HIV DRUG RESISTANCE

MEETING REPORT

WHO HIV DRUG RESISTANCE STEERING GROUP MEETING

OCTOBER 2013

World Health Organization

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TABLE OF CONTENTS

1. BACKGROUND

In 2004, WHO and the United States Centers for Disease Control and Prevention (CDC), in collaboration with partners (HIVResNet), developed a global strategy for the assessment and prevention of HIV drug resistance (HIVDR). Between 2004 and 2010, 101 surveys to assess transmitted drug resistance were conducted in 30 countries, and forty surveys to assess acquired HIVDR were performed in 12 countries. These surveys have generated invaluable data, published in 2012 in *WHO's HIV Drug Resistance Report,* on the magnitude of HIVDR transmission and emergence in low- and middle-income countries and have put to rest concerns that the rapid scale up of ART would generate widespread drug resistance.

Nevertheless, lessons learned from this initial implementation phase and the evolution of ART programmes have highlighted important limitations of the first generation of surveillance methods. First, due to the limited coverage of antiretroviral therapy at that time, the first generation of HIVDR surveillance methods explicitly sought to monitor HIVDR levels in a circumscribed geographical area using conveniently selected sites to facilitate implementation. Although important as general markers of programme performance, the fact that results were derived from convenient samples in defined geographic areas limited the ability to inform national and global level decision making with respect to optimal treatment regimens at the population-level. Country experiences also made clear the challenges inherent to the prospective method used to assess acquired HIV drug resistance, particularly the high costs of maintaining a prospective cohort and issues with the quality and integrity of the clinical and demographic data collected.

In the light of these lessons, WHO launched in 2012 a consultative process to revise existing surveillance methods with a view towards simplifying their operational design and improving their feasibility and uptake. Revised methods were developed in consultation with a broad group of programme managers, technical experts and virologists.

In order to review the outcomes of this process, a meeting of the HIVDR Steering Group was held on 1-2 October, 2013 to discuss the draft revised methods and obtain the group's expert input and advice. The meeting also reviewed the governance arrangements of WHO's HIV Drug Resistance Network to optimize the Steering Group's functioning as WHO's key advisor on HIVDR issues.

2. MEETING OBJECTIVES

i. Review and provide feedback on the proposed revised methods for the surveillance of transmitted, pre-treatment and acquired drug resistance.
ii. Discuss governance arrangements of the WHO HIVDR area of work.

3. KEY EXPECTED OUTCOMES

The meeting's key expected outcomes were: (i) advice to WHO on the revised surveillance methods and (ii) agreement on the governance and structure of the HIVDR work.

4. MEETING PARTICIPANTS

WHO standard Declarations of Interest (DoI) forms were completed by Steering Group members. Four members declared potential conflicts of interest. Sergio Carmona has received research support from Roche for a research unit developing an assay that is still under validation and that has currently no commercial value. Annemarie Wensing received research and unrestricted educational grants belonging to the university as well as subsidized travel to international conferences and workshops, paid for by BMS, Gilead, Janssen, MSD, ViiV healthcare and Virology Education. Jonathan M Schapiro has served within the past four years as a consultant, advisor and has received honorarium and research support from Abbot, BMS, GSK, ViiV Healthcare, Pfizer, Janssen-Cilag, Roche, Gilead, Teva, Virology Education and Merck. Robert Shafer received and still receives remuneration for consulting from Celera and Siemens Health Care. He also received and still receives research funding from Hoffman LaRoche, Gilead Sciences, Bristol-Myers Squibb, Celera and Siemans Health Care. As none of these interests were deemed substantively conflicting with the meetings purpose and topics, the individuals declaring those interests were allowed to fully participate in the meeting.

5. SUMMARY OF DISCUSSIONS

5.1 Opening and election of the Chair

Dr. Joseph Perriëns, Coordinator, HIV Commodities and Technologies (HIV Department, WHO), opened the meeting. Avelin Aghokeng (IMPM-IRD/CREMER, Yaounde, Cameroon), was nominated Chair of the meeting and was accepted without objections by the group.

5.2 Rationale and overview of revised methods

The group was briefed on the rationale for the introduction of revised methods. The original surveillance methods, developed in 2005, were designed for an early phase of ART scale-up characterized by low ART coverage and limited number of individuals on ART. At that stage, ART was available only at a few selected sites, mostly in urban areas. To reflect this reality, the original HIVDR surveillance and monitoring strategy focused on sentinel sites and relied on convenient sampling to select sites where enrolment would be possible. The focus was on clinic functioning, and results were area/region-specific. Survey findings were designed as an alert that would trigger more in depth investigations.

However, availability and coverage of antiretrovirals have increased dramatically in low- and middle-income countries since 2003. As of December 2012, almost 10 million people were receiving antiretroviral therapy in 149 low- and middle-income countries, with over 800,000 pregnant women receiving ARVs for MTCT. ART is now accessible across more than 30,000 ART facilities worldwide. The roles and uses of antiretrovirals are being increasingly expanded, both for treating and preventing HIV infection, and a number of countries have already approved their use in the context of pre-exposure prophylaxis for specific to be of greater relevance for decision making, while being sufficiently flexible to be implemented in multiple epidemiological settings. The ultimate goal is to obtain nationally representative results that can inform national programming.

Broadly, the HIVDR surveillance strategy elements tabled for discussion at the steering group included the following 5 elements:

1. TDR: transmitted drug resistance in populations likely to be naive and have been recently infected
2. PDR: Pre-treatment drug resistance in populations initiating ART
3. ADR: Acquired drug resistance in populations receiving ART at different time points
4. HIV drug resistance surveillance in ART-naive children less than 18 months recently diagnosed with HIV using Early Infant Diagnosis (EID) testing
5. EWI: Early Warning Indicators for HIVDR

Within this architecture, TDR survey results are particularly useful to inform the selection of optimal pre-exposure prophylaxis (PrEP), post exposure prophylaxis (PEP) regimens, and on ART programme functioning to minimize HIVDR emergence and its transmission; PDR survey results inform the selection of optimal first-line combinations; and ADR surveys results inform the selection of optimal second-line regimens.

It was highlighted that, under certain circumstances, routine HIVDR testing may also be used to assess HIVDR prevalence at the population level. However, it was stressed that losses along the cascade of viral load testing and genotyping can lead to biased estimates and inappropriate public health decision making (see section 5.14).