JOINT WHO AFRO – EMRO - HQ "NEW DR−TB DRUG INTRODUCTION EXPERIENCE EXCHANGE WORKSHOP FOR THE WHO AFRICAN AND EASTERN MEDITERRANEAN REGIONS", 4th-5th NOVEMBER 2015, NAIROBI, KENYA
- SUMMARY REPORT -

Background

WHO has recently issued policy recommendations regarding the use of newly approved anti TB medicines, namely Bedaquiline and Delamanid, as well as re−purposed drugs classified as Group 5 in the WHO *Companion Handbook of 2011 Guidelines for Programmatic Management of Drug-resistant Tuberculosis* (PMDT). The new medicines are increasingly being introduced in the treatment regimens of multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB. Given the essential role of the regional Green Light Committees (rGLCs) as the primary point of contact for country guidance and advice on PMDT, a series of workshops have been planned by WHO for the rGLC members and their respective rGLC Secretariat Focal Points, and partner organizations to brief them on WHO policy and encourage them to ensure that treatment principles and drug orders are aligned with the current WHO guidelines both in countries and among partners.

WHO/AFRO and EMRO, in collaboration with HQ, convened the second of such workshops in Nairobi, Kenya, 4−5 November 2015. The meeting was attended by the members of the rGLCs for the African and the Eastern Mediterranean Regions, the respective rGLC Secretariat Focal Points, and representatives of partner organizations, UNION, KNCV, Foundation Damien MSH, USAID, GDF, as well as NTP of Somalia. A total of 23 participants attended the workshop. A number of the facilitators presented remotely via Skype (WHO HQ, USAID, and the Global Fund)

The objectives of the workshop were:

1. To provide an update on current WHO policy recommendations on the use of new drugs, as well as those in Group 5, in the treatment of DR−TB patients, and how to introduce the drugs into programmatic use;
2. To share experiences of countries and partner organizations who have introduced new and/or re−purposed drugs in to the treatment of DR−TB countries; and
3. To plan the next steps for the introduction of new drugs and re−purposed drugs for the treatment of DR−TB patients in the countries of the WHO African and Eastern Mediterranean Regions.

SESSION 1: Update on current WHO Global and regional policies, guidance and plans – Chaired by Dr. Dr Hind Satti (Chair, r-GLC AFRO)

The session featured seven presentations and panel discussions on the current WHO global, regional policies guidance and plan, followed by the update by the two regional GLCs and partners providing the procurement of the drugs (GDF and USAID).

The presentation on WHO strategic plan for new drugs and regimens focuses on new drugs. The introduction of new drugs containing regimen should be a multistage (planning,

preparations, pilot and scale-up) and multi partners process to develop the best approach for each country / area.

The participants stressed the possibility of the cumulative effect of the different anti TB drugs. There is also the potential risk of cross resistance between Clofazimine and Bedaquiline that needs to be further explored. The development of Bedaquiline resistance is not yet well documented, and a DST method is still under validation by the SNRL network.

Key points:

- National and stakeholder engagement is needed;
- Attention needed for the prevention of misuse and emergence of resistance;
- Policy implementation under programme conditions: both safe and feasible;
- Need to collect due information to inform policy making national and globally and inform scale-up; and
- Need to speed up the development of laboratory systems.

The main areas covered by the "update on current WHO PMDT policies and guidance" included recommendations on Palliative care, Ethics, and TB and human rights. The presenter shared also the key recommendations on infection control. However the quality of evidence is low for administrative, environmental and personal protection measures.

Dr Falzon's presentation was on "Safety monitoring of drugs used to treat DR-TB patients". The use of new drugs forces us to revisit pharmacovigilance. The presenter urged participants to be pro-active, to look for adverse events actively and promptly report them when they occur. He explained how to do this as per the recommendations in the WHO's Pharmacovigilance policy document and the Companion Handbook. Participants were urged to obtain these documents and read through them for more information.

The presentations on the rGLC updates were presented by the respective rGLC chairs and constituted the third part of session 1.

