information is available for most countries in the South East Asia and Western Pacific WHO regions. Since it has been demonstrated that Hantaan virus is frequently associated with rural, urban and laboratory rodents, HFRS represents an important and potentially fatal disease threat to many countries. In countries where this disease has been recognized many hundreds or thousands of hospitalized cases occur every year. It is recommended that WHO assist in obtaining information from these countries and coordinate the distribution of information concerning incidence, prevalence, morbidity, mortality, etc., to all interested countries. Only after a complete systematic review of the circulating virus and the disease status in countries for which no information exists can a complete situation analysis be prepared.

6.2 Objectives

6.2.1 A basic objective would be to determine the distribution of Hantaan virus in the Western Pacific and South East Asia regions and to estimate the prevalence and impact of HFRS in member countries.

6.2.2 A second objective should be an increased competence and capability in member countries to institute an operational programme to include disease surveillance, diagnosis, research, prevention and control.

Specific objectives for the control and prevention of HFRS are perhaps premature until there exists a full assessment of the disease problem and potential for spread. However, it should be emphasized that all basic research into transmission mechanisms, reservoirs, vectors (if any) etc., should be conducted with the ultimate objective of disease control. Specific mechanisms of control must await the results of such investigations.

6.3 Targets

6.3.1 To carry out epidemiological survey of suspected clinical disease as well as a random sampling of residents in presumptive endemic areas to include urban and rural communities.

6.3.2 To conduct sera surveys for Hantaan virus antibody in rodents. Serum collection should include specimens from port cities (possible importation by shipping), rural and urban areas and laboratory rodents.

6.3.3 Initial survey sera should be sent to the WHO Collaborating Centre (HFRS); however, following the demonstration of evidence of Hantaan virus infection in a country, every effort should be made to develop qualified diagnostic capabilities in that country.

6.3.4 To create increased awareness of the clinical symptoms, diagnostic signs, laboratory tests and treatment modalities among the physicians of member countries. Associated with the distribution of information to physicians should be some mechanism for reporting this disease to responsible authorities and to the WHO Collaborating Centre (HFRS).

6.3.5 To incorporate information on HFRS and the Hantaan virus serology data in a publication similar to the "Dengue Newsletter" with the widest possible distribution; frequent bulletins should be issued to disseminate information concerning epidemics or potential disease threats.

6.3.6 To foster the rapid distribution of technical information on improved diagnostic tests as they are developed, and to provide a comprehensive clinical description of the disease syndromes for distribution to laboratories and health workers responsible for primary health care.

6.4 Strategies and approaches

The main strategies, at present are:

6.4.1 To create awareness in countries of both South East Asia and the Western Pacific regions of the potential public health importance of HFRS.

6.4.2 To strengthen national diagnostic facilities and epidemiological investigation capabilities, and

6.4.3 To support countries in case of outbreaks.

6.5 Activities

The following activities should be considered by WHO for implementation as soon as possible.

6.5.1 Dissemination of information on HFRS to member countries of Western Pacific and South East Asia regions to increase awareness and assist in the collection of basic epidemiological and ecological information.

6.5.2 Specific support to the WHO Collaborating Centre (HFRS) for the preparation and distribution of inactivated antigens and other diagnostic reagents.

6.5.3 The planning and execution of a laboratory training programme to be conducted at the WHO Collaborating Centre for HFRS. This training programme should be made available to qualified virologists from member countries and should be conducted as soon as possible to facilitate the surveillance as indicated in the first objective.

6.5.4 The identification of a WHO-HFRS consulting team to rapidly respond to requests for assistance from member countries. Circumstances requiring assistance might be epidemics of suspect HFRS disease or imminent disease threats. A rapid response requires contingency planning to include supplies, equipment, personnel and WHO coordination.

