

Technical Assistance for the Establishment of a Pharmacovigilance and Medicine Safety System in Rwanda

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February 2009



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This report is made possible by the generous support of the American people through the U.S. Agency for International Development (USAID), under the terms of cooperative agreement number GHN-A-00-07-00002-00. The contents are the responsibility of Management Sciences for Health and do not necessarily reflect the views of USAID or the United States Government.

Abstract

The need to monitor the safety of new essential medicines used in public health programs is recognized in Rwanda. The Rwanda Ministry of Health is leading current efforts for the establishment of broad-based medicine safety surveillance system. Such a system will have the capacity for conduct Pharmacovigilance, medicine information, and patient safety activities. One strategy for identifying what is need for the establishment of such a system is to review the WHO recommended basic steps for the setting up of Pharmacovigilance center then identify and address gaps. The establishment of such new service also requires capacity building, therefore, the four-tier hierarchy of capacity building needs: structures, systems and roles; staff and infrastructure; skills; and tools was also used to develop recommendations for improving Rwanda capacity for Pharmacovigilance and medicine safety activities.

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Nwokike, J. 2009. *Technical Assistance for the Establishment of a Pharmacovigilance and Medicine Safety System in Rwanda*. Submitted to the U.S. Agency for International Development by the Strengthening Pharmaceutical Systems (SPS) Program. Arlington, VA: Management Sciences for Health.

Key Words

Pharmacovigilance, Medicine safety, Surveillance, Capacity building

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ACRONYMS

ADR	Adverse drug reaction
ARV	Antiretroviral medicines
ART	Antiretroviral therapy
DTC	Drug and therapeutics committees
EML	Essential medicine list
HIV/AIDS	Human immunodeficiency syndrome/Acquired immune deficiency syndrome
MOH	Ministry of Health
M&E	Monitoring and evaluation
NPMC	National Pharmacovigilance and Medicine information Center
PTF	Pharmacy Task Force
STG	Standard treatment guideline
TOT	Training of trainers
TB	Tuberculosis
TRAC	Treatment and Research AIDS Center
UMC	WHO program for international drug monitoring, the Uppsala Monitoring Center
WHO	World Health Organization

INTRODUCTION

The need for the more scrutiny on the safety of health products is well recognized in developed countries. In resource-constrained settings, the importance of Pharmacovigilance is increasingly being recognized. One of the key factors for this recognition is the increased availability of new essential medicines used in mass treatment health programs like HIV/AIDS, TB, and Malaria. There is no complete understanding of the safety of these and indeed other new medicines at the point they are authorized for use. Data on the safety of new medicines are mainly derived from pre-authorization clinical trials in controlled settings. Clinical trials for the evaluation of safety, efficacy and quality of new medicines are conducted in limited number of patients with strict inclusion criteria often excluding special patient groups like those with comorbid conditions, children, elderly and pregnant women. There is often no long-term exposure to the product during clinical trials and the new drug may not have been tested in some racial groups who may end up taking the medicines. These limitations of pre-authorization clinical trials enforces on the importance of monitoring safety of all medicines. Besides the discovery of new drug-induced disorders including rare serious adverse drug reactions, ADR that were not known during clinical trials, monitoring the safety of health products post-authorization can provide useful information for the characterization and quantification of prevalence and risk factors of known ADRs and can alert cases of counterfeit products.

Burden of ADRs

It is estimated that ADRs are the 4th to 6th leading cause for death in the USA even while excluding medication errors, noncompliance, overdose, drug abuse, and therapeutic failures.¹ ADRs costs countries health resources, some countries spend up to 15-20% of their hospital budget dealing with drug complications.² Even though data is not available for many developing countries, it is projected that ADR burden may be higher due to the high prevalence of HIV/AIDS, TB, and Malaria and other co-morbid conditions; different genetic and nutritional status; weak regulatory capacity to weed out substandard products; widespread use of complementary and alternative medicines; and lack of resources for routine monitoring for early signs of toxicity. One of the early sources of ADR data related to the use of antiretroviral, ARV medicines in developing countries comes from the Medicines san frontiers, MSF ART program in Khayelitsha near Cape Town, South Africa. The Khayelitsha activity report noted that 10% of patients on zidovudine, nevirapine, and stavudine were switched due to adverse events in a period of three years.³ Also in Kenya, 65% of 283 patients receiving ARVs in large urban slum

¹ J. Lazarou, B. Pomeranz, and P. Corey, "Incidence of Adverse Reactions in Hospitalized Patients: A Meta-analysis of Prospective Studies," *Journal of the American Medical Association* 279, No. 15 (1998): 1200-1205.

