

Sentinel Site-Based Pilot Active Surveillance Pharmacovigilance in the Vietnam ART Program: Technical Assistance for Protocol Development

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About SPS

The Strengthening Pharmaceutical Systems (SPS) Program strives to build capacity within developing countries to effectively manage all aspects of pharmaceutical systems and services. SPS focuses on improving governance in the pharmaceutical sector, strengthening pharmaceutical management systems and financing mechanisms, containing antimicrobial resistance, and enhancing access to and appropriate use of medicines.

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ACRONYMS

ART	antiretroviral therapy
CCM	country coordinating mechanism
CDC	US Centers for Disease Control and Prevention
DI & ADR	Drug Information and Adverse Drug Reaction Monitoring Center (Vietnam)
GF	Global Fund
HCMC	Ho Chi Minh City
HUP	Hanoi University of Pharmacy
MSH	Management Sciences for Health
PAC	Provincial AIDS Committee
PV	pharmacovigilance
SCMS	Supply Chain Management System
SOP	standard operating procedure
SPS	Strengthening Pharmaceutical Systems
SWOT	strengths, weaknesses, opportunities and threats
TDH	Tropical Disease Hospital
TOT	training of trainers
USAID	United States Agency for International Development
VAAC	Vietnam Administration of AIDS Control
WHO	World Health Organization

BACKGROUND

The Ministry of Health and other key stakeholders in Vietnam are strengthening the pharmacovigilance (PV) system in their country. A notable step was establishment of the National Drug Information and Adverse Drug Reaction Center (DI&ADR Center) at the Hanoi University of Pharmacy (HUP) in 2009. The USAID-supported Strengthening Pharmaceutical Systems (SPS) Program of MSH is collaborating with the national stakeholders to support this process. Over the last one year or so, the key events in which SPS and its predecessor (RPM Plus) collaborated to provide technical assistance to the local partners were: 1-day consensus meeting which developed a PV framework for Vietnam that included active surveillance as a key element (March 2009); a 3-day training of trainers course on pharmacovigilance for staff from public health programs and other key local stakeholders (March 2009); development of a 1-year workplan for the DI&ADR Center, and development of a strategy to support potential inclusion of a PV component in Global Fund Round 10 application (July 2009); training of DI&ADR Centre staff on drug information and pharmacovigilance, including development of standard operating procedures (SOPs) and forms for drug information service, and revision of the spontaneous reporting form (September-October 2009). The Supply Chain Management System (SCMS) Program of MSH provided complementary support to the Center by procuring a set of key drug information and pharmacovigilance reference books (January 2010), and organizing a study tour for its staff to visit South Africa and Namibia to learn about these countries' experiences with drug information and pharmacovigilance activities (March 2010).

With these developments, the Vietnam Administration of AIDS Control (VAAC) and the DI&ADR Center have expressed interest in initiating a sentinel site-based pilot active surveillance pharmacovigilance within the ART Program. SPS facilitated preparatory work for this process by arranging two technical staff to visit Vietnam from 16 to 29 January 2010—Dr. Mohan Joshi from SPS, and Dr. Andy Stergachis from the University of Washington's Department of Global Health, which is a partner organization for SPS. This report describes the activities conducted during the above visit. Also appended to the report is the draft protocol developed for the pilot activity.

Purpose of Trip

The primary purpose of the Vietnam visit by Drs. Joshi and Stergachis in January 2010 was to assist the VAAC, DI&ADR Center and other key stakeholders to carry out preparatory work to design a pilot initiative on pharmacovigilance-related active surveillance within the ART Program.

Scope of Work for Dr. Joshi and Dr. Stergachis

- Provide a briefing and debriefing for USAID and CDC/Vietnam, as requested
- Analyze the findings of mapping of ART care and treatment carried out from January 11 to 15, 2010

- Carry out ART site visits and discussions with relevant in-country stakeholders in Hanoi and Ho Chi Min City
- Develop a draft of an active surveillance protocol that takes into account the currently prevailing circumstances and opportunities within the ART program in Vietnam
- Work with in-country counterparts on the selection of sentinel sites for active surveillance
- Present to VAAC and other stakeholders the draft protocol and obtain their feedback
- Carry out any additional information gathering or in-country discussions that might be needed (as informed by the feedback) to help revise the protocol
- Provide an exit briefing to VAAC and DI-ADR Center
- Submit a report after the completion of the trip

The request for country clearance (RFCC) sent to USAID/Vietnam is attached as *Annex 1*.

ACTIVITIES

The final agenda of various meetings and activities for Drs. Joshi and Stergachis during the period of their visit is in *Annex 2*. Given below is a summary of the main activities.

In-briefing to USAID/Vietnam

Dr. Joshi, Dr. Stergachis, and MSH/SCMS Vietnam Country Director Ms. Juanita Folmsbee provided in-briefing to Mr. Xerses Maneck Sidhwa, Health Officer, and Dr. Nguyen Thi Minh Ngoc, HIV/AIDS Care and Treatment Specialist at USAID Office on January 19th, 2010. Using a PowerPoint presentation, the team provided an overview of the planned active surveillance work along with the details of the scope of work for the visit. Dr. Joshi also took the opportunity to provide hard and electronic copies of the report of his previous visit to Hanoi that was undertaken in September-October 2009 to strengthen DI&ADR Center staff capacity for their drug information and pharmacovigilance functions.

ART Site Visits

Just prior to the Vietnam visit by Drs. Joshi and Stergachis, a mapping of seven antiretroviral therapy (ART) facilities was carried out at Dong Da Hospital OPC, Tay Ho Hospital OPC, Bach Mai Hospital OPC in Hanoi, and Binh Thanh OPC, District 10 OPC, Pediatric Hospital No.01 OPC, and Tropical Disease Hospital (TDH) OPC in Ho Chi Minh City (HCMC). This mapping was done from January 11th to 15th, 2010 by MSH/SCMS Senior Medicines Program Manager Dr. Hoang My Gerard, MSH/VAAC Program Associate Ms. Doan Thi Nga, and National DI-ADR Center/HUP pharmacist Ms. Vu Lan Huong.

To supplement this mapping, Dr. Joshi and Dr. Stergachis also went to three antiretroviral therapy (ART) sites identified by VAAC during their in-country visit—one in Hanoi and two in HCMC. Given below are the dates of visits and the staff that Dr. Joshi and Dr. Stergachis met. The three sites visited represented three different levels of care, i.e., national level (Bach Mai Hospital), provincial level (Tropical Diseases Hospital), and district level (Binh Thanh OPC).

Bach Mai Hospital (January 18)

- Dr. Pham Thanh Thuy, Deputy Chief of Infectious Disease Department
- Dr. Do Duy Cuong, OPC Chief
- Dr. Trinh Thi Ngoc, Chief of the Infectious Disease Department

Tropical Diseases Hospital (TDH) OPC (January 25)

- Dr. Vo Minh Quang (MD): Vice Head of Dept. of Planning and Generalizing – TDH, Head of HIV/AIDS OPC
- Pharm. Do Thi Cam Nhung: In charge of drug management and dispensing
- Mr Bui Hoang Thien Tan, Mrs Phan Ngoc Thuy Dung: Data keeper

Binh Thanh OPC (January 26)

- Dr. Dang Phi Bang: OPC Head

- Dr Tran Thi Viet: Treatment Doctor
- Dr. Ngo Thi Anh Dong: Counselor – Doctor
- Pharm. Ngo Thanh Binh: Dispenser
- Nurse Ngo Thi Kim Hoang: Admin

All these mapping visits were aimed at observing the facilities and discussing with their staff to understand the typical ART clinic and recording activities in order to help design the pilot protocol in as much an integrated manner as possible with the existing care process.

Meeting with HUP Officials

On January 19th, Dr. Joshi, Dr. Stergachis, and Ms. Folmsbee met with HUP's Rector Professor Le Viet Hung, Vice-Rector and Director of the DI&ADR Centre Professor Nguyen Dang Hoa, and the Head of the International Relations Office Ms. Dinh Thi Hien Van. Additional HUP staff present were Ms. Phan Quynh Lan, and DI&ADR Centre's Vice-Director Ms. Vo Thi Thu Thuy. USAID staff Dr. Nguyen Thi Minh Ngoc also attended the meeting. MSH/Vietnam staff Ms. Pham Thi Hanh Nguyen provided translation services during the discussion.

The MSH team discussed with the HUP officials about various aspects of PV activities, including the preparatory work for active surveillance pilot. During the discussion, Prof Hung and Prof Hoa expressed that HUP is keenly interested in developing relevant curricula for in-service as well as pre-service education on pharmacovigilance. They asked MSH/SPS to provide technical support to reform/develop such curricula and to prepare a cadre of expert local teachers and trainers through training of trainers (TOT) courses.

Visit at HCMC Provincial AIDS Committee (PAC)

On January 25, Drs. Joshi, Stergachis and Gerard along with Ms. Nga visited PAC in HCMC and discussed with the following officers:

- Dr. Luu Tuyet Hoa (PhD): Vice Head of HCMC AIDS Committee Office
- Dr. Van Hung, and Dr. Hoang Trong Tam: Staff members in the Department of HIV/AIDS Treatment and Care
- Pharm. Dang Thi Ngoc Diep: Staff in the Department of HIV/AIDS Treatment and Care

The PAC staff expressed that the proposed active surveillance pilot would be a valuable step toward improving pharmacovigilance within the ART Program in Vietnam.

Briefing of CDC and WHO Representatives

On January 22, Dr. Joshi, Dr. Stergachis, and Ms. Folmsbee met with Dr. Socorro Z. Escalante, Technical Officer for Pharmaceuticals, WHO/Vietnam. They informed her of the active surveillance initiative and also discussed about WHO-SPS collaboration to provide technical assistance to the related national counterparts for including a potential PV component within the Global Fund (GF) Round 10 application. Similarly, the team briefed Dr. Nick Medland, Senior Treatment Advisor, CDC/Vietnam on January 27. The team explained to him the draft design of the active surveillance pilot. Dr. Medland recommended proposing more frequent (e.g. 2-monthly)

supervision visits of the ART sites by PAC during the first six months of the pilot in order to ensure high levels of compliance to the protocol, and help address any constraints that could emerge during the initial period.

On January 29, the MSH team had a second meeting with Dr. Escalante (WHO) about the next steps regarding WHO-SPS support for the development of a PV component for potential inclusion in GF Round 10 grant proposal. Also present in that meeting was Ms. Van from HUP. The MSH team discussed about two draft documents developed by SPS to help support this process—a stepwise strategy for the PV proposal development, and a situation analysis template. Dr. Escalante, Ms. Van and the MSH team agreed to continue communications to identify appropriate next steps as further information from CCM and GF evolve and to work collaboratively to support the overall process.

Presentation of the Draft Design of the Active Surveillance Pilot to VAAC and HUP staff

Based on the available local documents, ART mapping, and discussions with the DI&ADR Center staff and other stakeholders, Drs. Joshi and Stergachis developed a draft protocol while in Vietnam. They presented the suggested design and the details of the pilot to VAAC and HUP staff on January 28. The PowerPoint presentation used for this debriefing is attached as *Annex 3*.

The following stakeholders were present during the debriefing:

- Dr. Bui Duc Duong, Deputy Director of VAAC
- Dr. Tran Van Son, Deputy Head of Care and Treatment Department, VAAC
- Pharmacist Nguyen Thi Vu Thanh, Specialist of Care and Treatment Department, VAAC
- MSc. Vo Thi Thu Thuy, Deputy Director, DI&ADR Centre, HUP
- Dr. Nguyen The Hung, Specialist, DI&ADR Centre, HUP
- Dr. Nguyen Hoang Anh, Specialist, DI&ADR Centre, HUP
- Dr. Socorro Escalante, Technical Officer, Pharmaceuticals, WHO Vietnam Country Office
- Dr. Masaya Kato, Medical Officer, HIV/AIDS Care and Treatment, WHO Vietnam Country Office
- Pharmacist Vu Lan Huong, Specialist, DI&ADR Centre, HUP
- Dr. Nguyen Thi Minh Ngoc, HIV/AIDS Care and Treatment Specialist, USAID/Vietnam

On behalf of MSH, Ms. Folmsbee, Dr. Joshi, Dr. Stergachis, Dr. Gerard, Ms. Thi, and Ms. Pham participated in the meeting.

