World Health Organization

TECHNICAL UPDATE

HIV DRUG RESISTANCE

HIV DRUG RESISTANCE SURVEILLANCE GUIDANCE: 2015 UPDATE

DECEMBER 2015

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ACRONYMS AND ABBREVIATIONS

ADR	Acquired HIV drug resistance
ART	Antiretroviral therapy
DBS	Dried blood spot
EID	Early infant diagnosis
EWI	Early warning indicators
HIVDR	HIV drug resistance
PDR	Pre-treatment HIV drug resistance
WHO	World Health Organization

INTRODUCTION

Unprecedented scale-up of antiretroviral therapy (ART) has been observed over the past decade: at the end of 2015, 16 million people were receiving ART in low- and middle-income countries. However, the emergence of HIV drug resistance (HIVDR) can compromise the effectiveness of antiretroviral drugs, thereby jeopardizing the efficacy of ART to further reduce HIV incidence and HIV-associated morbidity and mortality.

HIVDR emerges when HIV replicates in the presence of antiretroviral drugs. If HIVDR becomes widespread, the drugs used to treat HIV infection may become ineffective. To date, levels of HIVDR in countries scaling up ART remain manageable; however, they are slowly increasing. For example, in East Africa, resistance rates to non-nucleoside drugs (such as nevirapine and efavirenz) have recently been reported as above 10%.

Although new ART recommendations ("treat all") and the scale-up of pre-exposure prophylaxis using antiretroviral drugs are likely to further increase levels of HIVDR, concerns about resistant virus should not preclude adoption of a treat-all approach.

To minimize the emergence and spread of HIVDR, the World Health Organization (WHO) recommends HIV treatment scale-up be accompanied by measures to monitor and improve the quality of ART delivery and surveillance of HIVDR[1,2].

At country level, the strategy endorses:

1. country ownership through
   a. formation of a national HIVDR working group;
   b. integration of the national HIVDR strategy into the National Strategic HIV Plan; and
   c. integration of HVDR activities into routine Monitoring and Evaluation function.
2. HIVDR assessments including
   a. surveillance of HIVDR; and
   b. annual monitoring of early warning indicators (EWI) of HIVDR
3. leveraging of enablers
   a. use of WHO-designated laboratory for HIVDR testing; and
   b. identification and allocation of resources
4. use of all available information to minimize the emergence and transmission of drug-resistant HIV; and
5. timely dissemination of information

Recommendations include the following priority assessment activities:

1. monitoring EWI of HIVDR;
2. surveillance of pre-treatment HIV drug resistance (PDR) in populations initiating ART; and
3. surveillance of acquired HIV drug resistance (ADR) in populations receiving ART[3].

Due to greater operational complexity, WHO no longer recommends the routine implementation of surveys of transmitted HIVDR among recently infected populations. However, in limited circumstances, if the results will influence a planned public health intervention, surveys of transmitted HIVDR may add value by documenting transmission of drug-resistant virus in specific populations or geographic areas. Countries considering surveillance of transmitted HIVDR are encouraged to contact WHO to discuss its relevance and proposed methodology.

This update provides an overview of the essential elements that programme managers should include in programme planning to prevent and monitor the emergence of HIVDR. It also describes programmatic relevance and use of data.

1 Consolidated strategic information guidelines for HIV in the health sector. World Health Organization. World Health Organization, Geneva, Switzerland. 2015. Available at: http://who.int/hiv/pub/guidelines/strategic-information-guidelines/en/

2 Global Health Sector Strategy on HIV, 2016–2021. World Health Organization. World Health Organization, Geneva, Switzerland. 2016. Available at: http://www.who.int/hiv/strategy2016-2021/en/

3 When countries reach optimal coverage of VL testing for routine patient monitoring, remnant VL specimens can be used to inform HIVDR surveillance, if specimens are accessible for genotyping and no major biases are identified.

MAIN COMPONENTS

1. EWI of HIVDR

The first and most important step is to assess whether ART programmes deliver services with the quality required to minimize the emergence of HIVDR. This assessment is achieved through the use of a set of indicators known as "EWI of HIVDR". These indicators should be integrated into the routine monitoring and evaluation systems of ART programmes. Results should be used to identify gaps in service delivery, for which corrective actions may be taken at the ART clinic or programme level to optimize overall programme performance.

