

# Vector-borne diseases

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*Report of an informal expert consultation  
SEARO, New Delhi, 7–8 April 2014*



**World Health  
Organization**

Regional Office for South-East Asia

SEA-CD-300  
Distribution: General

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Printed in India

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## Acronyms

ACT	artemisin-based combination treatment
APDP	Asia–Pacific Dengue Partnerships
Bti	Bacillus thuringiensis israelensis
CBC	complete blood count
CDS	communicable diseases
CFR	case-fatality rate
COMBI	communication for behavioural impact
DALY	disability-adjusted life years
DDT	dichlorodiphenyl trichloroethane
DEN-V	dengue virus
DF	dengue fever
DHF	dengue haemorrhagic fever
DSS	dengue shock syndrome
EDS	expanded dengue syndrome
GIS	geographical information system
GPARC	global plan for artemisinin resistance containment
HiAP	health-in-all-policies
IEC	information, education and communication
IRS	indoor residual spraying
ITN	insecticide treated nets
IUs	implementation units
IVM	integrated vector management
JE	Japanese encephalitis

LF	lymphatic filariasis
LLIN	long-lasting insecticidal net
MDA	mass drug administration
M&E	monitoring and evaluation
MoH	Ministry of Health
NGO	nongovernmental organization
NTD	neglected tropical diseases
PCO	pest control officer
PHC	public health centre
PKDL	post kala-azar dermal leishmaniasis
PPP	public–private partnership
R&D	research and development
RDT	rapid diagnostic kits
SEAR	South-East Asia Region
spp	species
ULV	ultra low volume
USAID	US Agency for International Development
VBD	vector-borne diseases
VCRC	Vector Control Research Centre, Puducherry, India
VL	visceral leishmaniasis
WHO	World Health Organization
WHOPES	WHO pesticide evaluation scheme
WS	warning signs

# 1. Background

Vector-borne diseases are major public health problems, particularly in tropical and sub-tropical regions and places where access to safe drinking-water and sanitation systems is a challenge. They are considered diseases of the poor, being endemic in low-income groups or in areas where the vicious cycle of diseases and poverty exists. Some are associated with high stigma, discrimination and taboo. While all these diseases are preventable and curable, the disease burden and economic impact are very high and unacceptable in this modern era. Some of these diseases are fatal if not treated, while others leave patients disfigured and disabled. They account for 17% of the estimated global burden of all infectious diseases.

In the WHO South-East Asia Region (SEAR), the vector-borne diseases (VBD) that are of major public health importance are: malaria, dengue, Japanese encephalitis (JE), chikungunya, lymphatic filariasis and kala-azar.

Globally, in 2012, there were an estimated 207 million cases of malaria and 627 000 deaths. Although the highest burden of malaria is in sub-Saharan Africa, with deaths mainly among children under five years, the South-East Asia Region ranks second with 2.038 million cases and 1226 malaria deaths reported in 2012. These figures could be just the tip of the iceberg, since malaria in this Region occurs mainly in remote hard-to-reach areas where access to health-care services and disease surveillance remains a challenge.

The world's fastest growing vector-borne disease is dengue, with a 30-fold increase in disease incidence over the last 50 years. The incidence of dengue has grown dramatically around the world in recent decades. More than 2.5 billion people – over 40% of the world's population – are now at risk from dengue. WHO currently estimates there may be 50–100 million dengue infections worldwide every year. An estimated 500 000 people with severe dengue require hospitalization each year, a large proportion of whom are children. About 2.5% of those affected die.

JE is a leading cause of viral encephalitis in Asia with nearly 68 000 clinical cases reported annually. JE distribution is very significantly linked to



irrigated rice production, combined with pig rearing. Outbreaks of this disease occur frequently. While most JE virus infections are mild or without apparent symptoms, approximately 1 in 250 infections results in severe disease. The case-fatality rate (CFR) is as high as 30% among those with disease symptoms; and 30 – 50% suffer from lasting damage to the central nervous system.

Chikungunya occurs in Africa and Asia, including the Indian subcontinent. From February 2005 onwards, major outbreaks of chikungunya occurred in the islands of the Indian Ocean. A large outbreak of chikungunya in India occurred in 2006 and 2007. Several other countries in SEAR were also affected. Since 2005, India, Indonesia, Maldives, Myanmar, and Thailand have reported over 1.9 million cases. Outbreak was also confirmed in Bhutan in 2012.

An estimated 120 million people in 73 countries are currently infected with filariasis. The SEAR accounts for around 63% (876 million) of the 1.39 billion people living in areas endemic to filariasis. The Region contributes approximately 57% of the total global burden of 5.1 million disability-adjusted life years (DALY) lost due to lymphatic filariasis.

An estimated 200 000–400 000 cases of kala-azar and 20 000 – 30 000 deaths occur in the endemic countries annually. Bangladesh, India and Nepal are among the six countries that account for over 90% of the kala-azar or visceral leishmaniasis (VL) cases worldwide.

Efficient and effective implementation of current tools led to significant reduction of malaria, kala-azar and lymphatic filariasis (LF) and these diseases are now being targeted for elimination. However, additional tools and innovative delivery mechanisms to implement existing interventions and those that may be available in the near future are needed to accelerate control towards elimination and prevent resurgence of transmission.

The vector-borne viral diseases – dengue, JE and chikungunya – pose serious challenges due to outbreaks that require urgent actions as well as long term and sustainable solutions.

## 2. Objectives

In view of the above, an informal consultation with experts on vector-borne diseases was organized during 7–8 April 2014 with the following objectives:

- to review the status of vector-borne diseases of public health importance in the WHO South East Asia Region;
- to identify major challenges in prevention and control of vector borne diseases in SEAR; and
- to suggest public health actions for incorporation in national policy/programme as well as to WHO for combating vector borne diseases.

