

Report of the Eleventh Meeting of the WHO Technical Advisory Group on Leprosy Control

New Delhi, India, 30 September 2011



**World Health
Organization**

Regional Office for South-East Asia

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Printed in India

Contents

	<i>Page</i>
1. Introduction	1
2. Report of the Tenth TAG Meeting	1
3. Review of the global leprosy situation	1
4. Mechanisms to monitor the progress in terms of the global target of reducing the rate of new cases with G2D.....	2
5. Review of the global surveillance for drug resistance in leprosy and the next steps.....	3
6. Report on the progress of multicentric Uniform-MDT (U-MDT) study.....	3
7. Promoting research to develop new antileprosy drugs and regimens.....	4
8. Participation of persons affected by leprosy in leprosy services	5
9. Other issues	5
10. Conclusions and recommendations	5

Annexes

1. Terms of Reference of the WHO Technical Advisory Group on Leprosy Control	7
2. Agenda	9
3. List of participants	10

1. Introduction

The Eleventh Meeting of the WHO Technical Advisory Group (TAG) on Leprosy Control was held in New Delhi, India, on 30 September 2011, immediately following the Global Programme Managers' Meeting held at the same venue on 28–29 September 2011. The meeting was attended by members of the TAG; experts invited from the areas of chemotherapy research, drug resistance surveillance and social science, as well as representatives from the International Federation of Anti-Leprosy Associations (ILEP) and Regional Advisers from the WHO regions. The meeting was chaired by Dr H. J. S. Kawuma. The terms of reference of the WHO Technical Advisory Group on Leprosy Control, programme of the meeting and the list of participants are given in Annex 1, 2 and 3, respectively.

Dr Samlee Plianbangchang, Regional Director, WHO South-East Asia Region, SEARO, New Delhi while welcoming the participants appreciated the role of TAG in providing excellent technical advice to the Global Leprosy Programme over the years. The programme has been successful in reducing the leprosy burden over the past decade as seen by the declining trends in new case detection globally as well as in the WHO regions. However, Dr Samlee cautioned, "we must continue to be vigilant and sustain leprosy control activities so that new cases are diagnosed and cured in a timely manner and encouraged to live a normal productive life. In order to achieve this, all components of the referral system need to be integrated."

2. Report of the Tenth TAG Meeting

The report of the Tenth TAG Meeting held in New Delhi, India, on 23 April 2009 was approved by all members.

3. Review of the global leprosy situation

Dr Kawuma reviewed the current leprosy situation in his presentation. WHO received reports from 130 endemic countries on leprosy situation as of end of 2010. During the year a total of 228 474 new cases were reported, while 192 246 patients were still on register for treatment at the end of 2010. The disease continued to show a declining trend in new case detection. However, the decline is not uniform in all regions or countries. In fact some countries (Philippines, Sri Lanka and Sudan) showed increased new case detection during 2010.

During the year, about 13 000 new cases were reported to have presented with grade-2 disabilities (G2D) at the time of diagnosis, majority of these (72.3%) were from

Africa and the South-East Asia Region. The rate per 100 000 population for G2D is highest (0.40) for Africa and lowest (0.03) for the Western Pacific Region. The proportion of G2D among new cases reported was highest in China and Sudan (23%) and lowest in Marshall Islands (0%).

An increasing number of countries are reporting relapses on a regular basis to WHO. A total of about 2300 relapses were reported in 2010. So far no dramatic fluctuations have been noticed in the trend of reporting on relapses as this is an important proxy indicator for monitoring the efficacy of multidrug treatment (MDT) and possible emergence of drug-resistant strains of *Mycobacterium leprae*. The reporting on cure/treatment completion rates is not yet optimal, particularly from endemic countries in Africa. In general cure rates are better for paucibacillary (PB) than multibacillary (MB) cohorts of patients. The prevalence–detection ratio (P/D ratio) is unacceptably high in three of the five reporting WHO Regions, indicating relatively suboptimal case-holding strategy in programmes.