EWI monitoring assesses retention on ART, drug supply continuity, adherence to prescribed ART, viral load suppression, and coverage of viral load testing.

Standardized definitions and performance targets have been developed for each EWI, along with a colour-based scorecard system, in which "red" signals situations that require corrective action and "green" signals satisfactory performance.

It is recommended that EWI be monitored annually at all treatment sites. If this is not feasible, EWI may be monitored through a nationally representative sample of clinics, with the goal to progressively add more clinics in subsequent years until all of them are included. This approach will generate a reliable overview of a national programme's performance.

EWI monitoring should be integrated into routine monitoring and evaluation systems, to minimize costs and strengthen existing data collection and reporting processes.[1]

If EWI data are not routinely available, the following costs should be taken into account when planning for their abstraction:

1. sensitization of staff at treatment sites to the relevance of measuring performance against a series of standardized indicators, and how these can be used to improve service delivery;
2. organization of data abstraction and data entry (i.e. training and salaries for data abstraction and data entry to ensure high-quality data are obtained);
3. supervisory costs related to data quality assurance (e.g. travel to sites, per diem costs, etc.);
4. data analysis (e.g. data manager, statistician, etc.); and
5. report writing and dissemination, and use of data for clinic and programme optimization.

Responsibility for data abstraction can be assigned to existing clinic staff or, alternatively, new staff may be recruited for this task for a limited time. Abstraction costs depend on the number and location of sites, the size of the patient population, whether records are paper- or electronic-based, and ultimately whether abstraction is integrated with other routine monitoring activities.

Past experience monitoring EWI suggests that data abstraction in sites working exclusively with paper records

Table 1: Recommended high-priority activities for the surveillance of HIVDR

Type of survey	Population of interest	Outcome measure	Programmatic relevance	Recommended periodicity
PDR	Individuals initiating ART	Nationally representative estimate of HIVDR among individuals about to start ART	Presence of resistance prior to ART initiation can compromise both the therapeutic and prevention benefits of first-line ART. Results inform the choice of drugs to be included in first-line treatment, as well as pre- and post-exposure prophylaxis.	Priority element. To be repeated every 3 years
ADR	Individuals receiving ART for (a) 12 (±3) months and (b) at least 48 months	Nationally representative estimates of viral load suppression and levels /patterns of HIVDR in individuals who have been on ART for 12 (±3) months and/or ≥ 48 months	Viral load suppression is a strong indicator of regimen and programme performance. ADR may compromise the effectiveness of second- and third-line ART, as well as pre- and post-exposure prophylaxis. Adult and paediatric ADR surveys should be conducted separately.	Priority element. To be repeated every 3 years

1 The retention, viral load suppression, and drug stock-out indicators are WHO-recommended global indicators to the health sector response. Estimates of viral load coverage and adherence to ART can be measured by data abstraction from routinely recorded information in patient records.

may take two to three days per site at an average cost of US$ 500 per clinic.

To support EWI implementation, a data abstraction tool can be found at: http://www.who.int/hiv/pub/meetingreports/ewi_meeting_report/en/.

2. Surveillance of HIVDR: high-priority activities

WHO recommends that countries use the methods listed in Tables 1 and 2 for the surveillance of HIVDR. Table 1 lists high-priority activities and Table 2 lists activities to be considered in specific circumstances.

As a matter of national policy, some countries provide routine viral load and HIVDR testing to individuals initiating or failing ART. WHO is currently in the process of developing guidance for these countries on how to use such routinely collected data to inform public health decision-making.

Due to greater operational complexity, WHO no longer recommends the routine implementation of surveys of transmitted HIVDR among recently infected populations. However, in limited circumstances, where results are likely to directly influence a planned public health intervention, implementation of these surveys may be warranted.[2]

2.1. Surveillance of PDR in populations initiating ART

In 2014, WHO and partners developed and published new methods to assess PDR. The WHO-recommended PDR survey method generates a nationally representative prevalence estimate of HIVDR among populations initiating ART. Its main objective is to inform the selection of optimal regimens for first-line treatment and post-exposure prophylaxis (and, when used, pre-exposure prophylaxis).

