

# **Report of Meeting on Sentinel Surveillance for Drug Resistance in Leprosy**

**22–23 August 2011, Hyderabad, India**



**World Health  
Organization**

Regional Office for South-East Asia

# Meeting on Sentinel Surveillance for Drug Resistance in Leprosy

*A Report*  
*22-23 August 2011, Hyderabad, India*

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## 1. Background

The fight against leprosy has been a great success largely due to the development of multidrug therapy (MDT) in 1981. Resistance to dapsone has been reported since the late 1960s but convincing data supporting the existence of clofazimine-resistant strains of *M. leprae* have not been reported. . Since rifampicin is the backbone of MDT, it is important to monitor the emergence of rifampicin-resistant mutants.

In addition, several new anti-mycobacterial drugs are either under development or are in the market against other infections. The emergence of drug resistance is a concern and a threat for many disease control programmes, especially when secondary prevention (chemotherapy) is the main component of the control strategy. To meet the challenge of containing the disease and to sustain the declining trend of leprosy in endemic countries, it is essential to keep a vigil on drug sensitivity patterns in leprosy-endemic communities.

## 2. Objectives

The objectives of the meeting were:

- to review the drug resistance surveillance data;
- to review trends in relapses reported by the national programmes; and
- to discuss recent advances in techniques for diagnosing drug resistance and in therapy for drug resistant cases.

## 3. Opening session

Opening remarks were made by Dr V. M. Katoch, Director-General, Indian Council of Medical Research (ICMR) and Dr Myo Thet Htoon, Team Leader, WHO Global Leprosy Programme.

Professor Emmanuelle Cambau, Department of Bacteriology and Hygiene, Faculty of Medicine, Paris, France was nominated as chairperson and Dr Vijayalakshmi Valluri from Blue Peter Public Health and Research Centre, Hyderabad, India and Dr Khin Saw Aye, Immunology Research Division, Department of Medical Research (Lower Myanmar) were nominated as rapporteurs.

A total of 40 participants including experts from the sentinel sites (Brazil, China, Colombia, India, Nepal, Mali, Madagascar, Myanmar, Philippines, Viet Nam and Yemen), researchers from the reference laboratories and partner organizations attended the

meeting. The programme and list of participants are provided in Annex 1 and Annex 2 respectively.

#### 4. Updates: 2010 surveillance activities

Dr Myo Thet Htoon updated the surveillance system data. In 2010-2011, there were 14 participating countries: Burkina Faso, Madagascar, Mali and Mozambique for African Region, Brazil and Columbia for American Region, Pakistan and Yemen for Eastern Mediterranean Region, India, Myanmar and Nepal for South-East Asia Region and China, Philippines and Viet Nam for Western Pacific Region. In addition, 10 reference laboratories were involved.

The current surveillance data are based on detecting drug resistant *M. leprae* in relapse cases of leprosy. Dr Myo Thet Htoon recalled the definition of a relapse case which was decided at the previous meetings: (1) the re-occurrence of the disease at any time after completion of a full course with WHO recommended MDT with (2) the appearance of definite new skin lesions and/or an increase in the bacteriological index of two or more units at any single site compared to the same site at a previous examination. The procedure is to seek for mutations in the *rpoB*, *folP* and *gyrA* genes from a skin sample (skin smear or biopsy) from a lesion with a BI of 2+ or above.

In 2010, reports were received from eight countries (China, Colombia, India, Myanmar, Viet Nam, Pakistan, Philippines, and Yemen). A total of 109 MB relapse cases were reported: 80 with a bacteriological index (BI) of 2 and more and 75 cases with new skin lesions. There were no child cases reported and a majority of relapses were among males (84%).

Of these 109 relapse cases, 88 were tested for drug resistance. DNA amplification was reported to be negative for dapsone in 16 and for rifampicin in 17 cases (18%), which is much less than in 2009. Results of resistance associated with gene mutations were the following: nine dapsone resistance cases and one rifampicin resistance. This resulted in 12.5% secondary resistance to dapsone (9/72 results of *folP* sequencing) and 1.4% secondary resistance to rifampicin (1/71 results of *rpoB* sequencing). No mutation of the *gyrA* gene associated to ofloxacin resistance was reported.

