Indicator-Based Pharmacovigilance Assessment Tool: Manual for Conducting Assessments in Developing Countries

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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.

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Key Words

pharmacovigilance, medicine safety, surveillance, capacity building

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CONTENTS

ACRONYMS

ADR	adverse drug reaction
ARV	antiretroviral
CMS	Central Medical Stores
DIC	drug information center
DTC	drug and therapeutics committee
EMEA	European Medicines Agency
FDA	U.S. Food and Drug Administration
HF	health facility
HQ	headquarters
ICH	International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use
IPAT	Indicator-Based Pharmacovigilance Assessment Tool
MAH	marketing authorization holder
MoH	Ministry of Health
MRSCA	medicines and related substances control act
MSH	Management Sciences for Health
NDA	national drug authority
NMP	National Medicines Policy
NPMIC	National Pharmacovigilance and Medicine Information Center
PHP	public health program
PIC/S	Pharmaceutical Inspection Co-operation Scheme
QSL	quality surveillance laboratory
SOP	standard operating procedure
SPS	Strengthening Pharmaceutical Systems
TB	tuberculosis
UMC	WHO Collaborating Centre for International Drug Monitoring, *The Uppsala Monitoring Center*
WHO	World Health Organization

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This report was developed by—

Jude Nwokike (SPS Technical Lead on Pharmacovigilance)

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EXECUTIVE SUMMARY

Purpose

Opinions vary about the scope and attributes of an optimally functional pharmacovigilance and medicine safety system. Furthermore, no universally adopted performance or outcome metrics exist for assessing pharmacovigilance systems. These challenges have major implications for low- and middle-income countries where efforts to strengthen pharmacovigilance have been sporadic and uncoordinated. Consequently, a need exists for the development of a monitoring tool for a pharmacovigilance and medicine safety system. Such a tool is needed to benchmark stakeholders' functions; diagnose system strengths, weaknesses, and gaps; and monitor and evaluate interventions. This Indicator-Based Pharmacovigilance Assessment Tool (IPAT) was developed as a comprehensive performance metric for pharmacovigilance and medicine safety systems.

Scope

IPAT is suitable for evaluating the current state of collection, analysis, and interpretation of data on the safety aspects of medicine regulation as well as to ensure safe use of medicines at public health programs, health facilities, and the health care worker and consumer levels. The analysis of data derived from IPAT could be used to develop recommendations and identify priority interventions to improve critical aspects of the pharmacovigilance and medicine safety system.

Development Process

Management Sciences for Health's Strengthening Pharmaceutical Systems (MSH/SPS) Program reviewed the literature and identified published and unpublished reports of indicators and performance metrics for pharmacovigilance and medicine safety systems. Results identified 15 relevant reports with approximately 200 indicators addressing areas ranging from regulatory pharmacovigilance to medication safety. SPS aligned the identified indicators into key pharmacovigilance components, then proposed new indicators to address gaps. The first list of candidate indicators was assessed using explicit criteria for objectivity, reliability, relevance or adequacy, measurability, validity, and practicability. The 88 candidate indicators were presented in three rounds of Delphi consultations (see the Delphi Group section of the Introduction for further information), which involved exploring and distilling the opinions of pharmacovigilance experts in an iterative process. The Delphi group, with 12 respondents in eight countries, generated 27 responses. The group members weighted the indicators based on whether they considered them "core" or "supplementary." The indicators chosen by the Delphi group were used to formulate relevant assessment questions, and the group then reviewed those questions. SPS then pilot-tested the final draft of the indicators and assessment tool in Rwanda and evaluated the indicators for relevance and feasibility in South Africa. Feedback from the pilot testing was used to further refine the tool. Three external consultants also reviewed the tool.

Contents

IPAT has 43 indicators—26 core and 17 supplementary—that address five pharmacovigilance and medicine safety system components: (a) policy, law, and regulation; (b) systems, structures, and stakeholder coordination; (c) signal generation and data management; (d) risk assessment and evaluation; and (e) risk management and communication. The indicators are also classified by "structure," "process," or "outcome" according to the product or result they measure. IPAT is modular; different segments of the health system can use the indicators relevant to them to monitor various medicine safety issues.

Intended Users of this Manual

IPAT can be used by national medicine regulatory authorities, public health programs, health facilities, and all other stakeholders concerned with pharmacovigilance and medicine safety.