## 3. Opening

The informal expert consultation on vector-borne diseases was inaugurated by Dr Poonam Khetrpal Singh, Regional Director, South-East Asia Region of the World Health Organization, In her opening address (Annex 1), Dr Poonam highlighted the importance of this consultation and said that vector-borne diseases (VBD) kill over a million people annually, putting half the world's population at risk. VBD involve a diverse group of parasites and viruses, spreading to humans through vectors including mosquitoes, bugs, ticks, mites, flies and freshwater snails. These vectors are versatile creatures rapidly adapting to changing ecological and environmental conditions, thus challenging the control interventions available. She further stressed that we need to discuss how better we can understand the epidemiology and pathophysiology of these diseases and sustain improvements in case management. We need better data and stronger evidence on the disease burden and its health, social and economic impacts. We need to explore creative ways of working together both within and between countries.

Dr Rajesh Bhatia, Director, Communicable Diseases highlighted the objectives of the consultation. Professor Pratap Singhasivanon from Thailand and Dr Suman Rijal from Nepal were nominated Chair and Rapporteur of the consultation. See agenda and list of participants at (Annexes 2 and 3)

## **4. Overview of VBD in SEAR**

VBD account for 17% of the global burden of all infectious diseases. They are also considered as diseases of the poor, since they are endemic in low income groups or where the vicious cycle of diseases of poverty exists. Priority VBD in SEAR include malaria, dengue, kala azar or VL, JE, LF, chikungunya and schistosomiasis of which LF, kala-azar and schistosomiasis are targeted for elimination. One or more VBD are found in all Member States of the Region.

Malaria is endemic in 10 countries (except Maldives). Significant progress has been made in the control of malaria in SEAR in the last decade. Sri Lanka is maintaining zero indigenous transmission since November 2012 and Bhutan and Democratic People's Republic of Korea are in pre-elimination phase. Reported cases and deaths have also decreased in the last decade. However the emergence of resistance to artemisinin-based combination treatment (ACT) seriously threatens the achievements.

SEAR contributes to more than half of the global burden of dengue and all Member States in the Region except Democratic People's Republic of Korea are reporting dengue. Five countries (India, Indonesia, Myanmar, Sri Lanka and Thailand) are among the 30 most highly endemic countries in the world. In spite of the control efforts, there is a significant increase in number of dengue cases over the years though significant improvement has been made in case management and reduction of CFR to below 0.5%.

Kala-azar is known to be endemic in Bangladesh, India and Nepal where 147 million people are at risk. A kala-azar elimination programme has been implemented since 2005 in these three countries to reach the target by 2015. There has been a decreasing trend in the cases in all these three countries over the last few years. Recently sporadic cases are reported from Bhutan and Thailand. The reduction in the kala-azar cases in the Region provides the window of opportunity to reach the elimination target. However efforts need to be augmented, like polio eradication, for all the activities: active case-finding and early treatment, integrated vector management, information, education and communication/BCC and strengthening of monitoring and supervision. Availability of effective, safe

and short regimen e.g single-dose liposomal amphotericin B and combination regimens provided the tools for supervised treatment. The major challenge to the elimination programme is post kala-azar dermal leishmaniasis (PKDL), an important reservoir especially for the inter-epidemic period. Limited information is available on the true burden of PKDL and its diagnosis and treatment is not well standardized.

SEAR has been an endemic home for LF, where 63% (875 million) of the population are at risk and half of the infected people live. It is endemic in all countries except Bhutan and Democratic People's Republic of Korea while mass drug administration (MDA) has been stopped in three (Maldives, Sri Lanka, Thailand) out of the nine endemic countries.

JE is endemic in seven out of the 13 countries in the Region with an estimated 68 000 cases and 20 400 deaths occurring annually in Asia. This is the only VBD where an effective vaccine is available and is being provided free of cost in all the endemic countries. The challenge for JE is getting quick access and availability of intensive care facilities.

Schistosomiasis in SEAR is limited to only two districts in Indonesia.

In spite of the success achieved so far, challenges for the control of VBD in the Region include: inadequate community awareness and engagement, poor understanding of vector bionomics, inadequate vector control measures and emerging insecticide resistance. Rickettsial infection has shown an increasing trend and should be added to the list of VBD in the Region.

#### **4.1 Dengue: control, drugs and vaccines**

Dengue is the most rapidly expanding arboviral disease and its outbreaks exert a huge burden on populations, health systems and economies in most tropical countries. Currently, there is no vaccine available to prevent dengue infection, nor are there any specific drugs for the treatment. Dengue control has been primarily dependent on the control of the *Aedes aegypti* mainly through source reduction by clean-up campaigns and larviciding with insecticides. Biological agents like larvivorous fish, cyclopes and ovitraps were unsustainable or not accepted by the community. The successes of these measures have been limited and in spite of all efforts, the

number of cases continues to increase e.g. Singapore has experienced outbreaks in 2005 and 2010 and similarly Sri Lanka in 2009. The peak occurrence in dengue has been related to the onset of the monsoon rains.

*Wolbachia*-infected *Aedes* mosquitoes have a significant decrease in the life span and thus reduced vectorial capacity. The role of *Wolbachia*-infected mosquitoes in the prevention of dengue infection is undergoing field trials in Indonesia and Viet Nam and the results are keenly awaited. Although no licensed dengue vaccine is yet available, several vaccine candidates are under development, the live attenuated virus vaccines and live chimeric virus vaccines are undergoing clinical evaluation.

Active involvement of the community is critical to the control of dengue, however the sustainability of community participation is challenging. Strategy for effective IEC activities is required. In addition to the health sector a multisectoral approach is required. Education of the children has been shown to be an effective approach and school curriculum should lay more emphasis on health education including hygiene, sanitation, vector control, waste disposal etc. Innovative approaches for better surveillance can help to detect outbreaks early. A School Absenteeism Syndromic Surveillance System Model in Bangkok school children is being studied. Here the school absenteeism database is being used to assist disease (dengue) surveillance and outbreak prediction and the final results of this interesting model is awaited.