The definition of relapse was discussed, in order to increase the likelihood of including only "true" relapses and decrease the inclusion of cases of reversal reactions or those with high initial BI, who may remain smear-positive for some time after the completion of treatment with MDT.

## 5. Country presentations on relapse cases

### 5.1 Brazil

The source of the data presented by Dr Philip Suffys, was SINAN – National Information System of Communicable Diseases. Dr. Suffys mentioned that there were 1375 relapses reported during 2010. The male to female ratio among relapse cases was 1.82; majority of relapses were reported among MB cases (85%). Only about 1.4% were under the age of 15 years. The bacilloscopy results were available for 63.8% of the cases, of these 38.3% were positive. No resistant cases were observed among the relapse cases in 2010 compared in the period 2007-2008, where four cases with one strain mutated in *rpoB* only, one strain mutated in *folP1* and *rpoB* and two more strains with SNPs in *folP1*, *rpoB* and *gyrA* were detected as validated by Dr. Matsuoka's laboratory.

### 5.2 China

Dr Shen Jianping from the National Centre for Leprosy Control mentioned that China is detecting about 1500 new cases and about 150 relapses (after dapsone monotherapy and after MDT) are being reported every year since 1986. During 2010, 1324 new cases were reported. The number of relapses reported for the year was 96 (61 after dapsone monotherapy and 35 after MDT). The number of relapses in 2010 is much smaller than previous years due to efforts to improve the quality of relapse diagnosis and confirmation. Dr Jianping concluded by mentioning that WHO's recommendation of multidrug therapy regime is still effective for the treatment of leprosy. Thus, drug resistance in China may not be a serious problem.

### 5.3 Madagascar

Drug surveillance data from Madagascar was presented by Dr Ramarolahy Emerantien Benoit. The National Leprosy Programme was initiated in 1992 and the leprosy elimination goal was reached by 2006. The WHO drug surveillance study was initiated in 2011. A stable new case detection and prevalence rate was observed from 2006 to 2010. In 2010, 1521 new cases were detected of which 84% were MB cases. In 2010, eight relapse cases were reported and in the first half of 2011, 10 relapse cases were reported. Two relapse cases reported in 2011 were tested for drug resistance by applying molecular tools and were reported to be negative for PCR of *rpoB*, *folP* and *gyrA* genes. Both the cases were first diagnosed in 1977 and 1992 and reported as clinical relapse in 2011. Some of the problems mentioned were lack of capacity to collect samples at local level, delay in reporting from health centres and confusion between relapse and reaction. Future perspectives mentioned were establishing sentinel sites in larger centres, training of local health staff on sampling techniques, improving clinical information of relapse at local level and improving early reporting of relapse cases.

## **5.4 Mozambique**

Dr. Cynthia Sema presented the data on Mozambique and said leprosy is endemic in three provinces (Niassa, Cabo Delgado and Nampula) in north Mozambique. A decrease in prevalence was seen in these provinces from 2005 to 2010. Niassa province reported a decrease from 2.4 to 0.6; Cabo Delgado from 5.7 to 1.6 and Nampula reported a decrease in prevalence from 6.1 to 0.6. The national prevalence rate showed a decrease from 2.5 in 2005 to 0.5 in 2010.

New case detection rate showed a decrease from 24.8 to 6.5 in Niassa province, Cabo Delgado province showed a decrease in new cases from 2005 (57.8) to 2010 (17.7). In Nampula province there was a decrease in new case detection rate from 69.8 in 2005 to 7.2 in 2009 followed by a slight increase in new cases in 2010 (9). The national new case detection rate decreased from 27.7 in 2005 to 5.8 in 2010. Future perspective is to create and operate eight sentinel sites for the study of resistance to drugs used to treat leprosy throughout the country.

## **5.5 Nepal**

General information about Nepal was presented by Dr. Mahesh Shah, Anandban Hospital, Kathmandu, which was followed by drug surveillance studies presented by Dr Deanne Hagge the next day. The new case detection rate decreased from 1.5 in 2008/2009 to 1.12 in 2010/2011. Proportion of child cases was reported as 5.19 in 2010/2011. There was an increase in Grade-2 deformity from 2.72 in 2009/2010 to 3.47 in 2010/2011. Future perspectives include strengthening the referral centres; improving access of unreached groups, strengthening new case detection activities and an orientation programme on human rights for leprosy-affected people.