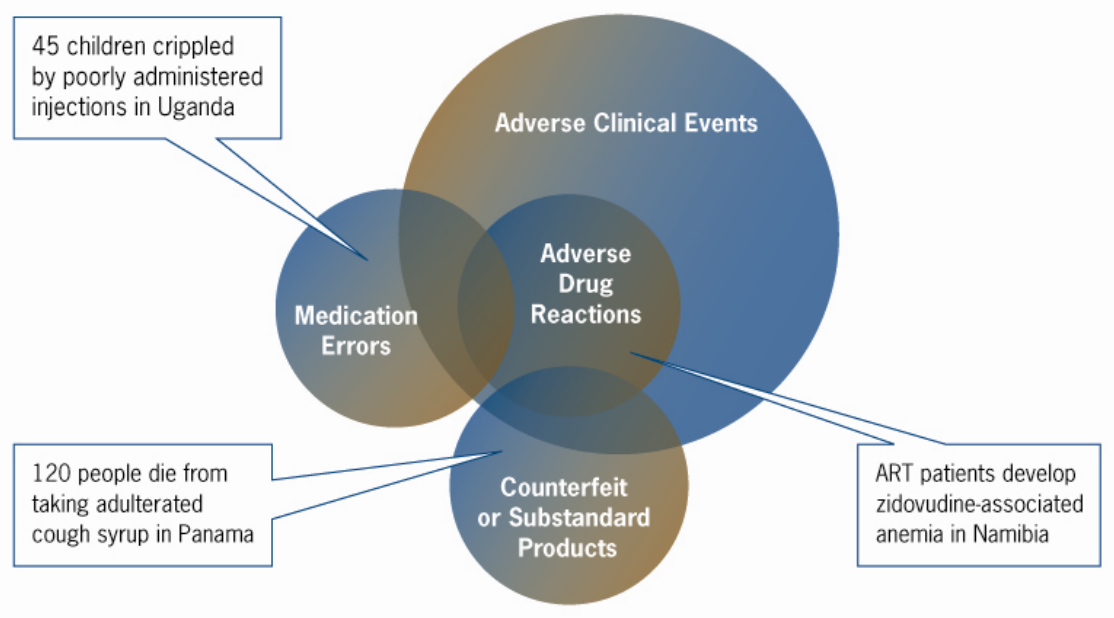
INTRODUCTION

The definition and scope of pharmacovigilance has evolved to recognize the importance of the systems approach for monitoring and improving the safe use of medicines. The World Health Organization (WHO) defines *pharmacovigilance* as the science and activities relating to the detection, evaluation, understanding, and prevention of adverse reactions to medicines or any other medicine-related problems.[1] Pharmacovigilance has been further defined as the processes and science of monitoring the safety of medicines and taking action to reduce risk and increase benefit.[2] However, no consensus exists on what constitutes a well-functioning pharmacovigilance or medicine safety system. Currently, there are no universally adopted performance metrics for assessing pharmacovigilance systems. Such a measurement tool is greatly needed to enable stakeholders to agree on scope, functions, and activities within the purview of pharmacovigilance; to assess the status of their pharmacovigilance system and diagnose the system's strengths, weaknesses, and gaps; to design and plan interventions based on local situations, existing regulatory capacity and priorities, identified system gaps, and available resources; to monitor and evaluate pharmacovigilance and medicine safety activities; and to compare pharmacovigilance activities across regions and programs, as well as across countries.

The development of performance metrics for pharmacovigilance and medicine safety systems requires common agreement on what the scope of such a system includes. Pharmacovigilance has been referred to as postmarketing surveillance, which is crucial to quantify previously recognized adverse drug reactions, to identify unrecognized adverse drug events, to evaluate the effectiveness of medicines in real-world situations, and to decrease mortality and morbidity associated with adverse events.[3] The scope of pharmacovigilance therefore covers product quality; medication errors, including therapeutic ineffectiveness; and previously known or unknown adverse drug reactions (ADRs) as depicted in figure 1. All these areas are equally important to the drug regulatory authority as to the consumer and the clinician. The spectrum of the pharmacovigilance and medicine safety system thus needs to be visualized as all activities involved in a continuum from regulatory pharmacovigilance to ensuring safe use of medicines. The processes of risk identification, risk assessment, and risk mitigation describe the entire series of processes addressed during pharmacovigilance. Performance metrics are therefore required to enable standardized, consistent, and routine monitoring and evaluation of pharmacovigilance and medicine safety systems. Such a tool will be useful in establishing current capacity for safety monitoring and will allow longitudinal measurement of progress after interventions are implemented. In the health sector, performance metrics or indicators have been defined as measures of structure, process, and outcomes of health care that can be used to guide and

[1] World Health Organization. 2002. *The Importance of Pharmacovigilance: Safety Monitoring of Medicinal Products*. Geneva: WHO.
[2] European Commission. 2006. *Assessment of the European Community System of Pharmacovigilance: Final Report—Final version, 25 January 2006*. Submitted by Fraunhofer Institute Systems and Innovation Research, Karlsruhe, Germany, to the European Commission Enterprise and Industry Directorate-General, Unit F2, Pharmaceuticals. http://ec.europa.eu/enterprise/pharmaceuticals/pharmacovigilance/docs/acs_consultation_final.pdf.
[3] Eguale, T., et al. 2008. Detection of adverse drug events and other treatment outcomes using an electronic prescribing system. *Drug Safety* 31(11):1005–16.

monitor the quality and appropriateness of health care delivery with the aim of health care improvement.[4]



Source: 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.

Figure 1. Scope of pharmacovigilance

A pharmacovigilance system or medicine safety system is the coordinated and interdependent functioning of activities to improve benefits and reduce harm related to the use of medicines by the public through the efficient mobilization of various stakeholders and resources at all levels and in all sectors. Performance metrics are needed to enable the monitoring and evaluation of all the interlinked activities involved in the medicine safety system. Such indicators would ideally allow different players working in various aspects of medicine safety to pick and choose relevant indicators for self-assessment. Therefore, a collection of modular indicators that could address different aspects of regulatory pharmacovigilance and safe clinical use of medicines is required to achieve optimal monitoring of safety activities across all stakeholders.