There is also a need for strengthening the surveillance system including the reporting from the private health-care facilities. Legislation making dengue a notifiable disease would be supportive. Close coordination of the control programmes, health-care facilities, and the municipality, would help in preparedness for better management of the dengue cases during outbreaks.

Though the primary prevention of dengue infection has not been successful, clinical care of dengue fever has improved with CFR being reduced to less than 0.5% in the Region. Sustaining this low mortality is a challenge. Uniformity and standard clinical care practices need to be emphasized and include private and tertiary care doctors in the training courses. In Thailand, a comprehensive document for dengue control covering 14 areas, which extends from policy development to community

involvement has been in use. This document could be an excellent example to replicate for the control of other VBD in the Region. The two dengue guidelines i.e., TDR (2009) and SEARO (2011) lack harmonization and this needs to be addressed.

With the currently available tools, the control of dengue by 2025 is unlikely to be achievable. There is a need for a vaccine. Also more accurate rapid diagnostic kits (RDT) are needed as the current diagnostic tests in use (NS1Ag) have a low sensitivity. Predictors for severe disease would be very helpful during screening of cases during outbreaks. There is also need for innovative research for development of antiviral drugs and antiplasma leakage drugs to be able to further decrease the mortality in dengue patients.

## **4.2 Clinical management of dengue: Thailand success story**

Thailand's success story about reducing dengue CFR from about 14% in 1958 and 0.09 % in 2013 and until now is an example for other endemic countries. This achievement and the sustainability are due to many factors, but the credit goes to the strong national policy and commitment from the higher administrators. Medicines, medical equipments, intravenous solutions (both crystalloid and colloid), and blood bank that are needed in the care of dengue patients are to be provided. Laboratory support necessary for early diagnosis and clinical management especially complete blood count (CBC) has to be available 24 hours in all hospitals and may be procured by the primary health-care centres. Capacity-building for doctors, nurses and other health-care personnel has to be done regularly according to the national guidelines including annual strengthening of dengue case management in newly graduated doctors and nurses. Good referral system for high-risk or more severe patients with clear indications should be available for personnel in every level. In addition, community education about the cause of dengue illness, home-care and warning signs of shock that they must look for to bring the patients back to the hospital as soon as detected is crucial. Dengue shock syndrome (DSS) patients have good consciousness, only look weak and tired.

Lessons learnt are early clinical diagnosis and follow up with only simple laboratory CBC is important to guide clinical management, not the RDT that is not sensitive enough and does not guide clinical management.

Capacity-building for health-care personnel is not enough, community education is also important.

This success story can be applied to other VBD provided they have the above necessities, i.e. strong policy, national guidelines, necessary medicines, equipment, laboratory support and capacity-building for health-care personnel. Good referral system and community education are also important factors.

The two different dengue classifications and clinical practice guidelines sometimes create a confusion; one is the original WHO classification since 1975, 1986, 1997 and the latest update 2011 (WHO-SEARO), another that is newly suggested and much different TDR, 2009 guideline. The TDR 2009 guidelines suggest a new classification; dengue, dengue warning signs (WS) and severe dengue! This emphasizes WS which are so non-specific and can be found in other acute febrile illnesses. This non-specific WS has resulted in increasing the number of admissions to at least 2–3 times and 20 times for the Out-patient Department. Besides increased work load, it also causes more complication of fluid overload and other complications. In contrast, the original WHO classification that classifies dengue into dengue fever (DF), dengue haemorrhagic fever (DHF), DSS and expanded dengue syndrome (EDS) stresses on plasma leakage, which may lead to shock and complications or organ(s) failure. Close monitoring of this important pathophysiologic change of plasma leakage can help to prevent shock and less severe diseases.

Future challenges include development of more sensitive and cheaper RDT, better than the current NS1Ag, finding the predictors of severe diseases than can reduce the workload for doctors and nurses, effective dengue vaccine(s) to all stereotypes of dengue, anti-dengue or anti-plasma leakage drugs.

### **4.3 Dengue vaccine**

Though there is a high level of country interest, no vaccine for dengue has been licensed yet. A number of candidates are in the 'pipeline'. The history of development of dengue vaccine in the Region dates back to 1994, when partnership between Sanofi Pasteur and the Vaccine Development Centre, University of Mahidol, Bangkok, Thailand, was established. Later, 2001

witnessed proof of the concept of a tetravalent live attenuated dengue vaccine in two doses and a booster; and start of the development of a second generation vaccine obtained by recombinant technology. Classical live vaccine approach was abandoned in 2004, due to reactogenicity and under-attenuation of serotype 3. This led Sanofi Pasteur to adopt a new approach, with a second generation live attenuated vaccine. Bill & Melinda Gates Foundation supported, in 2006, the Paediatric Dengue Vaccine Initiative (PDVI), a Consortium working to accelerate the introduction of a dengue vaccine for children in endemic countries and in 2007 phase –II clinical studies gave positive results (proof of concept). In 2009, Sanofi Pasteur dengue vaccine entered Phase–III clinical study. From 2011, partnership with the International Vaccine Institute to support Dengue Vaccine Initiative, a non-profit advocacy group, is focusing on raising awareness of dengue fever and supporting the development and introduction of dengue vaccination, funded by Bill & Melinda Gates Foundation.