Conducting this survey requires the following:

- identification of a representative sample of 15–40 clinics from a list of all clinics initiating ART in the country; and
- HIVDR genotypes from patients initiating ART on or after a predefined survey start date.

The number of patients to be included in the survey will vary according to a number of factors, such as the number of sites, but will typically fall within the range of 300–500. It is recommended that the duration of patient enrolment be limited to six months to ensure results are available in a timely fashion.

Operationally, individuals initiating ART at the selected clinics will be enrolled in the survey regardless of their prior exposure to antiretroviral drugs. However, information on prior antiretroviral drug exposure must be obtained upon enrolment, and will be used at the data analysis stage to distinguish prevalence of HIVDR among initiators with and without prior exposure to antiretroviral drugs. WHO recommends the implementation of PDR surveillance every three years.

To estimate the cost of implementing a PDR survey, the following six main budget categories should be considered:

1. protocol development and training;
2. survey coordination;
3. site support visits;
4. laboratory (e.g. cost of genotyping and shipment of specimens);
5. technical support (e.g. protocol adaptation and analysis); and
6. report production, printing and distribution.

Assuming a sample size of 460 specimens from 20 sites, and genotyping costs of US$ 150 per specimen, the estimated budget is approximately US$ 240 000 (see Table A1 in the Annex). All figures should be adapted to reflect

Table 2: Activities that should be considered in specific circumstances

Type of survey	Population of interest	Outcome measure	Programmatic relevance	Recommended periodicity
HIVDR among infant less than 18 months old	HIV-positive infant < 18 months old newly diagnosed with HIV and treatment-naive	Nationally representative estimate of HIVDR among infants newly diagnosed with HIV using EID	Results inform the choice of first- and second- line paediatric ART regimens	Implementation recommended prior to the update of paediatric ART guidelines at the national level

2 Countries considering implementation of surveys of transmitted HIVDR are encouraged to contact WHO to discuss methodology and anticipated public health action or ART programme actions.

the local context and costs. Several laboratories in the HIVResNet network offer genotyping at no or considerably reduced cost. Countries that can use these laboratories can significantly reduce survey costs.

A generic concept note for the surveillance of PDR has been developed and is available for country adaptation (http://www.who.int/hiv/pub/drugresistance/pretreatment_drugresistance/en/). As well as providing a technical description of the survey method, the concept note addresses various issues related to survey implementation.

2.2 Surveillance of ADR in populations receiving ART

The ADR survey methodology is designed to yield nationally representative point prevalence estimates of:

1. programme-level viral load suppression; and
2. the prevalence of HIVDR in populations receiving ART for 12 (±3) months and populations receiving ART for at least 48 months.

The level of viral load suppression in a population, as measured in a representative sample of treatment sites, is a strong indicator of regimen and programme performance. The description of resistance patterns in patients failing treatment informs the selection of second-line and potentially third-line regimens.

Implementation of an ADR survey requires the following:

- identification of a representative sample of 17–40 clinics from a list of all clinics dispensing ART in the country; and
- enrolment of consecutive eligible patients who have been receiving ART for a defined time period (e.g. 12 months and/or at least 48 months) on or after a predetermined survey start date.

Specimens are obtained from the sampled patients and viral load is assessed. Specimens from individuals with viral loads greater than 1000 copies/ml are subsequently genotyped.

The number of patients to be included in the survey will vary according to a number of factors, but should typically fall within the range of 400–600. It is recommended that the duration of patient enrolment be limited to six months to ensure the results are available in a timely fashion. WHO recommends implementing ADR surveillance every three years.

Separate surveys should be conducted among adult and paediatric populations, as different ART regimens are used in each group.

To estimate the cost of an ADR survey, the same budget categories described for the PDR survey should be considered. For the early time point (12 ±3 months) – assuming a sample size of 460 specimens collected from 20 sites, and viral load and genotyping costs of US$ 60 and US$ 150 per specimen, respectively – the generic estimated budget is approximately US$ 205 000 (see **Table A2** in the Annex).

For the late time point (≥ 48 months) – assuming a sample size of 560 specimens from 20 sites, and similar genotyping and viral load costs – the generic estimated budget is around US$ 230 000 (see **Table A3** in the Annex).

