KALA-AZAR ELIMINATION PROGRAMME

REPORT OF A WHO CONSULTATION OF PARTNERS

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Kala-Azar Elimination Programme

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Geneva, Switzerland
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1. Background

More than 147 million people in the WHO South-East Asia Region are at risk of contracting the *Leishmania* parasites that cause visceral leishmaniasis (kala-azar), a life-threatening disease. Bangladesh, India and Nepal have the largest burden of the disease in the Region, with recent, sporadic cases being reported from Bhutan and Thailand as well. These five countries renewed their commitment to eliminating kala-azar from the Region at a side event held during the thirty-second meeting of Ministers of Health of WHO’s South-East Asia Region (Sixty-seventh Session of the Regional Committee for South-East Asia) in Dhaka, Bangladesh on 9–11 September 2014. This renewed commitment calls on WHO and other partners to support the efforts of Member States in achieving the elimination target before the set date of 2017.¹

1.1 Opening session

The opening session was moderated by Dr Daniel Argaw Dagne, Head of the Leishmaniasis Control Programme, WHO Department of Control of Neglected Tropical Diseases.

Dr Jean Jannin, Coordinator, Innovative and Intensified Disease Management, WHO Department of Control of Neglected Tropical Diseases, delivered the opening remarks and stressed the following points:

- The WHO Roadmap’s target² for regional elimination of visceral leishmaniasis will be achieved by or before the set target date of 2020.
- Government commitments are commendable and essential.
- Synchronization is important.
- Gilead is committed to donating liposomal amphotericin B (AmBisome).
- The UK Department for International Development is supporting capacity-building and surveillance and improving access to AmBisome.
- The number of cases and deaths has reduced markedly.
- An estimation of the current case burden and the population at risk is important.
- All countries in which visceral leishmaniasis is endemic are adopting the same elimination strategies.
- Member States in the Region should scale up implementation of single-dose AmBisome.
- The surveillance system and active case detection should be reinforced.
- Vector control strategies and activities should be strengthened.

Dr Daniel Argaw Dagne presented the objectives of the meeting, which were:

1. To jointly review the progress and identify challenges regarding the implementation of kala-azar elimination in the WHO South-East Asia Region;

2. To elaborate and review the specific activities, contribution and engagement of partners in elimination efforts in the Region for harmonized, coordinated implementation of interventions; and

3. To provide a forum for sharing country experiences, joint planning and review of progress.

¹ Health Ministers commit to eliminating kalar azar [media advisory]. New Delhi: WHO Regional Office for South-East Asia; 2014 (http://www.searo.who.int/mediacentre/releases/2014/pr1581/en/).
He emphasized that the set target of elimination by 2020 is achievable and sustainable through accelerated, scaled up interventions implemented in a coordinated and harmonized way. These efforts are not possible through a single institution or an organization but through a strong partnership of all stakeholders.

The rapporteurs of the meeting were Dr Keshav Yogi, Dr Saurabh Jain, Dr Suman Rijal and Dr Rahul Kumar. Dr Daniel Argaw Dagne compiled the notes of the rapporteurs and wrote the meeting report. Annex 1 contains the meeting agenda and Annex 2 the list of participants.

1.2 Update on first meeting of Programme partners

The session was chaired by Dr A.C. Dhariwal, Director, National Vector Borne Disease Control Programme, India. Dr Daniel Argaw Dagne summarized the first meeting of partners (London, September 2014), which was attended by 16 partners, including new partners.

The issues and recommendations of the meeting concerned six specific areas: case management; surveillance and information; vector control; communication; strengthening coordination; and collaboration. Countries were encouraged to follow the action plan agreed at the meeting.

1.3 Status of kala-azar in the South-East Asia Region

Dr Rajesh Bhatia, Director, Communicable Diseases, WHO Regional Office for South-East Asia, presented the status of the Programme in the Region. He thanked all the partners for their support and contributions.

Elimination of kala-azar is a priority programme in the Region as reflected by it being one of the flagship programmes of the Regional Director. A memorandum of understanding among five endemic countries of the Region was signed in 2014. A document on the process of verification of the elimination of kala-azar as a public health problem in South-East Asia was published also in 2014. A new Regional Taskforce has been established to advise on practical measures to facilitate elimination. A Regional Strategic Framework for Elimination of Kala-azar (2016–2020) has been drafted and will be finalized in 2015 through informal consultation.

Three countries in the Region have sustained transmission of kala-azar: Bangladesh, India and Nepal. Two other countries, Bhutan and Thailand, have also reported cases in recent years. Some 147 million people living in the Region are at risk, with an estimated 100 000 cases per year and 15 000 reported cases. More than 80% of cases are from India.

All three countries have made significant progress towards the targets of the Kala-Azar Elimination Programme. The number of cases has decreased by 59%, mortality by 85% and case fatality by 61%. Nepal has eliminated the disease at district level and sustained the situation for the past 2 years. Bangladesh has achieved the elimination target in 90% of endemic upazilas. India has achieved the target in more than two thirds of endemic blocks. These endemic countries have adopted liposomal amphotericin B as the first treatment option.

Despite these achievements, some challenges remain. A changing epidemiological pattern has been observed, with new foci reported. Nepal, for instance, has lately observed a wider geographical distribution, with new cases reported from hilly areas. The burden and limited evidence of the disease,
based on interventions against post kala-azar dermal leishmaniasis (PKDL) in the Region, pose further challenges. Other challenges include ensuring an uninterrupted supply of diagnostics; vector control interventions (coverage, monitoring and insecticide resistance); cross-border surveillance and information-sharing; and capacity for verification of elimination.

Sustaining the achievements and advocating political support and enhanced implementation of the Programme, maintaining strong surveillance, ensuring effective cross-border collaboration, and strengthening monitoring and evaluation are possible only through a strong and committed partnership.

2. Country presentations

2.1 India

Dr A.C. Dhariwal, Director, National Vector Borne Disease Control Programme, presented an update on the status of the Programme in India.

The number of cases and deaths has decreased. More than 70% of endemic blocks have achieved elimination. Compared with the data reported in 2011 the number of cases has reduced by 72% and the number of deaths by 86%. Of the cases reported in 2014 some 77% were from 157 (26%) blocks which reported more than 1/10 000 population. In 2014 the incidence rate was below 1/10 000 population in 74% of blocks and below 1/10 000 in 305 (70%) blocks for 3 consecutive years; 88 (20%) blocks have reported no cases for 3 consecutive years. There is a decreasing trend also in the number of PKDL cases.

The Programme is monitored by periodic joint monitoring missions involving government and partners. The WHO National Polio Surveillance Project is also a stakeholder and has provided support for coordination in three states. Other national and international partners include the Rajendra Memorial Institute of Medical Sciences, the National Centre for Disease Control, the Central Health Education Bureau, the Drugs for Neglected Diseases initiative, Médecins Sans Frontières, PATH India, CARE India and the KalaCORE Consortium. These partners have supported training; treatment of patients with AmBisome; information, education, communication and behaviour change communication; supervision and monitoring; pharmacovigilance; research; vector control (indoor residual spraying); and diagnostics.

A CORE group has been formed at ministry (national) level to support and advocate the Programme. The group is represented by various sectors and provides policy and technical guidance to the Programme.