#### **4.4 Role of tertiary care hospitals in management of VBD**

Haphazard treatment policies in tertiary care hospitals in management of VBD are a problem. Moreover, tertiary centres may also have other priorities like acute cardio/cerebro-vascular episodes, etc. Unavailability of advanced serological tests in many centres, overcrowding, lack of standardization of procedures, scarcity of trained technical laboratory personnel, delay in obtaining results in appropriate frame, lack of adequate funding for VBD management, training and retraining of the staff, and regular accreditation of the laboratories are some of the major challenges for managing VBD at tertiary centres. Tertiary centres should tie up with primary and community health care centres for providing them technical support and mentoring technical staff of the peripheral institutions.



## **5. Emergence and spread of resistance in malaria and kala-azar**

### **5.1 Resistance in malaria**

SEAR reports around two million malaria cases annually and India contributes to half of them. In the past parasite resistance to monotherapies (quinine, chloroquine, SP, mefloquine, atovaquone) have developed quite rapidly (1–12 years) after introduction of the drug.

After WHO recommended the use of ACT in view of the widespread resistance to chloroquine and SP, all the SEAR countries opted for ACT for treatment of *P. falciparum* malaria. But in recent years, there have been reports of failure to ACT from India, Myanmar and Thailand. While the failures have been attributed to the failure of partner drugs, artemisinin resistance has also emerged in the Greater Mekong Sub-region. Global plan for artemisinin resistance containment (GPARC) has been in place since 2011 which defines the priorities to contain and prevent artemisinin resistance. The five action pillars of GPARC are: (i) stop the spread of resistance parasites; (ii) increase monitoring and surveillance to evaluate the threat of artemisinin resistance; (iii) improve access to diagnostics and rational treatment with ACT; (iv) invest in artemisinin resistance-related research; and (v) motivate action and mobilize resources. It has been observed that in spite of regulations, artemisinin monotherapy continues to be sold and made available over the counters in the Region. WHO and partners have intensified efforts to contain the emergence and spread of ACT resistance. A technical expert group on drug resistance and containment has been constituted in WHO HQs.

To prevent / contain the spread of drug resistance, the efficacy of these medicines should be monitored at various sentinel sites including the sites along international borders. Fortunately, we also have a marker for artemisinin resistance and one can have an early warning of the ensuing resistance. Further, there are various new molecules like OZ 439, spiroindolones (KAE609), imidazolopiperazine (KAF156) in the pipeline and can have potential to replace in case resistance to artemisinin develops.

## 5.2 Resistance in kala-azar

Treatment of kala-azar patients is one of the main strategies for control. Currently available drugs for the treatment of kala-azar are limited and most of them are toxic. Resistance to pentavalent antimonials has been observed in India since the 1990s and this has also spread to the endemic areas in Nepal. Miltefosine, the only oral drug, has been the first line of treatment since 2007. However, its efficacy has been shown to be reduced in India over the last decade while in Nepal, 20% of patients experienced relapse at one year follow-up after treatment and children had a higher risk of relapse compared to adults. The treatment failure was not associated with drug resistance, reinfection or reduced drug levels, but increased metacyclogenesis was observed in parasites isolated from the relapse patients. Moreover, pharmacodynamic modelling studies have shown a reduced exposure in children with the currently recommended doses (2.5 mg/kg/day for 28 days).

Miltefosine has not been reported to have developed natural resistance till now, but isolates showed *higher* tolerance in PKDL-treated patients (two rounds of treatment). Paromomycin resistance has been reported in natural populations and is also easily induced *in vitro*. To delay the emergence of resistance, combination regimens have been recommended in the long run. However, it has been reported that resistance is easily obtained experimentally in combinations with miltefosine/paromomycin and SbIII/paromomycin being the most susceptible.

Currently, simplified tools are available for assessing drug resistance and molecular tools are being developed. There is a need to monitor the efficacy of therapy and to monitor the resistance of the drugs currently being used by establishing reference laboratories. In addition, the quality of the drug and directly-observed therapy needs to be ensured.

## 6. VBD in neglected populations

Most of the VBD are also neglected diseases and affect the people from the lowest socioeconomic profile. Kala-azar affects the poorest of the poor and is predominantly seen in the *Mushahar* community in Bihar in India and

Nepal. Access to health care is a challenge for these communities. Districts in India have been categorized according to the proportion of tribal population (ST) as per the 2011 census, <10% ST (381 districts), 10–29.9% ST (104 districts) and 30% or more ST (124 districts). In the districts with  $\geq$  30% ST (20.4% of total districts), the proportion of total malaria, falciparum malaria and deaths was 46%, 70% and 46% respectively. There are four common VBD prevalent in tribal and marginalized populations. These are malaria, filariasis, dengue and chikungunya. Implementation of the control activities is quite a challenge due to difficult accessibility, remoteness, inadequate water supply and weak health infrastructure. Moreover migration and increased movement of the population in search of livelihood makes it difficult. Shortfall in supplies e.g RDT/ACT and insecticide treated nets (ITN) and long-lasting insecticide nets (LLINs) is also known to occur.

There is a need to upscale the activities to overcome these challenges including capacity-building and strengthening of health-care facilities and filling up the vacancies as a priority. IEC/BCC activities strategy for the tribal population needs to be reinforced, which should, in particular emphasize environment management for reducing the breeding areas for the vectors. Tools for protection against mosquito bites during outdoors and better understanding of the health-seeking behaviour of these neglected populations is required.