VAAC's Deputy-Director Dr. Doung commented that the proposed pilot would be very valuable for Vietnam. Regarding the choice of three sentinel facilities proposed for the pilot, he suggested that it would best to select one facility from each of the three levels of care delivery—national, provincial, and district. This would help inform the feasibility and the potential for future scale-up of the program at these various levels of care in Vietnam. The MSH team responded that this valuable suggestion would be included in the revised draft of the protocol. The team also suggested for VAAC to make the final selection on which sites would be best to participate in the pilot after the necessary review and approval process is over.

During the discussion, Dr. Masaya Kato from WHO provided the following highly useful comments:

- GF is moving toward making PV a compulsory part of GF grant application. So this pilot initiative is very timely and important.
- Vietnam is introducing a National Standard Form for patient monitoring (2051 form). So it will be good to think about the possibility of integrating the proposed active surveillance form into that national 2051 form. But this will need to be done once the pilot phase is over and the form finalized through any necessary revisions.

De-briefing with USAID/Vietnam

Ms. Folmsbee, Dr. Joshi, Dr. Stergachis, and Dr. Gerard debriefed USAID staff on January 29. The mission officials present were Dr. Ngoc, Mr. Sidhwa, and Dr. Jonathan Ross, Director, Office of Health. The team described the proposed framework for the pilot along with other details including the roles and responsibilities of the various stakeholders. The team highlighted that a lot of attention was paid to design the suggested pilot to fit as much as possible within the existing structures and functions of the ART Program and the DI&ADR Center.

Revision and Finalization of the Draft Protocol

After returning from Vietnam, Dr. Joshi and Dr. Stergachis worked further on the draft protocol for the pilot active surveillance activity. They accommodated the suggestions obtained from the local stakeholders during their visit and also made other necessary changes to improve the structure, flow and details of the protocol. The finalized draft is appended to this report as *Annex 4*.

NEXT STEPS

Immediate Follow-up Activities

- Send the finalized draft of the protocol for active surveillance pilot to VAAC and DI&ADR/HUP officials for review and approval
- Address comments and feedback on the protocol that may be received from VAAC and DI&ADR/HUP
- Follow-up with VAAC regarding final selection of ART sites for the pilot activity
- Collaborate with WHO/Vietnam to provide technical assistance to national stakeholders in case they decide to include a PV component in the GF Round 10 application

ANNEX 1. REQUEST FOR COUNTRY CLEARANCE

TO: Ngoc Nguyen Thi Minh, HANOI/HHA

FROM: Management Sciences for Health (MSH)/Strengthening Pharmaceutical Systems (SPS) Program, Cooperative Agreement # GHN-A-00-07-00002-00

SUBJECT: Request for country clearance for travel to Hanoi, Vietnam for Mohan Joshi, MSH/SPS, and Andy Stergachis, University of Washington

COPY: Jonathan Ross, HANOI/HHA
Xerses Sidhwa, HANOI/OPH
John MacArthur, USAID/ANE/ID/RDM/A
Anthony Boni, GH/HIDN/HS, CTO SPS
Veerle Coignez, GH/HIDN
Juanita Folmsbee, SCMS Vietnam Country Director, MSH
Ned Heltzer, Vietnam Technical Coordinator, MSH
Douglas Keene, Director, MSH/SPS
Sameh Saleeb, Deputy Director, MSH/SPS
Francis Aboagye-Nyame, Deputy Director, MSH/SPS
Mohan Joshi, SPS Country Program Manager for Vietnam, MSH/SPS
Andy Stergachis, University of Washington

1. The Strengthening Pharmaceutical Systems (SPS) Program wishes to request country clearance for the proposed travel to Hanoi, Vietnam for Dr. Mohan Joshi, Senior Technical Manager for AMR and SPS Country Program Manager for Vietnam, and Dr. Andreas Stergachis, Professor of Epidemiology & Global Health, University of Washington, from January 16th to the 29th, 2010.

2. Background:

The Government of Vietnam has recently launched its National Drug Information and Adverse Drug Reaction Monitoring Center (DI & ADR) to strengthen pharmacovigilance activities in the country and the Vietnam Administration of AIDS Control (VAAC) is interested to initiate a pilot active surveillance activity within the ART Program. The U.S. President's Emergency Plan for AIDS Relief (PEPFAR) Vietnam Program views this as an opportunity to build on its ongoing support to HIV/AIDS care, treatment, and prevention programs, which include training for practitioners, clinic support, procurement of medicines and supplies, and development of a supply chain. Strengthening the pharmacovigilance system will demonstrate PEPFAR's commitment to a broader health systems approach to promote safe and effective use of HIV/AIDS medicines, but also medicines for malaria, TB, child health, and methadone-substitution programs. In July 2009, the SPS Program provided a technical support visit by its Senior Program Associate, Ms. Helena Walkowiak, to work with the Center staff to draft a one-year work plan, and to develop a strategy for including pharmacovigilance activities in a proposal to the Global Fund to Fight AIDS, Tuberculosis and Malaria. In September-October 2009, SPS provided further support through a visit by Dr. Mohan Joshi to provide technical

assistance to strengthen the newly established Center's staff capacity to carry out drug information and pharmacovigilance activities. SPS will now build on these foundations and collaborate with VAAC, DI/ADR Center, and other stakeholders to help initiate a pilot active surveillance activity within the ART program in Vietnam.

3. Purpose of Proposed Visit:

The primary purpose of the Vietnam visit by Drs. Joshi and Stergachis is to assist the VAAC and other key stakeholders to carry out preparatory work to design a pilot initiative on pharmacovigilance-related active surveillance within the ART Program.

4. Scope of Work for Dr. Joshi and Dr. Stergachis:

- Provide a briefing and debriefing for USAID and CDC/Vietnam, as requested
- Analyze, interpret and synthesize the finding of mapping of ART care and treatment (scheduled to be carried out by SPS, VAAC, and DI-ADR Center from January 11th to 15th) to inform further work on the development of the active surveillance protocol
- Carry out ART site visits and discussions/interviews with relevant in-country stakeholders in Hanoi and Ho Chi Min City
- Develop a customized draft of an active surveillance protocol that takes into account the currently prevailing circumstances and opportunities within the ART program in Vietnam
- Work with in-country counterparts on the final selection of sentinel sites for active surveillance
- Present to VAAC and other stakeholders the draft protocol along with recommended next steps in the implementation of active surveillance in Vietnam, and obtain their feedback
- Carry out any additional information gathering or in-country discussions that might be needed (as informed by the feedback) to help revise the protocol and the recommended next steps
- Provide an exit briefing to VAAC and DI-ADR Center
- Submit a report after the completion of the trip

5. Anticipated Contacts:

- Representatives of USAID/Vietnam
- Representatives of CDC
- Staff of the Vietnam Administration for AIDS Control (VAAC)
 - 1. Dr. Bui Duc Duong, Vice Director of VAAC
 - 2. Dr. Do Thi Nhan, Head of Care and Treatment Department
 - 3. Doan Thi Nga, Pharmacist, Care and Treatment Specialist
- Representatives of the DI & ADR Center and the Hanoi School of Pharmacy
 - 1. Prof. Nguyen Dang Hoa
 - 2. Ms. Dinh Hien Van
 - 3. Ms. Phan Quynh Lan
 - 4. Ms. Vo Thi Thu Thuy

- PEPFAR implementing partners including Family Health International (FHI), Medicins de Monde (MDM), Harvard Medical School AIDS Initiative (HAIVN), and Life Gap/CDC, as appropriate
- Representatives of other organizations, as appropriate
 1. Dr. Soc Escalante, Pharmaceuticals Consultant, WHO

6. Logistics:

Dr. Joshi and Dr. Stergachis will arrive in Hanoi on or about January 16, 2010 and depart on or about January 29, 2010.

7. Funding:

The in-country work will be paid for with USAID/SPS funds.

8. Action:

Please inform the MSH/SPS Program whether country clearance is granted for the activity to take place as proposed. Please confirm receipt and reply via e-mail to the attention of Anthony Boni, USAID/G/PHN/HN/HPSR, at aboni@usaid.gov, tel (202) 712-4789, fax (202) 216-3702. Please send carbon copies to Veerle Coignez at vcoignez@usaid.gov, Douglas Keene at dkeene@msh.org, Juanita Folmsbee at jfolmsbee@msh.org, Sameh Saleeb at ssaleeb@msh.org, Francis Aboagye-Nyame at fnyame@msh.org, Mohan Joshi at mjoshi@msh.org, and Nicolette Regis at nregis@msh.org. Thank you for Mission cooperation.

ANNEX 2. AGENDA



Dr Mohan and Dr Andy's agenda for Jan.18 - 29, 2010

(development of pilot ART active surveillance protocol)

<i>Day/Time</i>	<i>Meetings/Activities</i>	<i>Location</i>
Jan. 18, Monday, 10:00—12:00 AM	In-briefing with Juanita/mimi	SCMS office
14:00—16:00 PM (approved by VAAC)	ART site visit at OPC Bach Mai Hospital	Bach Mai Hospital
Jan. 19 Tuesday, 10:00—12:00 AM	Brief-in with USAID 1. Xerses Sidhwa, Health Officer 2. Dr Nguyễn Thị Minh Ngọc, HIV/AIDS Care and Treatment Specialist	USAID office in Hanoi
Jan. 19, Tuesday 14:00—17:00 PM	Meeting with HUP officials 1. Prof. Le Viet Hung (HUP) 2. Prof. Nguyen Dang Hoa (HUP) 3. Ms. Dinh Hien Van (HUP) 4. Ms. Phan Quynh Lan (HUP) 5. Ms. Vo Thi Thu Thuy (HUP) 6. Dr Prof. Andy Stergachis (MSH) 7. Dr Prof. Mohan Joshi (MSH) 8. Ms Juanita Folmsbee (MSH) 9. Ms Pham thi Hanh Nguyen (MSH) 10. Dr Nguyen Thi Minh Ngoc (USAID)	HUP 13-15 Le Thanh Ton, Hoan Kiem, Hanoi
Jan. 21, Thursday 8:00 AM—16:00 PM	Working on the finding of mapping of ART care and treatment (carried out by SPS, VAAC, and DI-ADR Centre from January 11 to 15)	SCMS office in Hanoi
Jan. 22, Friday, 10.00—11.00 AM 14:00—17:00 PM	Meeting with Dr. Soc Escalante, WHO/Vietnam Working with DI&ADR Centre staff 1. Vice director Võ Thị Thu Thủy 2. Doctor Nguyễn Thế Hùng 3. Doctor Nguyễn Hoàng Anh 4. Vũ Lan Hương 5. Nguyễn Phương Thúy	MSH/SCMS office in Hanoi DI&ADR Centre, HUP
Jan. 23 -24	WEEKEND (travel to HCMC)	

***Sentinel Site-Based Pilot Active Surveillance Pharmacovigilance in the Vietnam ART Program:
Technical Assistance for Protocol Development***

Jan. 25, Monday (<i>approved by VAAC</i>) 9:30—12:00 AM 14:00 – 16:00 PM	<ul style="list-style-type: none"> • Meeting with PAC officials, HCMC • TDH ART site visit 	PAC HCMC office TDH
Jan. 26, Tuesday, 9:30 -12:00 <i>(approved by VAAC)</i>	ART site visit at OPC Binh Thanh	OPC Binh Thanh
Jan. 27, Wednesday, 12:30—1:30 PM	Debriefing with Dr. Nick Medland, CDC/Vietnam	
Jan. 28, Thursday, 14:00–16:00 PM	Debriefing meeting with VAAC and DI-ADR Centre staff 1. Dr Prof. Bui Duc Duong (VAAC) 2. Dr. Tran Van Son (VAAC) 3. Ms. Doan thi Nga (MSH/VAAC) 4. Ms. Võ Thị Thu Thủy (DI&ADR Centre) 5. Doctor Nguyễn Thế Hùng (DI&ADR Centre) 6. Doctor Nguyễn Hoàng Anh (DI&ADR Centre) 7. Ms Juanita Folmsbee (MSH) 8. Ms Hoang My Gerard (MSH) 9. Dr Prof. Mohan Joshi (MSH) 10. Dr Prof. Andy Stergachis (MSH) 11. Dr Nguyen Thi Minh Ngoc (USAID) 12. Dr. Nick Medland (CDC)	VAAC office
Jan. 29, Friday 12.15—1.30 PM 3:30 – 4:00 PM	Meeting with Dr. Soc Escalante (WHO) and Ms. Van (HUP) Debriefing meeting with USAID/Vietnam 1. Dr. Jonathan Ross, Director, Office of Health 2. Mr. Xerses Sidhwa, Health Officer 3. Dr Nguyễn Thị Minh Ngọc, HIV/AIDS Care and Treatment Specialist	HUP USAID office