For EMR, Dr Essam highlighted the latest information about TB and MDR-TB burden as per the WHO's Annual GTB report 2015. The 27% MDR-TB detection among notified cases was discussed. Members who responded agreed with it. For instance Pakistan, which has the majority of the cases in EMR, still has a low coverage of detection both among previously treated and the new TB cases. This is because DST is targeted mainly at previously treated cases, who contribute a small proportion of the overall caseload in Pakistan.

On the AFR side, Dr Hind Satti gave an overview of DR-TB in the region among previously treated cases. DST coverage saw a sharp increase between 2013 and 2014. Major challenges in the region at country level are lack of expansion plans, contact tracing and still low case finding. Challenges in AFRO for scale up. Major challenges relate to: human resources; the type of treatment model which is usually hospital based, especially for high burden countries, instead of ambulatory; and inadequate planning for expansion and funding of all the components of the scale up.

The update from GDF was done by Nigor Muzafarova. She stressed that the usual lead time for GDF sourced medicines is 4-6 months. The price of Bdq ranges from USD 900-3000 per

patient treatment. Dr Mukadi presented on the USAID-Janssen Bdq donation programme. The programme aims to supply 30,000 patient courses over 4 years to eligible countries.

The discussion focused on how countries can access the donation programme, and the support that GLC members can provide to countries. The participants agreed to highlight the participation on GLC members in supporting countries for the introduction of new TB drugs.

SESSION 2: Sharing experience of countries and partner organizations who have introduced new and/or re-purposed drugs for the treatment of DR-TB cases – Chaired by Dr Hind Satti rGLC AFR (Day 1) and Dr Essam Elmoghazy Chair of rGLC EMR (Day 2)

This session aimed at sharing the experience of countries from the two regions (Lesotho, Niger, Pakistan, Somalia, South Africa and Sudan) and partners (UNION) in introducing the new DR−TB drugs.

Dr A Trebucq presented the UNION's support activities to introduce the shorter MDR-TB treatment regimen, particularly in countries of West Africa. Subsequent discussions focused on the follow up of patients and the need of solid evidence before scale−up of said shorter regimen.

GDF shared its experience on access to Linezolid, which is different to that of South Africa. South Africa clarified that the main issue the country has faced has been due to the country's procurement system which Pfizer has not complied with.

Dr Satti presented the ENDTB project in Lesotho. This 4 year project has as its main objective to expand access to the new DR−TB drugs in 17 countries, and to provide capacity to NTP's to conduct a clinical trial of 9 novel DR−TB treatment regimens with the aim of producing evidence for the use of the new drugs in 5 to 8 priority new regimens used to treat DR−TB.

Dr Souleymane Hassane, representing Damien Foundation, shared the experience of Niger with its use of the following 6 drugs – clofazimine, high dose isoniazid, imipenem/cilastin, amoxicillin/clavulanate,. bedaquiline and linezolid. Several patients have been treated with different regimens over the years, 57 patients having been treated with 9 month regimen treatment (9MTR) He shared the results of a published paper which showed that there were no relapses after 9MTR use in 34 patients. He noted that 7 "pre−XDR" and XDR−TB patients have already been enrolled on various longer regimens.

Dr Al Agab shared the experiences from Sudan, with the notification of 2 XDR−TB since 2014 but not yet treated, and the lack of a PV framework. She pointed out the current lack of country policy on new drugs, but there are plans to correct this and follow the WHO minimum recommendations.

Dr Hergeye shared the experiences of Somalia. also highlighting the absence of a PV framework, policy on new drugs, weak HR for MDR-TB management, and the need to establish an NRL and a country−wide laboratory network.

Lastly, Dr Sabira Tahseen presented from Pakistan, highlighting the high detection rate (10%) of mono-resistance to R (using GeneXpert). Said detected patients are enrolled on the MDR-TB treatment regimen. Treatment monitoring is based on solid culture, causing a prolonged intensive phase whilst awaiting the culture results. FQ resistance is observed to be high. In relation to pharmacovigilance, although there is a checklist for TB symptoms with the data being entered into an electronic recording system, there is no data for PV and no surveillance for adverse effects is in place. The country is planning to introduce new DR−TB drugs soon, however there is no framework or process for introduction of the new drugs and process in place yet, and obtaining approval to procure the new drugs is time consuming.

