National Strategy on HIV Drug Resistance Monitoring and Surveillance in Nepal 2014 – 2020

Government of Nepal
Ministry of Health and Population
National Centre for AIDS and STD Control
Kathmandu, Nepal

Supported by :

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COUNTRY OFFICE FOR Nepal

National Strategy on HIV Drug Resistance Monitoring and Surveillance (HIVDR) for Nepal 2014 – 2020

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Foreword

Since the inception of the antiretroviral therapy (ART) in 2004, there has been a substantial increment of people on ART in Nepal. Despite the obvious benefits that rapid scale-up has had on AIDS-related morbidity and mortality, the potential for widespread emergence and transmission of HIV drug resistance (HIVDR) to antiretrovirals (ARVs) has been a major ongoing concern.

National Strategy on HIV Drug Resistance Monitoring and Surveillance (HIVDR) for Nepal – 2014 – 2020, summarizes a comprehensive package of HIVDR surveys that should be implemented in Nepal while scaling-up and maintaining populations on ART.

We are thankful to Dr Polin Chan, WHO Consultant and Dr Supriya Warusavithana, WHO-Nepal for providing technical guidance for development of this strategy in coordination with the members of the Technical Working Group on HIV Testing, Counseling, Treatment, care and PMTCT.

DR Singh

Dr Dipendra Raman Singh
Director

1. Background

The estimation and projection conducted in 2013 estimated that Nepal has approximately 40,723 persons living with HIV (PLHIV) and prevalence of HIV was 0.23%[1]. This also projected that the overall HIV epidemic in Nepal is on a decline. Modelling suggests that new infections continue to reduce from 1,437 in 2011 to 818 in 2015. The ART need in 2012 was projected to be 26,876 while 860 HIV positive pregnant women were estimated to require PMTCT services.

The epidemic remains a concentrated epidemic with new infections occurring among key populations including people who inject drugs (PWID), male and female sex workers (SW) and their clients, men who have sex with men (MSM) and male labour migrants. However, there is geographical variability of the modes of transmission within regions of the country. As an example, the issue of migration-linked HIV transmission seems to be more important in the Far and Midwestern regions of Nepal.[2]

1.1 Expansion of access to ART

Antiretroviral treatment (ART) was established within the national programme in 2004. As of mid-2014, the National Center for AIDS and STD Control (NCASC) reported approximately 9,000 people on ART from 52 centers, double the numbers receiving treatment in 2011 (5,867 individuals). Nationally approximately 100 children are receiving ART. The PMTCT programme is in its nascent stage, and is in process of being integrated into the Maternal and Child Health programme of Family Health Division of Department of Health Services. Early infant diagnosis (EID) is available, with capacities established in the National Public Health Laboratory (NPHL) since January 2014. Prior to this, samples for EID were sent to Bangkok, Thailand for testing.

The NCASC has already held consultations to adapt the WHO 2013 treatment guidelines[3] for adults, adolescents, pregnant women and children. In brief, the recommendations follow WHO guidance for earlier treatment at the CD4 threshold of ≤500 cells/mm^3. For pregnant women, national guidance now recommends provision of Option B+ (lifelong ART). Similarly, the updated national guidelines for treatment in children are aligned with the WHO 2013 guidance. ART requirements are projected to increase, however because the majority of people registering at ART services have low CD4 counts, this increase will not be significant in the short-term.

1 Government of Nepal (2013). National Estimates of HIV Infections in Nepal 2013.

2 Government of Nepal (2013). Review of the HIV response in Nepal, May-June 2013.

3 WHO (2013). Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach.

Funding for ARV drugs is dependent on the Global Fund to Fight AIDS, TB and Malaria (GFATM) where Nepal has received funding through the Single Stream Funding (SSF) grant which consolidates grants for Rounds 7 and 10. The country has applied for the New Funding Model (NFM) for 2015 -2017.

1.3 Current implementation of HIVDR activities

HIV drug resistance (HIVDR) surveillance has been prioritised within the strategic information framework in the National HIV/AIDS strategy 2011-2016.[4] HIVDR is articulated as part of the national public health surveillance in HIV, with emphasis on the core elements of Early Warning Indicator (EWI) monitoring and also to conduct HIVDR surveys.[5] Emergence of HIVDR will impact effectiveness of the treatment programme as well as increase the costs for ART. Current costs of ART based on global reports indicate the lowest prices of 100-150 USD for first-line regimens depending on drug type (zidovudine or tenofovir-based), 250 USD for second-line ART and 2,000 USD for third (salvage) regimens.[6,7]

EWI monitoring was piloted in 3 treatment sites (Kathmandu Valley) in 2013, with subsequent expansion to 14 additional sites by mid-2014. NCASC has planned to scale-up EWI monitoring EWI at 75% of all ART sites by 2017 and 100% thereafter, with the support of partners.