## **6. Technical discussion**

### **6.1 High throughout routine drug resistance surveillance in leprosy: present and future technologies**

Dr Varalakshmi Vissa presented the molecular tools she developed at the Department of Microbiology, Immunology and Pathology in Colorado State University. Each new or relapsed case is studied for genome strain typing by MVLA, SNPs detection or RFLP analysis, and detection of resistance-associated mutations. Genome typing can show transmission of leprosy in a community. Detection of mutations was set through a real-time PCR method using High Resolution Melt Curve assays (HRM) that permits detection of targeted mutations without sequencing.

## 6.2 Being prepared to detect for resistance to second-line drugs: new fluoroquinolones, clarithromycin and TMC207

Dr Cambau presented data on mechanisms of action and resistance for second-line drugs such as clarithromycin, minocycline, moxifloxacin, ethionamide and the new TMC207 (ex. R207910). Other drugs in development were presented at another presentation on the second day of the meeting. Some of these drugs are widely used for the treatment of common respiratory and urinary tract infections. Consequently, these antibiotics can select resistance mutants outside the treatment of leprosy. Similarly, ethionamide and TMC 207 will likely be used against tuberculosis. For all these drugs, the mechanisms of resistance are already known in other bacteria and mycobacteria although no drug resistant strain of *M. leprae* was described for clarithromycin, minocycline and TMC. Consequently, the molecular tools will be ready if we need to detect for resistance: detection of mutations in *rrs*, *rrl*, *atpe*, *gyrB* and *ethA* genes to be added to the *rpoB*, *gyrA* and *folP* genes sequenced.

## 7. Country presentations on drug resistance surveillance data

### 7.1 Brazil

Dr Rosa Castália França Ribeiro Soares presented the data on drug resistance surveillance carried out in Brazil. A total of 132 relapse cases (116 MB and 16 PB) were diagnosed at seven sentinel sites in Brazil, of whom only 59 were recruited for surveillance. New skin lesions were reported in 49 cases and more than 2+ BI at any sites were reported in 39 cases. However, this number is only about 10% of the total reported relapses in Brazil in 2010. Results of sequencing for drug resistance in leprosy are available from 40 relapse cases show no mutation in dapsone, rifampicin and ofloxacin controlling genes.

Some experimental procedures were also presented. For patients' sample collection, skin smears were taken from at least four sites and samples were washed within a sterile tube filled with 1 mL 70% ethanol. Specific pairs of primers were used for amplification of resistance genes to rifampicin (*rpoB*), dapsone (*folP1*) and ofloxacin (*gyrA*) and results were reported according to the presence or absence of mutations. DNA aliquots of positive samples for drug resistance mutations and the same number with the absence of mutations were forwarded to FIOCRUZ/RJ Laboratory and three other reference labs in Brazil. 10% of all Brazilian samples were forwarded from FIOCRUZ to Dr. Masanori Matsuoka's lab in Japan. For cases for whom skin lesion biopsies can be obtained in reference centres, samples were kept at 4°C and shipped to the Microbiology Laboratory of the Instituto Lauro de Souza Lima, Bauru/SP, where the Shepard technique was performed for inoculating bacilli in mouse footpad.

## 7.2 China

The data on surveillance carried out in China was presented by Dr Hongsheng Wang. About 1300 new cases were detected in 2010 and about 100 relapse cases were reported. The proportion of MB cases among all newly detected cases has increased gradually during the past ten years. The classification of leprosy is as per WHO recommendation. MDT was implemented in the whole of China in 1986. Sample collections, transportation, storage, DNA extraction and PCR were performed according to WHO guidelines. DNA sequencing was completed by Shanghai Sheng Gong Biology Company.

A total of 10 patients were tested for the presence of drug resistant mutations. Among them, six were relapses after MDT, and four with persisting high BI after MDT. All samples were positive for PCR amplification of *M.leprae* DNA. Only one relapse patient displayed *rpoB* gene mutation.

