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IMPROVING MEMBERSHIP INVOLVEMENT AND RESOURCE MOBILIZATION THROUGH BETTER COMMUNICATION

Discussions at the Stop TB MDR-TB WG meeting in Tbilisi, resulted in the MDR-TB Core Group (CG) deciding to strengthen communication and coordination within the Working Group, to build more effective links with other Stop TB Working Groups and seek more active members.

This newsletter will be produced periodically to inform Working Group members and interested stakeholders about the strategic vision, operational plans and concrete achievements of the MDR-TB WG. It will also provide a means of highlighting developments and events relevant to the care of people with drug-resistant tuberculosis and control of the pandemic, such as the launch of the new edition of the World Report on Drug Resistance.

There are several subgroups housed within the Stop TB Partnership working groups. Effective linkage between the Working Group subgroups is ensured by representation of all subgroup chairs on the MDR-TB Core Group which has resulted in improved collaboration between the different subgroups, benefiting from the complementary expertise and experience within the Working Group. In addition, individual Core Group members

function as the liaison with other Working Groups, such as the HIV/TB Working Group, the Global Laboratory Initiative, and the Infection Control and Public Private Mix subgroups.

However, more importantly, the MDR-TB Working Group is about achieving the goals and targets set out in the Global Response Plan for MDR and extensively drug resistant (XDR) TB. Future MDR-TB newsletters will continue to focus on concrete outputs and the challenges the Global MDR-TB and XDR-TB response plan pose.

The newly established Drug Resistance TB Mobilization subgroup will also launch a dynamic web-based platform for discussion, exchange and activation: reaching out to engage new energies to mobilize greater resources for the battle against drug resistance.

Many partners, representing many different institutions, countries and communities worldwide are active members of the Core Group and subgroups. However, more work needs to be done to seek investment and resources to achieve these goals. Read more about the DR-TB mobilization subgroup: www.dr-mobilization.org

If you are interested in joining the MDR-TB Working Group or any of the subgroups please contact the MDR-TB WG secretariat pavelsonsm@who.int or see the MDR-TB website:

» www.stoptb.org/wg/dots_plus/default.asp?AM=MDR

Kitty Lambregts-van Weezenbeek (Chair)
Case Gordon (Vice-Chair / Chair of the DR Mobilization subgroup)

MDR-TB CORE GROUP MEETS TO ADDRESS CHALLENGES TO IMPLEMENTATION



Sandra Roelofs, First Lady of Georgia addresses participants in Tbilisi

The Core Group of the Stop TB Working Group on MDR-TB met twice in Capetown, South Africa during the IUATLD Conference and in January 29-30, 2008, in Geneva, Switzerland to analyze progress to date and a work plan for further implementing the Global MDR-TB and XDR-TB Response Plan. The Core Group discussed issues around research, the Green Light Committee (GLC), access to 2nd line drugs, the Retooling Taskforce, development of regional MDR-TB centers of excellence and advocacy and resource mobilization. The meeting also reviewed the outcomes of the Working Group meeting which was held in Tbilisi, Georgia in September 2007. The Tbilisi meeting highlighted the crisis in second-line drug-procurement.

One of the five priority areas highlighted by the research agenda for drug resistant TB endorsed by the Working Group in Tbilisi is to improve MDR-TB treatment strategies. A meeting organized by the STOP TB Partnership and hosted by Partners in Health will be held on 10-12 June 2008 in Boston, USA, to set priorities and timelines for clinical trials and other research such as simplified treatment regimens and development of a strategy to seek resources for such research. Read more about the research agenda:

» www.stoptb.org/wg/dots_plus/assets/documents/Revised%20DR-TB%20Research%20Agenda.pdf

As reported in Tbilisi, during the sixth meeting of the MDR-TB working group, there is an alarming shortage of 2nd-line drugs for patients with MDR-TB. The newly established Drug Management sub-group, with representatives of PIH, MSH, MSF, KNCV, Project HOPE, the Global Drug Facility and WHO Pre-Qualification has been instrumental in supporting GDF to address the global shortage of quality-assured 2nd-line drugs. There has been encouraging progress on documenting the shortages, drug by drug, and that is a critical first step in attracting new suppliers. The Global Drug Facility (GDF) team has assembled useful reports showing the outstanding orders received from approved GLC projects for each major medication. The procurement challenges include logistical issues, such as delivery, registration, customs, communications and execution problems; short-term issues around order scheduling and production; and long-term drug shortages, which will only be resolved by attracting new suppliers for the market. The Drug Management sub-group and the GDF have made progress on all three of these fronts, as reported in more detail below.