Key points:

- There is a common and urgent need to strengthen pharmacovigilance as part of health system strengthening in many countries in the two regions.
- Countries do not have policy in place for the introduction of new DR−TB drugs.
- Laboratories need to strengthen their capacity to be able to conduct SL DST.

SESSION 3: Plan the next steps for the introduction of new drugs and re-purposed drugs for the treatment of DR-TB patients in the countries of the WHO African and EMRO regions – Chaired by Dr Essam Elmoghazy, Chair of rGLC EMRO

This session featured presentations on the new Memorandum of Understanding (MoU) between WHO and GF to support rGLC and the next steps for each region.

Dr Yassin presented the GF's approach and the MoU for the rGLCs and the roles expected under the MoU. The discussions focused on the GF's expectation that rGLCs should review all related TB control aspects of MDR−TB management. Some participants thought that this was too extensive a demand, but the overall consensus was that this essential to prevent the development of MDR-TB.

There was a discussion about the role of the rGLCs in approving GDF SLD orders. The conclusion was that the rGLC may provide ‘advice’ following a review of the order to GDF. However the rGLCs are not there to approve or disapprove a GDF SLD order.

The chairs of the two regions presented their respective next steps for the introduction of the new drugs and re-purposed drugs for the treatment of DR-TB patients in the countries of the WHO African and Eastern Mediterranean regions. The following next steps were proposed by the respective rGLC Chairs:

r-GLC EMRO

- Arrange briefing meeting to MDR−TB focal persons and partners in the countries. This will cover all aspects of introducing new medicines. Planned for June 2016

- rGLC members and secretariat will support countries for refreshing their PMDT plans through missions, on-line support and other means are requested throughout 2016.
- Briefing will also be included in consultant training planned for May 2016.

For EMR, it was suggested to also include the Gulf countries. Samiha noted that the Gulf countries are not supported by the GF, but EMRO will try to include them. It was observed that Oman and Bahrain have the capacity already in place to introduce the new drugs.

The plan for missions was endorsed and it was requested that partners already engaged at the country level should be included in these missions. It was highlighted that engaging such partners is very important towards building country capacity.

It was noted that a lot of preparation will be required before the proposed briefing meeting in 2016. Questions were asked about the planned consultant training. EMRO mentioned that the rGLC-EMR is planning to enrich their courses using the support of partners, such as UNION and KNCV. Fraser noted that many consultants have been recently trained, and that they need to be better utilised for missions and TA activities.

r-GLC AFRO

1. Programmatic management
- Plan TA to support countries to rationally introduce new TB drugs;
- Coordination of partners and stakeholders support;
- To support participation of private sector;
- Regional training on new drugs;
- Support and advice on guidelines update; and
- Strengthen and update reporting and recording forms.

2. Regulations
- Map requirements and support countries to register new drugs where needed;
- Advise and support countries to update their national guidelines and protocols;
- Explore inclusion of new drugs in the respective country's essential drug list; and
- Advise and support projections and procurement of new drugs.

3. Laboratory aspects
- Support trainings on FL and SL DST;
- Training of consultants to provide TA;
- Support accreditation of NRLs and EQA systems; and
- Support and coordinate with other laboratories initiatives.

4. PV
- Provide TA to develop aDSM;
- Regional training on PV; and
- Community participation.

5. Advocacy

- Advocate for reduction of the cost of new drugs; and
- Support countries to update their NSP to cover community participation on community-based PV.

For AFRO, the suggestion was given to group some of the above proposed activities. It was noted that some activities may need strengthened co-ordination between partners. Fraser shared the information that WHO will hopefully making a recommendation in relation to the shorter MDR−TB treatment regimens in 2016. This will provide many opportunities, but may also add complexities.

Dr Agnes Gebhard from KNCV shared that the Nigeria mission noted that the scale−up of Xpert to detect *M.tb* is happening fast. If Xpert is used to detect *M.tb* in low rifampicin resistance (RR) areas, there is a need to repeat the Xpert test due to the potential for false positive results in such low prevalence areas. She also shared that a new Xpert cartridge to detect FQ resistance is expected next year.