2. Development of the Nepal HIVDR strategy

WHO published the first global strategy for HIVDR monitoring and surveillance for countries scaling up ART with the public health approach in 2004.[8] In 2012, WHO updated its global strategy on HIVDR monitoring and surveillance[9]. The revised WHO strategy builds on existing HIVDR implementation experience in countries. As well, protocols for the different surveillance components were updated to provide countries with simplified standardised guidance which include:[10]

- Update of the EWI guidance and tools
- Revision of the HIVDR protocols for Acquired HIVDR (ADR) and Transmitted HIVDR (TDR)

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4 Government of Nepal (2011). National HIV/AIDS Strategy 2011-2016.

5 Government of Nepal (2011). Nepal surveillance guidelines: annex on the national strategy for surveillance of HIV drug resistance.

6 MSF (2014). Untangling the web of antiretroviral price reductions, 17th edition – July 2014.

7 WHO (2014). Access to antiretroviral drugs in low- and middle-income countries: technical report July 2014.

8 Bennett DE, Bertagnolio S, Sutherland D, Gilks CF. The World Health Organization's global strategy for prevention and assessment of HIV drug resistance. Antivir Ther. 2008;13(Suppl 2):1–13.

9 WHO (2012). WHO global strategy on HIV drug resistance monitoring and surveillance.

10 WHO guidelines for HIVDR surveys available at: http://www.who.int/hiv/topics/drugresistance/en/

- Development of two new protocols (a) to assess HIVDR in ART-naïve infants less than 18 months of age and (b) Pretreatment HIVDR among people initiating treatment (PDR).

A consensus meeting to discuss and prioritise HIVDR monitoring and surveillance activities was held by NCASC with the support of WHO on 6 August 2014. The objectives were to develop the Nepal HIVDR strategy (2014-2020) based on revised WHO 2012 global strategy and protocols. Guiding principles for country-led planning were (a) relevance to the epidemic and treatment scale-up context and (b) feasibility and sustainability of implementation. Among the types of HIVDR surveillance, the surveys to assess HIVDR in infants less than 18 months; and for transmitted drug resistance was noted to be not feasible in the country. This was because of the lack of appropriate sample size due to declining incidence; and inadequate numbers of EID samples for the survey in infants.

The three priority HIVDR elements selected include:

- EWI monitoring, as part of routine M&E activities
- Acquired HIVDR surveillance (ADR) in people receiving ART
- Pretreatment HIVDR (PDR) among people initiating treatment

National laboratory strengthening for public health surveillance in HIV drug resistance is an important element under the global HIVDR strategy to ensure sustainability of routine HIVDR surveillance. The NPHL was nominated as the nodal laboratory responsible for the implementation of surveys and laboratory aspects for HIVDR, in collaboration with NCASC. HIVDR testing capacity is not yet established in NPHL and thus planned HIVDR surveys will require additional technical assistance from WHO-designated regional reference laboratories for HIVDR genotyping.

2.1 Nepal HIV drug resistance monitoring and surveillance strategy, 2014-2019

Goals:

- The goal of HIV drug resistance monitoring and surveillance in Nepal is to provide evidence for decision-making and public health actions on the antiretroviral treatment programme.

Vision:

- Prevention of the development of HIV drug resistance in the antiretroviral treatment programme and among patients so as to ensure the effectiveness and sustainability of the public health approach to universal access to ART.

Mission:

1. Implement HIVDR monitoring using early warning indicators (EWI) as part of routine M&E to provide clinic-level information on functioning of the ART programme.
2. Implement HIVDR surveys as part of public health surveillance in HIV to monitor trends for the emergence and evolution of HIV drug resistance.
3. Take public health actions to strengthen the ART programme and related services so as to prevent emergence of HIVDR among people receiving treatment.

2.1.1 Mission I: HIVDR monitoring of EWI

EWIs are quality of care indicators which assess factors associated with emergence of HIVDR. These indicators are core indicators designed to be monitored at all ART clinics as part of routine monitoring and evaluation. The results provide clinic-specific information which can be used for local action to improve patient care, and for national (or subnational) programme for public health action. EWI-5 on viral load suppression has not been conducted on the current EWI reporting cohort of 2011-2012. Routine viral load monitoring under the programme is being scaled-up in 2014.