The Sub-group has made the long-term shortage problems their most urgent priority. The goal is to have at least 3 Quality-Assured suppliers for each drug. At present there are two for only a few drugs and there is only one approved supplier for the most important medicines.

The Core Group also established the new DR Mobilization subgroup. The terms of reference (ToR) have been formulated and a call for members is currently being made. Further information on joining this sub group and its terms of reference can be found at www.dr-mobilization.org or through the sub group's secretariat at Stop TB Partnership.

The DR Mobilization subgroup plans to activate at the XDR Task Force Meeting 9-10 April in Geneva, and quickly reach out to a very broad base of the global health community, media and decision makers from diverse sectors. The drive for dignity, drugs and diagnostics begins.

Finally, the Core Group also approved the MDR-TB Working Group amended ToR which is now operational. The ToR has been distributed to all MDR-TB WG members.

ACCESS TO DRUGS: PROGRESS SINCE TBILISI

At the Tbilisi meeting of the Stop TB Partnership Working Group on MDR-TB, there was considerable focus on an alarming shortage of 2nd-line drugs for patients with MDR-TB, and on the complete inadequacy of the 2nd-line drug supply, relative to the projections of patient enrollment in GLC projects over the next several years.

Since the Tbilisi meeting, the GDF team and a newly-formed Sub-Group on Drug Management have made some progress on resolving the most immediate shortages of key drugs, and have made significant and encouraging progress towards resolution of the long-term supply-demand imbalances. The addition of new staff at the GDF has afforded significant improvement in GDF's ability to keep up with demand for information and assistance from projects, suppliers and IDA in processing orders, resolving logistical issues, forecasting demand and encouraging new suppliers into the market. With regard to the short-term issues, a team from the GDF and IDA travelled to Russia in December to seek resolution of barriers and miscommunications that have led to long delays on drug deliveries. The problems of delayed shipments and shortages for Russian projects are by no means resolved, but there has been meaningful progress. We also received great news from Eli Lilly and Company in late January; the company increased its commitment of discounted-price Capreomycin by 500,000 vials for 2008. This brings Eli Lilly's total commitment of Capreomycin for GLC projects to 860,000 vials for the year.

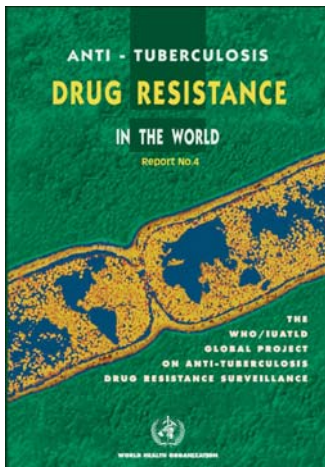
The GDF team has now developed a tracking mechanism for monitoring delayed deliveries and is working with IDA to understand both the causes of delay and how they can be avoided in the future. As the GDF, GLC members, consultants and the sub-group members have focused more intently on

resolving these problems, we have uncovered more problems than we were initially aware of in Tbilisi. This is unfortunate, but unsurprising – the first thing you find when you move to resolve serious problems is that they are more extensive than originally understood. But there are now processes in place whereby the GDF team is documenting the delays and shortages, moving to resolve them expeditiously and reviewing progress regularly with the Drug Management Sub-Group.

With regard to increasing long-term supply, GDF has now documented Current Orders and the 2008 Forecast Demand and Available Supply (from quality-assured sources) for each of the key drugs. These reports are being summarized into brief GDF Product Profiles, which will be sent to pharmaceutical companies who are already producing the needed drugs, but who are either not making product available to GDF or are not yet quality-assured. Plenty of suppliers have shown interest in producing for GLC-approved projects and GDF is now in a position to supply the companies the information they need to turn this interest into available supply over the next 12-18 months. The goal is to have at least 3 quality-assured suppliers for each drug. We now have two suppliers, at most, for only a few drugs, and have only 1 quality-assured supplier for many of the drugs in shortest supply.