Fraser supported Agnes' point on the need to retest RR in low prevalence area, and that may require re-visiting the diagnostic algorithms. He also noted that WHO will be re−looking at the SL LPA again in early 2016.

Dr Subroto commented that while Xpert scale-up is happening fast in many countries, often the specimen collection/transport/storage systems are not well addressed at the country level.

Another point was raised about the rGLC role and autonomy to conduct missions going beyond country demands, as country demand may not be sufficient. Fraser noted that this is an on-going discussion and will be discussed in the 4th GDI Core Group meeting on 1 December 2015. However it needs to be remembered that rGLC network is currently heavily dependent on funding from the GF, and activities are linked with what is in the MoU. The rGLCs now have an advisory role and not a controlling one. However it is important the roles of partners in the activities be enhanced.

The meeting ended with a closure speech from the respective rGLC chairs.

N.B
Each rGLC took the opportunity of this meeting in Nairobi to have a separate rGLC meeting after the end of Day 1.

Annex

- **List of Participants**
- **Photo group**
- **Agenda**

Annex 1: List of Participants

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Annex 2 : Group Photo

Annex 3: **Agenda**

Day 1: 4 November 2015
Chair: Hind Satti

09.00 – 09.15	Welcome and Workshop objectives Local briefing	R Sall WHO AFRO, S Baghdadi WHO EMRO UNDSS, Kenya
Session 1 09.15 – 10.30	Objective: To provide updates on current WHO global and regional policies, guidance and plans • How to introduce the new and repurposed drugs into programmatic use for the treatment of DR-TB patients • Update on current WHO policy recommendations on the use of new drugs (i.e. Interim Guidance on Bedaquiline and Delamanid) in the treatment of DR-TB patients	 GTB (F Wares) GTB (F Wares)
10.30 – 11.00 Coffee		
Session 1 11.00 – 13.00	• Update on current overarching WHO PMDT policies and guidance, including recommendations on the use of Group V drugs and repurposed drugs in the treatment of DR-TB patients and ethics and palliative care • Safety monitoring of drugs used to treat DR–TB patients • Discussions	GTB (E Jaramillo) GTB (D Falzon) ALL
13.00 - 14.00 Lunch		
Session 1 14.00 – 15.30	• Update from the AFR rGLC and EMR rGLC Chairs • Update from GDF on Group V products availability, policy to access these drugs and updated prices • Perspectives on the introduction and access to new drugs for DR–TB treatment, and an update on the bedaquiline "donation programme" and its coordination with other partners and programmes • Discussions	H Satti (AFR rGLC) E Elmoghazy (EMR rGLC) GDF (N Muzafarova) USAID (A Golubkov) ALL
15.30 – 16.00 Coffee		
Session 2 16.00 – 17.30	Objective: To share experiences of countries and partner organizations who have introduced new and/or re–purposed drugs for the treatment of DR–TB cases • Presentation from countries and partner organizations who have introduced new and/or re–purposed drugs in to the treatment of DR–TB countries • Discussions	 N Ndjeka (South Africa), A Trebucq (UNION), H Satti (Ethiopia, Lesotho, Nigeria), S Hassane (Fondation Damien) ALL

Day 2: 5 November 2015
Chair: Essam Elmoghazy

Session 2 continued 09.00 – 10.30	• Presentation from countries and partner organizations who have introduced new and/or re–purposed drugs in to the treatment of DR–TB countries continued • Discussions	S Agab (Sudan), MA Hergeye (Somalia), S Tahseen (Pakistan) ALL
10.30 – 11.00 Coffee		
Session 2 ctd 11.00 – 13.00	• Introduction and access to new drugs for DR–TB treatment under the Global Fund's funding model • Discussions	Global Fund (M Yassin) ALL
13.00 - 14.00 Lunch		
Session 3 14.00 – 15.30	Objective: To plan the next steps for the introduction of new drugs and re–purposed drugs for the treatment of DR–TB patients in the countries of the WHO African and Eastern Mediterranean Regions • Discussions	ALL
15.30 – 16.00 Coffee		
Session 3 ctd 16.00 – 16.30	• Discussions continued	ALL
16.30 – 17.30	Wrap up, next steps and closure	H Satti, E Elmoghazy, R Sall, S Baghdadi