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**MULTIDRUG-RESISTANT AND EXTENSIVELY DRUG-RESISTANT
TUBERCULOSIS IN THE AFRICAN REGION:
SITUATION ANALYSIS, ISSUES AND THE WAY FORWARD**

Report of the Regional Director

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BACKGROUND

1. Tuberculosis (TB) is a high-priority disease in the WHO African Region. The Global TB Control Report 2009¹ shows that, in 2007, the African Region, which accounted for an estimated 12% of the world population, contributed 22% of notified TB cases. Case notification rates have increased from 82:100 000 in 1990 to 158:100 000 in 2007. An estimated 51% of TB patients tested in 2007 were HIV-positive, making HIV infection the single most important risk factor for TB incidence in the Region. The current TB trends need to be reversed for the African Region to meet the Millennium Development Goals (MDG).
2. At its Fifty-third session in 2003, the WHO Regional Committee for Africa adopted Resolution AFR/RC53/R6 – Scaling up interventions against HIV/AIDS, tuberculosis and malaria in the WHO African Region. Subsequently at its Fifty-fifth session in Maputo, Mozambique, in 2005, the Regional Committee declared TB an emergency in the African Region.²
3. Multidrug-resistant TB (MDR-TB) is defined as TB caused by organisms that are resistant to at least isoniazid and rifampicin. Extensively drug-resistant TB (XDR-TB) is MDR-TB that is also resistant to any one of the fluoroquinolones and to at least one of four injectable second-line drugs (amikacin, capreomycin, kanamycin and viomycin). Between January 2007 and December 2009, a total of 22 032 new MDR-TB cases were reported by 33 countries. An estimated 1501 new XDR-TB cases were reported by eight countries³ during the same period.
4. Thirty-three countries have notified MDR-TB and XDR-TB cases but only 20 of them are known to have structured treatment programmes in place.⁴ Seventeen of the treatment programmes have the approval of the WHO Green Light Committee (GLC) which is a WHO mechanism for reviewing country MDR/XDR-TB Programme funding proposals for their consistency with WHO guidelines for management of drug-resistant TB. Even where treatment programmes exist, not all confirmed cases are receiving treatment due to unavailability of programme policies, tools and adequate supply of second line anti-TB medicines.
5. The Stop TB Strategy, launched in 2006, addresses among others the global threat of drug-resistant TB. In 2008 WHO published Global MDR-TB Management Guidelines⁵ and the Regional Office drafted a framework for the control of drug-resistant TB. In April 2009, 27 MDR-TB high-burden countries including Democratic Republic of the Congo, Ethiopia, Nigeria and South Africa met in Beijing, China, where they issued a Call for Action against drug-resistant TB.⁶ At its Sixty-second session, in May 2009, the World Health Assembly adopted Resolution WHA62.15 on Prevention and Control of Multidrug-resistant TB and Extensively drug-resistant TB. In the same year, the WHO Regional Committee for Africa at its Fifty-ninth session in Kigali, Rwanda, adopted Resolution AFR/RC59/R7 calling upon countries to implement actions

¹ World Health Organization 2009, Global tuberculosis control: epidemiology, strategy, financing, WHO Report 2009, Geneva, Switzerland (WHO/HTM/TB/2009.411).

² Resolution AFR/RC55/R5, Tuberculosis control: the situation in the African Region. In: *Fifty-fifth session of the WHO Regional Committee for Africa, Maputo, Mozambique, 22–26 August 2005, Final Report*, by which the Ministers of Health of countries of the African Region declared TB an emergency in the Region.

³ Botswana, Burkina Faso, Kenya, Lesotho, Mozambique, Namibia, South Africa and Swaziland.

⁴ Botswana, Burkina Faso, Cameroon, Democratic Republic of Congo, Ethiopia, Guinea, Kenya, Lesotho, Liberia, Malawi, Mozambique, Namibia, Nigeria, Rwanda, Senegal, South Africa, Swaziland, Tanzania, Uganda and Zambia.

⁵ WHO, Guidelines for programmatic management of drug-resistant TB, WHO/HTM/TB/2008, Geneva, World Health Organization, 2008.

⁶ The Beijing "Call for Action" on Tuberculosis control and patient care: together addressing the global MDR-TB and XDR-TB epidemic.

to prevent, monitor and manage drug resistance to AIDS, TB and malaria.⁷ Several global health initiatives including the Global Fund are in place to support TB control in the Region.

6. Given the emergence and spread of resistance to TB medicines, this technical paper highlights the issues and challenges and proposes the way forward in the prevention and control of MDR-TB and XDR-TB in the WHO African Region.