There is a great deal of work yet to do, but the progress since Tbilisi has been encouraging and the GDF and the Drug Management Sub-Group hope to report more progress in the months to come.

HIGHEST RATES OF DRUG-RESISTANT TUBERCULOSIS EVER RECORDED



WHO released the fourth edition of the Anti-Tuberculosis Drug Resistance in the World report in February, which shows the highest rates ever recorded of tuberculosis resistant to standard drug treatments. Estimates from the data (collected between 2002-2007 in 83 countries and territories), indicate nearly half a million cases of multi-drug resistant TB (MDR-TB) emerged in 2006, or about 5% of the nine million new TB cases annually.

MDR-TB has now reached unprecedented levels (up to 22% of new

cases) in some countries of the former Soviet Union. In Baku City, the capital of Azerbaijan, nearly a quarter of all new TB cases (22.3%) were reported as multidrug-resistant (MDR). Proportions of MDR-TB among new TB cases were 19.4% in Moldova, 16%, in Donetsk, Ukraine, 15% in Tomsk Oblast in the Russian Federation and 14.8% in Tashkent in Uzbekistan. Estimates also indicate that in Eastern Europe and Central Asia one in five people with TB have MDR-TB. It is also now widespread in provinces of China where 7% MDR-TB among new cases has been detected.

These rates surpass the highest levels of drug resistance published in the last report in 2004.

“These findings should sound an alarm”, said Dr Mario Raviglione, Director of the WHO Stop TB Department. “Drug-resistant TB is an expanding threat, and it will continue to worsen if we do not take more aggressive action as a global community. In addition to addressing drug-resistant TB, countries need to do better at getting prompt diagnosis and treatment to people with drug-sensitive TB-this is the best way to prevent the development of drug resistance.” However, levels of resistance such as these make it

clear that countries have no option but to find and treat those with MDR-TB at a far higher rate than they are doing now.

Raising concern even further is the fact that XDR-TB has been found in over 45 countries and is on average 10% of the MDR-TB cases in the former Soviet Union.

In Africa, we still do not have a full understanding of the situation due to the lack of laboratory and survey capacity, but the suspicion is that MDR-TB and XDR-TB is more widespread than is currently thought. Only six countries in sub-Saharan Africa were able to provide drug resistance data for the fourth report. Most countries in the region lack equipment and trained personnel needed to identify drug-resistant TB. While the report finds generally low levels of resistance in the countries surveyed, recent experiences in South Africa show that high HIV levels and the occurrence of MDR-TB and extensively drug resistant (XDR) TB can result in extremely high mortality particularly among those who are also co-infected with HIV.

Trend analysis shows that, while in Russian oblasts the situation is further deteriorating, in the Baltic countries serious intervention measures have resulted in the decline in the number of cases. Thirteen years ago, Estonia and Latvia were singled out by WHO as drug-resistant TB hotspots. Today, in the wake of substantial investment and a sustained assault on MDR-TB,

“The survey provides an overview and vista from which the desolation can be seen through the shadows - another 500,000 people this year with MDR/XDR but without access to quality drugs, diagnostics or dignity. The DRS shines a light on this global abuse of human rights and this affront to both medical and moral standards, which words and statistics alone will not change. Clearly, the time to act is now. DR Mobilization - we’re all in this together.”

Case Gordon, Activist and Vice-Chair MDR-TB Working Group

rates in these two Baltic countries are stabilizing for the first time, and TB notification rates are falling.

The report was launched on February 26-27 in Washington D.C., Geneva, and Brussels to ensure that national governments and the international community take immediate and urgent action, including increasing financial investment, to address the complexities linked to MDR-TB and XDR-TB. If we continue with current levels of funding and implementation we could seriously compromise TB control gains already made.

One sign that governments are taking these findings seriously was seen in Washington DC where there was a hearing on MDR-TB at the Africa and Global Health Sub-Committee of the Foreign Affairs Committee. The objective of the hearing was to explain the implications of data to key decision makers. The hearing was attended by four members of Congress. Dr. Mario Raviglione, Director of the Stop TB Department, WHO reported the main findings of the report to Congress. Dr J. Gerberding, Director of US CDC; Dr K. Hill, USAID Assistant Administrator; Dr M. Dybul, Global HIV/AIDS Coordinator also testified. It was very well attended and was followed with interesting questions and discussion.