ANNEX 3. POWERPOINT PRESENTATION ON THE SUGGESTED FRAMEWORK FOR THE ACTIVE SURVEILLANCE PILOT

Pharmacovigilance Active Surveillance Pilot in the ART Program in Vietnam

Mohan P. Joshi, MBBS, MSc, MD
Strengthening Pharmaceutical Systems (SPS), MSH
and

Andy Stergachis, PhD, RPh
School of Public Health, University of Washington

Presentation to VAAC and HUP, Hanoi, Vietnam
28 January 2010



1

Purpose of Current Visit to Vietnam, 16-29, January 2010

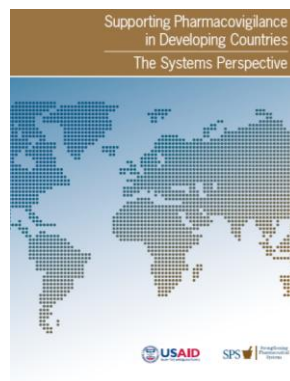
- Assist national stakeholders to design a pilot active surveillance activity in the ART program through:
 - Analyzing findings of ART Care Mapping
 - Briefings with stakeholders
 - Site visits: Hanoi (1); HCMC (2)
 - Development of draft protocol
 - Consultations with HUP, DI & ADR, PAC
 - *Presentation to VAAC, HUP, DI & ADR, WHO*



2

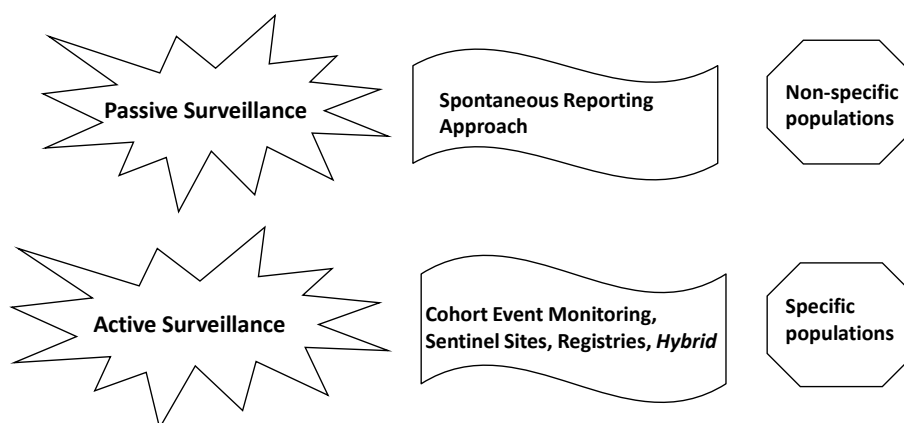
Why A Growing Interest in Pharmacovigilance of ARV?

- Rapid scale-up of ARVs
- Life-long therapy
- High level of treatment adherence required
- Short-term and long-term toxicities
- Presence of underlying diseases and concomitant medication use
- Inform development and updating of treatment guidelines with local data



3

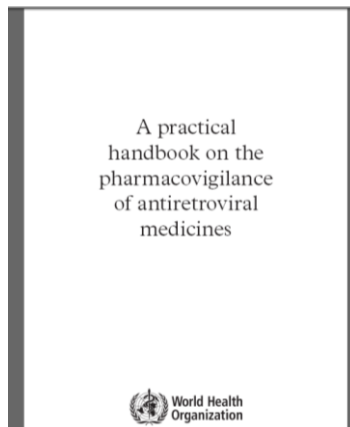
Comprehensive Monitoring Approach Using Passive and Active Surveillance



4

Active Surveillance

- “Systems whereby active measures are taken to detect adverse events.
- This is managed by active follow-up after treatment and the events may be detected by asking patients directly or screening patient records”



5



Why Active Surveillance?

This surveillance can be helpful especially for:

- Measuring rates and risk of ADRs
- Identifying risk factors for risk management
- Assessing safety in special vulnerable populations
- Early possible recognition of new adverse reactions for benefit-risk assessments
- Complimenting other methods, such as spontaneous adverse drug reaction reporting

6



Sentinel Sites Active Surveillance

- Sentinel Sites
 - Focusing on selected care delivery sites
- Advantages
 - Ease of adding surveillance to existing care delivery, infrastructure
 - Good way to pilot procedures and approaches for lessons learned and future scale-up
 - Can be efficient by focusing on a smaller number of sites and training is easier

7



Overall Goal of Pilot

Implement a pilot initiative on pharmacovigilance active surveillance within sentinel sites in the Vietnam ART Program to generate local, evidence-based information for use in improving patient safety and outcomes

8



Specific Aims of Pilot

1. Develop and field-test procedures and tools for sentinel site active surveillance of ARTs.
2. Determine the incidence of and risk factors for suspected adverse drug events in ART naïve adults receiving HAART
3. Evaluate the feasibility and sustainability of this pilot for future roll-out in order to support evidence-based decision-making, including review of standard treatment guidelines.

9



The 6 W's of Active Surveillance

What

- Pilot active surveillance for ART Pharmacovigilance
- Both ADEs and treatment switches

Where

- 3 sentinel sites (1 in Hanoi and 2 in Ho Chi Min City)
- Possible sites: Dong Da, TDH, Binh Thanh

How

- Asking questions actively during ART start & follow-up
- Recording information in structured form

When

- From the beginning of treatment
- Followed up for 18 months in the “pilot” phase

For Whom

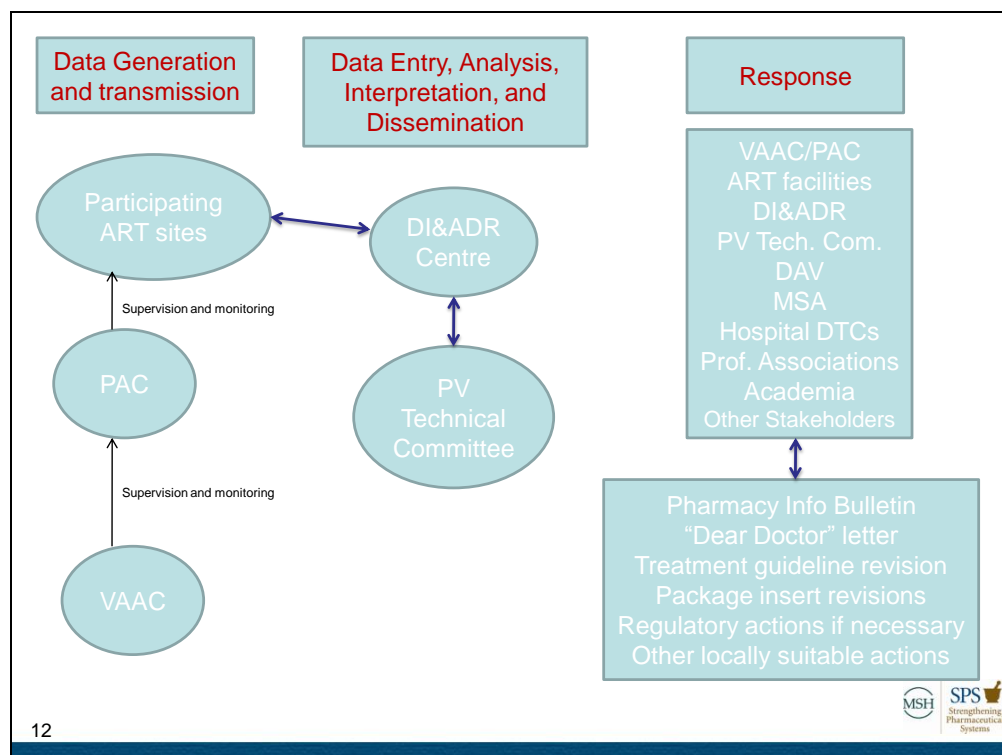
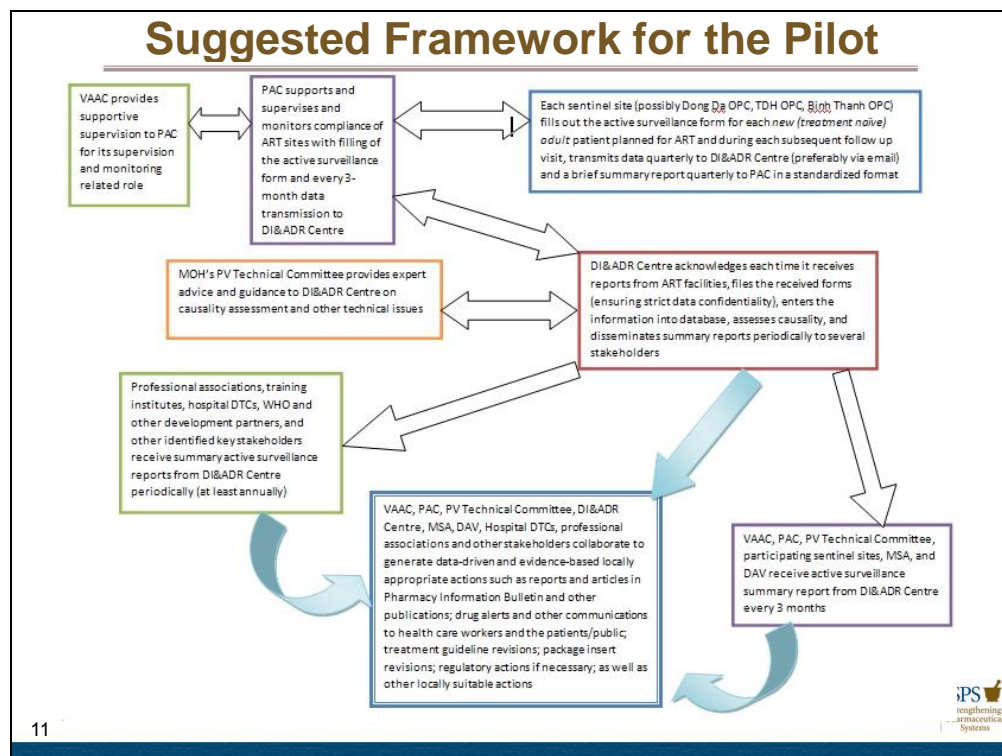
- New (ART Naïve) adult patients eligible for ART

By Whom

- Participating ART Sites
- DI&ADR Centre, VAAC, PAC, other stakeholders

10





Possible Sentinel Sites

Characteristic	Dong Da	TDH	Binh Than
Geographical Location	Hanoi	HCMC	HCMC
Staff			
Doctor	4	7	4
Pharmacist	2	4	2 (pharmacy dispensers)
Nurse	5 (2 also do computer work)	8	2
IT staff	2 (nurses)	2	1
New (<i>treatment naïve</i>) Adult ART Pts/month	Avg. 15	Avg. 90	Avg. 30
Presence of automated records	Yes	Yes	Yes

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Recruitment and Follow-up

Prospective recruitment of new ART treatment naïve patients from the Sentinel Sites

Total # of cohort = 600 patients

Target #s to be determined for each site

Follow from Start of ART

Record during usual care

**ADR/
ADE present**

**No ADR/
ADE present**

18 months of follow-up

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[illegible]