Due to the overlap of certain survey implementation costs (e.g. training, protocol development, on-site supervision), countries are strongly encouraged to include both time points when designing and implementing ADR surveys. This combined approach increases the amount of data collected, while optimizing the use of resources and capacity. The combined implementation of both time points, assuming similar sample sizes obtained from 35 sites, is estimated to cost approximately US$ 335 000 (see **Table A4** in the Annex).

Further optimization of resources and capacity may be achieved by simultaneous implementation of a survey of PDR and surveys of ADR at both time points. This option provides the maximum amount of information. The combined implementation of a survey of PDR and surveys of ADR at both the 12 (± 3) and 48+ month time points, assuming sampling from a total of 30 sites (20 in operation for 48+ months and 10 in operation for less than 48 months) is estimated to cost approximately US$ 373 300 (see **Table A5** in the Annex).

All figures should be adapted to reflect the local context and costs. Several designated laboratories within the HIVResNet network offer genotyping at no or considerably reduced cost. Countries that can use these laboratories can significantly reduce survey costs.

A generic concept note for the surveillance of ADR has been developed and is available for country adaptation (http://www.who.int/hiv/pub/drugresistance/acquired_drugresistance/en/). Similarly to the PDR concept note, it provides a technical description of the survey method and addresses various issues related to survey implementation.

3. Surveillance of HIVDR: activities for specific circumstances

3.1 Surveillance of HIVDR among treatment-naive infant less than 18 months old

The purpose of this survey is to assess the prevalence of HIVDR among treatment-naive infants younger than 18 months who have been newly diagnosed with HIV using early infant diagnosis (EID). The survey is particularly relevant in settings where many infants are exposed to or acquire HIV infection.

The survey method requires the genotyping of a representative sample of remnant dried blood spots (DBS), collected for paediatric polymerase chain reaction-based HIV diagnosis, and stored at EID laboratories. If possible, all laboratories where EID is performed in the country should participate in the survey and, thus, contribute to the overall sampling. The average sample size is estimated to be approximately 500.

Since the survey uses remnant specimens, most implementation costs are related to data entry, specimen shipping and handling, genotyping, technical support for analysis, and report production and distribution. Assuming an average genotype testing cost of US$ 150, the generic estimated survey cost is approximately US$ 140 000 (see **Table A6** in the Annex).

USE OF DATA FOR ART PROGRAMME OPTIMIZATION

High-quality treatment programmes are critical to minimizing the emergence of HIVDR. Monitoring EWI of HIVDR and performing surveillance of HIVDR provide countries with evidence that can be used to optimize patient and population-level treatment outcomes.

EWI of HIVDR

EWI monitoring uses scorecarding, which facilitates an at a glance understanding of clinic and programme performance. It also facilitates resource allocation to clinics and identifies the gaps in service delivery that require the most attention. Exploring differences in performance between clinics can lead to documentation and sharing of best practices within countries. This information can be used to allocate resources to the clinics most in need and to address the most pressing gaps in service delivery. EWI monitoring is designed to be implemented annually at all clinics, or to be scaled up in a representative fashion over time. It facilitates a local- and national-level understanding of key factors correlated with treatment optimization and minimization of resistant HIV.

Examples of actions that may be taken based on EWI results include:

- strengthening of general clinic and pharmacy record-keeping to facilitate future rounds of reporting;
- strengthening of communication and integration between pharmacy and clinic records to identify patients at risk of HIVDR due to missed pill pickups;
- engagement of defaulter tracing mechanisms to support retention on ART;
- support for and strengthening of supply chain management; and
- advocacy for high levels of coverage for viral load testing.

Surveillance of PDR in populations initiating ART

PDR surveys are designed to be repeated every three years, with results providing evidence to support choice of nationally recommended first-line ART regimens and regimens used for pre- and post-exposure prophylaxis. For example, survey results may be used in the analysis of cost effectiveness to inform the pace of change to integrase inhibitor or boosted protease, or use of individual-level PDR testing to guide regimen selection.