Dr. Mario Raviglione, Director Stop TB Department, WHO reporting to the Africa and Global Health Sub-Committee of the Foreign Affairs Committee, USA, on MDR-TB

At the same time, PEPFAR reauthorization for an additional five year period is under consideration by the US Congress. The \$50 billion proposed package includes \$4 billion for TB and \$5 billion for Malaria. This is an authorizing bill and funds would still need to be secured during the annual appropriations process if this is passed.

TB drug resistance requires urgent action today. Existing treatments and diagnostics must be made available to more people and we must have laboratory networks which are able to provide rapid diagnosis of drug resistance for all TB patients including those co-infected with HIV. Investment in research and development for new diagnostics, new drugs effective against resistant strains and an effective TB vaccine must be increased significantly if we are to respond effectively and stop MDR-TB in its tracks.

Read the full report:

» www.who.int/topics/tuberculosis/en/

THE GLOBAL LABORATORY INITIATIVE: INCREASING THE PROFILE AND ROLE OF LABORATORIES

Capacity to diagnose patients with drug-resistant TB is severely limited and it is currently estimated by WHO that less than 5% of existing MDR-TB cases are being detected. Over the past year, however, the profile and role of the laboratory has changed on both technical and political agendas. To address the massive scale-up of laboratory capacity needed in response to the epidemics of HIV-related and drug-resistant TB, the subgroup on Laboratory Capacity Strengthening (SLCS) of the Stop TB Partnership and the Supranational Reference Laboratory Network (SRLN) have been restructured into a TB Global Laboratory Initiative (GLI) with a secretariat provided by WHO. The GLI represents a network of international technical and funding partners involved in laboratory strengthening, working with national TB programs, nongovernmental organizations, and WHO offices at regional and country levels.

The GLI will formally be launched in May 2008. Several key GLI priority activities have already been identified, including country-specific roadmaps for laboratory strengthening, human resource development strategies, laboratory biosafety, and accreditation of laboratories to ensure quality. The SRLN will also be expanded, to assist in the scaling up of national reference laboratory networks and to provide important reference functions such as susceptibility testing of second line TB drugs. Addressing the need for rapid identification of MDR-TB and XDR-TB, policy guidance on programmatic implementation of drug susceptibility testing of second line drugs has been developed and will be released by WHO in April.

PROGRESS ON UNITAID MDR-TB STOCKPILE

The Stop TB Partnership's Global Drug Facility (GDF) will be able to call on a rotating stockpile of second-line drugs to respond quickly to supply challenges faced by MDR-TB programs approved by the Green Light Committee around the world.

A part of the UNITAID-funded MDR-TB Scale-Up Initiative, the stockpile will hold a full course of treatment for 800 patients, and will act as a buffer against the long lead times to which second-line drug orders are subject.

The drug market is in general driven by demand in the North, and while the bulk of actual demand is in developing countries, the global supply of WHO pre-qualified MDR-TB drugs is very limited. It is difficult to attract suppliers to offer affordable prices in an unpredictable market and the process of obtaining WHO Prequalification for drugs is, while crucial for quality assurance purposes, extensive and time-consuming. Furthermore, the relatively limited shelf-life of MDR-TB drugs leads to their being manufactured on demand, resulting in a mandatory delay in any order.

While UNITAID and other groups work to improve this global supply situation in terms of price, production capacity and quality, the GDF will be able to make use of the stockpile to help ensure an uninterrupted supply of drugs to MDR-TB programs around the world and to enable a more timely and cost-effective response when MDR-TB affects a community.

This new resource will also be available to allow more-rapid servicing of smaller orders as well as allowing UNITAID-funded MDR-TB programs to scale up the number of patients on treatment.

While the stockpile is set to be at full capacity later this year, its operations have begun and the benefits of the GDF-managed project are already in evidence. For example, stockpile drugs were used to complete an order that would otherwise have been delayed while waiting for the final component to be manufactured. In another example, stocks were used to replace drugs on the brink of expiry, ensuring uninterrupted treatment by the program.

In the context of WHO's recently released drug resistance survey, which found world drug-resistant TB levels to be at a record high, the implementation of a fully operational UNITAID rotating stockpile augurs well for a more streamlined and consistent supply of second-line anti-TB drugs and is welcome news in the fight against MDR-TB and the burgeoning threat of XDR-TB.