## 7.3 Colombia

Dr Nora Cardona-Castro from the Instituto Colombiano de Medicina Tropical gave a presentation on the results of the surveillance data carried out during 2011. Drug resistance surveillance is not part of Leprosy Control Programme (LCP) activities. Dr Nora described the leprosy situation in Colombia and a total of 289 cases including 243 new cases and 46 relapses (22 PB and 24 MB) were reported in 2010. In 2011, 133 cases (110 new cases and 23 relapses) were detected. A high proportion of relapses is a major warning for the Colombian Leprosy Programme but the causes of high reporting of relapses may be due to mis-diagnosis and mis-classification of patients (reactions). Resistance to rifampicin and dapsone were not seen in relapse cases in 2011 by mutation detection in *E.Coli* system. Group discussion suggested that for confirmation of detection of mutations for *folP* and *rpoB* in relapse cases must be sent to WHO recommended reference centre for further validation.

## 7.4 India

Dr Rupendra Jadhav, Dr Vijayalakshmi, Dr Ram Das and Dr Krishnamurthy each presented the results of the drug resistance surveillance carried out by the Stanley Browne Laboratory in Delhi, Blue Peter Public Health & Research Centre (BPHRC) in Hyderabad, National JALMA Institute for Leprosy and Other Mycobacterial Diseases and Damien Foundation India Trust, India, respectively.

The method of sample collection, transportation and testing from Stanley Browne Laboratory (SBL) in Delhi was as per the guidelines provided to the TLM centres (slides were also sent to the lab), samples to be kept at room temperature / 4°C and sent to SBL for PCR and sequencing at a later date (preferably at the end of every month) by routine transport without the need to control the temperature during transportation, or to take additional precautions for biohazard control. A total of 21 MB relapse cases were diagnosed at the sentinel sites but only 13 relapse cases were tested for drug resistance.

None of the samples tested so far from relapse cases showed mutation for rifampicin resistance; therefore, MDT can be used for treating such patients.

Blue Peter Public Health & Research Centre (BPHRC) in Hyderabad performed slit-skin smear and kept in 70% Ethanol, DNA extraction was done by DNeasy Kit. Individual PCR for *folp1*, *rpob*, *gyrA* and sequencing were carried out at a local laboratory. A total 30 relapse cases were diagnosed of whom only 17 cases tested for sequencing. The results did not show mutations in *folp1*, *rpoB* and *gyrA* in any of the PCR positive samples.

On behalf of National JALMA Institute for Leprosy and Other Mycobacterial Diseases (ICMR), Agra, Dr Ram Das presented results of 10 (BL/LL- 3 non-responder and 7 relapsed) cases. DNA was isolated and PCR-sequencing was performed for analysis of the mutation in *folP1*, *rpoB* and *gyrA* gene regions. Out of 10 samples, seven got amplified and three samples could not be amplified due to low bacilli load. Seven amplified samples were sequenced for *folP1*, *rpoB* and *gyrA* gene. The sequencing results of seven samples for *folP1*, *rpoB* and *gyrA* genes did not show any mutation. Dr Ram Das suggested that drug resistance in leprosy is very low in the MDT era. Further studies are needed with more non-responders and relapse cases for the detection of relevant mutations for deriving any meaningful conclusions.

Dr Krishnamurthy from the Damien Foundation India Trust presented 11 leprosy projects offering primary and secondary services. All have laboratory facilities. All new cases are subjected to slit-skin smear examination. In addition, three of the projects offer tertiary services and one of them is the sentinel centre for drug-resistance surveillance. Only one relapse case from among the cases managed by the projects was investigated and drug susceptibility test showed no resistance.

## 7.5 Mali

Dr Roch Christian Johnson presented the surveillance activities carried out in Mali and Burkina Faso. Sampling within countries was performed according to the clinical case definition for relapse, punch biopsy specimens were sent by DHL to Paris to the laboratory of Professor Cambau. A total of eight relapse cases were recruited in 2011, six cases from Mali and two cases from Burkina Faso. The results were negative PCR for *rpoB*, *folP1* and *gyrA* genes for rifampicin, dapson and ofloxacin from cases from Mali and no mutations of *rpoB*, *folP1* and *gyrA* genes from cases from Burkina Faso. Dr Johnson gave suggestions to improve the quality of sampling and the diagnosis of relapse and expand surveillance network to others countries.