A roadmap for the elimination of kala-azar was published in 2014\(^1\) with a target-oriented timeline up to block and village levels, with focus on highly endemic districts. The Prime Minister’s Office is also involved in monitoring of the Programme. Factors enabling implementation of the roadmap include the availability of resources, support from multiple partners, user-friendly diagnostic tests, strong political commitment at all levels and drugs donated through WHO.

The Programme is reviewed monthly by state, district and block-level task forces.

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Mobile vans are used to conduct active camp searches in endemic blocks. In 2014, more than 2000 search camps were held in 333 blocks. Of the 11 140 suspected cases detected, 387 (3.4%) tested positive using the rK39 rapid diagnostic test (RDT). Liaison with the Leprosy Elimination Programme has facilitated coordinated efforts for detection of PKDL cases resembling leprosy during search activities.

The current policy on indoor residual spraying is to conduct two rounds per year with DDT in villages reporting kala-azar cases in the previous 3 years and the current year. As the vector is showing resistance to DDT in some districts and acceptance of DDT among the community is poor, some policy changes have been made to introduce synthetic pyrethroid in one district in Bihar (Muzaffarpur), which has demonstrated 100% mortality. The Central Insecticide Board and the Ministry of Agriculture have been approached for permission to use synthetic pyrethroid also for sandfly control.

The new 2014 roadmap aims to strengthen information, education and communication as well as behaviour change communication with the help of development partners and to guide the uniform preparation of a micro plan.

Stirrup pumps will be replaced with hand compression pumps in one district (Vaishali) for efficiency.

The Programme provides financial incentives to accredited social health activists of US$ 5 for referring a suspected case and ensuring complete treatment, and US$ 3.2 for two rounds of indoor residual spraying. For patients and caregivers, US$ 8 for VL and US$ 32 for PKDL cases for loss of wages is provided.

Support from all partners is crucial in achieving the “last mile” and sustaining elimination in the country.

2.2 Bangladesh

Professor Dr Abul Khair Mohammad Shamsuzzaman, Director, Centers for Disease Control, presented an update of the Programme’s activities in Bangladesh.

Bangladesh is a signatory to the first memorandum of understanding on the elimination of kala-azar (signed by the health ministers of Bangladesh, India and Nepal in May 2005). Targeted activities are being carried out in line with the strategies adopted in the Region. The number of cases and deaths is decreasing. Most of the upazilas have achieved the elimination target and are sustaining the situation.

The elimination strategies adopted are early diagnosis and complete treatment; integrated vector management; effective disease surveillance; social mobilization and partnerships; and operational research. The main factors contributing to the Programme’s success are interventions and tools, such as rapid diagnosis with the rK39 RDT; treatment with liposomal amphotericin B (AmBisome); and indoor residual spraying using deltamethrin 5% wettable powder.

The following activities have proven highly effective: resource mobilization by engaging policymakers to steer the Programme; formation of a subdistrict kala-azar Committee; budget allocation from the Government; ensuring availability of drugs and diagnostics; community participation through advocacy; selection of target groups for capacity building; partnership development; and media mobilization.
Various levels of health-care providers have been trained to enhance capacity in the following areas: case identification; rapid diagnosis; case management; active case searches in the field; periodic follow up; indoor residual spray; reporting and recording; and surveillance.

Indoor residual spraying is carried out to reduce the density of adult sandflies. Bangladesh conducts six rounds of spraying. In 2014, of the 1,213,980 households targeted, 630,398 were covered. A report on pre-monsoon vector density showed a reduction in vector mortality of more than 99% after the second round of spraying in eight hyper-endemic upazilas.¹

Bangladesh has introduced two interventions to combat VL: (i) a no kala-azar transmission strategy; and (ii) larvicide spraying in breeding sites. The no transmission strategy involves household searches for cases of kala-azar and PKDL, entomological surveys, additional indoor residual spraying in areas where it has not been done recently and larvicidal spraying in breeding places such as chicken, cow and cattle sheds.

Long-lasting insecticide-treated nets are distributed for transmission interruption. Some 32,000 nets were distributed focally in 2014 to kala-azar patients in all endemic upazilas, with blanket distribution of 18,000 nets in one upazila.

Social mobilization activities include displaying billboards in selected sites, distributing information, education and communication materials, and singing folk songs on kala-azar during house-to-house case searches.

Bangladesh introduced AmBisome for the treatment of VL and PKDL in 2013. Some 15,000 vials of injectable AmBisome were provided through WHO.² In 2013, 560 cases of kala-azar were treated. In 2014, 685 VL and PKDL cases were treated.

The number of hyper-endemic upazilas has decreased from eight in 2012 to two in 2014 and in moderately endemic upazilas from 16 in 2012 to six in 2014. Some 19 upazilas reported 47 cases in 2014.

The Programme faces a number of challenges. These include increasing non or low compliance with PKDL treatment, development of drug resistance, inadequate information on vector bionomics and monitoring, asymptomatic carriers or reservoirs, and cases of relapse and treatment failure.

The progress and success of the Programme to date have been made possible through the support of various partners including Médecins Sans Frontières, WHO, the UK Department for International Development, the Special Programme for Research and Training in Tropical Diseases, and the Japan International Cooperation Agency.

2.3 Nepal

Dr Babu Ram Marasini, Director of Epidemiology and Disease Control Division, presented an update on the Programme in Nepal.

The number of new cases and deaths has reduced significantly. The elimination strategies adopted are early case detection and completion of treatment; vector control activities including distribution of long-lasting insecticide-treated nets; capacity building of health workers; maintenance of the supply chain; surveillance and research; partnership; pharmacovigilance; cross-border collaboration; and non-health interventions (a financial incentive equivalent to US$ 10 for cases having completed treatment).

The Programme has strengthened surveillance. Patient and laboratory registers are maintained at district level, and Programme districts provide monthly reports to the centre. Kala-azar is one of the six disease events included in the early warning reporting system (a hospital-based sentinel surveillance system). This reporting system has facilitated data collection from non-endemic (non-Programme) districts. Epidemiological and entomological verification are being carried out in non-endemic districts. However, surveillance should be strengthened further.

An independent assessment of the Programme carried out in 2014 documented a reduction in the number of cases and deaths in endemic districts as well as the emergence of small new foci in other districts.

Indoor residual spraying with alpha-cypermethrin is done twice a year in priority affected areas. The Programme is switching to deltamethrin. Improving the coverage and quality of spraying is a challenge in vector control activities.

Factors that have contributed collectively to the reduction in the number of cases and deaths include the availability of diagnosis and treatment; capacity building through orientation/training to physicians and health workers; indoor residual spraying and distribution of long-lasting insecticidal nets; provision of transport incentives to patients after completion of treatment; social mobilization and awareness; and socioeconomic interventions from non-health sectors.

The Programme needs to address the following areas: introduction of liposomal amphotericin B; training/orientation on the revised treatment protocol; further strengthening of disease and vector surveillance; active case-finding; epidemiological and entomological verification in non-endemic districts; and strengthening pharmacovigilance.

Despite the reduction in disease incidence and mortality, some challenges remain. The pattern in the distribution of the disease is shifting and new foci are emerging in non-Programme districts, including mountains, mountain valleys and urban areas, which may be related to climate change. Other important challenges include underreporting of PKDL cases, diagnosis of relapse and drug resistance, imported cases of cutaneous leishmaniasis in labour migrants and establishing effective cross-border coordination.