## **7. Social determinants of VBD, economic evaluation and sustaining integrated vector management (IVM)**

The social determinants of VBD include level of education, economic status, employment and decent work, housing and environment and effective health systems of preventing and treating ill-health. Education would include the number of years of schooling along with the literacy level of child bearing age women. Infection with VBD is associated with acute poverty, which also has an impact on morbidity and mortality. Good health requires a good health system. The key requirements for a good health system include: universality, comprehensiveness, equitability, effectiveness, responsiveness, accessibility, and quality. Most of the health facilities in the

developing countries are weak and health workers are few and/or unmotivated in addition to lack of basic drugs, equipments and supplies. This is also observed to some extent in the higher level health facilities. The budget allocation is not optimal and/or goes unutilized. For example, in Indonesia, the allocated budget for health in 2013 was less than 3% of gross domestic product (GDP) which remains below the WHO recommendation of 4–5% of GDP expenditure on health. The countries need to address health inequalities which will require better governance for health and development, promote wider participation in policy-making and implementation, strengthen global governance and collaboration and monitor progress and increase accountability. Multisectoral coordination is key in addressing VBD. During outbreaks of VBD, early detection is important for minimizing morbidity and mortality. Epidemic is considered as a non-natural disaster. Disaster is a function of hazard, vulnerability and the capacity of the local authority ( $D = H \times V / C$ ).

VBDs influence GDP and growth by many channels. Diffusion of VBD impacts on demographics, quantity and quality of labour and capital inputs etc. and if incidence reaches significant levels, can impact a variety of variables like human mobility, trade, investments, saving, and land use. Economic analysis is required to inform policy-makers regarding efficient resource allocation and the costs and consequences of elimination or eradication of the VBD. There are basically two types of economic analysis: (i) to measure the impact of VBD on economic outcomes which is widely used; and (ii) a practical and operational approach to undertake analysis to understand and inform investment decisions.

The impact of VBDs can be studied at macroeconomic and microeconomic levels. The former is undertaken at the cross-country level where the economic impact variable (ex. economic growth or per capita income) is seen as a function of VBD indicator and other covariates to study the impact of VBD on the selected outcome. In the micro-based approach, the impact of VBD is estimated at the individual or household levels. The micro-methods include the cost of illness, willingness to pay and (DALYs).

With regard to investment decisions, cost-benefit analysis which makes direct comparisons in monetary terms of costs and benefits and cost-effectiveness analysis helps to know which intervention is technically efficient. Costing is also required for national, regional and global financial

planning for control and eradication and becomes important for sustainable national programmes. Currently, there are few studies on economic analysis in SEAR. There is considerable scope and need for such analysis both for advocacy purposes and also to help sound policy-making where resources are scarce.

## **7.1 Integrated vector management (IVM)**

LF is targeted to be eliminated by 2020. It is expected that by 2017, 70% of all endemic countries will have met the criteria for stopping interventions i.e., MDA and will have entered the post-intervention (MDA) surveillance phase. By 2020, all endemic countries will have been verified as free of transmission or will have entered post-intervention (MDA) surveillance. In the elimination programme, there would be a continued need for IVM in the following situations: (i) areas with persistent infection even after eight rounds of MDA: to accelerate the interruption of transmission when applied in combination with MDA (ii) Post-MDA phase: reduce the subsequent risk of re-establishment of transmission (iii) Post-MDA phase: monitoring interruption of transmission through integrated /comprehensive vector surveillance. It is recommended that the organization and management of IVM be strengthened, a vector control be developed and the impact of parasites on humans, vectors and transmission be planned and monitored. It was strongly felt that entomological capacity, which is so crucial for successful implementation of the VBD control programmes, is extremely weak in all the Member countries in the Region. There is a need to build a core team of entomologists in each of the Member countries, provide capacity-building and facilitate networking amongst them. In addition, the stature of such people needs to be upgraded and a clear career ladder should be there to motivate them. They should be referred to as vector scientists.

## **7.2 Prioritizing VBD and strengthening health systems for its control**

VBD are quite complex. Different vectors transmit different diseases and a number of vector species are involved in transmitting one disease such as malaria. Even many sibling species have been identified in one vector species. Each species (sometimes sibling species of a species) have their

own bionomics, behaviour and geographical presence. Prioritization of issues in VBD control is important and takes into consideration several factors like morbidity, mortality and access to the affected population, availability of preventive tools – vaccination, preventive chemotherapy and environment-friendly vector control interventions, and whether the diseases are eliminable or eradicable and emergence of drug and insecticide resistance.

The gains made in the control and elimination of the VBD needs to be sustained. Monitoring the implementation, therapeutic efficacy and vector susceptibility studies need to be continued and strengthened. More research for better diagnostic tools and treatment regimens is required and there is a need for more operational research including innovations for health-care delivery in high transmission areas (reservoir of infection). An integrated approach with pooling of the resources would be most cost-effective. Cross-learning from different programmes should be adopted e.g. TB programme in medical curriculum and school curriculum emphasizing healthy practices. A balancing act between public and private health-care providers needs to be kept with the control programme playing the key role in coordinating the activities. Intersectoral cooperation and health-in-all-policies (HiAP) should be adopted.

Health system capacity is primarily dependent on adequate and trained human resources, financial resources availability, good health care and surveillance system and strong political will. In some of the Member States, the activities for the control of VBD is highly dependent on external donor support, including recruitment of health-care workers. It was felt that there should be less dependence on external funding for VBD programmes, particularly for human resources. Governments need to be prepared to take over investments in VBD control.

## **8. Intercountry cooperation**

Countries of the Region have witnessed outbreaks which may be local in origin, but pose an imminent and ongoing global threat, if not controlled at the source of origin. The spectrum of communicable diseases (CDS) in the countries is qualitatively similar.

Border regions between countries are prone to VBD for several reasons. Usually, large populations live in border areas and movement of people among countries of the Region is so intense due to the porous borders e.g. between India and Nepal. Poverty is high, health services are weak and access to health care is difficult. Integrated cross-border collaborations in the border areas for surveillance and control efforts are not coordinated. Insecticidal resistance and drug resistance have been more commonly observed in the bordering areas.

Actions for cross-border collaboration should include efforts to develop common or similar standards for diagnosis, treatment and surveillance. Coordination of vector control efforts in particular timing of indoor residual spraying (IRS) spraying on both sides should be attempted. Strategies and mechanisms for coordination between the Member States both at the central and regional levels including sharing of data and information on the trends of disease and outbreaks are required.