Concerns were expressed regarding the quality and completeness of the national data on leprosy. Efforts are required to improve the quality of recording and reporting of leprosy cases that are used to monitor the essential indicators. Programme evaluations and sample surveys can be used along with strengthened supervision to improve the quality of the information collected. Situational analysis should be used to identify high-burden areas within countries to prioritize activities. Further investigation of the operational aspects for implementation of contact examination and chemoprophylaxis for contacts to enhance the reduction in new cases is recommended.

4. Mechanisms to monitor the progress in terms of the global target of reducing the rate of new cases with G2D

Professor W.C.S. Smith introduced the topic of mechanisms for monitoring progress in using the global target of at least 35% reduction in the rate of new cases with grade-2 disabilities per 100 000 population at the end of 2015, compared with the baseline at the end of 2010. The rate of new cases with G2D when viewed together with other indicators can be used to estimate underdetection, to measure the need for physical and social rehabilitation, and to advocate for prevention of disabilities and promote collaboration with other sectors. There are several factors that affect new case-detection activities, such as effectiveness of information, education and communication (IEC), competence of health workers, quality of supervision and coverage of the programme. In addition, the starting level of G2D per population varies between countries and regions. For example Bangladesh, China and Philippines are starting at lower levels compared with countries such as Brazil, Mozambique and the Democratic Republic of the Congo. Professor Smith suggested that:

- all new cases should be assessed for grade-2 disabilities and the findings recorded and reported in standard formats;

- the WHO grade-2 disability grading should be used for collecting data for the population-based indicator as described in the Updated Operational Guidelines for the Enhanced Global Strategy to ensure uniformity.

Training by national programmes is important to ensure validity and reliability of grade-2 disability assessment, recording and reporting. Validation of data on a sample basis, where possible, is recommended.

5. Review of the global surveillance for drug resistance in leprosy and the next steps

The global surveillance for drug resistance in leprosy was introduced by Dr M. Matsuoka. After a brief history of chemotherapy of leprosy and occurrence of resistance to various antileprosy drugs, Dr Matsuoka introduced the developments in molecular methods to detect drug-resistant mutation in *M. leprae*. The paucity of information on the magnitude of drug resistance in leprosy was mainly due to tediousness and high cost of assessing drug susceptibility using mouse footpad methods in the past. However, limited reports/data do not necessarily mean low magnitude of the problem.

Today the main concern is about potential development of drug resistance to rifampicin, the sheet anchor of chemotherapy regimens in leprosy. The method used now is to screen for resistance by polymerase chain reaction (PCR) direct sequencing to detect mutations in drug resistance detecting regions (DRDR) in the *folP* (dapsone), *rpboB* (rifampicin) and *gyrA* (quinolone) genes. Samples of slit-skin smears preserved in ethanol are used. The mouse footpad is not used anymore for assessment of drug resistance.

The WHO surveillance network collects samples from MB patients who have taken a full course of MDT and have relapsed. WHO has established a network of sentinel centres in 16 endemic countries and a corresponding network of laboratory facilities for molecular testing of samples around the world. Dr Matsuoka concluded that:

- (1) the level of drug resistance in rifampicin is not a serious situation at present;
- (2) longitudinal surveillance should be continued to reveal the trend of drug resistance in leprosy as the drugs in use are not protected from unconventional use;
- (3) we have to watch out so that leprosy control avoids being threatened by drug resistance.

6. Report on the progress of multicentric Uniform-MDT (U-MDT) study

Dr B. Nagaraju reported on the progress of the multicentric study on Uniform-MDT (U-MDT) study for paucibacillary (PB) and multibacillary (MB) patients. This study is being

supported by the Special Programme for Research and Training in Tropical Diseases (TDR) in collaboration with the Global Leprosy Programme (GLP).

The recruitment for the study started in November 2003. The multicentric study involves six centres in India and two in China. A total of 3396 (2094 PB and 1302 MB) patients have been enrolled in the study. Sixteen per cent of them are children. Dr Nagaraju presented the results of the interim analysis on data available up to December 2010.

At the time of completion of treatment, more than 95% patients showed clinical improvement, which increased to more than 99% by the fourth year follow-up, in both PB and MB patients. So far six relapses (two PB and four MB) have been confirmed in the study. All relapses occurred within 13–28 months after treatment was discontinued. Discolouration due to clofazimine was milder and disappeared within few months. Of the 65 deaths recorded, none was related to leprosy. Dr Nagaraju concluded that the interim results were very promising and suggested that UMDT was acceptable, safe and effective in all types of leprosy. The final results will be available by 2015–2016.