More coordinated efforts at national, bilateral, regional and international levels are required to sustain the progress made and achieve elimination from the Region. Further research on climate change and the behaviour of kala-azar vectors is needed.
3. Partners’ presentations

3.1 KalaCORE Consortium Asia – *Leishmania* and HIV coinfection in Bihar

Dr Sakib Burza, Regional Coordinator for Asia, presented an update of the Consortium’s activities to combat coinfection with *Leishmania* and HIV, with focus on the situation in Bihar, India.

There is a long documented relationship of coinfection but data are sparse for the Indian subcontinent. In the African context, particularly northern Ethiopia, coinfection is well described (between 18% and 40% of VL patients are coinfected with HIV). There is a general lack of evidence and data on diagnosis, treatment and outcomes.

Coinfection has major clinical, diagnostic and epidemiological implications. People with HIV infection are particularly vulnerable to VL, which accelerates replication of HIV and progression to AIDS. Treatment outcomes are poor, and mortality in coinfected patients is higher than in non-HIV-coinfected patients regardless of the medicines used. Coinfected patients frequently relapse and may act as a reservoir for drug-resistant parasites. Furthermore, coinfected patients are thought to be more “infective”, which poses additional challenges to elimination efforts.

**HIV-VL in Bihar**

- The reported prevalence of HIV is 0.22–0.33%.
- According to the Kala-Azar Medical Research Centre, the HIV prevalence among adults and children increased from 0.88% to 2.18% during the period 2000–2006.
- Médecins Sans Frontières began routine testing of all adult patients (aged ≥ 14 years) in 2011.
- A total of 2130 consecutive patients were offered provider initiated counselling and testing. The diagnosis of HIV was confirmed in National AIDS Control Organisation testing centres.
- Some 2.4% of the 2130 patients were previously unknown to be HIV-positive.
- Unknown cases peaked at 5.4% in males aged 35–45 years and these cases are:
  - 8.2 times more likely to present with a history of relapse; and
  - more likely to present with severe anaemia.
- When pooled with previously diagnosed HIV cases:
  - 12.8% of males aged 35–45 years are coinfected; and
  - 6.1% of females aged 35–45 years are coinfected.

3.2 Médecins Sans Frontières – treatment of coinfection in Bihar

Dr Ritmeijer presented the experience of Médecins Sans Frontières in treating coinfection in Bihar, the results of studies of AmBisome and the risks associated with treatment in recent years.

**Coinfection**

- Initially, coinfection was treated using AmBisome (20 mg/kg) in four doses (5 mg/kg every 24 hours).
- No treatment failures or treatment-related mortality has been reported to date.
- Allergic reactions occurred in < 1/1000 of patients.
- The relapse rate was 2.5% at 18-month follow up.
- Coinfected patients were treated with the same regimen.
Long-term results following treatment with AmBisome (20–25mg/kg)

- Mean CD4 188 for patients on ART
- Mean CD4 101 for patients not on ART
- Mortality risk following treatment:
  - 14.3% at 6 months
  - 18.1% at 15 months (2.8% in non HIV-infected patients)
- Relapse risk (adjusted)
  - 16.1% at 12 months
  - 16.1% at 15 months (1.2% in non HIV-infected patients)
- ART initiated shortly after treatment was associated with:
  - a 64–66% reduction in the risk of mortality; and
  - a 75% reduction in the risk of relapse.

Start of single-dose AmBisome combination therapy study

- In 2012, the Drugs for Neglected Diseases initiative and the Rajendra Memorial Research Institute of Medical Sciences started a clinical trial comparing single-dose AmBisome with combination therapy.
- Coinfected patients were excluded from the study but were to be included in the surveillance register.
- Lengthy discussions concerned how best to treat coinfected patients given the lack of an evidence base, the relatively high relapse rate and the high short-term mortality with AmBisome (20 mg or 25 mg).
- Finally, the Ethics Review Boards of both institutions approved the physicians’ recommendations and the experts’ opinions.
- Use of combination:
  - AmBisome (30 mg/kg) in six divided equal infusions
  - miltefosine (14 days) of oral allometric dosing.

Risk of relapse

- The risk of relapse at 12 months was higher in the monotherapy group.
- In patients on ART the risk at 12 months was higher in the monotherapy group (16.2%) than in the combination group (6.4%).

Risk of mortality

- Combination treatment reduced early mortality.
- In patients on ART the overall mortality at 12 months was slightly higher in the combination group (11.2%) than in the monotherapy group (8.7%).

Recommendations of the expert working group meeting on HIV–VL co-infection (Patna, India, 1 September 2014)

- Given that 2–5.6% of VL patients are coinfected with HIV, all patients in whom visceral leishmaniasis is diagnosed (rK39 positive or otherwise) should be offered HIV testing with appropriate linkages to integrated or facilitated counselling and testing centres, where counselling and testing for HIV should be done with informed consent, as per national guidelines.

This recommendation will be implemented throughout the country but focus initially on four states: Bihar, West Bengal, Jharkhand and Uttar Pradesh.
• Medical officers at ART centres in states where VL is endemic should be sensitized and trained to suspect VL in all HIV-positive individuals having fever lasting > 2 weeks, hepatosplenomegaly and pancytopenia from an endemic area. Such patients should be referred for VL testing with rK39 (RDT). Those with rK39 positivity should be immediately linked to a facility where VL treatment is available. Those with rK39 negativity but high clinical suspicion for VL should undergo bone marrow aspiration for confirmation of diagnosis as per the algorithm.

• The diagnosis of VL in HIV-infected patients is made as for those who are HIV-negative (rK39 positive tests followed by bone marrow or splenic aspirate where indicated). Because rK39 may not be positive in all HIV coinfected patients due to low immunity, those with rK39 negativity but high clinical suspicion for VL should also undergo bone marrow aspiration and any further required investigations for confirmation of diagnosis, as coinfected patients may be rK39 negative but harbouring the infection.

• Atypical disseminated leishmaniasis is an AIDS defining illness (WHO clinical stage IV). However, VL is not defined as such in Indian national HIV/AIDS programmes (unlike in Africa, Brazil, Kenya and Sudan). The group recommended that this issue be discussed further with the National AIDS Control Organisation and WHO.

• Although VL is not recognized as an AIDS defining illness, the group recommended that as 79–97% of patients with VL will relapse if not started on ART, all coinfected patients should start ART irrespective of their CD4 counts. This recommendation will be discussed by the National AIDS Control Organization Technical Review Group on ART for approval.

• The group discussed dosing for AmBisome in coinfected patients, particularly in view of the RMRIMS-MSF study at Hajipur (Vaishali, Bihar). However, because control studies are not available it was decided to adopt the WHO recommendations on treatment of coinfected patients (40 mg/kg body weight as total dose, 3–5 mg/kg daily or intermittently for 10 doses, days 1–5, 10, 17, 24, 31 and 38).¹ AmBisome will be used in all 54 districts including in the four states where it is not proposed for use in treatment of visceral disease.

• Currently, there is insufficient evidence to recommend secondary prophylaxis. Moreover, there were concerns about resistance in cases of secondary prophylaxis because of the low dosages used.

• Treatment of VL should be started immediately. ART should begin after 7–10 days once patients have been adequately counselled and prepared for life-long ART.