ISSUES AND CHALLENGES

7. Despite almost universal adoption, by Member States, of the internationally-recommended DOTS Strategy, the African Region has a TB treatment success rate of only 79% (the set target is 85%) due to very high rates of preventable unfavorable outcomes such as patient default, transfer out and proportion of patients not evaluated at the end of treatment. Inadequate or poorly administered treatment regimens increase the probability of generating drug-resistant TB strains. Moreover MDR-TB and XDR-TB, especially when combined with HIV, may be contributing to the high TB mortality seen in certain settings. Furthermore, there is general lack of infection control measures in communities and health facilities, increasing the likelihood of infection with TB including drug-resistant forms.

8. In most National TB Control Programmes, control policies, manuals and guidelines have not been updated to include prevention and management of drug-resistant TB. National MDR-TB Guidelines are also not universally available due to the little attention that drug-resistant TB received in national programmes until the emergence of XDR-TB in the Region was reported in 2006. In addition, health system challenges such as lack of national strategic policy guidance, poor health infrastructure, poor access to diagnostic and treatment services, inadequate human resources for health and weak-to-ineffective systems of patient follow-up during treatment significantly hamper efforts to identify and effectively treat drug-resistant TB cases. Inaction in establishing strong TB programmes with sound policies for MDR-TB can lead to a new epidemic of drug-resistant TB with serious consequences for public health.

9. Diagnosis of drug-resistant TB is primarily bacteriological, requiring the existence of laboratory technologies and network for TB bacterial culture, antigenic or molecular analysis, and anti-TB Drug Susceptibility Testing. Provision of quality-assured laboratory services poses a major challenge to many countries in our Region. By the end of 2009, there were at least 13 countries in the Region⁸ that had no local capacity to perform TB culture and susceptibility testing of first-line anti-TB medicines for confirmation of MDR-TB. Regarding the diagnosis of XDR-TB, only Algeria and South Africa have local laboratory capability to conduct susceptibility testing of second line anti-TB medicines.

10. Given the lack of reliable data from the majority of Member States, the true magnitude of drug-resistant TB in the Region remains unknown. Surveillance and public awareness of drug-resistant TB are generally lacking. Only Botswana has undertaken representative countrywide surveys to determine the profile of drug-resistant TB over time. Between 2007 and 2008, seven countries carried out representative countrywide TB drug-resistance surveys⁹ and by the end of 2009, most of these countries had also conducted XDR-TB surveys.¹⁰

⁷ Resolution AFR/RC59/R7: Call for intensified action for HIV prevention and tuberculosis/HIV co-infection control in the African Region. In: *Fifty-ninth Session of the World Health Organization Regional Committee for Africa, Kigali, Rwanda, 31 August–4 September 2009, Final Report*. Brazzaville, WHO, Regional Office for Africa, 2009 (AFR/RC59/20), pp. 18–21.

⁸ Cape Verde, Central African Republic, Chad, Comoros, Congo, Gabon, Guinea-Bissau, Liberia, Mali, Niger, Sao Tome and Principe, Sierra Leone and Zimbabwe.

⁹ Botswana, Kenya, Lesotho, Mozambique, Namibia, Swaziland and Tanzania.

¹⁰ Botswana, Kenya, Malawi, Mozambique, Namibia, Swaziland and Tanzania.

11. Considering the airborne nature of TB transmission including MDR-TB and XDR-TB, it is important to ensure early diagnosis and containment of infectious cases while adhering to the best possible standards of care and infection control. Isolation facilities are generally lacking in health facilities and communities, hampering the containment of MDR-TB and XDR-TB cases and the reduction of facility-based and community-based transmission of infection. Inadequate administrative controls and poor ventilation in crowded health care facilities coupled with general inadequacy of personal protection and other infection control measures increase the risk of transmission of TB infection including drug-resistant TB.

12. Unlike first-line medicines, second-line medicines for the treatment of MDR-TB and XDR-TB are not adequately available in the majority of countries. The medicines are also not as effective as first-line medicines and tend to be associated with increased and severe adverse effects, making treatment compliance more difficult for patients. There is also limited global supply of quality-assured second-line medicines due to the limited number of international suppliers of these medicines. As a result, available country surveillance data indicate that a significant number of confirmed MDR-TB cases remain untreated. Of the 21 countries known to have MDR-TB treatment programmes, 17¹¹ have GLC-approved treatment programmes. This is partly due to the high cost of second-line anti-TB medicines as well as lack of budget line items for procurement of these medicines from national TB control budgets.

13. Even when second-line TB medicines are available for treatment of MDR-TB and XDR-TB, the very long required duration of treatment (at least 24 months) and the need to treat patients near their families as much as possible¹² pose major challenges. There is therefore need for operational research to determine how best to treat MDR-TB and XDR-TB in the communities.