² White T et al. Counting the cost of drug-related adverse events. *Pharmacoeconomics*, 1999, 15(5). 445-458.

³ Khayelitsha activity report, 2005. Comprehensive HIV Service Development at Primary Care Clinics The experience from Khayelitsha. Available from: http://www.msf.org.za/docs/Khayelitsha_report_July_2005.pdf Accessed: Jan 31, 2009.

in Nairobi from 2003-2005 experienced an adverse event, out of which 6% had severe toxicity. As at 18 months, only about 17% of patients had a probability of not experiencing any adverse event.⁴

Need for Pharmacovigilance systems

According to the World Health Organization, WHO pharmacovigilance is needed in every country, because there are differences between countries, and even regions within countries, with regards to the production and use of health products and these difference influence the occurrence of ADRs and other drug-related problems. Pharmacovigilance systems should be closely linked to drug regulatory authority. In many countries, national drug authorities are responsible of ensuring the quality, safety, and efficacy of the medicines consumed in the public and private sectors. Many drug regulatory authorities in resource-constrained settings require tremendous support to strengthen their regulatory duties including Pharmacovigilance. In many of these countries the HIV/AIDS, TB, and malaria programs can serve as pathfinders for the introduction or strengthening of Pharmacovigilance and medicine safety surveillance activities. It is in the interest of the public health programs that safety monitoring of is improved when there is mass drug administration involved. According to the WHO:⁵

Significant harm to a few patients can destroy the credibility, adherence to and success of a program. Rumours and myths about the adverse effects of medicines can spread rapidly and are difficult to refute in the absence of good data. Pharmacovigilance can provide these data. It can also provide evidence of other types of medicine-related problems including treatment failure, counterfeit medicines, poor quality medicines, interactions between medicine and food and the incorrect use of medicines. Good pharmacovigilance practice can generate the evidence that will inspire public confidence and trust.

⁴ Kim et al. Adverse Events in HIV-Infected Persons Receiving Antiretroviral Drug Regimens in a Large Urban Slum in Nairobi, Kenya, 2003-2005. Journal of the International Association of Physicians in AIDS Care (JIAPAC), Vol. 6, No. 3, 206-209 (2007)

⁵ WHO 2006. The safety of medicines in public health programmes: pharmacovigilance an essential tool. ISBN 92 4 159391 1. WHO Press

REVIEW OF EXISTING PLANS FOR THE ESTABLISHMENT OF PHARMACOVIGILANCE SYSTEM

Preliminary initiatives

The MSH/SPS program in Rwanda in collaboration with the Pharmacy Taskforce, PTF and other stakeholders developed the “Strategic approach for the establishment of a Pharmacovigilance system in Rwanda” document to articulate what needed to be achieved in efforts to establish functional Pharmacovigilance system. The document proposed modalities for the MOH authorities in Rwanda to work with local and international partners. From the review of the document, it was identified that the following plans had been developed:-

1. Preparation of a niche to host pharmacovigilance system:

Given the number of national and international partners that might be involved in supporting pharmacovigilance interventions at different levels, and the lack of experience in the country in this technical area, it is expected that the implementation of a pharmacovigilance system in Rwanda will require partners to progressively arrive to a common understanding of the objectives and results to be attained. Partners have agreed that this process will require the technical assistance of an expert with relevant experience in setting pharmacovigilance systems. The expert will assist and build the capacity of the local counterparts to define roles, responsibilities, functions and activities for the implementation of a national PV system. Some of the expected steps include:

- The Pharmacy Task Force, Malaria control program (PNILP), and Treatment and Research AIDS Center (TRAC) to hold advocacy meetings with top key MOH policy makers.
- Conduct pharmacovigilance training workshop for capacity building of local partners with support from the pharmacovigilance expert
- Develop national pharmacovigilance strategy. Some of the elements envisioned to be integrated in the pharmacovigilance national strategy include:
 - Set up a pharmacovigilance technical working group under the MOH.
 - Set up the pharmacovigilance unit (offices, HR, reporting lines, etc).
 - Subscribe to the WHO program for international drug monitoring and enroll as a WHO Uppsala Monitoring Center, UMC collaborating center
 - Ensure adequate coordination with other partners in interventions in the field of Pharmacovigilance and rational use of drug
 - Development of an action plan for implementation of priority activities discussed with the programs and other partners.

2. Establishment of an ADR system:

Indeed, a surveillance system for ADR is needed even for medicines with large experience of use, as there is always a possibility of finding new unknown effects, interactions or toxicities. The implementation of a comprehensive adverse drug reaction reporting system for all medicines should therefore be an objective for the national pharmacovigilance system, but it will require a progressive development over the years to become operational. As such, it is envisioned that the first stages of the implementation of the ADR reporting system in Rwanda will just target specific drugs.