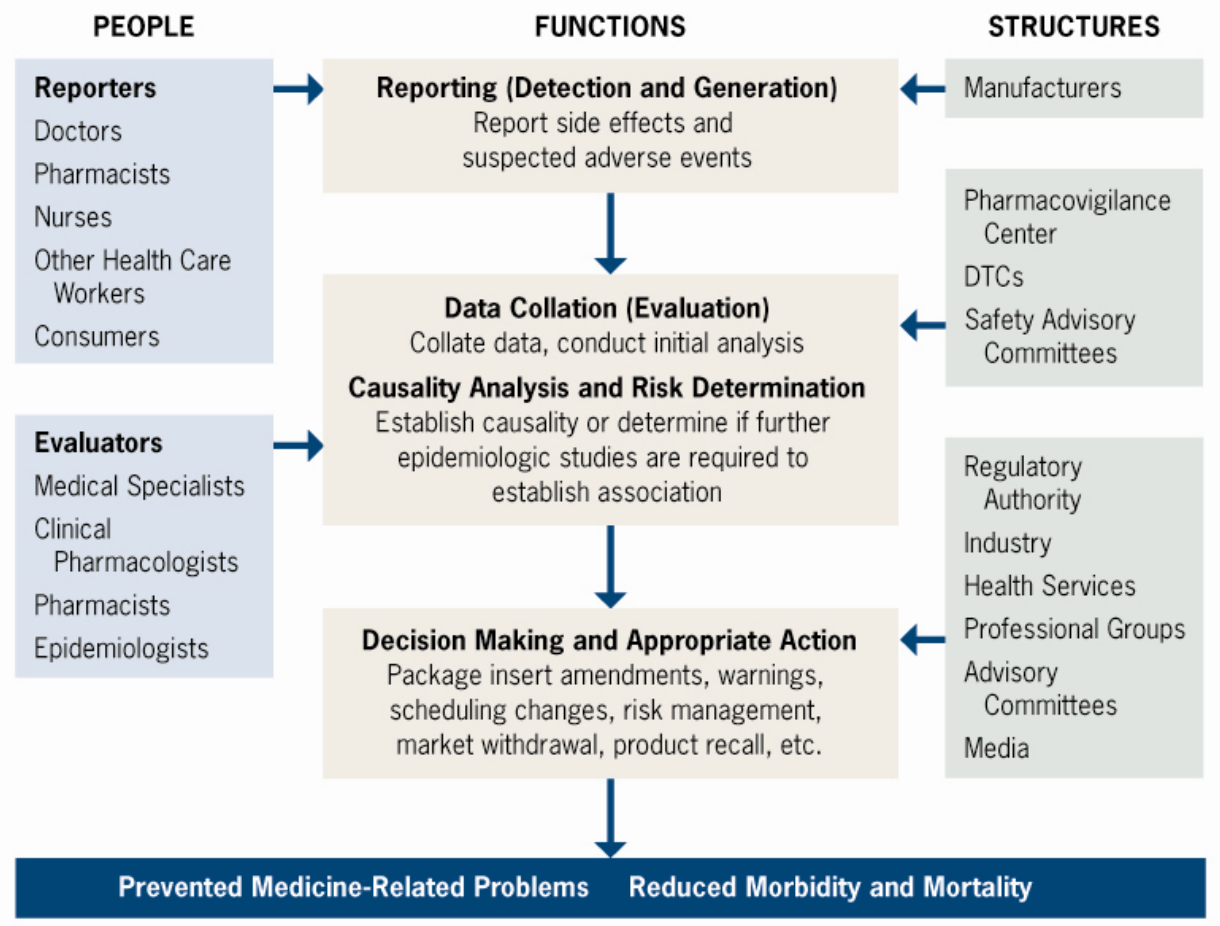
Pharmacovigilance: A Comprehensive Systems Perspective

A country's pharmacovigilance system should incorporate activities and resources at the facility, national, and international levels and foster collaboration among a wide range of partners and organizations that contribute to ensuring medicine safety. As a pharmacovigilance system matures, it may expand from a program based strictly on passive ADR surveillance that relies on

[4] Schaff, R., G. Schumock, and D. Nadzam. 1991. Development of the Joint Commission's indicators for monitoring the medication use system. *Hospital Pharmacy* 26:326–29, 350.

voluntary reports from health care providers or consumers to incorporate active surveillance methods that address priority safety concerns, such as the use of registries, sentinel sites, and follow-up of defined patient cohorts. Other system expansion efforts can include establishing a link between pharmaceutical quality assurance and ADR monitoring and developing mechanisms to communicate medicine safety information to health care professionals and the public.

Figure 2 illustrates the components of a comprehensive, ongoing pharmacovigilance system describing the **people**, **functions**, and **structures** of a pharmacovigilance and medicine safety system. The outcome of a pharmacovigilance system should be decreased medicine-related problems, with the ultimate impact being a reduction in medicine-related morbidity and mortality. This framework presents a comprehensive systems perspective of the medicine safety system.[5]



Source: 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.