6.5.5 A programme of WHO coordination for rodent control and monitoring of laboratory animals if indicated as a means of control of HFRS and approved by member countries

6.5.6 A survey of wild rodents and laboratory rodents in countries of the region where HFRS may be suspected.

6.6 Programme monitoring

At the present, the best indicators of programme success and progress will be in the information gathered by the WHO Collaborating Centre for HFRS. The Centre's reports can be compiled by WHO to define the major geographic areas of endemic HFRS and concentrate efforts in areas where information is lacking. The increase in the diagnostic capability as a result of WHO-sponsored training will become evident from serologically confirmed disease reporting in endemic areas or the ability to define areas free of Hantaan virus. Every effort should be made to provide diagnostic services and inactivated antigens to requesting countries. WHO could play an important role in reviewing the importation of infectious Hantaan virus into areas in which evidence for endemic HFRS is lacking. A systematic system of reporting to WHO would enable WHO to play an active role in the coordination and dissemination of information to the appropriate health officials in affected countries.

7. OTHER ARTHROPOD- AND RODENT-BORNE VIRAL DISEASES

7.1 Situation analysis

Some other arboviruses are recognised as current or potential disease problems. Because of the diversity within this group, each may require a separate outline of details but the same general objectives and strategies should apply to all. An increased diagnostic capability in Western Pacific and South East Asia countries would greatly facilitate the accumulation of the data base necessary for meaningful recommendations.

With reference to Ross River virus, some vectors have been identified, e.g. Ae. vigilax, Ae. polynesiensis and C. annulirostris, but there is an indication that as many as 18 vector species may be involved. There is thus a need for some work on the identification and ecology of the vectors. In some countries of the Western Pacific outbreaks of the virus have occurred through the introduction at airports. Hence airport sanitation and hygiene may be important for this virus. The methods of control of the vectors during outbreaks are similar to those for the control of the vectors of dengue virus.

8. RICKETTSIOSES, A PLAN OF ACTION FOR PREVENTION AND CONTROL

8.1 Situation analysis

As our knowledge and experience from different parts of the world accumulate, there is a realization that previously unrecognized rickettsial diseases are in fact contributing substantially to the acute febrile disease burden of many populations. Rickettsial diseases in South East Asia and the Western Pacific have been of great importance for a long time, but most medical research work was concentrated on diseases of dramatic clinical course and high mortality rate. The ecology of rickettsial diseases in Asia still needs elucidation. As human populations grow and their way of life changes, disturbing the ecosystem of rickettsial foci, an increase of rickettsial diseases is to be expected. It has to be said that rickettsial diseases are under-reported mainly for two reasons. Laboratory facilities for diagnosis are still limited in most of the countries of the regions. In many of the countries of the regions, abundant antibiotics are available to the public for self help in treating any fever cases. Antibiotics fortunately are effective in treating the diseases but often may have masked the magnitude of the problem.

Among the major groups of rickettsioses, scrub typhus and murine typhus are the most common occurrence in most South East Asian and Western Pacific countries.

8.1.1 Scrub typhus has been shown to occur in a surprising variety of climatological conditions and habitats. Very limited statistics are available on the magnitude of disease occurrence. From 1970 to 1980 it was reported in various countries such as China, India, Indonesia, Malaysia, Thailand and Viet Nam. The percentage of positive findings in sera from the general population varied from 2% (India) to 40% (Malaysia). Prospective studies in Malaysia and on the Pescadores Islands showed high rates of infection in the indigenous population.

8.1.2 Murine typhus is world wide in distribution and the disease appears to be more prevalent in the two regions than previously recognized. Serological studies of human cases in Burma showed 14% positive and of the general population the percentage of sero-positive individuals in Malaysia was 45% and in other South East Asian countries ranged from 6% to 22%. Infection among various rodent species in the urban and rural areas in these regions varied from 2% to 38%

8.1.3 Louse-borne typhus. No cases of this disease have been reported from South East Asia since 1978 or from the Western Pacific since 1969. It is important to point out that specific information is very sparse for vast areas of these regions, especially in the Himalayas and adjacent mountain ranges. The possibility of epidemics of louse-borne typhus still remains as a threat.

8.1.4 Q-fever and tick-borne rickettsioses were rarely reported and there is a lack of statistics on these diseases in the regions, except for Australia.

8.2 Objectives

8.2.1 To obtain more complete knowledge in the ecology/epidemiology of rickettsioses in different countries of the regions.

