ARE COUNTRIES USING GLOBAL FUND SUPPORT TO IMPLEMENT HIV DRUG RESISTANCE SURVEILLANCE? A REVIEW OF FUNDED HIV GRANTS

Karen F. Kelley,1 Emily Caudwell,2 Serge Xuref,2 Thuy Huong Ha,2 and Silvia Bertagnolio1

1World Health Organization, and 2The Global Fund to Fight AIDS, Tuberculosis and Malaria, Geneva, Switzerland

The Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund) is the largest funder of human immunodeficiency virus (HIV) prevention and treatment programs worldwide. Since 2002, the Global Fund has encouraged grant recipients to implement drug resistance surveillance (DRS) as part of treatment programs. We reviewed documentation of 147 grants funded in 2004–2008 (funding rounds 4–8) to assess grantees’ use of funds to support HIV DRS. Overall, 94 grants (64%) described HIV DRS as part of the national treatment program. However, only 32 grants (22%) specifically documented DRS as a grant-funded activity. This review provides baseline information suggesting limited use by countries of Global Fund financing to support HIV DRS. Additional assessment is required to evaluate barriers to using Global Fund grants to support DRS.

Although World Health Organization (WHO) surveys of human immunodeficiency virus (HIV) drug resistance (HIVDR) suggest that HIVDR rates remain limited at this time, HIVDR poses a threat to the success of antiretroviral treatment (ART) programs, endangering efforts to scale up and sustain these programs effectively. Ensuring the availability and appropriate use of antiretroviral drugs (ARVs) is crucial to safeguarding the continued efficacy of treatment and to optimizing patient outcomes. It also protects the value of investments made by national governments and by donors. As infected individuals begin treatment earlier and ARVs become more widely used to prevent HIV transmission, efforts to minimize HIVDR become increasingly important.

ART programs must be informed by routine programmatic evaluation to minimize first-line failure and potential HIVDR emergence and transmission. Routine, standardized, population-based surveillance of HIVDR is imperative and must be in place to detect an increase of HIVDR in a timely manner. Since 2004, WHO has developed and supported a global strategy to assess and prevent HIVDR, with implementation in >50 countries. To ensure sustainability of both drug resistance surveillance (DRS) in countries and the global surveillance system, it is crucial that ministries of health and development partners identify sustainable funding from both domestic and international sources to support and maintain this global approach to assessing HIVDR.

The Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund) is the largest funder of HIV programs worldwide and has enabled massive scale-up of treatment programs in low- and middle-income countries through successive rounds of funding. Recognizing the importance of investing in DRS as a component of treatment scale-up, the Global Fund Board issued a decision point in 2002 (GF/4/2) that “strongly recommended to Recipients that they implement mechanisms to monitor and contain resistance … according to existing international guidelines and, if necessary, drawing on budgeted requests for financial support from the Fund” [5]. The Global Fund has since put in place several mechanisms to encourage and support grantees to conduct DRS, including...
components of the procurement and supply management (PSM) plan required of grantees [6] (section 2.6 asks: “Is there a strategy for monitoring and containing drug resistance? If yes, describe briefly the elements of the strategy. If the strategy is not in place, describe plans to develop it”); the PSM guidance [7] (page 25 of the guide states: “[R]ecipients must ensure that systems are in place to monitor and contain resistance”); and the standard grant agreement with recipient countries (article 19 states: “The Principal Recipient shall implement mechanisms to … monitor and contain drug resistance”) [8]. In addition, grant monitoring assessments by local fund agents include an item requesting that they “comment on whether the Principal Recipient put into place and is … implementing systems to monitor … drug resistance” [9].

This review was undertaken to assess the extent to which grantees have used Global Fund resources to support HIV DRS.

**METHODS**

We reviewed key documents related to funded round 4–8 grants to identify (1) HIV DRS activities and plans in grantee countries and (2) grantee requests for funding of HIV DRS. Key documents included original grant proposals, detailed work plans, detailed and summary budgets, program grant agreements, and PSM plans. Available documentation for all round 4–8 funded grants was systematically reviewed using consistent search terms and validation procedures. Original grant proposals were available on the Global Fund public website [8]; all other grant documents were accessed through the Global Fund intranet. All documents were accessed during May–August 2010. Countries funded in >1 round are included at each occurrence.

Two indicators were used as proxy measures: (1) inclusion of HIV DRS in the country’s HIV treatment program, and (2) request for funds to implement DRS (Table 1). Grantees were considered to have documented HIV DRS as part of their treatment program if HIV DRS was described in either the grant proposal (as an ongoing or planned activity) or the PSM plan (by completing section 2.6 describing the “system established to monitor HIVDR”). HIV DRS was considered to be included as part of the grant’s funded activities if it was included as a component of the detailed proposal work plan, the detailed or summary budget, or the Program Grant Agreement (either in the Annex A program description or as an indicator in the performance framework).

**RESULTS**

One hundred forty-seven HIV grants were approved for funding in rounds 4–8 (round 4, 27; round 5, 26; round 6, 33; round 7, 26; round 8, 35). All funded grants included ART components in their work plans and budgets.

Of the 147 funded grants, 94 (64%) described HIV DRS as a component of the overall treatment program. The proportion of grants documenting DRS did not vary substantially by round (Table 2) or by region (data not shown).

Thirty-two of the 147 (22%) funded grants included DRS as a funded activity in the proposal. Once again, the proportion of grants including DRS did not vary substantially by round (Table 2) or by region (data not shown). We identified costed requests for HIV DRS activities for 24 grantees. The total funding requested in these 24 grants was $10,952,257 (median request, $144,865; range, $1875–$6,490,820). The majority of funding requested was to support surveys of acquired resistance among patients on treatment or for monitoring drug resistance early warning indicators. Two proposals requested funding to set up national HIV DRS networks, and 2 requested funding for training laboratory staff in resistance testing.