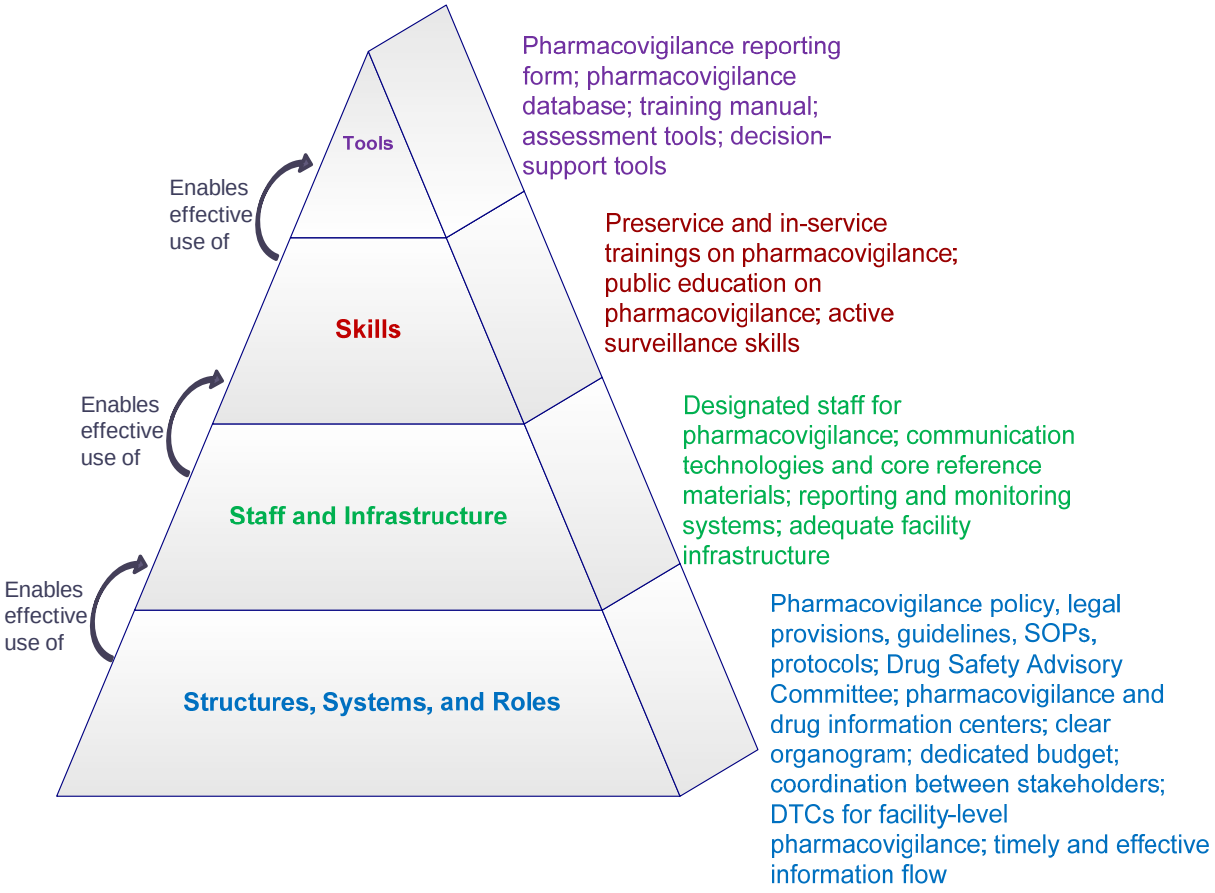
Figure 2. The Pharmacovigilance Framework

[5] 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.

Capacity Building for Pharmacovigilance

The development, establishment, functioning, and sustainability of a medicine safety system require the building of institutional capacities rather than mere ad hoc support with trainings and procurement of electronic tools. Capacity building is the creation of an enabling environment with appropriate policy and legal frameworks, institutional development that includes community participation, human resources development, and strengthening of managerial systems.[6] Capacity building for pharmacovigilance and medicine safety should address all processes for developing individual and system capacity and enable achievement of sustainable ability to manage effectively the safety of patients and health products.[7] According to Potter and Brough,[8] capacity building is achieved by applying a four-tier hierarchy of needs: structures, systems, and roles; staff and infrastructure; skills; and tools. In an effort to address requirements for medicine safety capacity building, how to attain each tier of this hierarchy of capacity building is reviewed individually. Figure 3 illustrates the respective capacities and resources that are required for developing and sustaining a functional pharmacovigilance and medicine safety system.

[6] Urban Environmental Management Web site. Urban Capacity Building, Defining Capacity building. Available at: http://www.gdrc.org/uem/capacity-define.html. Accessed January 24, 2009.
[7] 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.
[8] Potter, C., and R. Brough. 2004. Systemic capacity building: A hierarchy of needs. *Health Policy Planning* 19:336–45.



Adapted from: Potter, C., and R. Brough. 2004. Systemic capacity building: A hierarchy of needs. *Health Policy Planning* 19:336–45.