Some of the steps that would help to start implementing and ADR reporting system include:

- Select a list of priority medicines requiring monitoring ADR
- Develop and field test ADR reporting tools and systems
- Establish the mechanisms for reporting to ensure adequate and timely flow of information
- Gather and compile data, analyze the reports and produce reports
- Integrate ADR surveillance in the supportive supervision activities developed at district level.

3. Training and capacity building :

Training and capacity building at both central and peripheral levels are required for both creating a proper niche to host pharmacovigilance interventions and for the implementation of an ADR reporting system for ARVs, antimalarials, and in the future for other medicines. The first workshop to be conducted with the expertise of a consultant would be part of a capacity building intervention at the first stage. However, it is envisioned that training in specific technical areas, as well as on-going technical assistance and capacity building will be required in the short and medium term for full implementation of the strategic plan.

Some of the training activities will involve but are not restricted to the following ones:

i. Pharmacovigilance trainings:

- Training of trainers, TOT for key staffs, opinion leaders, and program managers. The primary objectives of the training will be to ensure that local stakeholders understand the science and practice of Pharmacovigilance and the advantages of having a pharmacovigilance system and are able to communicate that in subsequent trainings. This training will be facilitated by consultant and other international experts.
- A national training on pharmacovigilance to be conducted with some of the attendees of the TOT serving as facilitators, and with participation of representatives of the MoH and the public health programs.

- Trainers of provincial and district level will then start a cascade training targeting health facilities at all levels, with focus on doctors, prescribes, and nurses, and pharmacy staff.
- ii. Other capacity building interventions might include:
- On-going support to the pharmacovigilance unit and its members
 - The development and printing of job aids and other educational materials
 - The integration of pharmacovigilance in the formal training curriculum of Medical, Nursing and Pharmacy schools.

Other efforts

Also during the review of preliminary initiative, it was identified that a national orientation workshop was held for national institutions. The key objectives of this workshop was to obtain a common understanding of Pharmacovigilance and to develop basic tools that are required for the establishment of Pharmacovigilance in Rwanda. A proposed notification system including ADR form has been developed. The draft ADR form was pre-tested and favorable feedbacks were obtained from respondents. However, there were concerns about some formatting issues with the form. Besides the ADR form, the notification system identified key stakeholders that are crucial for the implementation of pharmacovigilance in Rwanda. It was identified that the drug and therapeutics committee, DTC was planned to play a key role in Pharmacovigilance system in Rwanda by serving as decentralization units. Both the proposed notification system and the draft work plan for the establishment of Pharmacovigilance relied heavily on the role of DTC in the implementation of Pharmacovigilance system in Rwanda. It was felt that this will assist in the institutionalization of Pharmacovigilance system. Since 2007 MSH/SPS has assisted the PTF in the establishment of DTCs in about eighteen district hospitals, with the purpose of addressing rational drug use related problems. MSH/SPS has continued to work with the PTF to establish a National Drugs and Therapeutics Committee (NDTC) as a national multidisciplinary body to ensure the systematic update of standard treatment guidelines, STGs, national formulary, NF, and Essential Medicines List (EML), and to coordinate DTCs activities in the country. DTCs at both peripheral and national levels are being implemented with capacity building interventions that involve general formal trainings, as well as coaching for work planning and rollout of activities. It was envisaged that DTCs could offer strategic entry points to implement drug safety interventions at health-facilities.

WHO recommended basic steps in setting up a Pharmacovigilance centre

Initial efforts at the establishment of Pharmacovigilance system in a country can be facilitated by the review and adaptation of experiences from another country with similar situations. In addition, the WHO document on safety monitoring of medicinal products, guidelines for the

setting up and running a Pharmacovigilance center⁶ clearly describes the key resources that are required and the necessary steps to aid in the process. Therefore the efforts currently on ground towards the establishment of Pharmacovigilance system in Rwanda was compared to the WHO basic steps in setting up a Pharmacovigilance center (Table 1.). The intention is that the findings will assist in identifying critical gaps in the current plan.

Table 1. Have existing plans met the WHO basic steps in setting up a Pharmacovigilance Centre?