In the last few years, there has been progress in harmonization of surveillance, diagnosis, treatment for kala-azar amongst the three endemic countries. However, there is no current mechanism in place for routine sharing of data. This becomes more relevant with elimination targets for kala-azar approaching. One of the crucial issues is strengthening of political commitment including renewal of Memorandum of Understanding (MoU) with emphasis on cross-border collaboration. The WHO Regional Office for South-East Asia should take the lead to help facilitate the coordination mechanisms between the Member States.

## **8.1 Health-in-all-policies (HiAP)**

HiAP is an approach to public policies across sectors that systematically takes into account the health implications of decisions, seeks synergies and avoids harmful impacts in order to improve population health and health equity. Control of VBD is not the sole responsibility of the health sector alone, as various other sectors like urbanization, irrigation, sanitation, etc. are also closely related. Tackling of public health issues due to pesticides and integrated pest management in agriculture primarily involves other ministries. Even if control is well implemented, currently we lack the tools to prevent all VBD e.g. no vaccines available for dengue, malaria, kala-azar, filaria or therapy to cure infections e.g. for adult worm causing filaria,

dengue. On the other hand, some interventions are effective against several vectors simultaneously and some vectors transmit several diseases. Therefore, there is a need for integration for decision-making process to optimize the best use of the limited resources.

There have been successful examples of this integrated approach for promoting healthy lifestyles and thus reduce the disease burden e.g. North Karelia Project in Finland and national programme to promote active, healthy lifestyle in Israel. The key areas of partnership include intersectoral approach, legislation and regulations, educational system and curriculum, information and mass media for public. At the foremost, there is a need to advocate this approach for VBD and a strategy needs to be developed for the Region.

## **8.2 Drug and vaccine development for VBD: how can endemic countries contribute?**

Most of the VBD are neglected diseases and affect populations mainly from low-income countries. They are a leading cause of mortality, chronic disability, and poverty. The efforts for developing newer drugs or vaccines have been extremely low. Developing a new drug takes 10 to 12 years on average and biopharmaceutical discovery is complicated and costly. Research and development (R&D) involves high capital cost and there is a long time gap between R&D investment and "commercialization" of the resulting technology. R&D investment is not appropriate; there are insufficient commercial returns for VBD and neglected tropical diseases (NTD).

Of the 850 new therapeutic products registered in 2000, only 1137 (4%) were indicated for NTD and of 148 445 clinical trials registered on 31 December 2011, only 2016 (1%) were for NTD.

Globally, these NTD represent a 11% health burden, based on a recent assessment of 2010 disability-adjusted life-years (DALYs) and there was about 0.6–1.3 new products/year for neglected diseases during 1975–1999, which increased to 2.4 during 2000–2011 and predicts 4.7 new products/year through 2018. Currently, 123 new products are in development for NTD, with over half (55%; 68) being vaccines or biological products, including 21 for malaria.



The world's major pharmaceutical companies joined forces with governments and leading global health organizations in 2012 to donate drugs and scientific know-how to help control or wipe out 10 neglected tropical diseases by 2020; including LF, kala-azar and schistosomiasis.

Drug development encompasses two main areas, discovery of new targets which is followed by development of drug candidates. The development takes many years. While discovery could be undertaken in the developed countries, institutions and universities of some of the Member countries e.g. India, Thailand which have the capacity, could also play an active role. The preparation of field site for clinical trials of candidate drug or vaccines well in advance could reduce the period for the development of the drug/vaccine.

With regards to safety monitoring, developing countries need to build their capacities to monitor side effects following post registration of drugs.

## **9 Research priorities in VBD**

The scenario amongst the VBD in the Region is varied. Most show a decreasing trend and are being targeted for elimination e.g. filaria, kala-azar while some are showing exponential increase e.g. dengue. There are still gaps in knowledge with regards to the pathogenesis, immunology, vector bionomics along with lack of ideal tools for vector control, diagnostic tests and drugs. On the other hand, operational research needs to be augmented and prioritized to support the control programmes.

The key priority areas for research for the different VBD in the Region are listed below:

- Dengue:
  - mapping for dengue serotypes from all the countries in the Region;
  - mathematical modeling to provide direction on where the emphasis should be made in dengue control;
  - innovative approach of models for community collaboration for dengue control;

- innovation research for better tools for diagnosis of dengue, dengue vaccines, antiviral drugs, anti plasma leakage drugs; and
  - research on prediction of dengue outbreaks including role of climate change, predictors of severe disease.
- Kala-azar:
- active case-finding in low and moderate endemic areas;
  - enhancing surveillance in newer foci to document the transmission and disease burden of kala-azar;
  - development of antigen detection diagnostic tests for kala-azar;
  - research on the role of the PKDL (different forms) and asymptomatic leishmaniasis infection in disease transmission;
  - validation of diagnostic tests and develop clinical algorithm for PKDL;
  - development of shorter and safer treatment regimens for PKDL;
  - study on vector bionomics and behaviour; and
  - development of alternative vector control tools.
- Malaria:
- validation of tools for protection for outdoor transmission of malaria;
  - mapping of mobile population in and out of the forest;
  - mapping of artemisinin resistance in all the countries in the region;
  - role of asymptomatics in the transmission of malaria; and
  - health-seeking behaviour for the treatment of malaria.
- Filaria:
- Why some IUs fail to achieve the target after several rounds of MDA and how the process can be accelerated;

- alternative strategies for filarial elimination in hot spot areas; and
  - validation of models on the method of follow-up after post MDA in filariasis.
- JE and chikengunya
  - All VBD
    - conduct of economic analysis with microeconomic and macroeconomic approach including cost-benefit and cost-effective analyses;
    - models to integrate HiAP for control of VBD;
    - evidence-based BCC and models for community participation for control/elimination of VBD;
    - effect of climate change in VBD;
    - development of molecular tools for monitoring drug resistance; and
    - monitoring insecticide resistance.