Surveillance of ADR in populations receiving ART

ADR surveys support choice of nationally recommended second- and third-line ART regimens. Their implementation, generally contemporaneously with PDR surveys on a rolling three-year cycle, not only provides HIVDR information, but also facilitates trend analysis and allows for nationally representative estimates of retention and viral load suppression.

Surveillance of HIVDR among infants less than 18 months old

Although not a high priority, this survey provides results that inform the choice of first- and second-line paediatric regimens. This survey is most useful when implemented prior to national updates of recommended paediatric ART guidelines. Results may be used to support rapid uptake of recommended protease inhibitor-based first-line ART regimens in infants younger than 18 months. Also, by estimating the level of resistance to non-nucleoside reverse transcriptase inhibitor, results will help guide usefulness of these antiretroviral drugs as a component of second- and third-line regimens.

ANNEX: GENERIC BUDGETS

The tables below provide generic estimated budgets for implementing the different surveys of HIVDR described in this document. All figures should be adapted to reflect the local context and costs. All costs are given in US dollars.

Table A1: Estimated budget for PDR surveillance among ART initiators

Number of sites: 20
Sample size: 460

Protocol development and training					
	Number of staff per site	Transportation costs	Per diem cost	Number of nights	Total
Training of site staff (1 day training)	2	$200.00	$150.00	1	$14 000.00
Production of protocol and training materials					$15 000.00
				Subtotal	$29 000.00

Survey coordination					
	Number of staff	Cost per staff/ month	Number of months	Number of sites	Total
Site coordination	1	$300.00	8	20	$48 000.00
Nurse incentive	2	$50.00	8	20	$16 000.00
National coordination	1	$1,000.00	8	1	$8 000.00
Data manager	1	$800.00	6	1	$4 800.00
				Subtotal	$76 800.00

Site support visits		
		Total
Study coordinator and driver	*Note: 2 days per visit, USD 50 per diem, 2 visits*	$8 000.00
Fuel	*Note: for six months*	$2 000.00
Air tickets to remote sites	*Note: 5 flights, USD 200 each*	$1 000.00
Local transportation		$1 000.00
	Subtotal	$12 000.00

Laboratory		
	Per unit	Total
Blood collection	$3.00	$1 380.00
DBS preparation and storage	$5.00	$2 300.00
Genotyping	$150.00	$69 000.00
Laboratory labor cost for genotyping		$2 500.00
Shipment of specimens	*Note: US$ 100 per site for national shipping, US$ 250 for international*	$2 250.00
	Subtotal	$77 430.00

Technical support	
	Total
Consultant (US$ 500 daily fee, US$ 200 per diem, 14 days) and flight	$1 800.00
Statistical support for analysis and interpretation	$10 000.00
Subtotal	$22 800.00

Report production, printing and distribution	
	Total
Report production and distribution	$10 000.00
Workshop to dicuss policy implication and actions required (15 outside participants, 15 local)	$10 500.00
Subtotal	$20 500.00
TOTAL	**$238 530.00**

Table A2: Generic budget for ADR surveillance (12-month time point)

Number of sites: 20
Sample size (12 months): 460
Estimated % with VL>1000 (12 months): 5%

12(±3) months

Protocol development and training					
	Number of staff per site	Transportation costs	Per diem cost	Number of nights	Total
Training of site staff (1 day training)	2	$200.00	$150.00	1	$14 000.00
Production of protocol and training materials					$15 000.00
Survey coordination					
	Number of staff	Cost per staff/ month	Number of months	Number of sites	Total
Site coordination	1	$300.00	8	20	$48 000.00
Nurse incentive	2	$50.00	8	20	$16 000.00
National coordination	1	$1 000.00	8	1	$8 000.00
Data manager	1	$800.00	4	1	$3 200.00
Site support visits					
					Total
Study coordinator and driver	*Note: 2 days per visit, US$ 50 per diem, 2 visits*				$8 000.00
Fuel	*Note: for 6 months*				$2 000.00
Air tickets to remote sites	*Note: 5 flights, US$ 200 each*				$1 000.00
Local transportation					$1 000.00
Laboratory					
				Per unit	Total
Blood collection				$3.00	$1 380.00
DBS preparation and storage				$5.00	$2 300.00
VL				$60.00	$27 600.00
Genotyping				$150.00	$10 350.00
Laboratory labor cost for genotyping and VL					$2 500.00
Shipment of specimens	*Note: US$ 100 per site for national shipping, US$ 250 for international*				$2 250.00
Technical support					
					Total
Consultant (US$ 500 daily fee, US$ 200 per diem, 14 days) and flight					$12 800.00
Statistical Suppport for analysis and interpretation					$10 000.00
Report production, printing and distribution					
					Total
Report production and distribution					$10 000.00
Workshop to dicuss policy implication and actions required (15 outside participants, 15 local)					$10 500.00
				TOTAL	**$205 880.00**