#	<u>WHO basic step</u>	<u>Existing plan (Completed/Initiated/Not initiated)</u>	<u>Comments</u>
1	Make contacts with the health authorities and with local, regional or national institutions and groups, working in clinical medicine, pharmacology and toxicology outlining the importance of the project and its purposes	Initiated	Consultations had been initiated but key informants stated that there is still a need for a lot of consultation. The committee set up for the establishment of pharmacovigilance had not met.
2	Design a reporting form and start collecting data by distributing it to hospital departments, family practitioners, etc.	Initiated	ADR notification form has been developed and pre-tested. Some respondents complained about some formatting issues. Consultant was asked to review the form
3	Produce printed material to inform health professionals about definitions, aims and methods of the pharmacovigilance system (Pharmacovigilance Guideline)	Not initiated	Consultant was requested to draft the outlines for the development of a national pharmacovigilance guideline
4	Create the centre: staff, accommodation, phone, word processor, database management capability, bibliography etc.	Not initiated	Consultant was requested to outline the structure, infrastructure, and resources required
5	Take care of the education of pharmacovigilance staff with regard, for example, to:	Not initiated	Consultant was requested to lead the development of draft curriculum
	data collection and verification		
	interpreting and coding of adverse reaction descriptions		
	coding of drugs		
	case causality assessment		
	signal detection		
	risk management		

⁶ WHO, 2000. Safety monitoring of medicinal products: Guidelines for setting up and running a Pharmacovigilance center. *the Uppsala Monitoring Centre (the UMC)*, WHO Collaborating Centre for International Drug Monitoring. ISBN 91-630-9004-X

6	Establish a database (administrative system for the storage and retrieval of data)	Not initiated	Consultant was requested to outline the structure, infrastructure, and resources required
7	Organize meetings in hospitals, academia and professional associations, explaining the principles and demands of pharmacovigilance and the importance of reporting	Not initiated	The strategic plan outlines that this will be covered under cascades of trainings
8	Promote the importance of reporting adverse drug reactions through medical journals, other professional publications, and communications activities	Not initiated	
9	Maintain contacts with international institutions working in pharmacovigilance, e.g. the WHO Department of Essential Drugs and Medicines Policy (Geneva) and the Uppsala Monitoring Centre, Sweden	Not initiated	Consultant requested to advice and initiate the process

Opportunities for the establishment of Pharmacovigilance system in Rwanda

Rwanda currently does not have a drug regulatory authority. There is also no system for monitoring the safety of health products. The PTF is currently in charge of some components of pharmaceutical services. The PTF's role is to supervise the effectiveness and quality of pharmaceutical product and ensure their availability and rational use at the national level. The major responsibilities of the PTF include:⁷

- Coordinate activities related to the implementation of the pharmaceutical policy
- Prepare laws and orders related to the functioning of the pharmaceutical practice
- Sets up the instructions governing pharmaceutical institutions
- Supervise the establishment of pharmaceutical institutions
- Organize the inspection as well as the supervision of pharmaceutical institutions
- Ensure the standardization and the quality of pharmaceutical product that come within Rwandan territory (registration, visa, authorization of importation, custom check up)
- Supervises the implementation of international conventions regarding drugs and other pharmaceutical substances
- Provide pharmaceutical information to Health professionals as well as to the public
- Set up cooperation with other national, regional and international institutions involved in supplying and controlling pharmaceutical products.

However, the ability of the PTF to fulfill these responsibilities and initiate the introduction of Pharmacovigilance in Rwanda is very limited. This is because of lack of skills, resources, and institutional capacity for the establishment of a national Pharmacovigilance service. Resources from the public health programs like HIV/AIDS, TB, and Malaria can support efforts at

⁷ Rwanda Ministry of Health. The Pharmacy Task Force. Available from: http://www.moh.gov.rw/tf_pharmacy.html
Accessed: Jan 31, 2009

establishing medicine safety surveillance system and drug regulatory authority. The Management Sciences for Health, MSH Strengthening Pharmaceutical Systems, SPS program in Rwanda provides technical assistance and support to the PTF towards the establishment of a Pharmacovigilance system in Rwanda.

CAPACITY BUILDING FOR ESTABLISHING MEDICINES SAFETY SYSTEM

The review of the existing plans for the establishment of a Pharmacovigilance system pointed to lack of institutional capacity for pharmacovigilance. Some activities related to the establishment of a Pharmacovigilance center, as recommended by WHO, has been initiated. In reality the current expectation from stakeholders in Rwanda is for the implementation of both medicine safety and drug information activities and it is apparent that what is needed is an all encompassing medicine safety surveillance system rather than merely the establishment of a Pharmacovigilance center. It was clear that Rwanda was looking for a system to facilitate the implementation of a whole spectrum of Pharmacovigilance, drug information, and patient safety activities. It became evident that the new system is desired to have a scope that will cover all of the following:

1. Monitor safety and tolerability of medicines used in Rwanda
2. Quantify and characterize occurrence of previously recognized ADRs in Rwanda
3. Conduct and coordinate spontaneous reporting and active surveillance activities
4. Determine real-life effectiveness of medicines used in Rwanda
5. Provide unbiased medicine information to health workers and consumers
6. Monitor the promotion and advertising of all health products
7. Improve rational use of medicines
8. Improve patient safety
9. Develop interventions to reduce medicine-induced morbidity and mortality

The development, establishment, functioning, and sustenance of such a medicines safety system in Rwanda require the building of institutional capacities. Capacity building is the creation of an enabling environment with appropriate policy and legal frameworks, institutional development, including community participation, human resources development and strengthening of managerial systems.⁸ Capacity building for medicines safety monitoring therefore should address all the processes for the development of individual and system capacity and enable Rwanda achieve sustainable ability to manage effectively the safety of patients and health products in Rwanda. According to Potter and Brough,⁹ capacity building should enable program execution independent of changes of personalities, technologies, social structures and resource crises. That is, it should imply developing sustainable, and robust, systems. Capacity building is achieved through applying a four-tier hierarchy of capacity building needs: structures, systems and roles; staff and infrastructure; skills; and tools. Therefore, in an effort to address requirements for medicine safety capacity building the requirements for attaining the above four-tier hierarchy of capacity building needs will be reviewed individually.

⁸ Defining Capacity building. Available from: <http://www.gdrc.org/uem/capacity-define.html> Accessed Jan 24, 2009

⁹ Potter C and Brough R. Systemic capacity building: a hierarchy of needs. Health Policy Plan. 19:336-345, 2004

Structures, systems and roles

The structural capacities required for the establishment of medicine safety system in Rwanda are related to the decision-making institutions and forums that will utilize a framework to oversee activities and take decisions. It is important that before implementation, the structure is clearly determined and agreed to by all stakeholders. Such questions like why there is a need for Pharmacovigilance and medicine safety activities will have to be addressed. Even when the need for Pharmacovigilance activities is determined, there is also a need for common understanding on the framework, approaches, and model for achieving set goals. It may not be suitable to borrow these approaches from developed countries without adaptation. Pharmacovigilance efforts in highly resourced countries focus more on the discovery of rare serious ADR. In many resource constrained settings pragmatic approach to health product safety monitoring is imperative. Such settings may benefit more from focusing on avoiding preventable adverse events, monitoring product quality issues, and improving rational use of drugs and patient safety through risk minimization. This can be achieved through applying Pharmacovigilance to all aspects of the pharmaceutical management cycle.¹⁰

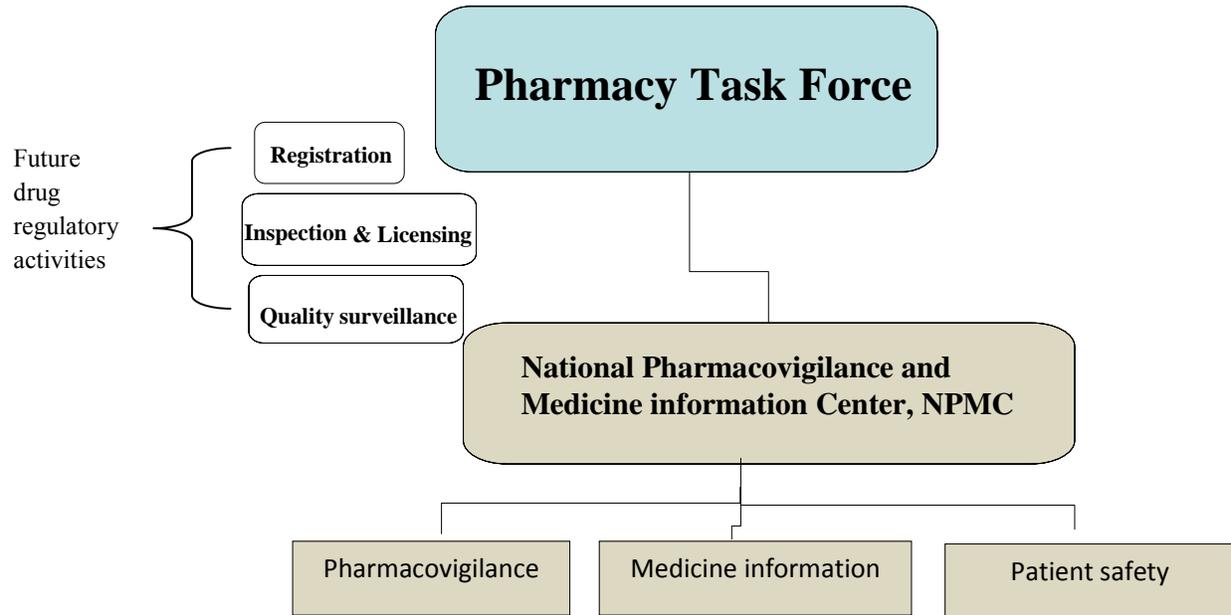
Rwanda plans for a structure that will monitor safety and effectiveness of health products in a routine and consistent manner. The following are the key outline of the structure, system, and roles that can support the development and implementation of monitoring safety and effectiveness in Rwanda:

- Scope of activities to be addressed by the National Pharmacovigilance and medicine information center, NPMC should cover aspects of Pharmacovigilance, drug information, and patient safety as shown in figure 1. below.
- The pharmaceutical information desk of the PTF can serve as a base for the development of the entire structure
- Resources proposed for the structure of the NPMC should be shared immediately with Ministry of Health and all stakeholders for buy-in

¹⁰ Pharmaceutical management is the set of practices aimed at ensuring the timely availability and appropriate use of safe, effective, quality medicines, health products, and services in any health care setting. MSH and WHO (Management Sciences for Health and World Health Organization). 1997. *Managing Drug Supply*. 2nd ed. West Hartford, CT: Kumarian Press.

Pharmaceutical management cycle is the process of selection, procurement, distribution, and rational use of essential medicines that occur within the available management support systems and is built on in-country medicines policy, law, and regulations.

Fig 1. Scope of functions of the NPMC



Beyond the mapping of key stakeholders, the establishment of a Pharmacovigilance and medicine safety system will require the design and adoption of means for the interaction and interrelationship of the discrete parts of medicine safety activities. Those discrete parts and instruments will include the policies, guidelines, standard operating procedures, and institutions and bodies involved and their roles and responsibilities. According to the WHO:¹¹

To attain a coherent pharmacovigilance system it is most important that guidelines and standards are developed, which describe the practical details of the intended information flow. Such standard operating procedures should include information on the following:

- ✓ *What constitutes a reportable adverse reaction?*
- ✓ *Who is expected to report an observation of a suspected medicine-related problem?*
- ✓ *The availability and practicalities of filling in a reporting form*

¹¹ WHO, 2000. Safety monitoring of medicinal products: Guidelines for setting up and running a Pharmacovigilance center. *the Uppsala Monitoring Centre (the UMC)*, WHO Collaborating Centre for International Drug Monitoring. ISBN 91-630-9004-X

- ✓ *Procedures for submission or collection of reports*
 - ✓ *Routines for assessment, follow-up and processing of case reports at the pharmacovigilance centre*
 - ✓ *Procedures for analysis of aggregated information and options for action*
 - ✓ *Good communication practices*
 - ✓ *A description of indicators by which the progress of the monitoring system may be measured.*
-

The Guidelines for medicines safety surveillance in Rwanda has been drafted and provides procedures and directions for addressing all issues related to medicines and patient safety in a comprehensive manner. The notification system for safety monitoring was developed and discussed with key stakeholders and their roles and responsibilities. The key standard operating procedures, SOPs that may be required for consistency and quality assurance in the services of the NPMC may include:

- Guidelines for the distribution and collection of ADR forms
- Guidelines for the receiving and entering of ADR reports
- Guidelines for operations of the Medicines safety committee
- Guidelines for the provision of medicine information
- Standard operating procedure for medicine safety communications
- Standard operating procedures for the NPMC decentralization units

Staff and infrastructure

The needed staffing for the NPMC and the related infrastructure for the running of the center has been articulated and proposed to the Ministry of Health. The NPMC requires a minimum of two staffs (one technical and one administrative) for the opening of operations of the center. Detailed specifications concerning the qualifications and skills of NPMC staffs and others who may provide technical support from time to time to the center have been drafted. In addition, a document with detailed listing of infrastructural requirements for running the center was drafted and submitted.

Skills

Pharmacovigilance and medicine safety is a specialized discipline and efforts should be made to develop and maintain skills. The cornerstone of current plan is to implement an initial training of trainers and subsequently a national training on Pharmacovigilance and medicine safety. There

are also plans for the implementation of a cascade of trainings, which will assist in developing more skills particularly amongst healthcare workers. Besides the local trainings, technical staffs of the NPMC and members of the drug safety advisory committee will require additional international trainings in signal detection and evaluation, risk minimization, and other topics in Pharmacovigilance and pharmacoepidemiology.