OVER 30,000 PATIENTS NOW APPROVED BY THE GREEN LIGHT COMMITTEE (GLC)

The **Green Light Committee** helps countries access treatment for drug-resistant tuberculosis. It is a mechanism that helps countries to implement the WHO Stop TB Strategy which calls for the control and prevention of MDR-TB through increased access to high quality second line anti-TB drugs and management of MDR-TB programs in line with WHO guidelines.

The Initiative consists of a Secretariat (provided by WHO), the Green Light Committee (an expert review, which is a subgroup of the Stop TB Working Group on MDR-TB, and a WHO advisory body) and the Global Drug Facility (GDF) the drug procurement arm of the Initiative). The GLC collaborates with the Global Fund and UNITAID. To help limit resistance to second-line anti-TB drugs, the Global Fund requires that all procurement of these drugs under Global Fund grants is conducted through the GLC Initiative.

UNITAID provides funding for second-line anti-TB drugs to GLC approved programs. Collaboration allows for negotiation of better prices by pooling procurement needs and resources of many programs. The GLC is now working in 53 countries on 104 projects and has approved 31,102 patients for medicines.

The Global Fund and GLC monitor the performance of MDR-TB programs, including program results and targets relevant to MDR-TB scale up. In order to start an MDR-TB program and receive second line anti-TB drugs, TB programs can submit applications to the GLC. For more information contact your WHO country or regional offices or see the following for fast track applications, FAQs and other useful information:

» www.who.int/tb/challenges/mdr/greenlightcommittee/en/index.html

UPCOMING EVENTS

GLOBAL HEALTH: CURRENT ISSUES, FUTURE TRENDS AND FOREIGN POLICY

When: 29 April 2008

Where: Royal College of Physicians, London

For more information:

[www.rcplondon.ac.uk/event/
details.aspx?e=1012](http://www.rcplondon.ac.uk/event/details.aspx?e=1012)

Conference Department.
Tel: +44 (0) 20 7935 1174
Ext. 436/252/300.

Email: conferences@rcplondon.ac.uk

Drawing together experts from the clinical and policy worlds, this conference will explore the growing UK debate on global health, with updates on communicable and chronic disease. The conference will be of interest to physicians, public health specialists, health care personnel, policy makers, political lobbyists, journalists, supranational organizations and NGOs.

XDR-TB TASKFORCE MEETING

When: April 8-10, 2008

Where: Geneva, Switzerland

For more information: jaramilloe@who.int

GREEN LIGHT COMMITTEE MEETING

When: April 11-12, 2008

Where: Montreux, Switzerland

For more information: sahakyani@who.int

INFECTION CONTROL TRAINING FOR THE EUROPEAN REGION

When: April 7-12, 2008

Where: Romania

For more information:
tuberculosis@euro.who.int

WHO EURO. Training for TB consultants of EURO region in infection control

GLOBAL LABORATORY INITIATIVE (GLI)

When: May 8-9, 2008

Where: Annecy, France

For more information: weyerker@who.int

WHO TRAINING COURSE FOR PUBLIC PRIVATE MIX-TB CONSULTANTS

When: April 14 - 19, 2008

Where: Sondalo, Italy

For more information:
www.euro.who.int/tuberculosis

Email: tuberculosis@euro.who.int

WHO Collaborating Centre, Global TB course

EUROPEAN LABORATORY STRENGTHENING TASK FORCE MEETING

When: May 5, 2008

Where: Banja Luka, Bosnia & Hercegovina

For more information:
www.euro.who.int/tuberculosis

Email: tuberculosis@euro.who.int

WHO TRAINING COURSE ON IMPLEMENTING THE STOP TB STRATEGY (MDR/XDR, TB/HIV, PPM, EMPOWERING PEOPLE WITH TB AND COMMUNITIES)

When: May 5-17

Where: Sondalo, Italy

For more information:
www.euro.who.int/tuberculosis

Email: tuberculosis@euro.who.int

WHO Collaborating Centre, Global TB course

WHO TRAINING COURSE ON COLLABORATIVE TB/HIV ACTIVITIES IN EUROPE (ENGLISH/RUSSIAN)

When: July 1-8, 2008

Where: Sondalo, Italy

For more information:
www.euro.who.int/tuberculosis

Email: tuberculosis@euro.who.int

WHO Collaborating Centre - European TB course