7. Promoting research to develop new antileprosy drugs and regimens

Dr V. Pannikar presented the next steps in promoting research to develop new antileprosy drugs and regimens. The primary objectives of developing new antileprosy drugs are (i) to simplify and shorten treatment duration; (ii) to improve the efficacy and safety of therapy; and (iii) to prevent development of drug resistance. However, there are many challenges in developing new drugs against chronic diseases such as, long follow-up for detecting relapses, requirement of a large number of study subjects in each arm, lack of suitable sites and personnel to conduct studies and high cost.

Currently there are six new antileprosy drugs in different stages of clinical development. These are: ofloxacin, clarithromycin, minocycline, moxifloxacin, rifapentine and TMC 207. Among these, moxifloxacin, rifapentine and TMC 207 have shown significant bactericidal activity against *M. leprae*, given either as a single or as multiple doses.

To accelerate the development of new drugs, Dr Pannikar suggested:

- developing rapid and simple methods for screening new compounds;
- developing new tests for measuring bactericidal activity precisely and rapidly;
- identifying surrogate markers for measuring sterilizing activity of drugs against *M. leprae*;
- upgrading research capacity of major leprosy institutions; and
- securing optimal resources for research activities.

8. Participation of persons affected by leprosy in leprosy services

Dr P.K. Gopal stressed the importance of strengthening participation of affected people in leprosy programmes. Affected people have been making tremendous contributions to their communities in various ways and now it is time to recognize their role in improving the quality of leprosy services. The Enhanced Strategy 2011–2015 has listed several areas where affected people can be involved as partners in the programme. WHO has prepared “Guidelines on strengthening participation of persons affected by leprosy in leprosy services”. These were developed in consultation and active participation of affected people, partners, experts and selected national programme managers.

Dr Gopal recommended that programmes:

- should work with affected persons and their organizations;
- facilitate removal of negative attitudes towards affected persons and their families;
- promote amendment and abolishment of discriminatory legislations; and
- provide opportunities and training to affected persons to strengthen their partnership with the programme.

9. Other issues

The Eighth Meeting of the Expert Committee on Leprosy was held in October 2010 in Geneva, Switzerland. The administrative clearance for the publication of its report is taking an unusually long time. The members urged that the report be printed and published as soon as possible.

10. Conclusions and recommendations

The TAG:

- (1) Endorsed the plan of action for the implementation of the Enhanced Global Strategy and its goal of reducing the occurrence of Grade 2 disabilities among new cases.
- (2) Concluded that renewed efforts will be needed to improve the quality of services for early detection, prevention and limitation of disabilities including improved management of leprosy reactions, strengthening of integrated referral systems, collection of monitoring data and activities for the socioeconomic rehabilitation of people affected by leprosy.

- (3) Recommended that countries carry out situational analysis to identify high-burden areas for the purposes of developing and implementing intensive and innovative approaches for controlling leprosy in those areas.
- (4) Considered that more specific efforts should be made to eliminate stigma and discrimination of people affected by leprosy by, among others, involving persons affected by leprosy in planning, advocacy and monitoring leprosy services.
- (5) Agreed that more innovative approaches will be needed to further reduce the disease burden due to leprosy and recommended that particular attention be paid to identify leprosy among high-risk groups such as contacts.
- (6) Appealed for further investigation of the operational conditions required for successful implementation of the available tools for diagnosis, immunoprophylaxis and chemoprophylaxis of leprosy.
- (7) Called for renewed efforts to improve the quality of information collected and used for calculating the essential monitoring indicators.

Annex 1

Terms of Reference of the WHO Technical Advisory Group on Leprosy Control

General Background

In 1995 the Leprosy Elimination Advisory Group (LEAG) was established by the Director-General to advise the former WHO Action Programme on Elimination of Leprosy (LEP) on implementation and management of the strategy to eliminate leprosy as a public health problem by the year 2000. This was defined as reducing the prevalence of the disease to less than one case per 10 000 population. It was disestablished in 1999 following WHO restructuring.