A strong coordination mechanism should be established between the National AIDS/Sexually Transmitted Infections Control Programme and the National Vector Borne Disease Control Programme at national and state levels in these four states. Monitoring and evaluation tools are needed to ensure proper coordination in tracking coinfected patients and facilitating regular reporting (along the lines of the coordination mechanism for HIV–TB coinfection).

Because coinfected patients will have multiple relapses even after HAART, retreatment with AmBisome (40 mg/kg) is the best option. Currently, there is no recommendation for combination therapy and further evidence is needed.

Implementation research for management of coinfection with *Leishmania* and HIV should be undertaken as per the WHO recommendations.

**Discussion and comments**

*On Leishmania and HIV coinfection*

Further information is needed on treatment of coinfection with high-dose AmBisome.

Screening of HIV and kala-azar is scalable in Bangladesh and Nepal.

*On PKDL*

Delhi is not endemic for kala-azar and the number of PKDL cases is not decreasing. One state has reported a case of cutaneous leishmaniasis. PKDL cases are reported also from non-endemic districts. PKDL cases pose an important challenge to VL elimination. More work on, and evidence for, the treatment of PKDL are required.

The number of PKDL cases is increasing in West Bengal, which warrants further study.

PKDL should be the priority; in one outbreak it was suspected to be the source of infection. The tools for diagnosis are inadequate. A PKDL consortium has been formed. Treatment with high-dose AmBisome has more side-effects than the low dose. MSF is conducting a study on low-dose AmBisome.

There is a need to generate more evidence on PKDL.

There is a huge gap in treatment of PKDL.

There are many unknowns regarding PKDL cases. Are all forms of PKDL responsible for transmission? How long and when do PKDL cases transmit the infection? What treatment regimen will help reduce infectivity?

Even if there is no evidence for what form of PKDL is infectious, such cases should be treated.

The health system and primary health-care services should be able to detect PKDL.

*On vector control*

Environmental measures and sanitation are important considerations for elimination. There is no evidence on the effectiveness of larvicides for VL control.
WHO recommends against switching from one synthetic pyrethroid to another (Nepal is switching from alpha-cypermethrin to deltamethrin for indoor residual spraying) because of the potential for cross-resistance to insecticides.

If there is resistance to alpha-cypermethrin, then there will be also resistance to deltamethrin.

Resistance to the insecticides used in indoor residual spraying may develop over time, spray operators may become fatigued and spraying is expensive.

Indoor residual spraying is effective in reducing vectors and their density. Evidence is available.

*On programmatic issues*

Working with other public health programmes such as malaria control also benefits VL elimination. In countries or areas with fewer cases, there should be early follow up.

Health screening of labour migrants with rK39 can be beneficial for early case detection.

Leprosy and VL are coendemic in some areas in Bangladesh, where combined searches should be done. Pharmacovigilance is important.

The Programme is based on incidence. What happens after elimination? Should the target be no case or no transmission? What should the strategies and target be for the next planning period?

The next target should be no case and no new case should be the indicator. An active surveillance system should be in place to detect cases.

Expertise on kala-azar should be preserved. Work should begin on post-elimination strategies and how to sustain elimination.

*On epidemiological surveillance*

There is a need to improve the notification system. Visceral leishmaniasis should be made a notifiable or reportable disease. An early warning system should be in place to detect cases early.

The numbers of foci should be taken as target indicators instead of the numbers of blocks, upazilas or districts.

The number of VL cases is decreasing in Nepal and the pattern of its distribution is changing, with cases being reported from hilly districts. Repeated outbreaks have been reported from some endemic areas where vector control activities are inadequate. Surveillance must be strengthened.

The second half of the session was chaired by Dr Shamsuzzaman (Bangladesh).
3.3 WHO – independent monitoring of indoor residual spraying in India

Dr Saurabh Jain reported on independent monitoring of the first and second rounds of indoor residual spraying carried out in 28 341 and 21 731 houses respectively in 2014. The monitoring involved 3591 squads in total.

Method

- Monitoring of preparedness at state, district and block levels
- Concurrent monitoring of spray squads
- Post-activity monitoring of sprayed villages
- Real-time feedback to district and state level for corrective actions
- Feedback to the Government of India.

The monitoring was done in 728 blocks of 65 districts, where 50 427 houses and 3615 spraying squads were monitored in both rounds.

Areas of improvement

- Fund flow at district level: 64% funding (first round); 59% funding (second round). Funds released to primary health-care centre level: just over 20%
- Micro-planning: available in 88% of districts; 76% and 89% of primary health-care centres had functional pumps for each squad during the first and second rounds.
- Spraying: uniform spraying
- Training
- Supervision
- Community awareness and participation.

Issues

- Low coverage
- Spray quality
- Number of cases increasing in some blocks
- Data on vector.

AmBisome rollout: a national roadmap is available.

Issues

- Cold chain
- Training
- Treatment of coinfection with HIV.

Partners in the Indian Programme organized a meeting in November 2014 involving government, WHO and partners at which the national roadmap and plan of action for the four states were presented and discussed.
3.4 WHO – indoor residual spraying for leishmaniasis control

Dr Rajpal Yadav identified the three criteria to ensure efficient indoor residual spraying against VL: when, what, and how to apply? The three requirements are: operators, application equipment, and insecticide formulation.

Application equipment
Stirrup pumps and compressor pumps. Stirrup pumps apply constant pressure. Errors may occur at various stages of spraying. Sources of application errors include: mixing and calibration errors leading to incorrect dosing; worn nozzles; pressure variation at nozzle; speed of spray lance (target speed is 0.44 m/sec); distance from wall and runoff (should be 45 cm from the wall); tank settling due to poor formulation; and poor maintenance of sprayers.

Existing field practices can be improved by fitting a control flow valve or other regulating device, and ceramic nozzle tips. Sprayers with control flow valves reduce operator load and fatigue. A comparison of discharge rates of pressure sprayers has shown better performance with ceramic nozzle plus control flow valve than brass nozzle and new ceramic nozzle alone.

New developments and technologies such as insecticides in water soluble bags, new PPEs and laser beams were also discussed. Water soluble bags are easy to calibrate and handle and for mixing, and reduce risks to operators and the environment.

Participants were informed of the availability of WHO resources on indoor residual spraying and insecticides. CDs were distributed at the meeting.

3.5 CARE India – elimination activities in Bihar, Jharkhand and West Bengal

Dr Sridhar presented the progress made during the past 6 months in domains supported by CARE India.

In 2014, more than 19 000 households from approximately 1000 villages in 24 districts (40 villages from each district) were monitored for indoor residual spraying in Bihar, India. The monitoring investigated households visited by spray squads versus households actually sprayed, and explored the reasons for non-spraying. Spraying was refused in 23% of households. Other reasons for non-spraying or partial spraying included perceptions of spraying (staining of walls, smell of insecticides, increase of leeches rather than reduced problems of mosquitoes or insects); food materials kept in rooms; no male members and adults at home; houses or rooms locked; households not informed on time; and houses under construction.

Insecticide-related and vector bionomics studies are planned for entomological surveillance in Bihar (6 sites), Jharkhand (1 site) and West Bengal (1 site). Teams are already on the ground in Bihar, trained and collecting data. Preliminary data suggest around 50% susceptibility to DDT; testing for deltamethrin is under way.