## **10. Conclusions**

After all the deliberations, different experts came to the following detailed conclusions.

### **10.1 Policy and programme**

- A regional network of institutes in tropical and infectious diseases should be built in the Region.
- Multisectoral collaboration (different ministries and partners) for control of VBD should be enhanced after identifying the roles and responsibilities of each sector.
- Environmental factors influence the transmission of VBD; thus issues like sanitation, and waste management should be strongly addressed as part of the control strategy.

- Community involvement in the control of VBD should be enhanced. Use of tools along with community initiatives need to go together.
- School curriculum should include the control of VBD and also public health measures like waste management, sanitation and hygiene for inculcating healthy practices in children.
- A core group of vector scientists should be built in each country and capacity building and networking between them supported. Entomologists would be better referred to as vector scientists and should also have a career ladder.
- Kala-azar in South Asia being on a decreasing curve in the last few years, efforts should be intensified by all the countries to reach the elimination targets.
- MoU on Elimination of Kala-azar in South Asia between the partner countries should be renewed.
- Criteria for verification of kala-azar elimination should be developed.
- Coordination mechanisms between the countries need strengthening for cross-border issues and migration.
- Dengue should be made a notifiable disease in all countries.
- Regulations for registration of diagnostic kits should be developed to ensure use of validated tests in the community and hospitals.
- The two WHO dengue guidelines (2009 and 2011) should be harmonized.
- Private hospitals should also be included in surveillance for dengue. National guidelines for the management of dengue should also be disseminated to private health-care facilities.
- Coordination must be ensured between public health programme, meteorological department and hospitals for better preparedness to deal with dengue cases.
- IEC/BCC activities for the community and media for all VBD should be enhanced. Social scientists should be included in control programmes.
- Listing of the comprehensive measures (14 points) should be elaborated for each VBD in the individual countries.

- Developing countries have the potential for a greater role in the research and development of VBD and also to support acceleration e.g. field site preparation for clinical trials.
- Availability of quality medicines for malaria should be ensured.

## **10.2 Technology and research**

- Mapping for dengue serotypes should be carried out in all the countries in the Region
- Mathematical modeling should be used to provide direction on where the emphasis should be made in dengue control.
- Innovation research should be undertaken for better tools for diagnosis of dengue, dengue vaccines, antiviral drugs, anti-plasma leakage drugs.
- Research on prediction of dengue outbreaks including role of climate change, predictors of severe disease should be conducted.
- Active case-finding should be undertaken in low and moderate endemic areas. Surveillance in newer foci should be enhanced to document the transmission and disease burden of kala-azar.
- Liposomal alphotericin B with a short regimen, efficacy and safety profile should be used as a first line regimen for treatment of kala-azar in the attack phase.
- Antigen detection diagnostic tests for kala-azar should be developed.
- Research on the role of PKDL (different forms) and asymptomatic infection in disease transmission should be conducted.
- Diagnostic tests should be validated and clinical algorithms developed. Shorter and safer treatment regimens for PKDL should be developed.
- Tools for protection for outdoor transmission of malaria should be validated.
- Mapping of mobile population in and out of the forest should be done.

- Mapping of artemisinin resistance: systematic review of published data surveillance and mapping for drug resistance in different countries should be done.
- Models on the method of follow-up post MDA in filariasis should be validated.
- Vector surveillance in the control activities should be strengthened.

### **10.3 Communities**

- Tribal districts/forested areas should have adequate supplies of LLIN/ITN, RDT and ACT. Coverage of IRS should be adequate. Capacity-building of human resources and infrastructure in tribal areas is important.

### **10.4 Funding**

- The primary funding for programme activities needs to be from the countries internal resources. They should be less dependent on external funding, particularly for human resources. WHO should support capacity-building and issues as per the individual country's needs.

## **11. Recommendations**

### **11.1 To Member States**

- (1) A national policy and strategy in the context of HiAP, with focus on sustainable multisectoral approaches that are less dependent on external resources, should be formulated and implemented to control and if feasible, strengthen the efforts to eliminate VBD.
- (2) A high-level multisectoral task force or committee should be established to oversee the development and implementation of the national policy and strategy.
- (3) The right mix and number of expertise should be developed and sustained involving all stakeholders as part of health system strengthening to effectively address VBD. Specifically, vector control teams including vector scientists, vector control specialists and technicians should be built, sustained and provided with the necessary

enabling environment and training programmes, including laboratory support for evidence-based vector control and career development should be conducted.

- (4) Generation of strategic information to inform policy and strategy development, planning and decision-making on VBD should be strengthened. This would include, among others, creating awareness among researchers in the public sector and private industry on the needs of programmes to control VBD, including drugs, vaccines, environmental control / management and operational research, investing in operational research; strengthening mechanisms for getting evidence into policy and practice; strengthening surveillance that encompasses VBD surveillance, entomological, ecological and behavioural surveillance; and optimizing the use of modern information technology.
- (5) Social scientists, civil society, community leaders, schools, local governments, private corporate sector and others should be engaged in designing and implementing sustainable approaches for intersectoral collaboration and community participation to control and eliminate VBD.
- (6) Economic and epidemiological analyses, including costing studies, mathematical modelling, on VBD should be conducted to support the need for sustainable financing for their control and elimination.