8.2.2 To increase capabilities of the countries to delimit the size of the problem and to cope with epidemics or other emergencies.

8.3 Targets

8.3.1 Phase 1: by 1984 all countries of the regions should have formulated a national plan of action for disease surveillance.

8.3.2 Phase 2: by 1986-88 the plan of action should have been implemented.

8.3.3 Phase 3: by 1987-1989 the knowledge acquired should have been applied for introduction of appropriate intervention measures.

Louse-borne typhus - health authorities of various countries should have a plan of better surveillance and information system to combat any emergency which may arise.

8.4 Strategies and approaches

8.4.1 Countries of the regions should develop national facilities for diagnosis of rickettsioses with the help of existing WHO Collaborating Centres for Reference and Research and WHO should designate a WHO Collaborating Centre for rickettsial (scrub typhus) reference and research in the two regions.

8.4.2 Manpower development should be organized in laboratory diagnosis, epidemiological surveillance and research through suitable training courses for each category.

8.4.3 Joint refresher courses for clinicians, epidemiologists and laboratory personnel should be organized. Suitable course curricula for these courses need to be developed.

8.4.4 Exchange of technical expertise between developing countries and between developed and developing countries should be encouraged and coordinated by WHO.

8.4.5 Lay reporting of fevers from areas ecologically defined as likely places for presence of rickettsioses should be introduced. In such cases where blood is taken for malaria/filaria diagnosis, filter paper blood collection should also be made and sent to appropriate laboratory for rickettsial serology.

8.4.6 Serological surveys should also be carried out in ecologically appropriate areas on both human and small mammal sera to define foci of rickettsial infection. Such surveys would be organized by appropriate laboratories as designated by the national authority as within the context of a WHO collaborative study.

8.4.7 The effectiveness of community education in leading to active participation of the community in rodent control and the problems of managerial and delivery aspects of health programmes should be studied.

8.4.8 National and international funding agencies should be asked to provide assistance for surveillance and research on rickettsioses.

8.5 Activities

8.5.1 All cases having high fever of unknown origin (FUO) should be reported to the respective health authority for future examination and investigation. Collaborative studies on the aetiology of FUO should be fostered between institutions on intra- and inter-country basis.

8.5.2 Prompt exchange and dissemination of information between workers in each country are also necessary.

8.5.3 Continued rodent control work should be carried out yearly with the cooperation of the community and agricultural authorities to maintain a very low density level.

8.5.4 Upgrading of laboratory facilities at all levels.

8.5.5 Improvement in reporting and recording systems are essential. To achieve this appropriate additional training of managerial personnel is required.

8.5.6 National authorities should develop firefighting teams and epidemiological help to assist in epidemic control.

8.5.7 The planned work on rickettsioses should be coordinated with governmental agencies outside health, including universities.

8.5.8 Collaborative studies are required on the development of a vaccine for scrub typhus. Research on simplified rapid serodiagnosis of rickettsioses including monoclonal antibodies should be encouraged.

8.6 Programme monitoring

To monitor the progress of this programme, annual assessments should be made of the number of personnel in various categories trained, surveys completed and their results, the effectiveness of information exchange and of the time taken for the institution of control measures.

9. RECOMMENDATIONS TO WHO

9.1 WHO should encourage the further development and production of existing vaccines and the transfer of these technologies. In view of the impracticability of substantially reducing the cost of producing inactivated viral or rickettsial vaccines, particular attention should be given to the development of live attenuated vaccines. Attention should also be paid to antiviral therapy.

9.2 WHO should encourage the development of laboratory techniques for rapid and early diagnosis of arthropod- and rodent-borne viral and rickettsial diseases. Particular attention should be paid to simple techniques suitable for use at peripheral laboratories and in the field. This should be linked to an active reagents programme - links between national laboratories and WHO Collaborating Centres for Reference and Research should be strengthened.

9.3 Training and refresher courses should be provided for all grades of laboratory personnel to improve the quality of work and ensure the standardization of diagnostic techniques. Refresher courses for clinicians and epidemiologists are equally important. A long-range programme of encouraging/recruiting scientists to support and sustain research should be contemplated.