Case recording and tracking formats have been revised and are in use in most blocks of Bihar and Jharkhand, online reporting of line-listed cases is starting, and mapping through geographical information systems is planned. Pharmacovigilance is being layered on by PATH.
The CARE team is on track to complete a validation exercise across Bihar and Jharkhand by mid-2015.

3.6 Bill & Melinda Gates Foundation – elimination activities in Bihar

Dr William Starbuck presented the progress of VL elimination in Bihar, India during the past 6 years. Human resources and commodities (drugs, rapid diagnostic tests and insecticides) are available in primary health-care centres, patients are presenting at centres, more than 13 000 accredited social health activists have been or are being trained, and incentive payments have been introduced. Vector-borne disease consultants and kala-azar technical supervisors are present in most districts as well as CARE district programme officers and link workers. The presence of laboratory technicians has improved across all districts. Microplans are up to date.

Funds are in place and more than 3000 new stirrup pumps provided by CARE are in use within Bihar. Miltefosine tablets and liposomal amphotericin B (single infusion) are being used for treatment. There is active partner cooperation and information-sharing. National and Bihar VL elimination roadmaps are in place, together with active support from the NVBDCP (Ministry of Health, Government of India) and key Government of Bihar officers. Spray teams are paid more regularly. Better training is given to the spray squads. Monitoring has improved, district magistrates now include VL in their monthly district task force reviews; and district medical officers are now accountable for coverage and quality of indoor residual spraying.

Discussion

On vector control

The number of spraying rounds depends on the length of transmission. The active ingredient of insecticides lasts for 6 months. One round of spraying before the rainy season is important.

The choice of insecticides should be made on the basis of susceptibility studies. If cattle sheds are sprayed then households should be sprayed with the same insecticides. The insecticide should be switched if there are early indications of resistance.

The quality of spraying is essential. There is a need for improved spraying and monitoring. The regulatory body for insecticides/pesticides is independent in Nepal, so approval is difficult. Nepal has two transmission seasons and two rounds of spraying are done using Hudson pumps.

3.7 KalaCORE – control and elimination of visceral disease

Dr Sakib Burza presented the work of the KalaCORE consortium in supporting control and elimination of VL.

The UK Department for International Development has funded an initiative of UK£ 27 million to assist elimination and control. The KalaCORE Consortium was awarded the bid. Its members include:

- the Drugs for Neglected Diseases initiative
- the London School of Hygiene and Tropical Medicine
- Médecins Sans Frontières
- Mott McDonald.
**Two regions**

– Africa: Ethiopia, South Sudan, Sudan
– South Asia: Bangladesh, India, Nepal

**Current status**

• Inception report approved January 2015
• Procurement approval expected in next weeks
• Start of global implementation slightly delayed; expected shortly
• Crucial activities have already begun
  – roll out of liposomal amphotericin B in India
  – preparation for support of passive pharmacovigilance.

**Planned project for India**

• Support training, upgrading and implementation of liposomal amphotericin B across three states.
  – District hospital-level training in 24 districts (completed in three states). Primary health care is planned (from February 2015 onwards).
  – More than 320 patients have been successfully treated so far.
  – Coordination with WHO AmBisome donation; roadmap plans are ongoing.
• Develop pharmacovigilance capacity within the National Pharmacovigilance Programme of India.
  – It is important to develop regional data for introduction of new regimen.
  – There are two projects: one supporting passive pharmacovigilance, the other focusing on active pharmacovigilance and sentinel surveillance.
• Strengthen active case detection strategies for PKDL and VL across highly endemic districts in Bihar and Jharkhand.
  – Recent comprehensive active case detection showed a ratio of 70:30 PKDL in West Bengal state
  – The epidemiological pattern is similar to that in Bangladesh, with falling VL incidence.
  – “Prevalence mop-up” is urgently required in Bihar and Jharkhand.
• Implement a comprehensive and innovative information, education, communication and behaviour change communication strategy for VL and PKDL across endemic districts in Bihar and Jharkhand.
  – Build on existing work from the World Bank; implement in mission mode.
  – Include information, education and communication on indoor residual spraying.
• Provide cascade training of accredited social health activists across endemic districts.
• Identify and train or initiate private care practitioners into elimination mode.
• Build capacity and skills of state epidemiologists and surveillance officers in surveillance, project management, and monitoring and evaluation.
• Second monitoring and evaluation and skilled human resources support for government facilities.
  – Central, Bihar and Jharkhand state and district-level support.
• Assess the quality of indoor residual spraying with insecticide quantification kits.
  – Work alongside CARE to develop sustainable monitoring of spray quality within the Programme.
• Improve access to diagnosis, treatment and improved information-sharing across trans-border areas.
  – Lessons learnt; ensure no opportunity is missed.

**Planned project for Bangladesh**

• Develop, pilot and scale up information, education and communication as well as behaviour change communication activities.
• Train front-line health workers.
• Build capacity at the Surya Kanta Kala-azar Research Center (SKKRC) hospital.
• Support disease mapping and surveillance and understanding of spatial transmission patterns.
• Second an expert in monitoring and evaluation to the national programme.

**Planned project for Nepal**

The main focus will be on training and surveillance support.
• Train district public health offices, vector control officers and female community health volunteers.
• Develop an information, education, communication and behaviour change communication strategy.
• Strengthen outbreak investigation response.
• Sustain medical entomology capacity.
• Provide direct monitoring and evaluation support to the Epidemiology and Disease Control Division.

**Operational research**

A number of areas will be focussed on across the Region:
• Gender bias and marginalized populations in access to care.
• Demonstration of the utility of insecticide rotation for indoor residual spraying.
• Development of standards for drug susceptibility monitoring and classification.

3.8 **Special Programme for Research and Training in Tropical Diseases – research on case detection and vector control in Bangladesh, India and Nepal**

Dr Pierro Olliaro summarized the ongoing support provided to the Programme in Bangladesh, India and Nepal through research on improved case detection and vector control.

In 2014, four “chronic fever” camps – a combined camp approach as an active case detection strategy – were organized in highly endemic villages or communities of the three countries. The camp team visited the identified communities to conduct camps after awareness activities with the support of local health functionaries and community volunteers. The fever camp approach adopted the following operational definitions, methods and tools: fever + spleen enlargement + rK39 = VL; rapid diagnostic test for malaria (Nepal only), suspected tuberculosis cases were referred to the district hospital for sputum smear, photographs of leprosy were used to distinguish them from PKDL, and existing bednets were impregnated with slow-release insecticides.
Two new VL cases, 2 PKDL cases, 2 leprosy cases and 2 TB cases were detected among 120 fever cases screened in the fever camp.

Considerable delays were observed within health services. In India and Nepal, delays occurred in patients presenting for and receiving treatment. A follow up study in Bangladesh and Nepal is in preparation.

In a sandfly mortality by intervention study, reduction of VL vector densities showed the same pattern: indoor durable wall lining was most effective even when covering only half of the wall.

3.9 Drugs for Neglected Diseases initiative – elimination initiatives in South Asia

Dr Suman Rijal explained how the Initiative is supporting the Programme in South Asia.

Short-course multidrug treatment randomized controlled trial
A total of 634 patients were enrolled in a randomized controlled trial in 2008 and 2009. Three potential short-term regimens were compared with standard monotherapy. The trial concluded that combination treatment is efficacious and safe, encourages adherence to treatment and reduces the emergence of drug resistance.