## **11.2 To WHO**

- (1) The adoption and implementation of HiAP should be promoted to address VBD. In this regard case studies should be conducted to be used as advocacy tool and orient key staff at WHO regional and country offices to advocate for HiAP.
- (2) Support should be provided for capacity development of vector scientists and vector control specialists and an enabling environment for networking provided to them to facilitate exchange of knowledge and expertise and to raise their profile in public health and in the scientific community.
- (3) Research to develop new tools or interventions or improve the use of existing tools against VBD should be promoted and whenever feasible, supported. Support in translating evidence into policy and practice should be provided.

- (4) A small multidisciplinary group should be commissioned to review the current state of knowledge and the gaps on vectors and VBD and a regular forum for dissemination of research agenda and research findings on vectors and VBD should be provided.
- (5) The existing road maps should be updated to accelerate control towards elimination of malaria, kala-azar, LF and schistosomiasis, and strategic investments to catalyse actions where needed provided for.
- (6) Generation of strategic information, including the conduct of economic and epidemiological analyses, including mathematical modelling, on VBD should be supported.
- (7) The Dengue case management guidelines should be synchronized and criteria for validation of kala-azar elimination developed.



## **Annex 1**

### **Opening address of Dr Poonam Khetrapal Singh, Regional Director, WHO South-East Asia Region**

It is my pleasure to welcome you all to this informal consultation on vector-borne diseases (VBD) which coincides with the theme of World Health Day 2014. WHO celebrates World Health Day every year to focus global attention on a disease of common interest to all of us. In the context of the South-East Asia Region, this year's theme on VBD is very apt and timely.

VBD are an important group of diseases, killing over a million people annually and putting half the world's population at risk. These often neglected diseases account for 17% of the global estimated burden of all infectious diseases. VBD involve diverse groups of parasites and viruses, spreading to humans through the bite of a diverse group of vectors, including mosquitoes, bugs, ticks, mites, flies and freshwater snails. These vectors are versatile creatures rapidly adapting to changing ecological and environmental conditions, thus challenging the control interventions available.

Malaria is endemic in all Members States of the Region, except Maldives, putting around 1.4 billion people at risk. WHO estimates 42 million cases and 27 000 deaths from malaria in the Region in 2012. Around 1.8 million people in the Region are at risk of dengue. In 2012 there were over 257 000 cases reported from the Region, which includes countries with the highest contribution to global dengue cases. Around 875 million people in the Region are at risk of lymphatic filariasis – the highest contribution to the global burden, with an estimated 60 million infected people. Kala-azar is endemic in Bangladesh, India and Nepal, with an estimated 100 000 cases annually, while sporadic cases are being reported from Bhutan and Thailand. An estimates 70 000 cases of Japanese encephalitis with 15 000 deaths are reported annually in the Region. Schistosomiasis persists in two districts of Central Sulawesi in Indonesia.

The Region has been making progress in controlling and eliminating most of the VBD. Malaria prevalence continues to decline, with five countries achieving more than 75% decrease in case incidence and two additional countries expected to achieve this target by 2015. Sri Lanka is in elimination phase with no locally acquired cases since November 2012, while Bhutan and the Democratic People's Republic of Korea are in the pre-elimination phase. Bhutan and the Democratic People's Republic of Korea continue to remain free from lymphatic filariasis (LF) and Maldives, Sri Lanka and Thailand are working on submitting the dossier for certification of LF elimination. Bangladesh, India, Myanmar and Nepal are making good progress in reaching the LF elimination target. Bangladesh and Nepal is making good progress in eliminating kala-azar, and India is committed to reaching the regional target.

However, there are still many challenges in eliminating these diseases as issues of public health concern. Environmental degradation and poor solid-waste management is creating more mosquito-breeding grounds than ever. Global warming and climate change are pushing vectors to new locations and higher altitudes while increasing the efficiency of the mosquitoes as vectors. Dengue and chikungunya keep on increasing in the Region. The emergence of malaria parasite resistance to medicines threatens progress, while vectors developing resistance to insecticides are posing greater challenges. While countries continue to make progress in eliminating the diseases, sustaining control measures and strengthening surveillance remain an issue. National capacities to meet these challenges need to be strengthened and communities must be educated and empowered to prevent these diseases. We need better tools to reach out to the difficult-to-reach pockets in countries. While efforts to develop a dengue vaccine continue, we need to discuss how we can better understand the epidemiology and pathophysiology of the disease and sustain improvements in case management. We need better data and stronger evidence on the disease burden and its health, social and economic impacts. We need to explore creative ways of working together both within and between countries. I hope this two-day consultation will advise and guide us on some of these issues and beyond, enabling us to better focus our agenda in controlling and eliminating VBD. We seek technical support from all the institutions and WHO collaborating centres.

I am also very pleased to know that all WHO collaborating centres working on VBD located in the Region are represented in this meeting. I hope you all had a pleasant journey and your stay here in New Delhi is comfortable.

## **Annex 2**

# **Agenda**

- (1) Opening
- (2) Overview, dengue, drugs and vaccines
- (3) Emergence and spread of resistance in malaria and VBD in neglected population
- (4) Social determinants and IVM
- (5) Intercountry cooperation and HiAP
- (6) Research priorities
- (7) Recommendations
- (8) Conclusion

## Annex 3

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Vector-borne diseases (VBD), account for 17% of the estimated global burden of all infectious diseases. Their burden and economic impact continue to be very high. In the WHO South-East Asia Region, the VBD of public health importance are malaria, dengue, Japanese encephalitis, chikungunya, lymphatic filariasis and kala-azar.

On the occasion of the World Health Day 2014, an informal consultation with experts on VBD was organized at SEARO, New Delhi on 7 and 8 April 2014. More than 20 experts across different specialties in medicine and public health in the Region attended the meeting and deliberated on various aspects of VBD including their situation and impact, drugs, diagnostics and vaccines, emergence and spread of drug resistance, social determinants, intercountry cooperation, health in all policies and research priorities.

After detailed discussions, the consultation made a set of recommendations to WHO as well as the Member countries.



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