## 7.6 Myanmar

Dr Kyaw Kyaw presented the results of the surveillance activities carried out at two sentinel sites in Myanmar. These are the Mandalay Special Clinic, Mandalay and the Central Special Skin Clinic, Yangon. A total of 12 relapse cases were recruited - seven cases from Yangon and Bago divisions and five cases from Mandalay and Magwe divisions. One to three skin smear samples were taken from each patient, kept without

blade in 70% ethanol tubes and sent to the reference laboratory of the Leprosy Research Centre (LRC), National Institute of Infectious Diseases (NIID), Japan. Results of DNA sequencing for drugs resistance revealed no mutations in *rpoB*, *folP1* and *gyrA* genes.

## 7.7 Nepal

The data on leprosy surveillance carried out in Nepal was presented by Dr. Deanna A. Hagge, Head, Mycobacterial Research Laboratory, Anandaban Hospital, Kathmandu, Nepal. The centre's inclusion in WHO's Global Surveillance of Drug Resistance in Leprosy was approved in October 2010 by the Government of Nepal and the Nepal Health Research Council (NHRC).

Data were presented on results of biopsy from five relapse cases (four from Anandaban, one from Lalgadh) in 2010 were explained, all are male MB patients with ages between 24 and 62 years old. Relapses occurred between 5-28 years post-MDT. The average BI from SSS was 3.7 from four sites. All are histopathologically described as "active" BB-LL cases. Samples were sent to Stanley Browne Laboratory in New Delhi for sequencing and results were awaited.

## 7.8 Philippines

Surveillance for drug resistance in the Philippines was presented by Dr. Irene B. Mallari, representing the Leonard Wood Memorial Research Centre, which is the designated sentinel site. Two MB relapse cases were diagnosed and samples were sent to the reference laboratory of National Hansen's Disease Programmes, Baton Rouge, Louisiana, USA for DNA sequencing. The results of both cases were sensitive to rifampicin, dapsone and ofloxacin.

## 7.9 Viet Nam

Dr. Nguyen Thi Hai Van gave a presentation on the results of the drug resistance surveillance carried out in Viet Nam. She presented the leprosy situation in Viet Nam. In 2010 the detection rate was 0.41/100,000 and the prevalence rate was 0.04/10,000 - MB proportion among new cases is 72.14%, children proportion among new cases is 3.9% and proportion of disability grade 2 among new cases is 18.66%. Five MB relapsed cases with BI>2+ were detected in 2011. All are male aged between 19 to 61 years. Sequencing results of these five relapse cases showed no mutations in *rpoB*, *folP1* and *gyrA* genes.

## 7.10 Yemen

Dr Abdul Rahim Al-Samie presented the data on leprosy surveillance of drug resistance conducted in Yemen in 2010. Yemen is a low-burden country for leprosy. The national leprosy elimination programme is completely integrated with the primary health care (PHC) system and run by leprosy specialized staff up to second national level and by

general staff in the lower levels. Since its inception, the NLEP has received support from WHO, GLRA, YELEP (local NGO) and MoPH. MDT according to WHO recommendations was introduced in the early 1980s.

The leprosy elimination target was achieved at country level in 2000. Data show a slow but steady decline in new cases, a persistent high rate of Grade 2 disability and satisfactory figures for treatment completion.

Dr Al-Samie also spoke about the sample collection facilities in the country. All relapse cases are suspected by the leprosy centres at the second national level and confirmed by medical supervisors from the HQ. The suspected relapse patients are requested to come to the national referral centre.

The number of relapses diagnosed yearly fluctuated due to many factors like over-diagnosis, mainly due to not following the stringent WHO criteria in the past. Sometimes, there was under-reporting due to non-confirmation of some suspected cases by the MO, especially in areas with security problems.