Figure 3. Systemic capacity building for pharmacovigilance

Constructing the IPAT

IPAT Development Process

Steps of the IPAT development process (see figure 4) included—

- Reviewing the literature to identify all published and unpublished indicators and performance metrics for pharmacovigilance and medicine safety systems
- Mapping and transcribing identified indicators and assessment questions into a dedicated spreadsheet (with data on source of the indicator, type, and use)
- Identifying and removing identical, repeated, or similar indicators and assessment questions

- Identifying areas of pharmacovigilance without available indicators available for monitoring and developing candidate indicators to address the gaps

- Listing all the identified candidate indicators, rephrasing and combining some where necessary, and generating a first raw draft of candidate indicators

- Using assessment criteria to assess and score the candidate indicators for objectivity, reliability, relevance or adequacy

- Developing and implementing an assessment of the indicators using the Delphi method, including recruitment of 15 members of the Delphi group and individually sending the candidate indicators to them

- Using the final set of adopted indicators from the Delphi group to formulate relevant assessment questions, and asking the Delphi group to review the assessment questions

- Generating assessment questions based on the candidate indicators and listing those questions alongside the indicators

- Generating the final draft of the indicators and assessment tools

- Developing the manual for the indicator-based assessment tools

- Sending the tools and manual to three external expert consultants for final review

Literature Review

To ensure that opportunities for learning from existing efforts are used, SPS conducted a literature review of indicators in the pharmacovigilance literature. SPS searched websites of some regulatory authorities, such as the U.S. Food and Drug Administration (FDA), the European Medicines Agency (EMEA), the Japan Pharmaceuticals and Medical Devices Agency, and websites of Canadian and Australian regulatory authorities, and the WHO Essential Medicines website, including the International Drug Monitoring Program. SPS also reviewed PubMed and pharmacovigilance journals including *Drug Safety*, *Pharmacoepidemiology and Drug Safety*, *Drug Information Journal*, *Health Affairs*, *Annals of Pharmacotherapy*, and *Journal of Health Informatics in Developing Countries* for indicators related to quality and safe use of medicines using the following key words: drug safety, drug safety indicators, pharmacovigilance indicators, pharmacovigilance metrics, medicine safety systems, and indicators for monitoring drug safety.

Fifteen relevant reports with approximately 200 indicators addressing areas ranging from regulatory pharmacovigilance to medication safety were found. The search confirmed the lack of a comprehensive set of indicators for pharmacovigilance encompassing both regulatory and medication safety indicators. Several indicators and performance metrics in drug regulation,