NCASC has piloted[11] and expanded EWI monitoring at 17 sites between 2013 and 2014. The results indicate issues with on-time pill pickup (ART adherence) and retention in ART care at 12 months, particularly in children. Death and lost to follow-up (LFU) were highly variable among clinics.[12]

The following are national plans for scaling up EWI monitoring, 2014-2019:

Table 1: EWI scale up plan

Survey type	2013-2014	2015	2016	2017	2018	2019
EWI	Piloted in 3 sites in 2013 and expanded to 14 more in 2014	Total of 36 sites out of 52 clinics	Total of ~40 sites	Reach 75% of eligible sites (~55 ART clinics planned by 2017)	Reach 100% of all eligible sites	

11 NCASC (2014). Moving towards HIV Drug Resistance monitoring in Nepal. Monitoring Early Warning Indicators: Report of the Pilot Survey.

12 NCASC (2014). EWI results from 17 sites.

2.1.2 Mission II: Public health surveillance of HIVDR, 2014-2019

NPHL is responsible to public health surveillance in infectious diseases. As part of national public health surveillance in HIV, HIVDR will be incorporated in the NPHL responsibilities in collaboration with NCASC.

The first priority survey to be conducted is on Acquired drug resistance (ADR), which is planned to be conducted in 2015. The ADR survey assesses prevalence of viral load suppression and describes HIVDR patterns in populations receiving ART at two time-points which are at 12 ± 3 months and ≥ 48 months. The results provide a nationally representative prevalence which can inform decisions around (a) how effective is the current national first-line regimen and (b) the optimal second-line regimen. Main ADR survey outcomes are presented in Table 2.

Table 2: Main ADR survey outcomes

	Outcomes	Time point: 12 (±3) months	Time point: ≥48 months
1.a	Prevalence of VL suppression (VL <1000 copies/mL) among individuals on ART	X	X
1.b	Prevalence of VL suppression (VL<1000 copies/mL) among individuals on first-line ART	X	X
1.c	Prevalence of VL suppression (VL<1000 copies/mL) among individuals on NNRTI-based first-line ART	X	X
2.a	Nationally representative measure of retention at 12 months	X	
2.b	Prevalence of VL suppression among individuals on ART, adjusted for retention	X	
3.a	Prevalence of HIVDR among individuals on ART with VL > 1000 copies/mL	X	X
3.b	Prevalence of HIVDR among individuals on first-line ART with VL >1000 copies/mL	X	X
3.c	Prevalence of HIVDR among individuals on NNRTI-based first-line ART with VL >1000 copies/mL	X	X
4	Prevalence of HIVDR among individuals on ART	X	X

In 2016, the PDR survey will be conducted to assess HIVDR prevalence among patient starting treatment, to inform decisions around the first-line regimen. The new recommendations of tenofovir-based regimens as the preferred first-line will be operationalised towards end of 2014. The PDR survey has six main outcomes: three of them are related to HIV drug resistance per se, while three others are related to how frequent individuals initiate ART with prior ARV exposure – Table 3.

Table 3: Main PDR survey outcomes

	Outcomes
1.	HIVDR outcomes
1a	Prevalence of HIV drug resistance among all ART initiators, regardless of prior exposure to ARVs
1b	Prevalence of HIV drug resistance among ART initiators without prior exposure to ARVs
1c	Prevalence of HIV drug resistance among ART initiators with NNRTI-based regimens without prior exposure to ARVs
2.	Prior ARV exposure
2a	Proportion of all ART initiators without prior exposure to ARVs
2b	Proportion of all ART initiators with prior exposure to ARVs
2c	Proportion of all ART initiators with unknown prior exposure to ARVs

The country plans to implement the surveys every 3 years as recommended by WHO to monitor trends.

Survey type	**2014/15**	**2016**	**2017**	**2018**	**2019**
ADR	X			X	
PDR		x			x

Note: WHO surveillance protocols for HIVDR surveys are available at: http://www.who.int/hiv/topics/drugresistance/en/

2.1.3 Mission III: Take public health action to strengthen the ART programme and related services so as to prevent emergence of HIVDR among people receiving treatment

Based on evidence generated from EWI monitoring and HIVDR surveys, the necessary public health action will be taken. Actions will be taken to strengthen the treatment programme and address loss from the continuum of HIV care based on findings from the 2013-2014 EWI exercise.

This may include:

- Strengthen record keeping and documentation (M&E)
- Review patient pill pick-up as an objective measurement of adherence and establish formal referral system to document transfer of care including tracking of whether patients actually reach the ART clinic which they have been referred to
- Trace patients who missed their appointment and those with LFU, to attempt to get them back into ART care
- Review the quality of patient care e.g. regularity of CD4 counts every 6 months, viral load monitoring, pharmacy stock-outs etc.
- Assess reasons why paediatric ART patients have worse on-time pill pick up compared to adults and implement appropriate interventions
- Understand the determinants for death e.g. baseline CD4 counts at enrollment in ART clinics, types of opportunistic infections (OIs), mortality during ART etc.
- Monitor and assess the quality of care and CD4 and viral load monitoring within decentralised ART care in dispensing centers
- Training of clinical care providers including para-medical staff.