According to relapse data, six relapse cases were suspected during 2010 by the programme. The samples were collected according to the WHO guidelines and sent to the Global Health Institute/Switzerland. Only three cases were found with sufficient *M.leprae* DNA. The bacilloscopy results of the remaining three samples were negative. The genotyping result for the three positive cases showed that they were all from different genotypes. They belonged to 2-E (East Africa like), 1-D (Asia, Madagascar but also found in South America) and 1-B (this one is rare, only found once in India and twice in French Indies).

## **8. General discussion**

### **8.1 Quality control: technology, logistics and reporting**

Dr Masanori Matsuoka presented data on the third round of quality control survey. Six samples were sent to the 17 reference laboratories of the network in nine countries. Among them, 13 labs reported results. Three samples contained DNA at various concentrations from a wild type strain and the other three contained a strain that was mutated in *rpoB*, *folP* and *gyrA*. Three laboratories had negative PCR results for some controls with a low concentration whereas only two laboratories did not provide sequencing results.

Dr Matsuoka also showed results he obtained (published in the Japanese Journal of Infectious Diseases 2011) on the efficiency of the FTA elute card compared to smears in ethanol suspension. Results on 192 samples demonstrated that PCR efficiency is similar with the two methods of skin smear collection.

## 8.2 *M. leprae* genomics: impact on transmission, new drug targets and resistance detection

Dr Diana Williams from Louisiana State University presented an overview on *M. leprae* genomics and the potential benefits for leprosy research. Several strains are being sequenced with representatives in various parts of the world. Microarray for transcriptome study is also developed. Genotyping is usually done by VNTR and SNPs analysis. This recently showed the story of the origins of leprosy and its further world-wide dissemination. It also confirms the armadillo-to-human transmission in Southern USA. PCR and new RT-PCR protocols are used for the detection of *M. leprae* DNA and the enumeration of bacterial cells in skin smears. Dr Williams described several molecular methods that can be used to detect mutations in the drug targeted genes and showed a new method that is under development (LIPLA system).

## 8.3 Outcome of management of drug-resistant leprosy cases using second-line drugs

Dr Kyaw Kyaw presented two cases of leprosy with rifampicin resistance he had to manage. The first case has a long history of leprosy treatment from 1973 onwards with DDS alone then associated with combination of DDS + clofazimine with or without rifampicin. The actual clinical status was relapse of lepromatous leprosy with BI5+ and a *M. leprae* strain with mutation in *rpoB* and *folP*. The patient was then treated with ofloxacin, clofazimine and minocycline successfully. The second case has also a long history of DDS monotherapy that ended with one year MDT. He relapsed in 2009 with new lesions and BI5+. The strain showed only a *rpoB* mutation. He was eventually treated successfully with DDS, ofloxacin, minocycline and clofazimine.

## 8.4 Current developments in search for new anti-leprosy drugs

Dr Cambau presented data on new antibiotics that could be useful in future for the treatment of leprosy. Ofloxacin (or levofloxacin), minocycline and clarithromycin are the usual second-line drugs with ethionamide being less active. Moxifloxacin is a new second-line drug that has showed efficacy in leprosy treatment. Promising drugs that showed efficacy in the mouse footpad model are rifapentine, a long-acting rifamycin and the new antituberculous drug TMC-207 (Tibotec). All the new antituberculous drugs (nitroimidazole derivatives for instance) that have been developed by the Global alliance against TB team should be further tested for leprosy. In conclusion we need to keep testing models for studying the activity of new drugs and drug combinations against *M. leprae*.

## 9. Conclusions and recommendations

- The participants acknowledged and appreciated the support provided by various partners and especially LEPRO India- Blue Peter Public Health & Research Centre (BPHRC), Hyderabad, India in hosting this meeting.
- The results of the ongoing drug resistance surveillance shows that MDT remains an effective treatment.
- In relapsed cases where previous records are not available, the presence of definite new lesions and BI of 2+ and more should be included for sentinel surveillance of drug resistance.
- The existing network of surveillance needs to be expanded to include more sentinel sites and collaborating laboratories.
- The quality control initiative introduced by the leprosy research centre, National Institute of Infectious Diseases, Tokyo, Japan, is an important component to drug resistance surveillance and is to be continued.
- Studies on efficacy of new antileprosy drugs should be initiated.
- Referral centres and their collaborating laboratories are encouraged to publish information on the clinical and other scientific aspects of relapse cases in relevant journals.
- Collaborating laboratories and sentinel sites are encouraged to do additional studies in new MB skin smear positive cases for primary drug resistance, but these results should be separated from those of the relapsed cases.