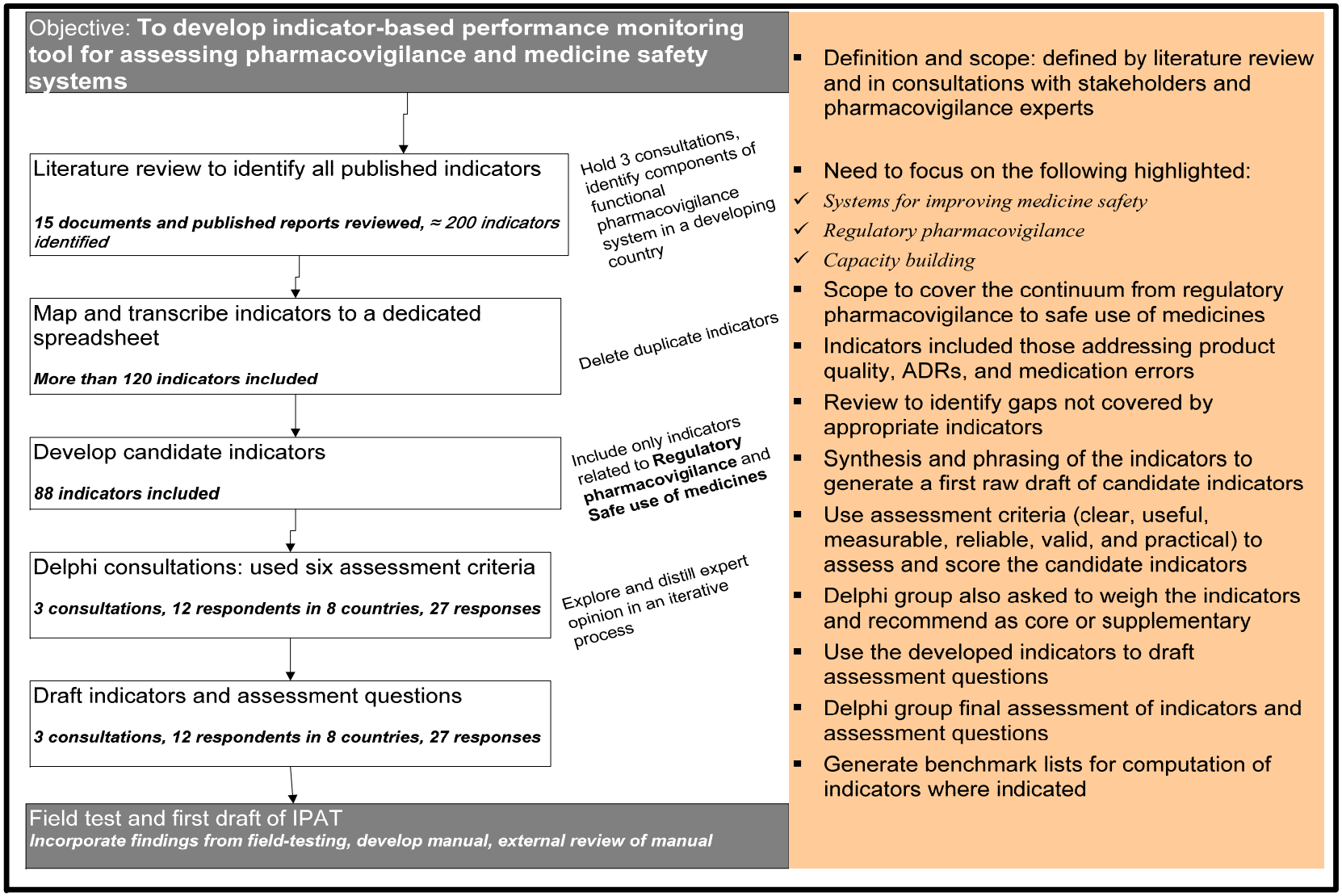


Figure 4. IPAT development process

rational use of medicines, and patient safety areas have groups of indicators that address aspects of medication safety. For example, with regard to ADR reporting, several publications use the "number of ADR reports" as an indicator. Regulatory pharmacovigilance seems to have received more attention in terms of indicator development. In the ADR monitoring section of the document *Effective Drug Regulation: A Multicountry Study*,[9] the WHO included a few indicators to help collect data to reflect the functioning of the pharmacovigilance system. In addition, the WHO Immunizations, Vaccines, and Biologicals program for strengthening national regulatory authorities recommends 9 indicators for monitoring adverse events following immunization.[10] Amrumpai and colleagues described their process for the development of the Thailand safety monitoring program indicators in which indicators were developed to support the regulatory authority specifically in the safety monitoring of new medicines. The Thai indicators provided broad-based drug safety–specific indicators for new drug monitoring programs.[11]

The most comprehensive listing of regulatory pharmacovigilance indicators is from the report *Assessment of the European Community System of Pharmacovigilance.*[12] This report, commonly referred to as the Fraunhofer report, was developed from a literature review and from interviews of the regulatory agencies in Europe. The Fraunhofer report, which defined pharmacovigilance as "the processes and science of monitoring the safety of medicines and taking action to reduce risk and increase benefit," used the Delphi survey method to develop indicators. The Delphi group was asked to rate the generated indicators according to their relevance, practicability, and interpretation. The Fraunhofer report finally assembled 67 indicators grouped under the following headings: data collection, data management, signal detection, safety issue assessment, decision making, communication/action, and general factors. The Fraunhofer report identified the critical success factors through the Delphi method. The critical success factors were defined as those elements of the whole process that determine its performance and can be modified to improve a system. From the literature review, this categorization (figure 5) was recognized as the first seen in published literature to identify the broader segments of the pharmacovigilance system processes. A few—but relevant—indicators were also identified from several WHO documents[13,14,15,16] and other reports that discussed pharmaceutical management, including the

[9] Ratanawijitrasin, S., and E. Wondemagegnehu. 2002. *Effective Drug Regulation: A Multicountry Study*. Geneva: WHO. http://www.who.int/medicinedocs/collect/medicinedocs/pdf/s2300e/s2300e.pdf.

[10] WHO Immunization, Vaccines, and Biologicals Joint Medical Products Assessment Tools of National Regulatory System Vaccines Assessment. 2004. Post-marketing activities including surveillance of adverse events following immunization (AEFI). https://apps.who.int/vaccines-access/vaccine_regulation/nras/nra_functions_table_jan2005.pdf.

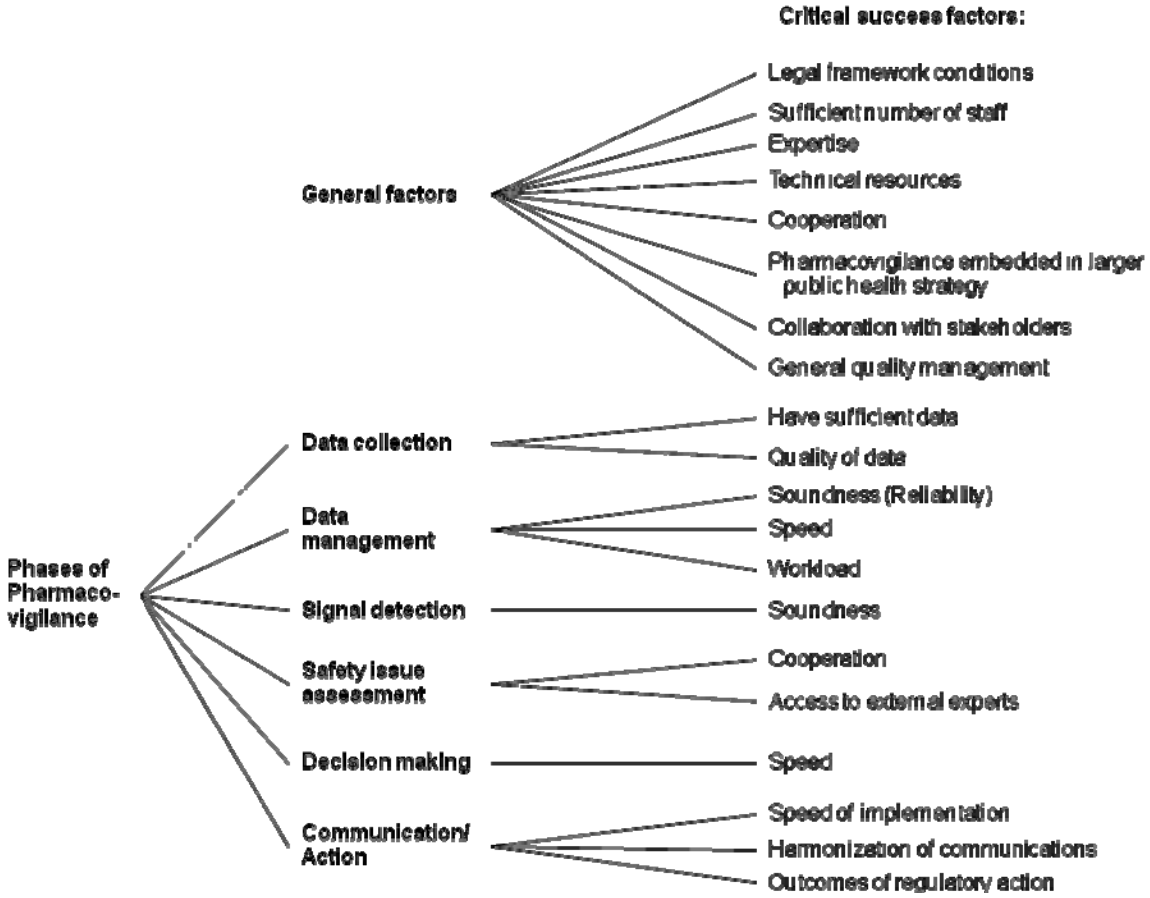
[11] Amrumpai, Y., N. Kiatying-Angsulee, and K. Chamroonsawasdi. 2007. Identifying safety indicators of new Drug Safety Monitoring Programme (SMP) in Thailand. *Drug Information Journal* 41:769–77.