Active Surveillance Form Part “A” - Baseline

PATIENT STATUS AT START OF ART – COPY FROM RECORDS						
Date of Birth: ____/____/____	Age: _____ Yrs	Facility <input type="checkbox"/> Dong Da <input type="checkbox"/> Bach Mai <input type="checkbox"/> Binh Thanh <input type="checkbox"/> Tropical Disease Hospital	Weight: _____ kgs	WHO Clinical Stage: 1 2 3 4 99 (if missing)		
CONDITIONS CHECK		MEDICATIONS (CURRENT AND WITHIN PAST MONTH)		LABORATORY TESTS		
Malnutrition				Test	Date	Result
Anemia				Hb (g/dl)		
Alcohol abuse				CD4		
Substance abuse				ALT		
Tuberculosis						
Renal disease						
Liver disease				Others (specify): Chlamydia		
Bacterial infection						
Other (specify)						
Other (specify)						

Active Surveillance Form - Part “B” From ART Start Through Follow-Up

PATIENT ENCOUNTERS FROM START-UP OF ART THROUGH FOLLOW-UP									
DATE OF VISIT _/_/	ART REGIMEN (code)	OTHER MEDICINES (code)	ADVERSE DRUG EVENTS (code)	OTHER ADVERSE EVENTS (code)	CHANGES IN DRUG REGIMEN (code)	OUTCOMES OF ADVERSE EVENTS (code)	ABNORMAL LABORATORY FINDINGS (list)	OTHER NOTABLE CONDITIONS (code)	COMMENTS
ART START VISIT									
FOLLOW-UP									
FOLLOW-UP									
FOLLOW-UP									
FOLLOW-UP									
FOLLOW-UP									
FOLLOW-UP									
FOLLOW-UP									
FOLLOW-UP									
FOLLOW-UP									
FOLLOW-UP									
FOLLOW-UP									
FOLLOW-UP									
FOLLOW-UP									
FOLLOW-UP									
FOLLOW-UP									

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Codes for Data Fields for the Form

ART REGIMEN CODES		OTHER MEDICINES CODES	CODES		CHANGES IN DRUG REGIMEN CODES	OUTCOMES OF ADVERSE EVENTS CODES	OTHER NOTABLE CONDITIONS CODES
Principal ART Regimens	Alternative ART Regimens		ADVERSE DRUG EVENT CODES	OTHER ADVERSE EVENTS CODES			
0 = AZT/3TC/NVP 1 = D4T/3TC/NVP	2 = AZT/3TC/EFV 3 = AZT/3TC/EFV 4 = TDF/3TC/NVP 5 = TDF/3TC/EFV 6 = AZT/3TC/DFP 7 = Other (Specify)	0 = None 1 = Cotrimoxazole 2 = Iron suppl. 3 = SP antimalarials 4 = Artemesinins Combinations 5 = Aspirin and other NSAIDs 6 = Paracetamol 7 = Antibiotics-Ciprofloxacin 8 = Antibiotics-penicillin 9 = Other (specify)	0 = None 1 = Abdominal 2 = Anemia 3 = Peripheral Neuropathy 4 = CNS 5 = Rash 6 = Fat changes 7 = Fatigue 8 = Headache 9 = Jaundice 10 = Lactic acidosis 11 = Lipodystrophy 12 = Nausea 13 = Pruritus 14 = Other (specify)	0 = None 1 = Hospitalized 2 = Dead 3 = suspected treatment failure 4 = other (specify)	0 = None 1 = Discontinued without treatment switch 2 = Dose reduced 3 = Switch ART regimen 4 = Other (specify)	0 = None 1 = Resolved 2 = Resolving 3 = Resolved with sequelae 4 = Not resolved 5 = Worsened 6 = Death 7 = Unknown	0 = None 1 = Pneumonia 2 = Kaposi's sarcoma 3 = Hookworm 4 = Malaria 5 = GI bleeds 6 = liver cirrhosis 7 = Blood disorders 8 = malnutrition 9 = Pregnancy 10 = other (specify)

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Suggested Roles and Responsibilities of Key Stakeholders (1)

■ ART Facilities

- Part A of Form: Completed by receptionist nurse
- Part B of Form: Completed by clinician or other clinical officer (if relevant)
- Computer Entry and Quarterly Transmission of Data: By IT person (or by other staff working with computer; alternatively can transmit copy manually)

■ VAAC and PAC

- VAAC: supportive supervision of PAC (quarterly)
- PAC: supportive supervision of ART sites (bi-monthly for the first 6 months, then quarterly)

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Suggested Roles and Responsibilities of Key Stakeholders (2)

■ DI & ADR Centre

- Sending acknowledgement whenever data are received
- Data management, analysis including causality assessment, update reporting (quarterly)

■ PV Technical Committee

- Expert technical advice to DI & ADR Centre

■ VAAC, PAC, DI&ADR Centre, PV Tech. Com., DAV, MSA and others

- Participation in appropriate responses based on locally generated data, including safety signals

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Resources Required

- **Training** of Sentinel Sites, DI & ADR staff, PV Technical Committee staff and other related stakeholders
- **Simple database** for computer entry of data at ART sites, and for data management at the DI&ADR Centre
- **Field-testing, printing, distributing** the *Pharmacovigilance Active Surveillance Form*
- **Operational:** Internet access, local travel, and IT support

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Protocol Outline

1. Overall Goal & Specific Aims
2. Background & Rationale
3. Methods
4. Quality Control and Training
5. Roles and Responsibilities
6. Strengths & Limitations
7. Evaluation of Pilot Activity
8. Annexes

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Summary of Methods

- Inclusion criteria: ART treatment naïve adults
- Setting: Sentinel sites (3-4)
- Sample size: 600 patients
- Follow-up: 18 months per patient
- Outcomes: ADRs and other selected AEs
- Data collection: baseline and follow-up using a structured form
- Training at onset and QA monitoring
- Data transmission, preferably by email

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Strengths & Limitations

- **Strengths**
 - Estimate ADR/ADE rates and risk factors
 - Pilot procedures and approaches for lessons learned and future scale-up
 - Strengthens overall pharmacovigilance & ART program
- **Limitations**
 - Sample size
 - Geographical representation
 - Duration of follow-up

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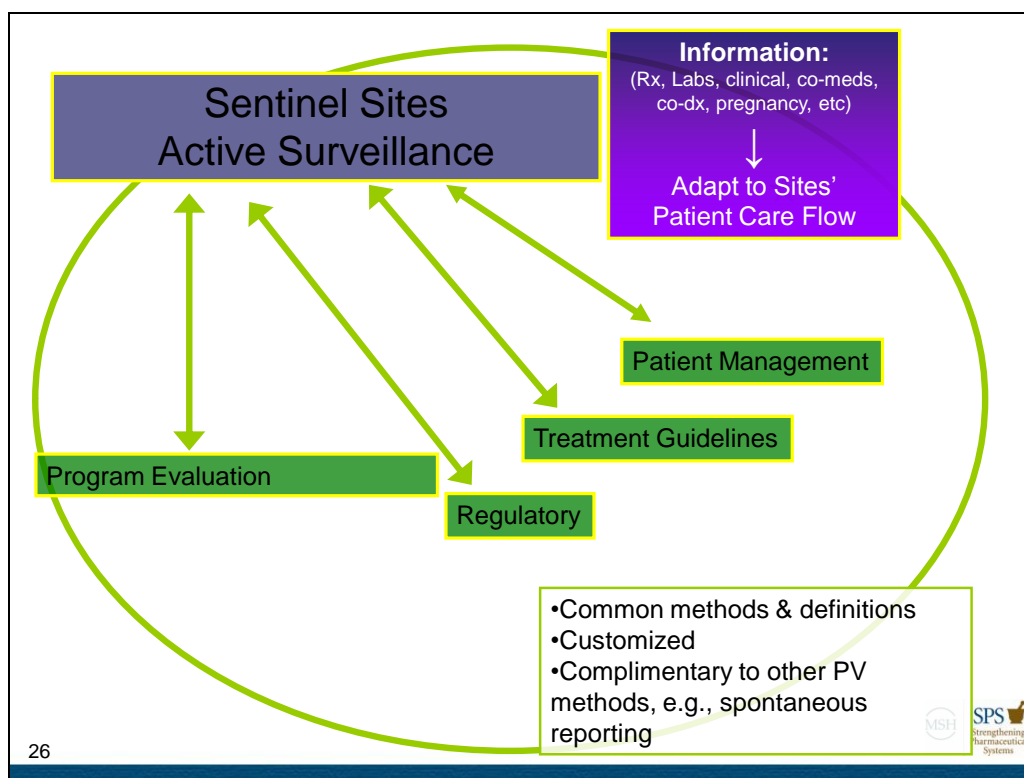
Approval & Other Considerations

- VAAC and HUP to determine approval process
- Data confidentiality & ethical issues:
 - “Because it is essential to record personal identifiers, the security, privacy and confidentiality of personal data need to be strenuously maintained.....should avoid attempting to obtain individual informed consent if at all possible because it will be time-consuming to try to explain the concepts of pharmacovigilance to each patient, will increase complexity and add to the cost, and could potentially compromise the validity of the results if many patients refuse to be enrolled. (It) is not a clinical trial or research study and does not interfere with treatment in any way. It is simply a process of observation data collection in the interests of public health.” *

* A practical handbook on the pharmacovigilance of antiretroviral medicines. WHO (2009) Draft



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Summary

This ART Program pilot active surveillance will:

1. Complement existing spontaneous reporting system
2. Create local data for improved medicine safety and patient outcomes
3. Evaluate feasibility and sustainability for future expansion to additional ART sites
4. Provide a model for similar initiatives by other public health programs in Vietnam

ANNEX 4. DRAFT PROTOCOL FOR THE PILOT ACTIVE SURVEILLANCE ACTIVITY

Appended as the following section of this report (*Annex 4*) is the draft protocol on “*Sentinel Site–Based Pilot Active Surveillance Pharmacovigilance in the Vietnam ART Program*”.

Sentinel Site–Based Pilot Active Surveillance Pharmacovigilance in the Vietnam ART Program

March 15, 2010

Draft Protocol submitted to the
Vietnam Administration of AIDS Control
and the
National Drug Information and Adverse Drug Reaction Monitoring Center,
Hanoi University School of Pharmacy



Strengthening
Pharmaceutical
Systems

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About SPS

The Strengthening Pharmaceutical Systems (SPS) Program strives to build capacity within developing countries to effectively manage all aspects of pharmaceutical systems and services. SPS focuses on improving governance in the pharmaceutical sector, strengthening pharmaceutical management systems and financing mechanisms, containing antimicrobial resistance, and enhancing access to and appropriate use of medicines.

Key Words

active surveillance, adverse drug reactions, antiretroviral therapy, pharmacovigilance

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ACRONYMS AND ABBREVIATIONS

3TC	lamivudine
ADR	adverse drug reaction
AE	Adverse event
ART	antiretroviral therapy
ARV	antiretroviral medicine
AZT	zidovudine
CD4	cluster of differentiation found on a subset of T-lymphocyte
D4T	stavudine
DAV	Drug Administration of Vietnam
DI&ADR Center	National Drug Information and Adverse Drug Reaction Monitoring Center
DTC	Drug and Therapeutics Committee
EFV	efavirenz
Global Fund	Global Fund to Fight AIDS, Tuberculosis and Malaria
HAART	highly active antiretroviral therapy
HCMC	Ho Chi Minh City
IT	Information technology
MSA	Medical Services Administration
NVP	nevirapine
OPC	outpatient clinic
PAC	Provincial AIDS Committee
PV	pharmacovigilance
SPS	Strengthening Pharmaceutical Systems (Program)
TB	Tuberculosis
TDF	tenofovir
VAAC	Vietnam Administration of AIDS Control
WHO	World Health Organization

SUMMARY

Proposed is a pilot system for monitoring the safety and tolerability of antiretroviral therapy (ART) at sentinel sites in Vietnam through sentinel site active surveillance. It aims to develop, implement, and demonstrate the local feasibility of a practical and sustainable pharmacovigilance system that could later be scaled up to monitor the safety of antiretroviral medicine (ARV) regimens across Vietnam. It also has applicability for future active surveillance of other medicines, settings, and populations. The active surveillance activity, developed in consultation with stakeholders, proposes to systematically document and quantify the presence or absence of ARV-related adverse events and to determine risk factors at three sentinel sites in Vietnam. For this pilot activity, it is proposed that the active surveillance be initiated and evaluated at three outpatient ART health care facilities, two in Ho Chi Minh City (HCMC) and one in Hanoi. Systematically collecting information about medicines used in a defined population can help ensure that medicines have an acceptable safety profile and are used safely.