Tools

Some critical tools aid the practice of Pharmacovigilance and medicine safety monitoring. The WHO/UMC has developed some very useful tools that countries participating in the international drug monitoring program are advised to subscribe to. Preliminary contacts have been made to initiate the process for Rwanda to apply for membership of the international drug monitoring program. Locally, the tools for the running of the center have been identified including the draft ADR notification form. This form was revised and has been converted to an interactive PDF format to enable electronic submission and transmission. The proposed ADR notification form is attached as Annex 1. One of the key challenges that limit spontaneous reporting in many countries is lack of time and the burden of reporting.¹² The development of innovative approaches for improving reporting is needed. The use of electronic forms is one approach and others include reducing the burden of reporting by simplifying the ADR reporting form. This will enable the busy clinician to provide an initial report with as little data as is readily available. The other essential data in the ADR form will be completed subsequently with help from the NPMC staff. These initial data (pre-report) can be generated through the clinician's case file and by making ADR reporting as part of the normal clinical administration of care to patients. For ADR reports that do not require expedited reporting, the basic data that is generated can be processed through the existing structures like the monitoring and evaluation, M&E systems. Integrating reporting into routine care administration and using existing channels like the M&E system are some of the strategies that can be considered in Rwanda.

Capacity for active surveillance

Spontaneous reporting as a Pharmacovigilance method is very useful for the identification of safety signals of rare adverse reactions and in the generation of hypothesis. However, spontaneous reporting systems has some limitations including lack of denominator, lack of controls, poor case documentation and under or over ascertainment. The importance of active surveillance in medicine safety is increasingly being recognized even in developing countries. However, efforts at developing skills and resources for the implementation of quality active surveillance activities are just being initiated in most of these countries. In Rwanda, there is interest at developing active surveillance systems particularly within the public health programs. Active surveillance methods are sentinel surveillance, case-control studies, cohort event

¹² Eland IA, Belton KJ, van Grootheest AC, Meiners AP, Rawlins MD, et al. Attitudinal survey of voluntary reporting of adverse drug reactions. *Br J Clin Pharmacol* 1994; 48: 623–627.

monitoring including registries and prescription event monitoring. Drug utilization studies and secondary use of health records and automated databases are also other methods that are becoming popular particularly in environments with electronic medical records. This is because of the current realization that medical records containing details of patients exposure to medicines, what worked and what did not, can be pulled together for better understanding of safety and effectiveness in real-life use. The capacity for active surveillance activities can be developed through the development of skills, human resources, and infrastructural capacity (particularly databases). Active surveillance may require more resources than spontaneous reporting but can be built on signals generated from spontaneous reports. The following steps can be considered in the initiation of active surveillance activities in Rwanda:

- Identify research priorities or medicine safety issue of high importance; these priorities can be determined through the review of signals from spontaneous reports, individual case safety reports, and case series
- Identify objectives of monitoring; WHO recommends that these objectives can be directed towards —
 - ✓ Identifying events that are likely to affect adherence to treatment; determine their rates and the risk factors that make these events more likely
 - ✓ Estimating rates of events so that risk can be measured and risk factors clearly identified and safety of medicines compared
 - ✓ Determining safety in pregnancy and in children
 - ✓ Monitoring for specific toxicities
- Identify active surveillance method and identify in-country capacity to implement method or seek collaboration within the region and internationally
- Develop protocol and implement study with local leadership

As part of building capacity for active surveillance activities and sharing the results of international collaborations, Rwanda can set up a system for participation in some collaboration of which examples include:

- The Antiretroviral Therapy in Lower Income Countries (ART-LINC); this is an international collaboration of treatment cohorts, the current database includes patients from 13 African countries
- The Data Collection on Adverse events of Anti-HIV Drugs (DAD); <http://www.cphiv.dk/DAD/About/tabid/106/Default.aspx> the DAD is a prospective multi-cohort of ART patients with the objective to assess the incidence of myocardial infarction in patients on ART
- TREAT Asia HIV Observational Database (TAHOD); <http://www.amfar.org/world/treatasia/article.aspx?id=3310>
- ART Cohort Collaboration (ART-CC); <http://www.art-cohort-collaboration.org/> includes 19 cohort studies from Europe and North America

- International Epidemiological Databases to Evaluate AIDS (IeDEA); <http://www.iedea-hiv.org/> central database of large sample size and standardized HIV/AIDS data
- The East African Network for Monitoring Anti-malarial Treatment; <http://www.eanmat.org/> monitors antimalarial treatment
- INDEPTH Network; <http://www.indepth-network.org/> uses demographic surveillance sites for evaluation of populations and their health
- Malaria in Pregnancy Consortium; <http://www.mip-consortium.org/>