[12] European Commission. 2006. *Assessment of the European Community System of Pharmacovigilance: Final Report—Final version, 25 January 2006*. Submitted by Fraunhofer Institute Systems and Innovation Research, Karlsruhe, Germany, to the European Commission Enterprise and Industry Directorate-General, Unit F2, Pharmaceuticals. http://ec.europa.eu/enterprise/pharmaceuticals/pharmacovigilance/docs/acs_consultation_final.pdf.

[13] WHO. 2006. *Using Indicators to Measure Country Pharmaceutical Situations: Fact Book on Who Level I and Level II Monitoring Indicators*. Geneva: WHO. http://www.sld.cu/galerias/pdf/servicios/medicamentos/using_indicators_to_measure_country_pharmaceutical_situations.pdf.

[14] WHO. 2009. Harmonized Monitoring and Evaluation Indicators for Procurement and Supply Management Systems Tracking the Performance of PSM Systems for ARVs, TB and Malaria Medicines. Working Document for Field Testing. http://www.who.int/hiv/amds/amds_me.pdf.

MSH *Rapid Pharmaceutical Management Assessment: An Indicator-Based Approach*[17] and the United States Pharmacopeia Drug Quality and Information Program.[18]



Source: European Commission. 2006. *Assessment of the European Community System of Pharmacovigilance: Final Report—Final version, 25 January 2006*. Submitted by Fraunhofer Institute Systems and Innovation Research, Karlsruhe, Germany, to the European Commission Enterprise and Industry Directorate-General, Unit F2, Pharmaceuticals. http://ec.europa.eu/enterprise/pharmaceuticals/pharmacovigilance/docs/acs_consultation_final.pdf.

Figure 5. Critical success factors

[15] WHO. 2004. *The World Medicines Situation*. Geneva: WHO. http://www.searo.who.int/LinkFiles/Reports_World_Medicines_Situation.pdf.
[16] WHO Global Program for Vaccines and Immunization, Expanded Program on Immunization. 1997. *Surveillance of Adverse Events Following Immunization: Field Guide for Managers of Immunization Programmes*. Geneva: WHO. http://www.who.int/vaccines-documents/DocsPDF/www9541.pdf.
[17] Rational Pharmaceutical Management Project, Latin America and Caribbean Health and Nutrition Sustainability Project, and Regional Program on Essential Drugs of the Pan American Health Organization. 1995. Rapid Pharmaceutical Management Assessment: An Indicator-Based Approach. Arlington, VA: MSH.
[18] United States Pharmacopeia Drug Quality and Information Program and collaborators. 2007. *Ensuring the Quality of Medicines in Resource-Limited Countries: An Operational Guide*. Rockville, MD: The United States Pharmacopeial Convention. www.usp.org/worldwide/dqi/resources/technicalReports.

SPS also reviewed patient safety indicators. The focus was on medication-related patient safety indicators, for example, those that have to do with medication errors. Such related indicators were transcribed from the several patient safety indicators that were identified.[19,20,21,22,23,24] The South Africa HIV/AIDS program also developed some indicators for monitoring adverse events to antiretroviral (ARV) medicines.[25] Beyond these, no performance monitoring tools exist for assessing where a country stands in addressing the entire continuum of medicine safety. The fragmentary indicators that currently exist are each used for monitoring safety in only a segment of the pharmacovigilance system. Clearly, a comprehensive pharmacovigilance performance metric will be very relevant. Countries at different stages in the development and implementation of their pharmacovigilance systems can use aspects that are relevant to them. Furthermore, a pharmacovigilance tool, when adopted, would support countries in their efforts to identify priorities and benchmark the development of their medicine safety system against that of other countries.