9.4 Attention should be given to upgrading biosafety laboratory standards in handling active viruses and rickettsiae.

9.5 Vector populations should be monitored regularly for density build-ups and susceptibility to insecticides.

9.6 WHO should continue to encourage the development of new methods of vector control including biological control.

9.7 Community health education to secure community participation in vector control, especially with reference to the control of Ae. aegypti and other vectors of dengue, should be strongly encouraged.

9.8 It is recommended that a suitable mechanism for continued bi-regional cooperation on the problem of arthropod- and rodent-borne viral and rickettsial diseases be established.

9.9 Surveillance of arthropod- and rodent-borne viral and rickettsial diseases should be strengthened and epidemiological information be distributed rapidly throughout the two regions.

ANNEX I

LIST OF PARTICIPANTS, OBSERVERS AND SECRETARIAT

PARTICIPANTS (TEMPORARY ADVISERS)

South East Asia region

BANGLADESH

Dr Farida Huq
Head
Microbiological Laboratory
Institute of Public Health
Dacca

INDIA

Dr K. Pavri
Director
National Institute of Virology
Pune

Dr A.N. Raichowdhuri
Director
National Institute of
Communicable Diseases
Delhi

INDONESIA

Dr M. Adhyatma
Director-General
Directorate Genral of
Communicable Disease Control
Ministry of Health
Jakarta

Dr Iskak Koiman
Head, Biomedis Research Centre
National Institute of Health Research
and Development
Ministry of Health
Jakarta

Dr Setiady
Head, Health Ecology Research and
Development
Ministry of Health
Jakarta

SRI LANKA

Dr U.T. Vitarana
Virologist
Medical Research Insitute
Colombo

THAILAND

Professor Natth Bhamarapavati
Rector
Mahidol University
Bangkok
(Also Principal National Organizer
of the meeting)

Dr Nadda Sriyabhaya
Director-General
Department of Communicable Disease
Control
Ministry of Public Health
Bangkok

Dr Suchitra Nimmannitya
Senior Paediatrician
Childrens Hospital
Bangkok

Western Pacific region

AUSTRALIA

Dr B. Gorman
Senior Virologist
Queensland Institute of Medical Research
Bramston Terrace
Herston, Brisbane
Australia 4006

CHINA

Dr Huang Weiquan
Epidemiologic Institute of
Guangdong Province

FIJI

Dr Bhagat Ram
Director
C.W.M. Hospital
Suva

JAPAN

Dr A. Oya
Director
Department of Virology and
Rickettsiology
National Institute of Health
Tokyo

MALAYSIA

Dr Tikki Pang
Lecturer
Department of Medical Microbiology
University of Malaya
Kuala Lumpur

NEW ZEALAND

Professor J.A.R. Miles
c/o PO Lake Hawea
Central Otago
New Zealand

PHILIPPINES

Dr J. J. Dizon
Director-General
Bureau of Health Services
Ministry of Health
Manila

REPUBLIC OF KOREA

Dr Ho Wang Lee
Director
Institute of Virology
Korea University
Seoul

SINGAPORE

Mr Ng Say Kiat
Head
Vector Control and Research Department
Ministry of the Environment
Singapore 3

SOCIALIST REPUBLIC OF VIET NAM

Dr Nguyen Duy Thanh
Director of the Infectious Diseases
Hospital Choquan
Ho Chi Minh City

OTHER TEMPORARY ADVISERS

Dr Scott B. Halstead
Professor and Chairman
Department of Tropical Medicine and
Medical Microbiology
University of Hawaii
Honolulu

Dr R. E. Shope
Director
Department of Epidemiology and
Public Health
Yale Arbovirus Research Unit
Yale University School of Medicine
New Haven, Connecticut 06510
USA

Colonel G.A. Eddy
Chief, Virology Division
United States Army Medical Research
Institute of Infectious Diseases
Fort Detrick
Frederick, Maryland 21701
USA

Dr J. A. Forbes
WPRO Consultant CDS Unit
Manila

Dr T. Umenai
Regional Adviser in Communicable
Diseases - Designate
WHO/WPRO
Manila