Besides direct participation in these collaborations, routine scanning of findings and publications from these sites can provide reassurance about safety or provide directions on safety concerns that may warrant local attention. Some useful resources for reference on implementing active surveillance studies include the Guidelines for Good Pharmacoepidemiology Practices, GPP¹³ and WHO publications.^{14,15}

Metrics for monitoring and evaluation

Plans for the establishment of Pharmacovigilance and medicine safety systems should also include the identification of performance indicators and monitoring and evaluation plans. The ultimate goal of medicine safety interventions are to reduce medicines-induced morbidity and mortality and improve rational use of medicines. The development of indicators and performance measures for the medicine safety activities can be initiated by determining the objectives, listing possible indicators (candidate indicators should meet the importance, measurability, reliability, and validity criteria), refine and select the best indicators, and field-test. The NPMC can develop some output indicator to monitor their activities including trainings, reports, ADR reports, etc. There should also be outcome indicators that measure how the activity of the center has improved medicine safety and health of the people.

¹³ International Society for Pharmacoepidemiology, ISPE. Guidelines for Good Pharmacoepidemiology Practices, GPP. PDS 2008; 17: 200–208

¹⁴ WHO (2006) The safety of medicines in public health programmes: pharmacovigilance an essential tool. ISBN 92 4 159391 1

¹⁵ WHO (2007) Pharmacovigilance for Antiretrovirals in Resource-poor Countries. WHO/PSM/QSM/2007.3

CONCLUSIONS

Increasingly access to new essential medicines particularly for HIV/AIDS, TB, and Malaria is improving through support from multiple global initiatives. Many developing countries are realising the need for building Pharmacovigilance systems. The establishment of medicine safety monitoring in Rwanda requires building new capacity, systems, and infrastructure but at the same time requires the strategic linking of the available local committees and resources that can leverage resources and ensure sustainability in medicine safety surveillance activities. This informed current efforts to utilize the pharmaceutical information desks of the Pharmacy Task Force as a base for the proposed National Pharmacovigilance and Medicine information Center, NPMC. It also informs the key role of existing committees particularly the drug and therapeutics committee to serve as the NPMC decentralization units. The need for capacity building requires a review of the WHO recommended basic steps in setting Pharmacovigilance center and each elements of the capacity building framework. There is also a specific need for the development of capacity for active surveillance activities in Rwanda.

ANNEX 1

REPUBLIC OF RWANDA



MINISTRY OF HEALTH

Print Form

Submit by Email

Form No:

ADVERSE EVENT REPORTING FORM

A. PATIENT INFORMATION			
Last Name	<input type="text"/>	Patient No. as noted in the Register	<input type="text"/>
First Name	<input type="text"/>	Date of birth	<input type="text"/> Weight (Kg) <input type="text"/>
Gender	<input type="text"/>	Pregnant	<input type="text"/> Address & Cell No. <input type="text"/>
B. HEALTH PRODUCT INFORMATION			
1. Suspected product	<input type="text"/>	Brand name/Manufacturer	<input type="text"/> Expiry date <input type="text"/> Manuf. date <input type="text"/>
2. Product quality problem (e.g. defects/malfunctions)	<input type="text"/>		Lot/batch No. <input type="text"/>
Indication: why was this product taken or prescribed	<input type="text"/>		Date started <input type="text"/> Date stopped <input type="text"/>
Route of administration	<input type="text"/>	Prescribed	<input type="text"/> Describe product quality problem <input type="text"/>
Dose	<input type="text"/>	Source of product	<input type="text"/>
C. ADVERSE EVENT INFORMATION			
Describe Adverse event	<input type="text"/>		Describe medication error/Patient safety event <input type="text"/>
Date event started	<input type="text"/>	Date event stopped	<input type="text"/> Outcome attributed to adverse event <input type="text"/>
If adverse event was treated, please describe	<input type="text"/>		
Readministered	<input type="text"/>	Did adverse event reappear upon readministration	<input type="text"/> Relevant history/lab test/pre-existing health condition <input type="text"/>
D. OTHER PRODUCTS USED (please enter all other health products used)			
Name of product used	<input type="text"/>	Dosage and route	<input type="text"/> Date started <input type="text"/> Date stopped <input type="text"/>
Name of product used	<input type="text"/>	Dosage and route	<input type="text"/> Date started <input type="text"/> Date stopped <input type="text"/>
E. REPORTER INFORMATION			
Last Name	<input type="text"/>	Address & Cell No.	<input type="text"/>
First Name	<input type="text"/>	Email Address	<input type="text"/>
Profession/Occupation	<input type="text"/>	Date	<input type="text"/> Signed By <input type="text"/>