3. Partnerships and resource needs

NCASC will be working in partnership with institutions, technical and developmental partners in the implementation of EWI and HIVDR surveys. In order to successfully operationalise the HIVDR five year strategy, the following budgets will be required:

Resource needs	Approximate budget	Tentative source/donor
ADR surveys (2015 and 2018)	200,000 USD per survey x 2= 400,000	2015 survey to be supported by WHO. Funds for 2018 ADR survey to be mobilized.
PDR survey (2016 and 2019)	200,000 USD per survey x 2=400,000	Funds for 2016 and 2019 ADR surveys to be mobilized.
EWI scale up	57,000 for 3 years	3 years funding (2015-2017) to be mobilized.

Technical assistance from WHO and other partners will be required and include the following key areas:

- Protocol development including site selection, sampling methods and development of tools
- Capacity building of NPHL for implementation of the laboratory component of the survey
- Facilitation with the regional reference laboratory for HIVDR genotyping
- Capacity building for analysis and interpretation of HIVDR results, as well as in dissemination
- Resource and fund mobilisation for the implementation

4. Operationalization of the ADR survey in 2015

A core working group will be constituted to coordinate work around implementing the ADR in 2015. A list of activities required for implementation of the surveys is detailed in Annex A.

The core working group includes:

Organisation	Designation of focal persons	Organisation role and responsibility
NCASC	Coordinator : member secretary TWG Logistic focal point Public Health expert	• Leadership and joint coordination with NPHL for implementation of the survey. • Resource mobilisation and timely transfer of funds and other resources e.g. procurement
NPHL	HIV focal person	• Co-chair with NCASC for the core working group • Project management and implementation of the survey according to guidelines
WHO Nepal	Medical Officer HIV	• Technical assistance for survey • Resource mobilisation as required
FHI360	Surveillance focal point Laboratory focal point	• Technical assistance for survey • Provide monitoring support during implementation
Clinical Experts	Bir Hospital: Dr Sushil TUTH: Dr Prem Paediatrics: Dr Laxman MCH focal point : Dr Indira	• Technical assistance for survey • Provide monitoring support during implementation
National Health Research Council (NHRC)	Representative	• Technical assistance for survey • Provide monitoring support during implementation

Annex 1

Gant chart (draft) for implementation of the ADR survey in 2015

HIVDR monitoring and surveillance Implementation roadmap (2014- 17), Nepal																																					
Updated by:																																						
Date/version #:																																					
Activities: planning list to implement the ADR in 2015	Responsible person	2014						2015												2016																	
		8	9	10	11	12		1	2	3	4	5	6	7	8	9	10	11	12		1	2	3	4	5	6	7	8	9	10	11	12				
Country planning meeting on HIVDR five year plan		x																																		
Draft and finalisation of Nepal HIVDR strategy and roadmap of activities		x																																		
Establish Core Group for coordinating implementation of ADR		x																																		
Program Data to be organised inorder to facilitate the sampling methodolgy for ADR		x																																		
Initial meetings to discuss details of implementation and planning survey, including resources required		x	x																																	
Prepare/refine budgets required for implementation of the ADR		x	x																																	
Discussions with WHO and other relevant experts on the sampling methodolgy for ADR		x	x	x																																
Draft protocol: preparation including methods, sample size, site selection																																				
Meeting around protocols and finalisation, expected 4-6 small meetings with experts nationally																																				
Tool preparation: field manuals, training, supervisor checklist for on site support, printing																																				
Communication with WHO for facilitation of support from regional reference lab which will perform the HIVDR genotyping (to establish the relationship, communications and technical assistance for labs early during the planning of the ADR survey)																																				
Funding approval process and transfer of funds to involved institutes																																				
Procurement of HIVDR commodities eg vacutainers for Viral load, DBS filter paper, personal protection equipment etc.																																				
Planning of logistics for transport of survey samples																																				
Training of sites: laboratory staff, clinical staff, focal person in charge of the ART center where data collection is to be heal																																				
Sample collection started																																				
On-site follow up as supervisory visits																																				
Samples sending to NPHL for storage																																				
Sending of collected samples to Regional Reference Lab (WHO facilitated)																																				
Analysis of results at the Regional Refernce Lab, and feedback to country																																				
Send sequences to WHO Geneva for validation and quality assurance																																				
Core group meeting including technical advisory experts: discuss validated findings																																				
National TWG: presentation of final results																																				
Dissemination in various forum: international/local conferences, RC and CST meetings, to central and state policy makers																																				
Write up in peer-review journal as publication: to be led by NPHL																																				
Approval process to share sequences with WHO Geneva for the purpose of the Global HIVDR Reporting																																				