VL: viral load

Table A3: Generic budget for ADR surveillance (48+ month time point)

Number of sites: 20
Sample size (48+ months): 560
Estimated % with VL>1000 (48+ months): 30%

					48+ months
Protocol development and training					
	Number of staff per site	Transportation costs	Per diem cost	Number of nights	Total
Training of site staff (1 day training)	2	$200.00	$150.00	1	$14 000.00
Production of protocol and training materials					$15 000.00
Survey coordination					
	Number of staff	Cost per staff/ month	Number of months	Number of sites	Total
Site coordination	1	$300.00	8	20	$48 000.00
Nurse incentive	2	$50.00	8	20	$16 000.00
National coordination	1	$1 000.00	8	1	$8 000.00
Data manager	1	$800.00	4	1	$3 200.00
Site support visits					
					Total
Study coordinator and driver	*Note: 2 days per visit, US$ 50 per diem, 2 visits*				$8 000.00
Fuel	*Note: for six months*				$2 000.00
Air tickets to remote sites	*Note: 5 flights, US$ 200 each*				$1 000.00
Local transportation					$1 000.00
Laboratory					
				Per unit	Total
Blood collection				$3.00	$1 680.00
DBS preparation and storage				$5.00	$2 800.00
VL				$60.00	$33 600.00
Genotyping				$150.00	$25 200.00
Laboratory labour cost for genotyping and VL					$2 500.00
Shipment of specimens	*Note: US$ 100 per site for national shipping, US$ 250 for international*				$2 250.00
Technical support					
					Total
Consultant (US$ 500 daily fee, US$ 200 per diem, 14 days) and flight					$12 800.00
Statistical support for analysis and interpretation					$10 000.00
Report production, printing and distribution					
					Total
Report production and distribution					$10 000.00
Workshop to discuss policy implication and actions required (15 outside participants, 15 local)					$10 500.00
				TOTAL	**$227 530.00**

VL: viral load

Table A4: Generic budget for ADR surveillance (combined 12 month and 48+ month time point)

Number of sites: 35

Sample size (12 months): 460

Sample size (48+ months): 560

Estimated % with VL>1000 (12 months): 15%

Estimated % with VL>1000 (48+ months): 30%

					Shared survey costs	12(±3) months	48+ months
Protocol development and training							
	Number of staff per site	Transportation costs	Per diem cost	Number of nights	Total		
Training of site staff (1 day training)	2	$200.00	$150.00	1	$24 500.00		
Production of protocol and training materials					$15 000.00		
Survey coordination							
	Number of staff	Cost per staff/month	Number of months	Number of sites	Total		
Site coordination	1	$300.00	8	35	$84 000.00		
Nurse incentive	2	$50.00	8	35	$28 000.00		
National coordination	1	$1 000.00	8	1	$8 000.00		
Data manager	1	$800.00	4	1	$3 200.00		
Site support visits							
					Total		
Study coordinator and driver	*Note: 2 days per visit, US$ 50 per diem, 2 visits*				$14 000.00		
Fuel	*Note: for 6 months*				$2 000.00		
Air tickets to remote sites	*Note: 5 flights, US$ 200 each*				$1 000.00		
Local transportation					$1 000.00		
Laboratory							
				Per unit	Total		
Blood collection				$3.00		$1 380.00	$1 680.00
DBS preparation and storage				$5.00		$2 300.00	$2 800.00
VL				$60.00		$27 600.00	$33 600.00
Genotyping				$150.00		$10 350.00	$25 200.00
Laboratory labor cost for genotyping and VL					$4 000.00		
Shipment of specimens					$250.00	$1 500.00	$2 000.00
Technical support							
					Total		
Consultant (US$ 500 daily fee, US$ 200 per diem, 14 days) and flight					$12 800.00		
Statistical Suppport for analysis and interpretation					$10 000.00		
Report production, printing and distribution							
					Total		
Report production and distribution					$10 000.00		
Workshop to dicuss policy implication and actions required					$10 500.00		
				Subtotal	$228 250.00	$43 130.00	$65 280.00
					Grand Total		**$336 660.00**