OVERALL GOAL AND SPECIFIC AIMS

Overall Goal

The overall goal of this proposed activity is to implement and evaluate a pilot pharmacovigilance active surveillance at three sentinel sites in Vietnam's ART program to generate local, evidence-based information to improve the systematic identification, diagnosis, management, and prevention of medicine-related morbidity and mortality in HIV-infected patients on highly active antiretroviral therapy (HAART).

Specific Aims

1. Develop, implement, and field-test procedures and tools for sentinel site active surveillance of ARTs.
2. Prospectively determine the incidence of and risk factors for suspected adverse drug events in treatment-naïve adults receiving HAART at sentinel site ART clinics.
3. Evaluate the pilot program and demonstrate the feasibility of using active surveillance as a sustainable platform for assessing the safety and use of HAART to help support evidence-based decision making, including review of standard treatment guidelines.

BACKGROUND AND RATIONALE

The government of Vietnam launched its National Drug Information and Adverse Drug Reaction Monitoring Center (DI&ADR Center) to strengthen pharmacovigilance activities in the country. Under the Rational Pharmaceutical Management Plus Program, Management Sciences for Health assisted the government of Vietnam and its partners in developing a framework for medication safety and pharmacovigilance that acknowledged the importance of active surveillance methods in support of public health programs, including the use of sentinel sites and follow-up of patient cohorts. This one-day national stakeholder consensus meeting held on March 25, 2009, was followed by a three-day training-of-trainers Introduction to Pharmacovigilance course for staff from public health programs and other key institutions. Since that time, the Vietnam Administration of AIDS Control (VAAC) and the DI&ADR Center, Hanoi University of Pharmacy, have expressed interest in initiating a pilot active surveillance activity within the ART program. In July 2009, the Strengthening Pharmaceutical Systems (SPS) Program, which is a follow-on to Rational Pharmaceutical Management Plus, made a technical support visit to the center's staff to draft a one-year work plan and to develop a strategy for including pharmacovigilance activities in a proposal to the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund). SPS subsequently provided further technical assistance to strengthen the capacity of the newly established center's staff to carry out drug information and pharmacovigilance activities. Building on these foundations, SPS has collaborated with VAAC and the DI&ADR Center and has obtained inputs from other stakeholders to develop this draft protocol for pilot active surveillance activity within the ART program in Vietnam.

The Need for Pharmacovigilance of Antiretroviral Medicines

According to the World Health Organization (WHO), *pharmacovigilance* is the science and activities relating to the detection, evaluation, understanding, and prevention of adverse reactions to medicines or any other medicine-related problems.¹ Despite their lifesaving and quality-of-life-improving effects, ARVs are associated with safety issues ranging from minor to more serious adverse drug reactions (ADRs), with both short- and long-term effects.² Major adverse events associated with the use of ARVs affecting patient adherence and outcomes include lipodystrophy, anemia and neutropenia, hypersensitivity reactions, hepatic disorders, acute pancreatitis, osteopenia and osteoporosis, and lactic acidosis.³ However, little is known about the epidemiology of the toxicity profiles of ARVs in low- and middle-income countries, despite the

¹ World Health Organization. 2002. *The Importance of Pharmacovigilance: Safety Monitoring of Medicinal Products*.

² World Health Organization. 2006. *Antiretroviral Therapy for HIV Infection in Adults and Adolescents: Recommendations for a Public Health Approach, 2006 Revision*. Geneva: WHO.
<http://www.who.int/hiv/pub/guidelines/artadultguidelines.pdf>.

³ Vietnam HIV/AIDS Treatment Guidelines (Part A: Diagnosis and Treatment of HIV/AIDS in Adults; Part B: Diagnosis, Treatment and Care for HIV/AIDS-infected Children).

importance of such information for regulatory and public health decision making.⁴ These countries have special factors and different, and medicine use and its safety may therefore vary considerably, including the presence of conditions such as tuberculosis (TB), malnutrition, reliance on traditional or alternative therapies, and likelihood of medicine interactions.⁵ ADRs are among the most important factors interfering with patient adherence to ART, thus monitoring and managing adverse reactions to ARVs is important.

Active Surveillance as a Tool for Pharmacovigilance within Public Health Programs

With expanded access to ARVs, recognition of the need to implement systematically conducted pharmacovigilance activities within public health programs is increasing.⁶ Linking and coordinating national pharmacovigilance activities with in-country public health programs supports overall system strengthening and can help achieve better program outcomes. The conduct of surveillance—that is, ongoing systematic collection, analysis, and interpretation of data—is not a new concept for HIV/AIDS programs.⁷ As a tool for pharmacovigilance, active surveillance involves methodically searching for exposures and health outcomes, often at sentinel site facilities.⁸ It consists of the systematic collection, analysis, interpretation, and dissemination of data regarding one or more medicine-related outcomes using observational methods.⁹ Through active surveillance, potential safety problems and their risk factors can be identified for specific populations of patients. Systematically collecting information about medicines used in a defined population can help ensure that medicines have an acceptable safety profile and that they are used safely. It also helps understand the scope of ADRs. Because these methods involve obtaining a denominator of persons exposed to medications of interest, calculation of rates of adverse drug events is possible.

⁴ Modayil, R. R., et al. 2010. Adverse Drug Reactions to Antiretroviral Therapy (ART): An Experience of Spontaneous Reporting and Intensive Monitoring from ART Centre in India. *Pharmacoepidemiology and Drug Safety* 19(3): 247–55. doi: 10.1002/pds.1907.

⁵ Pirmohamed, M., K. N. Atuah, A. N. Dodoo, and P. Winstanley. 2007. Pharmacovigilance in Developing Countries. *BMJ* 335(7618): 462.

⁶ World Health Organization. 2007. *A Practical Handbook on the Pharmacovigilance of Antimalarial Medicines*. Geneva: WHO. <http://www.who-umc.org/graphics/19449.pdf>.

⁷ U.S. Agency for International Development. Facility-Based Routine Surveillance. http://www.usaid.gov/our_work/global_health/id/surveillance/fbrsurveillance.html (Last Updated on: June 02, 2009).

⁸ Strengthening Pharmaceutical Systems (SPS). 2009. *Supporting Pharmacovigilance in Developing Countries: The Systems Perspective*. Submitted to the U.S. Agency for International Development by the SPS Program. Arlington, VA: Management Sciences for Health.

⁹ U.S. Centers for Disease Control and Prevention. 2001. Updated Guidelines for Evaluating Public Health Surveillance Systems: Recommendations from the Guidelines Working Group. *MMWR Recommendations and Reports* 50(RR13): 1–35. <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5013a1.htm>.

The importance of active surveillance as a systematic approach to medicine safety assessment and pharmaceutical systems strengthening has been cited by many in the field.^{10,11,12} An increasing number of low- and middle-income countries are establishing active surveillance methods for ARVs and other medicines important to public health programs. In 2007, the Tanzania Ministry of Health and Social Welfare, Tanzania Food and Drugs Authority, initiated a cohort event monitoring study of adverse reactions among users of ARVs in Tanzania. Beginning in August 2007, USAID–U.S. President’s Malaria Initiative supported a pilot pharmacovigilance system for antimalarials in Jinja, Uganda. More recently, the KwaZulu Natal Department of Health in South Africa received funding from the Global Fund to support the further development of pharmacovigilance activities in the province, including a provincial cohort event monitoring program intended to collect long-term data on safety and treatment outcomes in ART patients at eight sentinel sites in the province. In addition, a record-linking active surveillance activity is under way in Namibia on the association between zidovudine and the risk of anemia. Active surveillance can provide accurate and timely information for program and guideline development or change. Moreover, an active surveillance system will increase reporting of potential ADRs, thereby strengthening spontaneous reporting approaches to pharmacovigilance.

Sentinel Site Active Surveillance

Sentinel surveillance is the collection and analysis of data by designated institutions selected for their geographic location, medical specialty, and ability to report high-quality data. For example, district hospitals may be required to report specific conditions to quantify the burden of disease. Sentinel sites are often those facilities where pilot programs operate. Such sites are chosen based on certain functions and criteria that are highly relevant for a planned task. Considerations may include representativeness, ease of access, infrastructure support, reasonable patient flow; interest and commitment of the potential site; any ADR-related initiative or expertise already in existence; past performance; level of computerization of ART and patient-related data management; and quality assurance measures in place. Generally, sentinel surveillance is very useful for answering specific questions, but because sentinel sites may not represent the general population or the general incidence of disease, it may have some limitations in generalizing for national disease patterns and trends.¹³ Nevertheless, for new surveillance programs, sentinel site strategies are often chosen so that data are manageable in volume and concept and for logistical efficiency, as is the case in the active pharmacovigilance examples previously cited in this proposal (i.e., Tanzania, Uganda, and South Africa). Sentinel site surveillance has the following

¹⁰ Platt, R., L. Madre, and R. Reynolds. 2008. Active Drug Safety Surveillance: A Tool to Improve Public Health. *Pharmacoepidemiology and Drug Safety* 17(12): 1175–82. doi: 10.1002/pds.1668.

¹¹ Wise, L., J. Parkinson, J. Raine, et al. 2009. New Approaches to drug Safety: A Pharmacovigilance Tool Kit. *Nature Reviews Drug Discovery* 8(10): 779. doi:10.1038/nrd3002.

¹² World Health Organization. 2007. *A Practical Handbook on the Pharmacovigilance of Antimalarial Medicines*. Geneva: WHO. <http://www.who-umc.org/graphics/19449.pdf>.

¹³ USAID. Sentinel Surveillance. http://www.usaid.gov/our_work/global_health/id/surveillance/sentinel.html.

additional advantages: regular supervision, feedback, and logistical support can be provided because sentinel sites are located in fewer facilities; higher-quality data can be obtained from a few sites with intensive support of training, supervision, and logistics; and sentinel surveillance systems are less expensive to run and maintain than universal reporting systems.

Bridging the Gap: Generating Local Data to Inform Regulatory Actions, Treatment Guidelines, and Care Delivery

The optimal methodology for drug safety surveillance in resource-limited settings is likely to vary from site to site, but in general, the options are driven by the choice and assessment of outcomes of interest and the methods needed to reliably capture drug exposures. Toward this end, this pilot will make important contributions in terms of the choice and feasibility of data collection methodologies. The data collection tools developed and validated should be applicable to future expansions of active surveillance to other medicines, settings, and population groups as well as support future proposals addressing pharmacovigilance issues. A clear and growing need exists to understand better the benefits and risks of medicines under conditions of actual use. Most questions of drug safety can be answered only by observing and analyzing the use and outcomes of therapy in large populations during the postapproval phase.^{14,15} The targeted pharmacovigilance approaches adopted in this proposal will contribute to the knowledge base on this important matter and help develop in-country infrastructure for future active surveillance approaches. In addition to its methodological contribution, this project's results should help inform future revisions of in-country HIV/AIDS treatment guidelines and regulatory decisions. The proposed prospective, observational approach will contribute data to provide estimates of safety of ARVs as well as to conduct a pilot project involving the identification of signals and to evaluate suspicions of risk to provide for better estimates of benefit-risk profiles. In addition, from a patient care perspective, knowledge of factors that may affect the risk and management of adverse reactions, including other illnesses and conditions, the patient's other current medications, the availability of alternative regimens, and the patient's history of medication intolerance, can lead to improved outcomes.

¹⁴ Committee on the Assessment of the US Drug Safety System. 2006. *The Future of Drug Safety: Promoting and Protecting the Health of the Public*. Washington, DC: Institute of Medicine.