## Annex 1

### Programme

#### Day 1: Monday, 22 August 2011

- 09.00-09.30 hours - Opening session
- Welcome address WHO and Blue Peter Public Health and Research Centre
  - Selection of chairperson and rapporteur
  - Introduction of participants

#### Setting the stage

- 10:00- 10:30 hours Drug Resistance: updates on current situation (*Dr Myo Thet Htoon*)
- *Discussion*

- 10:30 – 12:30 hours Country presentation on relapses: current situation, trends and case management (10 minutes each)
- Brazil (*Dr Rosa Castalia Soares*)
  - *Discussion*

#### Technical session

- 14:00 – 14:30 hours Continuation of country presentation on relapses
- China (*Dr Shen Jianping*)
  - Madagascar (*Dr Ramarolahy Emerantien Benoit*)
  - Nepal (*Dr Garib Das Thakur*)
  - *Discussion*

- 14:30 – 15:00 hours Being prepared to detect for resistance to second line drugs: new fluoroquinolones, clarithromycin, minocycline and TMC207 (*Professor Emmanuelle Cambau*)
- *Discussion*

- 15:00 – 15:30 hours High throughput routine drug resistance surveillance in leprosy: present and future technologies (*Dr Varalakshmi Vissa*)
- *Discussion*

**Day 2: Tuesday, 23 August 2011**

- 09:00-10:00 hours **Country presentations on drug resistance surveillance data: current practices for diagnosis, referral, investigations and results** (10 minutes presentation followed by discussion)
- Brazil (Dr Rosa Castalia Soares)
- China (*Prof Wang Hongsheng*)
- Columbia (*Dr Nora Cardona-Castro*)
- India (*Dr Rupendra Jahdavi, Dr V. Vijaya Laskmi, Dr Ram Das and Dr Krishnamurthy*)
- 10:30 – 12:30 hours **Continuation of country presentations** (10 minutes presentation followed by discussion)
- Mali (*Dr Mamadou Sidebe and Dr Roch Christian Johnson*)
- Myanmar (*Dr Kyaw Kyaw*)
- Nepal (*Dr Deanna Hagge and Dr Graeme Clugston*)
- Pakistan (*Dr Christine Schmotzer*)
- Philippines (*Dr. Irene Mallari*)
- Viet Nam (*Dr Tran Hua Khang*)
- Yemen (*Dr Abdul Rahim Al-Samie*)
- General discussion**
- 14:00-14:30 hours Quality control: technology, logistics and reporting (*Dr M. Matsuoka*)
- Discussion
- 14:30-15:00 hours Current developments in search for new anti-leprosy drugs (*Professor Emmanuelle Cambau*)
- Discussion
- 15:00-15:30 hours Outcome of management of drugs resistant cases using second line drugs (*Dr Kyaw Kyaw*)
- Discussion
- 15:30-16:00 hours Conclusion and recommendations
- 16:00- 16:15 hours Closing

## Annex 2

### List of participants

#### National Programme Managers

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The WHO Global Leprosy Programme organized a meeting on Sentinel Surveillance for Drug Resistance in Leprosy on 22-23 August 2011 at LEPRO India's Blue Peter Public Health and Research Centre, Hyderabad, Andhra Pradesh, India. A total of 40 participants including experts from the sentinel sites, researchers from the reference laboratories and partner organizations attended the meeting. Currently, there are four participating countries: Burkina Faso, Madagascar, Mali and Mozambique from the African Region, Brazil and Colombia from the American Region, Pakistan and Yemen from the Eastern Mediterranean Region, India, Myanmar and Nepal from the South-East Asia Region and China, Philippines and Viet Nam from the Western Pacific Region. In addition, 10 collaborating reference laboratories are involved in molecular testing for drug resistance. Results of ongoing drug resistance surveillance show that MDT remains an effective treatment.



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