**DISCUSSION**

WHO has defined and recommends a specific set of activities for surveillance of HIVDR [4]. WHO and its technical partners,

<table>
<thead>
<tr>
<th>Table 1. Review Framework for Round 4–8 Grants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indicator</td>
</tr>
<tr>
<td>HIV DRS in the country’s HIV treatment program</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Request for funds to implement DRS</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: DRS, drug resistance surveillance; HIV, human immunodeficiency virus; HIVDR, HIV drug resistance; PSM, procurement and supply management.
including WHO HIVResNet (http://www.who.int/hiv/topics/drugresistance/hivresnet/en/index.html), have provided technical assistance to >50 countries to adapt and implement their national HIVDR strategies, which should be integrated into the national HIV prevention and care plan and existing evaluation structures. DRS results provide an evidence base to support optimal use of available ARVs and minimize clinic and program factors associated with the emergence of HIVDR, thus optimizing patient care. WHO has worked closely with the Global Fund to support applicants and grantees to ensure that HIV DRS is considered an important component of ART scale-up, including issuance of technical guidance on HIVDR for Global Fund applicants to support inclusion of strategy elements into Global Fund proposals [11].

In theory, information on a country’s HIV DRS should be documented in several parts of the Global Fund proposal, whether or not the applicant has included DRS in its formal work plan or budget. It is somewhat encouraging that the majority (64%) of funded proposals included information on ongoing or planned HIV DRS in their proposal documentation, indicating a high level of awareness of the importance of HIVDR.

However, it is surprising that only 32 of 147 (22%) funded grants took advantage of Global Fund financing to support or expand DRS. It is possible that these countries had adequate financing for their national DRS activities and did not require additional support from the Global Fund. It is also possible that the available documentation did not enable a robust assessment of specific funding requests because costs of DRS could be hidden in other budget areas such as monitoring and evaluation or commodities. However, parallel assessments carried out on funding requests for tuberculosis DRS and malaria DRS indicated that a much higher percentage (>60%) of round 4–8 proposals requested specific funding for these activities (Global Fund, unpublished data).

Although prioritization of activities is country driven and owned, the Global Fund has established policy and administrative procedures to encourage recipients to implement effective DRS as part of an overall approach to treatment scale-up. This review indicates that only 64% report the existence of DRS within their national ART programs. The Global Fund and its network of technical partners may consider more strongly advocating the inclusion of DRS activities into grant proposals through existing administrative and policy mechanisms at country, regional, and global levels, including information notes, guidance to technical review panels, and country coordinating mechanisms. The Global Fund can also consider prioritizing actions in specific countries, for example, countries with the highest HIV prevalence or largest absolute case numbers or those scaling up treatment most rapidly.

Data for this review were restricted to existing sources, which did not enable an assessment of the quality or comprehensiveness of work implemented or planned by grantees. Although the Global Fund formularies used by grant applicants request details on the country’s mechanisms for drug resistance prevention and assessment, the level of detail provided by recipients was inconsistent, often incomplete, or of poor quality. The data also did not enable an assessment of implementation of funded activities.

This review assessed use of Global Fund resources to support HIV DRS in countries scaling up ART. Despite data limitations, our findings indicate that HIVDR may not have been considered an integral component of treatment programs in approximately 36% of grantee countries engaged in significant treatment scale-up and that there was limited use of Global Fund resources to support HIV DRS in grantee countries during this period.

HIVDR emergence and transmission remains low in the majority of the areas and populations assessed through WHO DRS methods [12]. However, as ART roll-out continues, increased rates of HIVDR may occur. Recent data document moderate (5%–15%) levels of transmitted HIVDR in specific geographic regions [13]. These data underscore the importance of HIV DRS to guide public health programs and to support practices to minimize emergence and transmission of HIVDR. This review provides background and baseline information. Additional reviews may be useful to assess the quality and comprehensiveness of DRS activities financed by the Global Fund and assess the reasons why the majority of grantees did not include HIV DRS in their proposals.

Table 2. Drug Resistance Surveillance in Grant Documentation, Approved Global Fund Grants Rounds 4–8

<table>
<thead>
<tr>
<th>HIV DRS in the country’s HIV treatment program</th>
<th>Round 4, No. (%)</th>
<th>Round 5, No. (%)</th>
<th>Round 6, No. (%)</th>
<th>Round 7, No. (%)</th>
<th>Round 8, No. (%)</th>
<th>Total Rounds 4–8, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Request for funds to implement DRS</td>
<td>19/27 (70)</td>
<td>13/26 (50)</td>
<td>21/33 (64)</td>
<td>16/26 (62)</td>
<td>25/35 (71)</td>
<td>94/147 (64)</td>
</tr>
<tr>
<td>Total</td>
<td>10/27 (37)</td>
<td>6/26 (23)</td>
<td>6/33 (18)</td>
<td>4/26 (15)</td>
<td>6/35 (17)</td>
<td>32/147 (22)</td>
</tr>
</tbody>
</table>

Abbreviations: DRS, drug resistance surveillance; HIV, human immunodeficiency virus.
Notes

Disclaimer. The conclusions and opinions expressed in this article are those of the authors and do not reflect those of their respective organizations.

Supplement sponsorship. This article was published as part of a supplement entitled “The World Health Organization HIV Drug Resistance Prevention and Assessment Strategy: Global, Regional, and Country Progress,” sponsored by The Bill & Melinda Gates Foundation (38180).

Potential conflicts of interest. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References