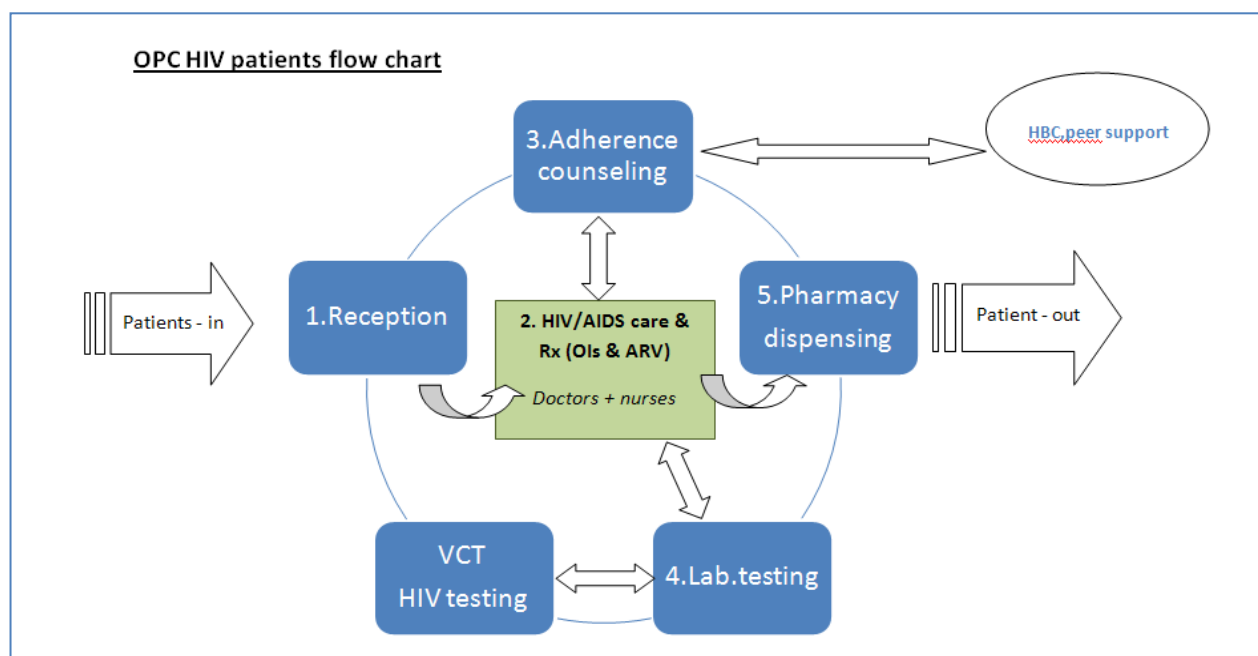
¹⁵ Lang, T., D. Hughes, T. Kanyok, J. Kengeya-Kayondo, V. Marsh, et al. 2006. Beyond Registration—Measuring the Public-Health Potential of New Treatments for Malaria in Africa. *Lancet Infectious Diseases* 6: 46–52.

METHODS

Sentinel Sites

Based on the mapping of services and data recording in ART clinics and site visits (figure 1), the initial pilot program is proposed for implementation in three ART outpatient clinics (OPCs) that will serve as the sentinel sites—two clinics in Ho Chi Minh City and one in Hanoi. The proposed sites represent the following different levels of care delivery within Vietnam—

- National level: national HIV/AIDS treatment facilities
- Provincial level: general hospitals
- District level: district-level health centers, which are the central point where comprehensive medical services are provided for persons with HIV/AIDS



Note: HBC = home-based care; OIs = opportunistic infections; VCT = voluntary counseling and testing.

Figure 1. General overview of OPC HIV patient flow in Vietnam

Table 1 describes selected characteristics of three sites that were visited during the ART care and mapping process to help inform the development of this protocol. This table shows some key characteristics relevant for the selection of the pilot sites, such as geographical location of the facility, number of key health care staff involved in ART, and average monthly number of patients who meet the suggested inclusion criteria. The sites shown in table 1 are displayed for

illustrative purposes only; the final decision regarding selection of the actual sites for the pilot rests with the VAAC.

Table 1. Characteristics of Three Sites, One or More of Which Could Serve as Sentinel Sites for the Pilot

Characteristics	Dong Da Hospital OPC	Tropical Disease Hospital OPC	Binh Than OPC
Geographical location	Hanoi	HCMC	HCMC
Staff			
Clinician	4	7	4
Pharmacist	2	4	2 (pharmacy dispensers)
Nurse	5 (2 also do computer work)	8	2
Information technology staff	2 (nurses)	2	1
Average number of new (treatment-naïve) adult ART patients per month	15	90	30
Presence of automated records	Yes	Yes	Yes

Data Sources

Proposed is a data collection strategy that relies mainly on abstracting and recording of sources of data that are already contained in the clinical records of patients who are newly placed on HAART. ARV treatment, and collecting and recording of patient information in Vietnam is conducted in accordance with Ministry of Health guidelines and protocols. For example, the treatment protocol for people living with HIV/AIDS specifies that information should be collected about medical history, clinical stage, side effects and interactions of prescribed medicines, and diagnosis of other diseases, including laboratory tests where indicated. A detailed schedule of follow-up visits is also specified as are provisions for assessing and promoting treatment adherence and treatment effectiveness. Specifically, information from the following *existing data sources* from the sentinel sites will be used for this activity—

- Pre-ART Register and ART Register
- Outpatient Record

One *new data collection form* is proposed for use by the sentinel sites to systematically abstract and record information for this active surveillance activity. The form is designed to be completed by a health care provider when he or she sees the patient. It is intended to capture information on baseline status and on medication and adverse events during start-up of therapy and subsequent follow-up visits through active questioning and recording performed by the attending health care providers. Table 2 lists the suggested minimum data set for this active surveillance activity that

guided the development of the proposed data collection form. The form is included as Annex 3. The first section of the form, designated as Part A, is for recording baseline information before ART is initiated. The second section of the form, designated as Part B, is for recording ART regimens as well as suspected adverse event–related information from ART start through each follow-up visit of the patient to the outpatient clinic.

Table 2. Minimum Data Set for the Proposed Active Surveillance Pharmacovigilance Pilot

Type	Variable(s)	Currently Recorded?	Comment
Patient data	Unique patient ID number	Yes	Necessary for record linkage
	Assigned code number	No	Can be used if concerns about confidentiality exist
	Contact details	Yes	Including treatment supporter if available
	Age/date of birth, gender, weight/height (BMI), pregnant, other notable conditions	Yes	Routinely recorded in the Outpatient Records and Pre-ART and the ART Register
Medicine exposure data	ARV drug name, strength, dose	Yes	Contained in Outpatient Record and ART Register
	Date ARV initiated and stopped	Yes	Contained in Outpatient Record and ART Register
	Adherence to ARV	Yes	Contained in the Checklist for Adherence Assessment During Treatment and the Outpatient Record
	Concomitant medications	Yes	Contained in Outpatient Record and ART Register
Outcome data	Adverse drug event and outcome	Yes	Recorded; however, will need to be recorded more systematically for active surveillance
	Classifications of seriousness and severity of outcome	No	New information needed to be collected for active surveillance
	Effect of challenge/rechallenge if applicable	No	New information needed to be collected for active surveillance
	Laboratory values	Yes	Only selected laboratory tests are to be recorded on the form

Selection of Patients

The inclusion and exclusion criteria for patient enrollment in this active surveillance activity are specified below.

- *Inclusion criteria:* adult treatment-naïve HIV/AIDS patients (older than 16 years of age) who attend clinic and are enrolled for ART initiation

- *Exclusion criteria:* pediatric and adolescent HIV/AIDS patients and treatment-experienced adult HIV/AIDS patients (i.e., those persons with previous or currently ongoing treatment with ARVs)

Patient Outcomes

The following outcomes should be recorded on the Active Surveillance Form: suspected ADRs and other selected adverse events (AEs), such as hospitalization, death, and suspected therapeutic failure. Clinicians or other recording health care staff should be asked to make no judgment on causality, and normal clinical terms or descriptions should be used. Specifically, health professionals will be asked to record the following types of events—

- All *new AEs* even if minor
- Abnormal *changes* in laboratory tests compared with a previous examination
- Suspected lack of *effectiveness*
- *Admission to hospital* with date and cause
- The first observation of *pregnancy* of any duration
- All *deaths* with date and cause
- Possible *drug interactions*

Duration of Surveillance and Duration of Pilot Activity

Because this is a pilot project, an 18-month follow-up for each person recruited into the active surveillance is proposed. The three sentinel sites suggested as examples in table 1 have the potential for recruiting at least 500–600 adult treatment-naïve HIV/AIDS patients over a four- to six-month period. The cohort recruitment at each sentinel site is proposed to continue until a predefined patient number for that site is reached. Selection of sites that receive higher number of new ART-naïve adult patients is likely to help hit the required target number more quickly. For example, given their average numbers reported to date, the three suggested sentinel sites could recruit up to 135 new ART-naïve adult patients per month, with a busy OPC such as the Tropical Disease Hospital accounting for two-thirds of that total.

Each recruited patient will be followed from the start of ART for 18 months, and data updates will be requested from sentinel sites on a quarterly basis. It is expected that active surveillance information will be integrated into usual care and collected every time the patient comes for follow-up, which typically is once a month for stabilized patients. The standard practice at the ART OPCs includes efforts made to track patients who do not present for follow-up visits. For the overall pilot activity, a period of about 28 months is proposed, commencing upon receipt of necessary approvals. The overall proposed period accounts for a 1-month training at the beginning of the activity and a 3-month analysis and reporting period at the end of the activity. It also allows at least 18 months of follow-up for every patient recruited into the active surveillance.

Data Entry and Analysis

Data entry will be done using a simple database. As data accumulate, descriptive frequency tables for demographics, medicine use, and adverse drug events will be presented periodically. As the program matures and more data accumulate, statistical analysis will be performed to understand and present various AE profiles, such as incidence rates, predictors of adverse events, and relative risks. Frequencies and risks of adverse drug events will be compared by medicine category. Multivariate models will be developed to identify predictors of adverse drug events, taking into account potential confounders (table 3).

The incidence rate of an event will be calculated as the number of events divided by the total number of patient-months of follow-up, that is, for ADRs by type. Estimates will be given with 95 percent confidence intervals assuming a Poisson distribution. Regression models will be used to investigate factors associated with the occurrence of the endpoint events.

Table 3. Variables to Be Used in Analyses

Variable Name	Category	Type
HAART regimen	Primary exposure	Categorical
Age	Confounder	Continuous
Gender	Confounder	Binary; male or female
Baseline CD4	Confounder	continuous
Baseline hemoglobin	Confounder	Continuous
Baseline co-illnesses	Confounder	Categorical
Co-trimoxazole use	Confounder	Binary; yes, no
Baseline comorbidities	Confounder	Categorical
Duration of HAART	Effect modifier	Continuous

One of the goals of the surveillance program is to link itself with WHO resources and participate in the Uppsala Monitoring Center global safety surveillance support and at the same time derive benefit from a supranational global network.

Sample Size Estimation

A cohort of approximately 500 to 600 persons on ART gives a 99 percent chance of identifying an adverse drug event that is expected to occur with an incidence of 1:100 and a 92 percent chance of identifying an adverse drug event occurring at a rate of 1:200 persons in one of the ART groups. As table 4 shows, larger sample size increases the likelihood of identifying less common AEs. However, detecting rare adverse drug events requires sample sizes beyond the scope of this pilot project. The key objective of the pilot is to demonstrate feasibility of the program, which will help in scaling up the program in future, thus leading to larger sample sizes that help in detecting less common adverse drug events. Besides providing information on such

feasibility issues, the proposed pilot will help characterize AEs that are commonly encountered in terms of their incidence and risk factors.

Table 4. Relationship between Sample Size and Probability of Observing an AE: Percent Probability of Observing at Least One AE in the Sample by AE Expected Incidence

Expected AE Incidence: 1 Event out of ... Patients							
Sample Size	100	200	500	1,000	2,000	5,000	10,000
200	86.47	63.21	32.97	18.13	9.52	3.92	1.98
300	95.02	77.69	45.12	25.92	13.93	5.82	2.96
500	99.33	91.79	63.21	39.35	22.12	9.52	4.88
700	99.91	96.98	75.34	50.34	29.53	13.06	6.76
1,000	100.00	99.33	86.47	63.21	39.35	18.13	9.52

Source: WHO. 2009. *A Practical Handbook on the Pharmacovigilance of Antiretroviral Medicines*.

QUALITY CONTROL OF DATA AND TRAINING

Training needs to be defined and provided. Topics to be covered include defining AEs and ADRs and the purpose of pharmacovigilance and the pilot surveillance system. Emphasis will be placed on what to report and how to report using the pilot system.