Combination treatment Phase III trial
A Phase III, open label, randomized and non-inferiority study on a combination regimen was carried out in Bangladesh between 2010 and 2012. A total of 602 patients were enrolled in the study. A 99.4% final cure rate at 6 months was observed with the combination regimen of liposomal amphotericin B and paromomycin. The finding of the study has been shared with the Government. The combination regimen has yet to be adopted.

Field level pilot project
A pilot project on “Safety and effectiveness of new treatment modalities at field level in India (2011–2014)” was done. Based on the findings of the study, the National Vector Borne Disease Control Programme of India has revised its drug policy to include single-dose liposomal amphotericin B as the first treatment choice and the combination of miltefosine and paromomycin as the second treatment of choice.

DNDi continues to support the rolling out of single-dose AmBisome as per the national roadmap for elimination of kala-azar (KalaCORE, MSF); generate data on long-term relapse (12 month follow-up) on the cohort of 1102 patients treated in the pilot study, and PKDL occurrence within 24 months of follow up; support treatment facilities for second choice treatment (miltefosine and paromomycin); strengthen active pharmacovigilance through sentinel sites including documentation of long-term outcome as per the national programme guidelines and establishment of drug sensitivity monitoring of the parasite at the Rajendra Memorial Research Institute of Medical Sciences in Patna.

However, there is evidence of increased relapse even after 6 months of treatment. An expert committee recommended generating evidence of 12-month outcomes in a Phase I study. Results are expected in the second quarter of 2015.

A cohort longitudinal study on the occurrence of PKDL with different regimens, infectivity studies, pharmacokinetics in skin and clinical trials for better regimens is planned. A Phase II clinical trial of three treatment regimens to assess the safety and efficacy of treatment in India and Bangladesh with
AmBisome monotherapy and combination therapy (AmBisome and miltefosine) is ongoing. These studies will provide additional data and evidence on the treatment of PKDL.

3.10 Médecins Sans Frontières – update on activities in Bangladesh and India

Dr Koert Ritmeijer summarized MSF’s engagement with VL elimination in India (since 2007) and in Bangladesh (since 2010) as well as its core membership of KalaCORE (since September 2014). In India, MSF works in collaboration with the Rajendra Memorial Research Institute and the National Vector Borne Disease Control Programme.

From 2007 to 2014, the cure rate was 99.3% among 8752 VL patients treated with AmBisome (20 mg/kg), of whom 0.3% passively returned with PKDL after treatment.

The response to treatment with liposomal amphotericin (30 mg/kg body weight) for PKDL in India therefore appears to be safe and effective.

RMRI and MSF have proposed a randomized clinical trial comparing liposomal amphotericin B (40 mg/kg) and combination liposomal amphotericin (30 mg) plus miltefosine (100 mg) for 14 days.

Control of VL started in Bangladesh in 2010 in two upazilas. AmBisome treatment (15 mg/kg; 3 x 5mg/kg on day 0, 1 and 5) shows a cure rate of 96.4% at 12 months. PKDL is treated with AmBisome (30 mg/kg; 6 x 5 mg/kg over 3 weeks).

Conclusions
- Demonstration of safety and effectiveness of AmBisome treatment of VL in routine programme settings (hospitalized and ambulatory).
- Development of evidence for safe and effective ambulatory treatment of PKDL with short-course AmBisome.
- Demonstration of evidence for safe and effective treatment of HIV–VL coinfection.
- Contribution to operational and clinical research in collaboration with partners.
- Contribution to elimination of VL with integrated activities: active VL and PKDL case detection and treatment free of charge, and support to vector control (indoor residual spraying).

3.11 International Centre for Diarrhoeal Disease Research, Bangladesh – activity update

Dr Dinesh Mondal provided an overview of the Centre’s work with partners to eliminate kala-azar in Bangladesh and a snapshot of ongoing activities.

- The Centre contributes to the Programme mainly through research and capacity building. Areas of research encompass epidemiology, diagnostics, clinical trials, vector studies and nutrition. The extensive network of partners works in close collaboration with the national programme.
- Current activities include:
  - An observational study for development of PKDL and VL relapse: cohorts of patients treated with different treatment regimens are being followed up. In a cohort of 289 cases
treated with single-dose liposomal amphotericin B for 24 months, the cumulative incidence of relapse was 3.6% for VL and 13% for PKDL.

- Strengthening the surveillance system of kala-azar by conducting an operational study to understand the feasibility of web-based surveillance within the health system. This will also be expanded to include pharmacovigilance. The training has been completed and it is currently being piloted in a few upazilas.
- Web-based surveillance is one of the important tools being studied in Bangladesh to strengthen surveillance of kala-azar.
- A study of the safety and cure rate of miltefosine in allometric dose for PKDL treatment in children and adolescents and to investigate association of nutritional and environmental factors with PKDL is ongoing.
- Studies on vector density and its correlation with climate variables. Regarding different environmental conditions acting as risk factor for kala-azar, studies in Bangladesh have demonstrated that humidity is significantly associated with increased density of the vector.

Indoor house lining has reduced the burden of kala-azar after use of long-lasting insecticide-treated nets. The Indian and Nepalese Programmes could consider using this intervention to control or sustain elimination.

3.12 Liverpool School of Tropical Medicine – collaborative work on vector control

Professor Janet Hemingway presented the School’s work on vector control in India, which is being carried out in association with RMRI, ICMR Institute, Bihar and CARE India.

The issues for indoor residual spraying with DDT are:

- the proportion of DDT used; ideally it should be 75%
- the isomers of DDT; one of the two isomers is inactive
- sedimentation rate of DDT
- susceptibility of DDT to insecticides.

Some recent activities undertaken in Bihar include subjecting five samples from different places to the HPLC method; none qualified as per WHO recommendations. Chemicals used as insecticide showed a faster sedimentation rate than WHO recommendations.

Communities contacted during the second round of indoor residual spraying in Bihar (September–November 2014) have reported improved coverage than during the first round (May 2014).

Sampling in 2000 houses has shown less than the one third of the recommended concentration of DDT on the sprayed walls. It was also observed that only 30% of the structures were sprayed.

The recommended dose of DDT in India is 1 g/m², in this case less than 0.3 g/m². There is enough circumstantial evidence of DDT resistance in Bihar that it is not confined to smaller areas but has a wide geographical spread.

In the present scenario DDT should be the last insecticide to be used in the public health programme when no other chemical is available.

Professor Hemmingway also mentioned the need to change spray pumps from the stirrup types to the WHO-recommended hand compression pumps. Stirrup pumps are less safe for users than hand
pumps and the chances of spillage with insecticide are greater. Also because chemical is sprayed on the wall there is more wastage.

3.13 Genesis Laboratories, Inc. – treatment of cattle to control sandflies

Richard Poche presented an initiative to control sandflies by treating cattle with systemic drugs.

- A new research concept aims to interrupt transmission of by treating cattle with fipronil. Cattle are an important source of blood meals for sandflies. The insecticide kills the adult vectors and hence plays an important role in the life-cycle of the sandfly.

- Laboratory experiments using insecticide-fed rodents to control ticks have been successfully demonstrated. More than 20 insecticides and insect growth regulators have been screened.