OBSERVERS

Dr Donald S. Burke
Chief, Virology Department
Armed Forces Research Institute of
Medical Sciences
Bangkok

Dr Joel Dalrymple
Virology Division
United States Army Medical Research
Institute of Infectious Diseases
Fort Detrick
Frederick, Maryland 21701
USA

SECRETARIAT

WHO Headquarters

Dr F. Assaad
Director
Division of Communicable Diseases
WHO Headquarters
Geneva

Dr T. Bektimirov
Acting Chief Medical Officer
Virus Diseases
Division of Communicable Diseases
WHO Headquarters
Geneva

Dr C.P. Pant
Chief, Ecology and Control of Vectors
Division of Vector Biology and Control
WHO Headquarters
Geneva

Dr Lim Boo Liat
WHO Inter-regional Vector Biology and
Control Research Unit No.2
Jakarta

WHO South East Asia region

Dr U Ko Ko
Regional Director
WHO Regional Office for South East Asia
New Delhi

Dr Chaiyan K. Sanyakorn
Director
Disease Control and Prevention
WHO Regional Office for South East Asia
New Delhi

Dr R. Chical
WHO Programme Coordinator and
Representative
Bangkok

Dr R. Krzysko
Regional Adviser in Communicable
Diseases
WHO Regional Office for South East Asia
New Delhi

Dr I.A.H. Ismail
Regional Entomologist
WHO Regional Office for South East Asia
New Delhi

WHO Western Pacific region

Dr H. Nakajima
Regional Director
WHO Regional Office for the Western
Pacific
Manila

Dr C.J. Ross-Smith
Director, Disease Control and Prevention
WHO Regional Office for the Western
Pacific
Manila

Dr L.S. Self
Regional Adviser in VBC
WHO Regional Office for the Western
Pacific
Manila

ANNEX II

A SUGGESTED OUTLINE FOR A PLAN OF ACTION

The focus is on diseases/group of diseases for the prevention and/or control of which some collaborative action is likely to be requested by countries to WHO bearing in mind WHO's coordinating role in technical cooperation between developing countries (TCDC) and the Organization's involvement in collaborative research.

For an effective action programme to become fully operative, it is best expressed within a standardized structured framework of planning, programming and budgeting. Since the views and recommendations will undoubtedly provide the WHO secretariat with valuable details for the purpose of programme formulation and development, reports should be presented in a uniform format, along the following lines:

Situation analysis

The situation analysis comprises a succinct statement on the load and impact of the disease/group of diseases in terms of:

- morbidity;
- mortality;
- physical, mental and social handicaps;
- economic loss, etc.

The statement should reflect the country reviews presented by participants from South East Asia and the Western Pacific regions

Objectives

Broad objectives reflecting the aspiration of countries in South East Asia and the Western Pacific regions by 1989 should be stated.

Targets

Within the broad objectives, well defined and time limited targets should be stated. Whenever possible targets should relate to problem reduction. It is recognized, however, that in many instances targets would be limited to defining in terms of extent and time, the desired activities within the programme (see below).

Strategies/approaches

A description of the best means to reach the target should be given and should reflect a consensus on the ranking of the different strategies/approaches. The ranking should in turn, reflect the cost-effectiveness within given time periods of the alternative strategies/approaches but should also take into consideration the appeal to public health authorities and funding agencies.

Activities

A series of actions/interventions should be developed to reach the given targets. For easy reference activities should be grouped within a well-defined functional framework, the following is a suggested grouping:

- application of existing echnologies to case management, epidemiological surveillance and disease control which may require for example:
 - manpower development (including managerial skills);
 - support of health services infrastructure;
 - development of management systems.

- Research and development of new tools through:
 - collaborative studies;
 - strengthening of national institutes;
 - health services research.

- Exchange and dissemination of information which includes the established information systems available to WHO, but also different meetings of workers in a given field, etc.

Programme monitoring

Consideration should be given to:

- milestones; and/or
- indicators.

which would help in monitoring the programmes.

= * =