Training sessions will be provided at the outset of the pilot to all key members of the sentinel sites, the VAAC, Provincial AIDS Committee (PAC), DI&ADR Center, and Pharmacovigilance (PV) Technical Committee. The active surveillance forms will be pretested and modified accordingly, including the precoded options on the form. To ensure credibility of results generated as part of the pilot, quality assurance tools such as standard operating procedures will be implemented.

The training of personnel at all sites will be performed before the initiation of the activity. Quality assurance procedures will also include at least annual visits to the participating sites by a designated monitor from VAAC, PAC, or DI&ADR Center. Site monitoring will include a review of a sample of source documents.

APPROVAL, DATA CONFIDENTIALITY, AND ETHICAL CONSIDERATIONS

The VAAC and Hanoi University of Pharmacy/DI&ADR Center will need to determine an approval process and obtain or provide a formal approval to initiate the pilot. This will be an observational activity with minimal risk where the information is collected from the patient and from the clinical history of the patient without any intervention. All patient identifiers will be encrypted. Procedures will be established and maintained to ensure the confidentiality of data and unauthorized persons will not have access to the data. Regarding these issues, the WHO 2009 *Practical Handbook on the Pharmacovigilance of Antiretroviral Medicines* (85–87) writes—

Because it is essential to record personal identifiers, the security, privacy and confidentiality of personal data need to be strenuously maintained...should avoid attempting to obtain individual informed consent if at all possible because it will be time-consuming to try to explain the concepts of pharmacovigilance to each patient, will increase complexity and add to the cost, and could potentially compromise the validity of the results if many patients refuse to be enrolled. [It] is not a clinical trial or research study and does not interfere with treatment in any way. It is simply a process of observation data collection in the interests of public health.

LIMITATIONS

The proposed activity has some limitations. For example, the duration of patient follow-up for this prospective study is limited to 18 months. Additionally, the geographic coverage of the sentinel sites is limited and cannot be generalized to the entire country of Vietnam.

SUGGESTED FRAMEWORK OF THE PILOT ACTIVITY AND ROLES AND RESPONSIBILITIES OF KEY STAKEHOLDERS

Suggested Framework

The suggested framework envisages an intersectoral surveillance system that functions in a coordinated manner to (a) generate data, (b) analyze and interpret data, and (c) create locally appropriate responses based on the data. As figure 2 depicts, the sentinel ART sites generate data, and the DI&ADR Center analyzes and interprets the data, leading to concerted responses by several pharmacovigilance stakeholders. The framework links the ART public health program group (VAAC, PAC, and ART sites) with the national pharmacovigilance center (DI&ADR Center), which is a highly desirable mechanism for building an interconnected and strong pharmacovigilance system.

Suggested Information Flow within the Sentinel Sites

This section contains a suggested flow of information within sentinel sites from a patient's and a health care worker's perspective. When new ART-naïve adult patients arrive at an OPC for the first time, the receptionist begins the process by filling out Part A of the Active Surveillance Form (Annex 3), primarily using patient information that is already included in the Registration Sheet for Enrollment in HIV/AIDS Care and Treatment Program form. Immediately following the initial visit, the Initial Visit section of the Outpatient Record is reviewed, and essential data elements for active surveillance are abstracted onto the Active Surveillance Form, preferably by a nurse. At follow-up visits, the physician or other clinical officer is requested to complete Part B of the Active Surveillance Form for each follow-up visit, indicating, for example, the presence or absence of adverse drug events. An information technology (IT) person on site then enters Active Surveillance Forms into a computer and transmits the data electronically from sentinel sites to the DI&ADR Center in accordance with prespecified intervals, for example, every three months. Alternatively, a copy of the Active Surveillance Forms can be transmitted to the DI&ADR Center manually.

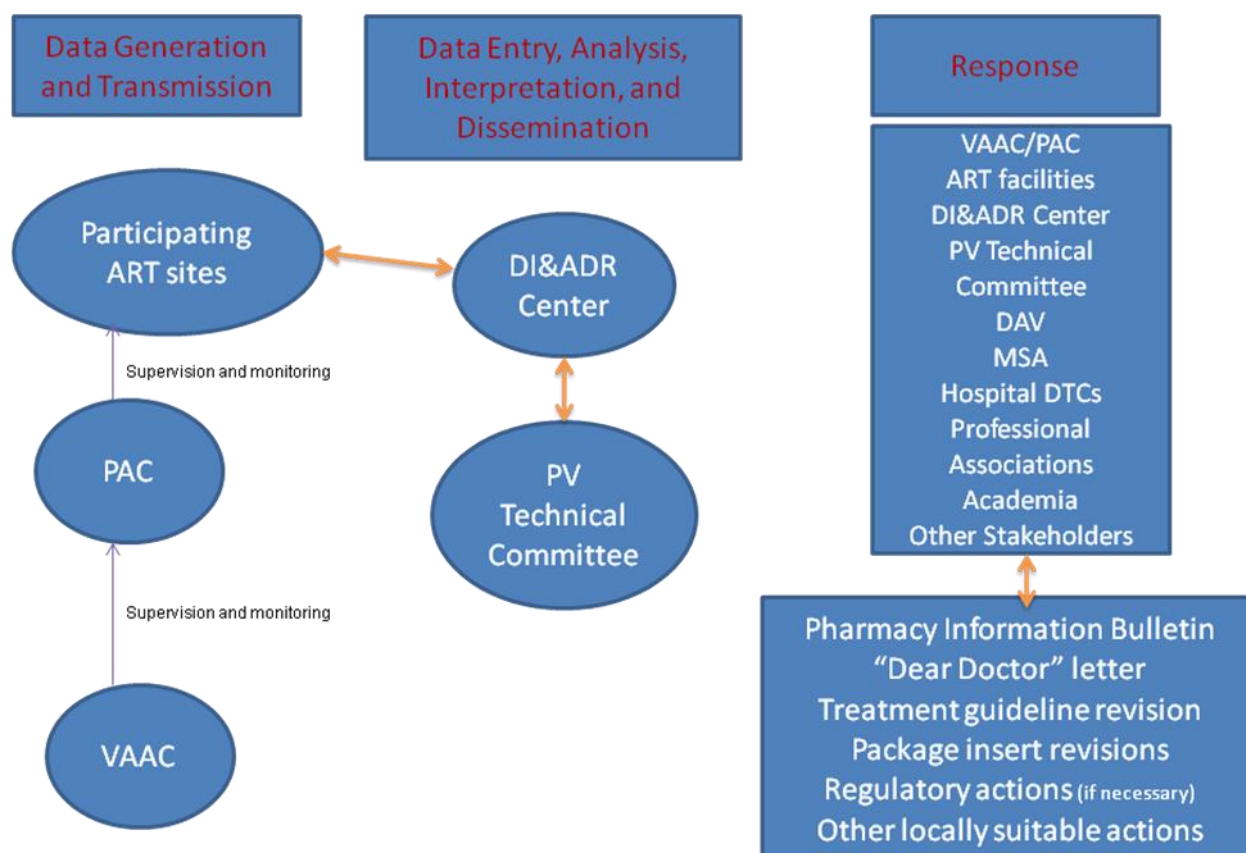


Figure 2. Suggested framework for pharmacovigilance active surveillance pilot in the ART program in Vietnam

Suggested Roles and Responsibilities

Roles and responsibilities of the various stakeholder groups for the pilot are suggested below and summarized in the box. These active surveillance–related roles were aligned as much as possible with their existing roles and functions.

- Each sentinel site fills out the active surveillance form for each recruited ART-naïve adult patient planned for ART. The form is filled when the ART is being initiated and subsequently thereafter during each follow-up visit. The sentinel site also transmits data quarterly to the DI&ADR Center (preferably via e-mail) and a brief summary report quarterly to the PAC in a standardized format.
- The PAC supports, supervises, and monitors compliance of ART sites with filling in the active surveillance form and transmitting the data quarterly to the DI&ADR Center.
- The VAAC provides supportive supervision to the PAC for its supervision and monitoring role.

- The DI&ADR Center acknowledges each time it receives reports from ART facilities, files the received forms (ensuring strict data confidentiality), enters the information into the database, assesses causality, and disseminates summary reports periodically to several stakeholders. It sends reports to the VAAC, the PAC, the PV Technical Committee, participating sentinel sites, the Medical Services Administration (MSA), and the Drug Administration of Vietnam (DAV) every three months. It also disseminates summary reports to professional associations, training institutes, hospital Drug and Therapeutics Committees (DTCs), and other identified key stakeholders, including WHO and other development partners, at least annually.
- The Ministry of Health's PV Technical Committee provides expert advice and guidance to the DI&ADR Center on causality assessment and other technical issues.
- The VAAC, PAC, PV Technical Committee, DI&ADR Center, MSA, DAV, hospital DTCs, professional associations, and other stakeholders collaborate to generate data-driven and evidence-based locally appropriate actions such as reports and articles in the Pharmacy Information Bulletin and other publications; drug alerts and other communications to health care workers and the patients or public; treatment guideline revisions; package insert revisions; regulatory actions, if necessary; and other locally suitable actions.

Box. Responsibilities of Stakeholders for Active Surveillance Pilot

ART Facilities

- Part A of Form: Completed by receptionist nurse
- Part B of Form: Completed by clinician or other clinical officer (if relevant)
- Computer entry and quarterly transmission of data: by IT person (or by other staff working with computer; alternatively, transmit copy manually)

VAAC and PAC

- VAAC: supportive supervision of PAC (quarterly)
- PAC: supportive supervision of ART sites (bimonthly for the first six months, then quarterly)

DI&ADR Center

- Sending acknowledgment whenever data are received
- Data management, analysis including causality assessment, update reporting (quarterly)

PV Technical Committee

- Expert technical advice to DI&ADR

VAAC, PAC, DI&ADR Center, PV Technical Committee, DAV, MSA, and Others

- Participation in appropriate responses based on locally generated data, including safety signals

Figure 3 is a schematic presentation of the interconnected roles and responsibilities of different stakeholders grouped according to the different elements of the active surveillance framework.

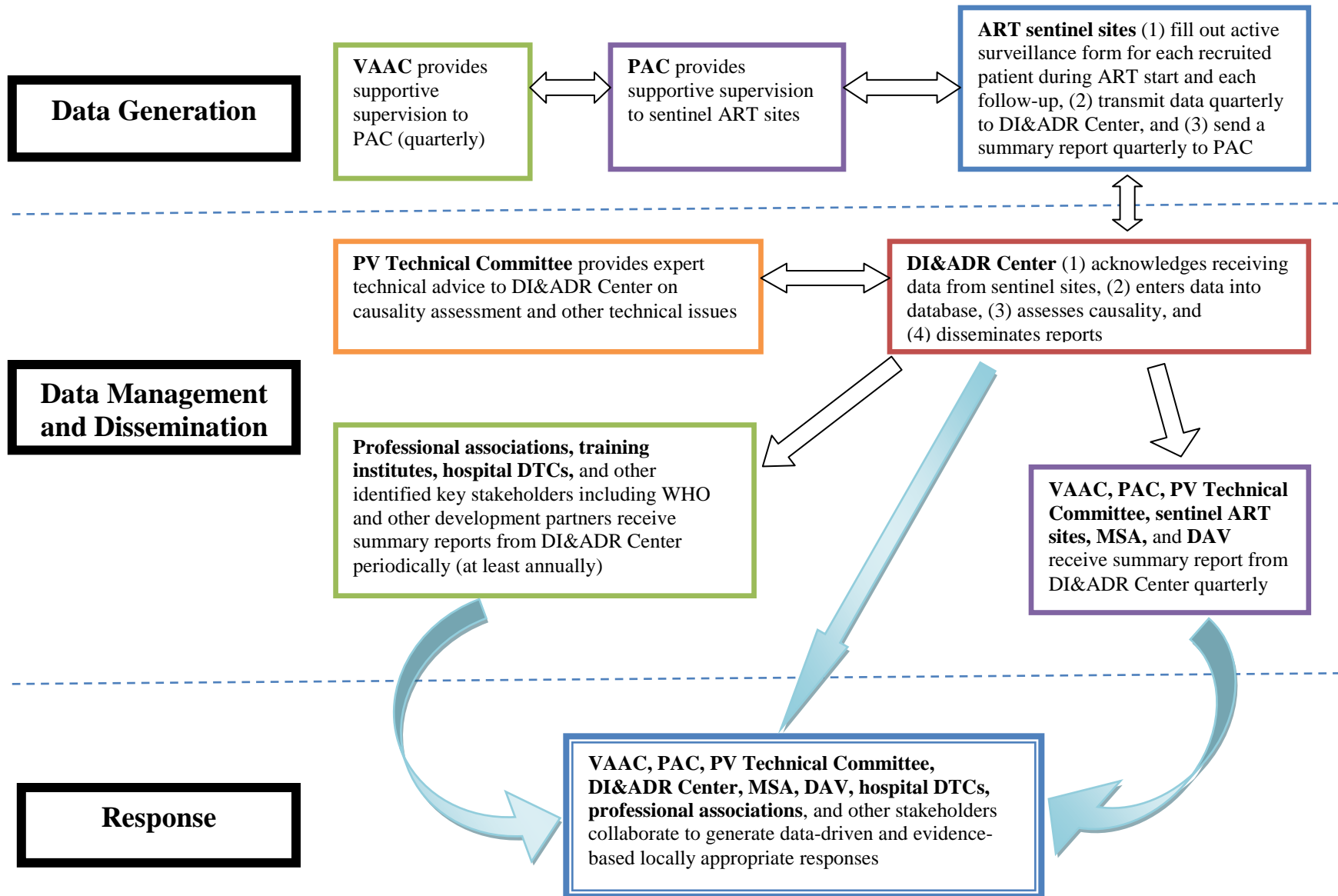


Figure 3. Framework of the Pilot Surveillance Activity, and Roles and Responsibilities of the Stakeholders