- The control of sandfly vectors in kala-azar transmission takes the following into consideration: cattle are a source of sandfly blood meals; treatment of cattle to deliver drug to eliminate vector adults is feasible; sufficient drug is eliminated in cattle’s faeces to kill sandfly larvae; therefore, a reduction in the sandfly density will reduce the number of cases of VL.

- Research has already shown that proximity of humans to cattle is major risk factor for VL and that more than 50% of sandfly blood meals are from cattle. Sandflies are capable fliers and are more peri-domestic than previously thought. Pilot field studies have shown a reduction in sandfly numbers when treating cattle with fipronil. Modelling sandfly control shows good potential in VL reduction by treating cattle with fipronil.

- The planned research in 2015 includes:
  - Conducting a dynamics study of VL in endemic villages in Bihar and evaluating the impact of disease elimination efforts in those villages.
  - Assessing the treatment of livestock with fipronil on sandfly density and Leishmania seroconversion of populations after application.
  - Conducting an animal safety and performance study on lactating cows and buffalos.

3.14 Institute of Tropical Medicine – activity update

Dr Epco Hasker presented the Institute’s involvement in research on leishmaniasis and the results of a collaborative study in Nepal on visceral disease.

- The Institute is engaged in the following areas of research:
  - evaluation of diagnostics (DAT, rK39, rK28) for visceral disease and markers for asymptomatic infections;
  - effectiveness of chemotherapy: resistance vs treatment failure;
  - effectiveness, cost and acceptability of new vector control methods; and
  - elimination: how to strengthen surveillance systems?

- Following increased reports of VL cases from non-endemic areas and hills in Nepal the Institute, along with the B.P. Koirala Institute of Health Sciences and WHO, conducted a recent study on “VL in new econiches: outbreak investigation in hill districts Nepal”. The key findings of this study showed:
– strong evidence for ongoing transmission of *L. donovani* in the hilly regions of Nepal considered hitherto as non-endemic;
– associations with local risk factors;
– cases among persons who had never travelled;
– no association with travel to endemic areas; and
– presence of *Phlebotomus argentipes* and of *L. donovani*.

3.15 NTD Modelling Consortium – key questions

Dr Deirdre Hollingsworth highlighted the Consortium’s ongoing work to address the questions: “Are we on track for the 2020 goals with the current strategies? If not, what other strategies will be required, and where?”

- The role of infectious disease modelling in public health policy could be helpful in:
  – modelling for public health policy on neglected tropical diseases;
  – frequency and timing of mass drug administration;
  – interpreting diagnosis data;
  – identifying the role of vector control; and
  – understanding what makes good modelling.

- The two modelling groups for VL are (i) Erasmus MC Rotterdam and (ii) Warwick University and the Liverpool School of Tropical Medicine.

- The four main types of intervention that can affect the transmission cycle are:
  – early and appropriate treatment of cases
  – vaccination to prevent susceptible patients from being infected
  – bednets by decreasing human biting rates
  – vector population control by decreasing its numbers and life expectancy.

- The plans for 2015 include:
  – January: review of previous modelling results
  – By end of March: initial analyses
    - Warwick/Liverpool – diagnostics
    - Erasmus – role of asymptomatic cases and PKDL in transmission
    - Analysis of case data
      ▪ in partnership with CARE India
      ▪ characterize patterns of diagnosis over time
      ▪ investigate variability between villages
  – By end of year one: can the goals be reached using the current tools?

3.16 Erasmus MC – update on modelling visceral disease in South Asia

Dr Epke Le Rutte presented the initial findings of modelling on VL and the two main conclusions: (i) screening of asymptomatic cases is ineffective in elimination; and (ii) the role of PKDL in elimination should be ascertained.
4. Summary of group work and recommendations

4.1 Vector control

During the meeting the break-out groups deliberated various issues.

- Blanket spray vs focal spray vs reactive spray vs withdrawal of spray in the Programme
  - Data on regional practices and evidence from reactive spray from malaria programmes.

- Cross-border issues of synchronization of spray activities in terms of compound used and timing of spray on both sides of border.

- Implementation of indoor residual spraying
  - Best practices for quality need to be documented.

- Funding, compliance and remuneration issues in operationalization of spraying activities

- Optimizing insecticide selection
  - DDT resistance is reported from various parts of Bihar, India. It is a reasonable assumption that such resistance is widespread and not focal. In the light of resistance to DDT and the excellent results from other chemicals such as deltamethrin there is a need to switch to other insecticides in India as soon as possible. This can be a key factor in elimination not only in India but also in the South-East Asia Region as Nepal and Bangladesh are also using alpha-cypermethrin and deltamethrin respectively in the spray programme.
  - At present, no viable compounds other than DDT are registered for sandfly control in India; there is an urgent need to register other compounds at the earliest.

- Additional vector control activities
  - Wall lining studies have proved to be useful in the control of sandflies.
  - Other methods of systemic use of insecticide through animals are also being explored.
  - A vector advisory group could be constituted to build and put forth evidence.

During the plenary the need for management of insecticide resistance was stressed. Various options – rotational use of insecticides, mosaic approach – are available to reduce the risk of resistance.

It is well accepted that a decrease in vector density is directly related with less risk for and less occurrence of VL. There is no clear cut evidence as to how many spray rounds are sufficient in a public health programme to control and eliminate sandfly vectors. It was mentioned that the Joint working group of India and Bangladesh in prevention, control, elimination and eradication of communicable diseases is sharing the necessary information about disease trends, outbreaks and other interventions in respective countries.

4.2 Case detection

Fever camps are considered to be resource intensive with little yield (e.g. only 1% of all cases in Bihar, India were diagnosed in camps). The camp approach depends on four main factors: (i) the level
at which it is organized, e.g. whether at village or sub-health centre or primary health centre; camps can be combined with screening for other diseases and programmes; (ii) the frequency of camps, e.g. whether annual, quarterly or monthly; (iii) the timing of camps, e.g. organization of camps coinciding with the peak of cases, i.e. March–April and October–November in Bihar, India; and (iv) the capacity of health personnel present during the camp, e.g. medical officers or trained paramedics or laboratory technicians at the camp.

An incentive approach for case detection is important and the role of community health volunteers, e.g. accredited social health activists in India, is key to improving case detection. Although such activists are important in referring suspects, the shifting of tasks for use of rapid diagnostic tests cannot be delegated as for malaria because kala-azar patients must be examined for spleen enlargement and test results remain positive in cured patients for some time after completion of treatment. Activists can best be engaged in generating awareness, referring suspects and following up patients.

Such an approach can also enhance case detection provided messages are communicated to vulnerable communities and patients and at all levels of health functionaries.

At present, it is not possible to estimate the burden of infection with serological tests.

The integration of PKDL case detection in leprosy elimination programmes was discussed. Leprosy is a major public health programme and resources and systems are available in areas where kala-azar is coendemic. It was noted that PKDL, although important as a reservoir, is a cosmetic condition and it is important to strengthen the capacity of health systems to sustain surveillance in scenarios of declining disease trends.

It was proposed that WHO invite organizations to submit data related to kala-azar and other leishmaniasis conditions. The group observed that cases of PKDL would be missed using the camp approach as camps focus more on fever cases and PKDL is a benign skin condition. Ideas about using spray squads during spray rounds or before indoor residual spraying searches could be explored.