In order to advise WHO on effective implementation of the intensified strategy and monitoring its progress, particularly in the areas of capacity building, MDT supply, communications and information, as well as monitoring and surveillance, the Director-General decided to establish a Technical Advisory Group on Leprosy Control (TAG) consisting of independent experts. There are currently nine members representing all WHO regions and having different expertise and vast experience in various fields. The first meeting of TAG was held in Geneva in 2000.

Terms of Reference

The WHO Technical Advisory Group on Leprosy Control is composed of experts who are independent of WHO. Members are chosen for their expertise in leprosy and programme management with particular reference to public health, epidemiology, community mobilization and advocacy, operational research, and disability prevention. They form a strong team with a good technical balance and geographical representation.

The members of this advisory body are selected and appointed by WHO and meet at least once a year. The period of membership is three years, with the possibility of extension.

The Technical Advisory Group's deliberations are open to representatives of national and international partners as observers to encourage open debate.

In addition, the Group may invite, as necessary, representatives from selected leprosy endemic countries and other experts to its meetings.

- To review and monitor the implementation of the Global Strategy to further reduce the leprosy burden and sustain leprosy control activities.

- To advise WHO on new strategies and approaches if necessary.
- To monitor progress in further reducing the leprosy burden.
- To give technical advice and guidance on sustaining leprosy control activities.
- To identify and facilitate implementation of a research agenda in order to improve the quality of leprosy control activities, including prevention of disabilities and rehabilitation.
- To support efforts related to reducing stigma and discrimination against individuals and families affected by leprosy.

Annex 2

Agenda

Friday, 30 September 2011

0900 - 0930 hrs	Opening Remarks by the Regional Director, SEARO Welcome by Chairperson Introduction of participants Selection of Rapporteur
1000 -1015 hrs	Approval of report on 10th TAG meeting held in New Delhi, India on 23 April 2009
1015 -1045 hrs	Review of the global leprosy situation (<i>Dr H.J.S. Kawuma</i>) - <i>Discussion</i>
1045 -1130 hrs	Discussion on mechanisms to monitoring progress in terms of the global target of reducing the rate of new cases with grade-2 disabilities (<i>Professor WCS Smith</i>) - <i>Discussion</i>
1130 -1200 hrs	Review of the Global Surveillance for Drug Resistance in Leprosy and next steps (<i>Dr M. Matsuoka</i>) - <i>Discussion</i>
1200 -1245 hrs	Report on the progress of multi centric Uniform-MDT Therapy (U-MDT) study (<i>Dr B. Nagaraju</i>) - <i>Discussion</i>
1245 -1330 hrs	Next steps in promoting research to develop new anti-leprosy drugs and regimens (<i>Dr V. Pannikar</i>) - <i>Discussion</i>
1430 -1515 hrs	Discussion on other social issues Participation of person affected by leprosy in leprosy services (<i>Dr P.K. Gopal</i>) - <i>Discussion</i>
1515 -1600 hrs	Conclusions and recommendations
16:00 hrs	Closing

Annex 3

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The Eleventh Meeting of the WHO Technical Advisory Group (TAG) on Leprosy Control was held on 30 September 2011 in New Delhi, India. The members of the TAG reviewed the global leprosy situation and the mechanisms for monitoring progress in terms of the global target of reducing the rate of new cases with grade 2 disabilities. The issues discussed were: the current status of research in chemotherapy; progress of Uniform MDT for all cases; the global surveillance for drug resistance in leprosy; identifying next steps forward; and the importance of strengthening participation of affected people in leprosy programmes.

The TAG unanimously endorsed the plan of action for the implementation of the "Enhanced Global Strategy to Further Reduce Leprosy Burden 2011-2015" and called for renewed efforts to: improve the quality of leprosy services; develop and implement intensive and innovative approaches for early detection and prevention of disabilities; and improved programme management. The report details the specific efforts considered to reduce and subsequently eliminate stigma and discrimination and to provide opportunities for leprosy research and socioeconomic rehabilitation of people affected by leprosy.



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SEA-GLP-2012.3