14. Most of the issues and challenges related to prevention and control of TB drug resistance revolve around the health system, e.g. limited access to general TB services, weak medicines procurement and supply management systems, weak TB laboratory infrastructure, inadequate funding, inadequate human resources for health, poor transport and communication systems, and weak strategic information and logistic systems. The actions proposed are therefore framed in the context of strengthening the overall health system.

ACTIONS PROPOSED

15. **Prevent the generation of drug-resistant TB strains:** Countries should improve programme performance indicators for Directly-observed Treatment, short-course (DOTS) services, especially TB treatment success rates. This can be achieved by improving treatment compliance and completion rates through strategies to reduce patient default and transfer out rates and minimize the proportion of patients not evaluated at the end of treatment.

16. **Develop and scale up programmatic management of drug-resistant TB:** Countries should update their policies by adapting WHO guidelines for programmatic management of drug-resistant TB in DOTS programmes.¹³ Furthermore, national programmes should ensure uninterrupted supply of second-line anti-TB medicines, their rational use and pharmacovigilance and establish or strengthen drug resistance monitoring systems and infection control. Countries should also update their human resource plans to ensure adequate human resource capacity to combat MDR-TB and XDR-TB. Likewise, systems for patient follow up and psychosocial

¹¹ Burkina Faso, Cameroon, Democratic Republic of the Congo, Ethiopia, Guinea, Kenya, Lesotho, Liberia, Mali, Mozambique, Nigeria, Rwanda, Senegal, Swaziland, Tanzania, Uganda and Zambia.

¹² WHO, Guidelines for programmatic management of drug-resistant tuberculosis, WHO/HTM/TB/2008.402, Geneva, World Health Organization, 2008.

¹³ WHO, Guidelines for programmatic management of drug-resistant TB “WHO/HTM/TB/2008”, Geneva, World Health Organization, 2008.

support must be developed and monitored. These should include advocacy, communication and social mobilization strategies.

17. Establish and sustain national drug-resistant TB surveillance systems: Countries should establish routine laboratory-based surveillance of resistance to first- and second-line TB medicines among previously treated cases and other high risk TB patients and groups. They should also conduct regular periodic representative Drug Resistance Surveys and establish standardized recording and reporting systems for drug-resistant TB as a logical extension of the regular TB recording and reporting system. In order to strengthen cross-border surveillance, countries should work with partners and strive to set up electronic surveillance systems and incorporate TB programmes in International Health Regulation committees in countries to minimize transmission within and outside borders while ensuring that all cases of MDR-TB and XDR-TB are notified.

18. Strengthen procurement and supply management systems for second line anti-TB medicines: Countries should review the essential drug list to include second-line anti-TB medicines and strengthen their procurement and supply chain management to ensure uninterrupted availability of good quality, affordable second-line medicines and related commodities. In this respect, countries are encouraged to apply for concessionarily-priced, quality-assured second-line anti-TB medicines through the GLC mechanism.

19. Develop and implement TB infection control measures: National programmes should incorporate TB infection control strategies within existing national infection control policies and guidelines, and implement administrative, environmental and personal protection infection control measures for MDR-TB and XDR-TB in all health facilities. Infection control should be taken into account in the design of health facilities, especially in the context of HIV/AIDS to avoid cross-infections. The dangers of cross-infection between HIV and TB should be clearly elaborated and health staff concerned should be fully briefed on control measures. Furthermore, in collaboration with relevant government departments, TB programmes should support the development, implementation and monitoring of infection control plans in all health facilities.

20. Mobilize financial resources for supporting implementation of the recommended actions: In the context of overall health system strengthening, countries should allocate sufficient funds from the national budget for control of TB including MDR-TB and XDR-TB. Countries should also mobilize additional resources from global and regional initiatives to complement their national resources. Countries with GLC-approved MDR-TB/XDR-TB programmes have access to low-priced second-line medicines which can be bought with resources from various global health initiatives. The use of such initiatives should go a long way to strengthen the overall health system.

21. Expand regional networks for diagnosis of MDR-TB and XDR-TB: WHO and other technical partners should work with national governments to establish and strengthen subregional capacity to perform supranational TB reference laboratory functions including the establishment of additional regional laboratories capable of identifying strains resistant to second-line anti-TB medicines in order to identify XDR-TB among confirmed MDR-TB cases. Member States need support from partners to strengthen national reference laboratory infrastructure and to access, evaluate, and scale up new diagnostic technologies as they become available.

22. **Undertake operational research:** The capacity to conduct clinical trials for new diagnostics and drugs should be improved in the Region. Countries with support of partners should perform operational research to determine how best to treat MDR/XDR-TB in the communities while taking appropriate infection control measures to reduce transmission.

23. The Regional Committee is requested to examine and adopt the actions proposed in this document.