4.3 Case management and treatment

Case management of VL was discussed country by country. Recommendations were made as follows.

4.3.1 India

- First treatment option: single-dose liposomal amphotericin B
- Second treatment option: combination paromomycin–miltefosine
- Lipid-based emulsions of amphotericin B are **neither** included in the WHO list of prequalified medicines, nor in the WHO Model List of Essential Medicines.

Information about procurement and manufacturers of drugs used in combination regimens such as miltefosine and paromomycin is available on the WHO website. The group recognized the challenges in procurement.

4.3.2 Bangladesh

- First treatment option: single-dose liposomal amphotericin B
- Second treatment option: combination paromomycin–miltefosine
– paromomycin is not registered in Bangladesh and is not considered an issue.
– miltefosine procured by the national programme is of inferior quality; this issue needs to be addressed.

4.3.3 Nepal

- First treatment option (in pipeline): single-dose AmBisome
  - WHO and KalaCORE have agreed to provide the support needed for roll out.

- Second treatment option: combination paromomycin–miltefosine

4.4 Drug forecasting (Bangladesh, India and Nepal)

WHO and KalaCORE will provide estimates of drug forecasting to national programmes.

4.5 Pharmacovigilance (Bangladesh, India and Nepal)

The need for high-quality pharmacovigilance (passive and active) has been identified and requires implementation.

5. Case management of post kala-azar dermal leishmaniasis

5.1 India and Nepal

First treatment option: miltefosine, 100 mg/day, orally for 12 weeks for patients weighing > 25 kg; 50 mg orally per day for 12 weeks for patients weighing < 25 kg, with appropriate counselling.

Second treatment option: liposomal amphotericin B (5 mg/kg per day by infusion two times per week for 3 weeks for a total dose of 30 mg/kg) as per WHO Kolkata meeting (i.e. in district hospitals where monitoring is available).¹

5.2 Bangladesh

First treatment option: miltefosine, 100 mg/day, orally for 12 weeks for patients weighing > 25 kg; 50 mg orally per day for 12 weeks for patients weighing < 25 kg, with appropriate counselling.

Second treatment option: liposomal amphotericin B (15 mg) subject to pending results as per Médecins Sans Frontières’ guidelines (i.e. in district hospitals where monitoring is available).

To date no natural resistance to miltefosine has been reported and there are no molecular markers as yet for drug resistance. KalaCORE is willing to undertake drug susceptibility studies. In all three endemic countries a laboratory network for drug resistance is required as for the poliomyelitis laboratory network. WHO is willing to collaborate and work with these laboratories for drug resistance.

6. **Drug procurement**

Countries and partners should ensure timely procurement of quality-assured drugs and products to avoid any rupture of stock.

7. **Research on post kala-azar dermal leishmaniasis**

The meeting identified the following needs for research on PKDL:

- Fast-track studies of infectivity to determine which patients should be treated.
- A new clinical trial of short duration treatments to determine end-of-cure time-points.
# Annex 1.  Agenda

**Tuesday, 10 February 2015**

**MODERATOR:** Dr A.C. Dhariwal, Director NVBDCP, DGHS, MOHFW, India

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<td>Registration</td>
<td>Participants</td>
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<td>09:00–09:15</td>
<td>Opening of the meeting and welcoming remarks</td>
<td>Dr Dirk Engels, Dr Jean Jannin</td>
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<td>09:15–09:30</td>
<td>Objectives of the meeting and Summary of the first meeting in London</td>
<td>Dr Daniel Argaw Dagne</td>
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<td>09:30–09:40</td>
<td>Status of KAEP in SEAR and key activities for 2015</td>
<td>Dr R. Bhatia</td>
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<td>10:00–12:30</td>
<td>STATUS OF KAEP – COUNTRY UPDATES</td>
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<td>10:00–10:30</td>
<td>India</td>
<td>Dr A.C Dhariwal</td>
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<td>10:30–11:00</td>
<td>Bangladesh</td>
<td>Prof. A.K.M Shamsuzzaman</td>
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<td>11:00–11:30</td>
<td>Nepal</td>
<td>Dr Babaram Marasini</td>
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<td>11:30–12:00</td>
<td>VL–HIV coinfection in India</td>
<td>Dr Sakib Burza</td>
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<td>12:00–13:00</td>
<td>Discussion</td>
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**MODERATOR:** Professor A.K. Shamsuzzaman, Director CDC, DGHS, MOHFW, Bangladesh

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<td>14:00–14:15</td>
<td>IRS independent monitoring and AmBisome roll-out</td>
<td>Dr Saurab Jain</td>
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<td>14:15–14:30</td>
<td>RMKI</td>
<td>Dr Pradeep Das</td>
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<td>14:30–14:45</td>
<td>Applications of IRS for leishmaniasis vector control</td>
<td>Dr R. Yadav</td>
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<td>14:45–15:00</td>
<td>Care, India/Bill &amp; Melinda Gates Foundation</td>
<td>Dr Sridhar Srikantiah/Dr W. Starbuck</td>
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<td>15:00–15:30</td>
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<td>16:00–16:15</td>
<td>KalaCORE (DFID VL consortium, South Asia)</td>
<td>Dr Sakib Burza</td>
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<td>16:15–16:30</td>
<td>WHO/TDR</td>
<td>Dr P.L. Ollario</td>
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<td>16:30–16:45</td>
<td>DNDI</td>
<td>Dr Suman Rijal</td>
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<td>16:45–17:30</td>
<td>MSF experience update in India and Bangladesh</td>
<td>Dr Koert Ritmeijer</td>
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**Wednesday, 11 February 2015**

**MODERATOR:** Dr B. Marasini, Director EDC, MOHP, Nepal

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<td>09:00–09:10</td>
<td>ICDDR,B</td>
<td>Dr Dinesh Mondal</td>
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<tr>
<td>09:10–09:20</td>
<td>LSTM</td>
<td>Professor Janet Hemingway</td>
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<td>09:20–09:30</td>
<td>ITM</td>
<td>Dr Epc Hasker</td>
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<tr>
<td>09:30–09:40</td>
<td>BHU, NIAID, NIH</td>
<td>Dr Shyam Sundar</td>
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<td>09:40–09:50</td>
<td>Genesis Laboratories, Inc.</td>
<td>Dr Richard Poche</td>
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<tr>
<td>09:50–10:00</td>
<td>VL modelling – South Asia update</td>
<td>Dr Epke Le Rutte</td>
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<td>10:00–10:10</td>
<td>NTD modelling consortium – VL work</td>
<td>Dr Deirdre Hollingsworth</td>
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<tr>
<td>10:10–10:30</td>
<td>Discussion</td>
<td>Participants</td>
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<td>11:00–13:00</td>
<td>Group work</td>
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<tr>
<td>14:00–15:00</td>
<td>Group presentations</td>
<td>Participants</td>
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<tr>
<td>15:00–16:00</td>
<td>Plenary discussion on the group presentations</td>
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<tr>
<td>16:30–17:00</td>
<td>Plenary discussion wrap up and closing</td>
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</tbody>
</table>
Annex 2.  List of participants

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LEISHMANIASIS

KALA-AZAR ELIMINATION PROGRAMME

REPORT OF A WHO CONSULTATION OF PARTNER
GENEVA, SWITZERLAND
10–11 FEBRUARY 2015

World Health Organization