VL: viral load

Table A5: Generic budget for combined PDR and ADR surveillance

Number of "old" sites (sites in operation for more than 48+ months): 50
Number of "new" sites (sites in operation for less than 48 months): 20
Example: 10 000 people on ART at "old" sites and 5 000 people on ART at "new" sites
Total number of sites sampled: 20 "old sites" and 10 "new" sites (total 30 sites)
Sample size (PDR): 410
Sample size (12 ± 3 months): 420
Sample size (48+ months): 520
Estimated % with VL>1000 (12 months): 15%
Estimated % with VL>1000 (48+ months): 30%

					Shared survey costs	PDR	12(±3) months	48+ months
Protocol development and training								
	Number of staff per site	Transportation costs	Per diem cost	Number of nights	Total			
Training of site staff (1 day training)	2	$200.00	$150.00	1	$21 000.00			
Production of protocol and training materials					$15 000.00			
Survey coordination								
	Number of staff	Cost per staff/month	Number of months	Number of sites	Total			
Site coordination	1	$300.00	8	30	$72 000.00			
Nurse incentive	2	$50.00	8	30	$24 000.00			
National coordination	1	$1 000.00	8	1	$8 000.00			
Data manager	1	$800.00	4	1	$3 200.00			
Site support visits								
					Total			
Study coordinator and driver	*Note: 2 days per visit, US$ 50 per diem, 2 visits*				$12 000.00			
Fuel	*Note: for 6 months*				$2 000.00			
Air tickets to remote sites	*Note: 5 flights, US$ 200 each*				$1 000.00			
Local transportation					$1 000.00			
Laboratory								
				Per unit	Total			
Blood collection				$3.00		$1 230.00	$1 260.00	$1 560.00
DBS preparation and storage				$5.00		$2 050.00	$2 100.00	$2 600.00
VL				$60.00			$25 200.00	$31 200.00
Genotyping				$150.00		$61 500.00	$9 450.00	$23 400.00
Laboratory labor cost for genotyping and VL					$4 000.00			
Shipment of specimens	*Note: US$ 100 per site for national shipping, US$ 250 for intl*				$250.00	$1 500.00	$3 000.00	$2 000.00
Technical support								
					Total			
Consultant (US$ 500 daily fee, US$ 200 per diem, 14 days) and flight					$12 800.00			
Statistical Suppport for analysis and interpretation					$10 000.00			
Report production, printing and distribution								
					Total			
Report production and distribution					$10 000.00			
Workshop to dicuss policy implication and actions required					$10 500.00			
				Subtotal	$206 750.00	$64 780.00	$41 010.00	$60 760.00
					Grand Total			**$373 300.00**

VL: viral load

Table A6: Generic budget for surveillance of HIVDR among treatment-naive infants less than 18 months old

Number of participating labs: 10
Sample size: 500

Protocol development and training		
		Total
Production of protocol and training materials		$10 000.00
Training of site staff (1 day training)		$14 000.00
	Subtotal	$24 000.00

Laboratory		
	Per unit	Total
Genotyping	$150.00	$75 000.00
Laboratory labor cost for genotyping	$250.00	$2 500.00
Shipment of specimens	$100.00	$1 250.00
	Subtotal	$78 750.00

Technical support		
		Total
Consultant (US$ 500 daily fee, US$ 200 per diem, 14 days) and flight		$12 800.00
Statistical support for data analysis and interpretation		$10 000.00
	Subtotal	$22 800.00

Report production, printing and distribution		
		Total
Report production and distribution		$10 000.00
Workshop to dicuss policy implication and actions required		$4 000.00
	Subtotal	$14 000.00
	TOTAL	**$139 550.00**

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