MONITORING AND DISSEMINATION OF THE PILOT ACTIVITY

It is important to monitor the progress of the pilot activity to identify any problems encountered in implementation to allow for refining and adapting implementation strategies, including training. Monitoring the pilot activity provides the basis for documenting lessons learned for subsequent decision making about possible scale-up of active surveillance pharmacovigilance beyond the pilot stage. In most instances, monitoring can be conducted by routine assessment of the Active Surveillance Forms; but in some instances, a need may exist for a limited amount of additional information gathered through selected interviews or assessment of source records. The following areas of focus are proposed for monitoring this pilot activity—

- Number of Active Surveillance Forms received and timeliness of their receipt
- Completeness of Active Surveillance Forms
- Data quality: Validity of data elements contained in the Active Surveillance Forms
- Simplicity and efficiency of the active surveillance activity, for example, time and effort involved in various phases of the activity

Feedback to the sentinel sites on the monitoring of the data collection for completeness and validity must be a regular part of data collection and interpretation. Feedback should be given promptly to sentinel sites in the event of inconsistencies in data collection, missing data, and other related issues that require immediate attention to ensure data quality.

The VAAC and DI&ADR Center will need to develop a plan to effectively communicate the results of the pilot activity to the various stakeholders.

After the pilot ends, the overall experience of its implementation, including results, achievements, and challenges, as well as recommendations for approaches to future scale-up should be disseminated to a wide group of related stakeholders.

ANNEX 1. DEFINITIONS¹⁶

Active (or proactive) safety surveillance

Systems whereby active measures are taken to detect adverse events. This is managed by active follow-up after treatment and the events may be detected by asking patients directly or screening patient records.

Adverse event

Any untoward medical occurrence that may present during treatment with a pharmaceutical product but which does not necessarily have a causal relationship with this treatment.

Adverse (drug) reaction (ADR)

A response which is noxious and unintended, and which occurs at doses normally used in humans for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function.

Causality assessment

The evaluation of the likelihood that a medicine was the causative agent of an observed adverse event. Causality assessment is usually made according to established algorithms.

Pharmacovigilance

The science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem.

Relationship assessment

The objective evaluation of the relationship between the administration of a medicine and a health event, taking into consideration duration of therapy to onset of event, response to dechallenge and rechallenge (if performed) and the presence of diseases or other medicines that could have caused the event. This process stops short of attempting to establish a causal relationship but is an essential preliminary.

Risk

The probability of harm being caused; the probability (chance, odds) of an occurrence.

Serious adverse event or reaction

A serious adverse event or reaction is any untoward medical occurrence that at any dose:

- results in death;
- results in inpatient hospitalization or prolongation of existing hospitalization;
- results in persistent or significant disability or incapacity;
- is life-threatening;
- is a congenital anomaly/birth defect.

¹⁶ These definitions are reproduced from the following WHO reference materials:

- WHO. 2009. *A Practical Handbook on the Pharmacovigilance of Antiretroviral Medicines*. Geneva: WHO.
- WHO/the Uppsala Monitoring Centre. 2000. *Safety Monitoring of Medicinal Products: Guidelines for Setting Up and Running a Pharmacovigilance Centre*. Uppsala, Sweden: the Uppsala Monitoring Centre.

To ensure that there is no confusion or misunderstanding about the difference between the terms “serious” and “severe,” the following note of clarification is provided:

The term “severe” is not synonymous with serious. In the English language, “severe” is used to describe the intensity (severity) of a specific event (as in mild, moderate or severe); the event itself, however, may be of relatively minor medical significance (such as severe headache).

Seriousness (not severity) which is based on the outcome of the event on the patient or action criteria serves as the guide for defining regulatory reporting obligations.

Signal

“Reported information on a possible causal relationship between an adverse event and a drug, the relationship being unknown or incompletely documented previously.” Usually more than a single report is required to generate a signal, depending upon the seriousness of the event and the quality of the information.

Spontaneous report

An unsolicited communication by health care professionals or consumers that describes one or more ADRs in a patient who was given one or more medicinal products and that does not derive from a study or any organized data collection scheme.

ANNEX 2. RECOMMENDED RESOURCES NEEDED AND STAFFING PLAN

The pilot is designed to fit into the existing structures and functions of the ART Program and the DI&ADR Center so resources related to new staff or structures are not anticipated. However, the following resources will be required to initiate the pilot:

- **Training** of Sentinel Sites, DI&ADR Center staff, PV Technical Committee staff, and other related stakeholders
- **Simple database** for computer entry of data at ART sites and for data management at the DI&ADR
- **Field-testing, printing, and distributing** the *Pharmacovigilance Active Surveillance Form*
- **Operational:** Internet access, local travel, and IT support

Additionally, for optimal efficiency of the pilot program, it is recommended that a focal person be identified, for example, a coordinator and data manager at the DI&ADR Center, and the primary contact person at each sentinel site. It is also recommended that a team of clinical reviewers representing the PV Technical Committee and other ART hospitals and organizations be identified to technically support the DI&ADR Center in causality assessment and other matters, including decisions on generating locally appropriate responses based on ongoing accumulation of data.

ANNEX 3. DATA COLLECTION FORM

VIETNAM ART PROGRAM – SENTINEL SITE ACTIVE SURVEILLANCE FORM FOR ART-NAIVE PATIENTS (PART A)

Patient Unique Identification Number:																																																																				
PATIENT STATUS AT START OF ART – COPY FROM RECORDS																																																																				
Date of Birth: ____/____/____	Age: ____ yrs	Facility <input type="checkbox"/> _____ <input type="checkbox"/> _____ <input type="checkbox"/> _____	Weight: ____ kgs	WHO Clinical Stage: 1 2 3 4 99 (if missing)																																																																
<table style="width: 100%; border-collapse: collapse;"> <tr> <th style="width: 40%; text-align: center;">CONDITIONS</th> <th style="width: 5%; text-align: center;">CHECK</th> <th style="width: 30%; text-align: center;">MEDICATIONS (CURRENT AND WITHIN PAST MONTH)</th> <th colspan="3" style="width: 20%; text-align: center;">LABORATORY TESTS</th> </tr> <tr> <td>Malnutrition</td> <td></td> <td></td> <td style="text-align: center;">Test</td> <td style="text-align: center;">Date</td> <td style="text-align: center;">Result</td> </tr> <tr> <td>Anemia</td> <td></td> <td></td> <td style="text-align: center;">Hb (g/dl)</td> <td></td> <td></td> </tr> <tr> <td>Alcohol abuse</td> <td></td> <td></td> <td style="text-align: center;">CD4</td> <td></td> <td></td> </tr> <tr> <td>Substance abuse</td> <td></td> <td></td> <td style="text-align: center;">ALT</td> <td></td> <td></td> </tr> <tr> <td>Tuberculosis</td> <td></td> <td></td> <td rowspan="4" style="text-align: center; vertical-align: middle;"> Others (specify): Creatinine </td> <td></td> <td></td> </tr> <tr> <td>Renal disease</td> <td></td> <td></td> <td></td> <td></td> </tr> <tr> <td>Liver disease</td> <td></td> <td></td> <td></td> <td></td> </tr> <tr> <td>Bacterial infection</td> <td></td> <td></td> <td></td> <td></td> </tr> <tr> <td>Other (specify)</td> <td></td> <td></td> <td colspan="3"></td> </tr> <tr> <td>Other (specify)</td> <td></td> <td></td> <td colspan="3"></td> </tr> </table>						CONDITIONS	CHECK	MEDICATIONS (CURRENT AND WITHIN PAST MONTH)	LABORATORY TESTS			Malnutrition			Test	Date	Result	Anemia			Hb (g/dl)			Alcohol abuse			CD4			Substance abuse			ALT			Tuberculosis			Others (specify): Creatinine			Renal disease					Liver disease					Bacterial infection					Other (specify)						Other (specify)					
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VIETNAM ART PROGRAM – SENTINEL SITE ACTIVE SURVEILLANCE FORM FOR ART-NAIVE PATIENTS (PART B)

Patient Unique Identification Number:									
PATIENT ENCOUNTERS FROM START-UP OF ART THROUGH FOLLOW-UP									
DATE OF VISIT _/_/_	ART REGIMEN (code)	OTHER MEDICINES (code)	ADVERSE DRUG EVENTS (code)	OTHER ADVERSE EVENTS (code)	CHANGES IN DRUG REGIMEN (code)	OUTCOMES OF ADVERSE EVENTS (code)	ABNORMAL LABORATORY FINDINGS (list)	OTHER NOTABLE CONDITIONS (code)	COMMENTS
ART START VISIT									
FOLLOW-UP									
FOLLOW-UP									
FOLLOW-UP									
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CODES

ART REGIMEN CODES		OTHER MEDICINES CODES	ADVERSE DRUG EVENTS CODES	OTHER ADVERSE EVENTS CODES	CHANGES IN DRUG REGIMEN CODES	OUTCOMES OF ADVERSE EVENTS CODES	OTHER NOTABLE CONDITIONS CODES
Principal ART Regimens	Alternative ART Regimens						
0 = AZT/3TC/NVP 1 = D4T/3TC/NVP	2 = AZT/3TC/EFV 3 = d4T/3TC/EFV 4 = TDF/3TC/NVP 5 = TDF/3TC/EFV 6 = AZT/3TC/TDF 7 = Other (specify)	0 = None 1 = Co-trimoxazole 2 = Iron suppl. 3 = SP antimalarials 4 = Artemisinin combinations 5 = Aspirin and other NSAIDS 6 = Paracetamol 7 = Antibiotics-ciprofloxacin 8 = Antibiotics-penicillin 9 = Other (specify)	0 = None 1 = Abdominal 2 = Anemia 3 = Peripheral neuropathies 4 = CNS 5 = Diarrhea 6 = Fat changes 7 = Fatigue 8 = Headache 9 = Jaundice 10 = Lactic acidosis 11 = Lipodystrophy 12 = Nausea 13 = Rash 14 = Other (specify)	0 = None 1 = Hospitalized 2 = Dead 3 = Suspected treatment failure 4 = Other (specify)	0 = None 1 = Discontinued without treatment switch 2 = Dose reduced 3 = Switch ART regimen 4 = Other (specify)	0 = None 1 = Resolved 2 = Resolving sequelae 3 = Not resolved 4 = Worse 5 = Death 7 = Unknown	0 = None 1 = Pneumonia 2 = Kaposi's sarcoma 3 = Hookworm 4 = Malaria 5 = GI bleeds 6 = Liver cirrhosis 7 = Blood disorders 8 = Malnutrition 9 = Pregnancy 10 = Other (specify)