Delphi Group

The Delphi method was used to develop the indicators. The Delphi method for collecting group judgment allows for asynchronous and spatially dispersed interaction that emphasizes individual contributions and individual choices, the body of which come to represent group choices through an iterative process.[26] The Delphi method describes an approach to group collaboration designed to foster the exploration and distillation of expert opinion. It allows individual participants to express and defend their choice of each candidate indicator with the aim of generating a body of expert opinion.[27] This method has been used previously and found suitable for the development of indicators.[28]

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[19] New South Wales Therapeutic Advisory Group, 2007. *Indicators for Quality Use of Medicines in Australian Hospitals.* http://www.ciap.health.nsw.gov.au/nswtag/QUMIndicators.html.

[20] Nigam, R., et al. 2008. Development of Canadian Safety Indicators for Medication Use. *Healthcare Quarterly* 11(Sp):47–53.

[21] Schaff, R., G. Schumock, and D. Nadzam. 1991. Development of the Joint Commission's indicators for monitoring the medication use system. *Hospital Pharmacy* 26:326–29, 350.

[22] American Hospital Association, Health Research and Educational Trust, and Institute for Safe Medication Practices. 2002. *Pathways for Medication Safety*. http://www.medpathways.info/medpathways/tools/tools.html.

[23] Gianino, M., et al. 2008. Indicators for preventable drug-related morbidity: Practical application in home-based care. *Pharmacoepidemiology and Drug Safety* 17:501–510.

[24] MacKinnon, Neil J., and Karen McCaffrey. 2004. *Health System Performance Indicators as a Tool for Maximizing Health Gain in Canada: Where Do Pharmaceuticals Fit?* A Report for Merck Frosst Canada, Ltd. http://www.merckfrosst.ca/assets/en/pdf/health_policy/PerformanceIndicators2004.pdf.

[25] Department of Health. 2004. Monitoring and Evaluation Framework for the Comprehensive HIV and AIDS Care, Management and Treatment Programme for South Africa. http://www.hst.org.za/uploads/files/monitorevaluation.pdf.

[26] Adler, M., and E. Ziglio. 1996. *Gazing into the Oracle: The Delphi Method and Its Application to Social Policy and Public Health*. Philadelphia: Taylor and Francis.

[27] The HERO e-Delphi system: Overview and implementation, October 2001. http://hero.geog.psu.edu/products/Delphi_white_paper.pdf.

[28] See, for example, European Commission. 2006. *Assessment of the European Community System of Pharmacovigilance: Final Report—Final version, 25 January 2006*. Submitted by Fraunhofer Institute Systems and Innovation Research, Karlsruhe, Germany, to the European Commission Enterprise and Industry Directorate-General, Unit F2, Pharmaceuticals. http://ec.europa.eu/enterprise/pharmaceuticals/pharmacovigilance/docs/acs_consultation_final.pdf.

A panel of experts with experience working on pharmacovigilance-related activities in developing countries were recruited into the Delphi group. Three rounds of Delphi exchange were used to obtain feedback from the group. Participants were not revealed to one another but were known to the moderator. This method ensures that all views are expressed and that opinion leaders do not bias feedback from other respondents.

Following the detailed literature review previously described, two persons independently collected relevant indicators and entered them into an Excel spreadsheet. The two lists were eventually harmonized and the indicators grouped according to selected themes. These indicators were aligned to key pharmacovigilance components. New indicators were proposed to fill gaps. The first set of indicators was presented in three rounds of Delphi consultations. In the first round, participants were given these global sets of indicators for review based on some selected assessment criteria, which have been used in the development of indicators.[29] These criteria evaluate whether the indicators are—

Clear: easily understood and calculated

Useful: reflects an important dimension of performance

Measurable: can be defined in quantitative or qualitative terms and used within existing constraints on information quality and availability
Reliable: permits consistent assessment over time among different observers

Valid: is a true measure of what it is meant to measure

Practical: can be obtained timely, at reasonable cost, frequently enough to inform the progress and influence decisions

Respondents were asked to insert "1" for each criterion they think the indicator meets. Therefore, an indicator that meets all six criteria gets a maximum score of 6. The questionnaire was sent to 18 participants. Twelve responses (66.7 percent) were received. Feedback from this first Delphi round was statistically analyzed using mean and standard deviation. The following rule was set for the inclusion of indicators in the next Delphi round.

[29] WHO. 2001. *How to Develop and Implement a National Drug Policy.* 2nd ed. Geneva: WHO. http://apps.who.int/medicinedocs/en/d/Js2283e/4.2.4.html.

Table 1. Criteria for Inclusion of Indicators

Category 1	**Standard deviation < 1.5; mean > 4.25** The responses from the Delphi group have a standard deviation of less than 1.5 and mean score for the criteria of more than 4.25 (maximum score 6) for that particular indicator
Category 2	**Standard deviation 1.5 ≤ 2.0; mean > 4.25** The responses have a standard deviation of from 1.5 to less than or equal to 2.0 and mean score for the criteria of more than 4.25
Category 3	Standard deviation < 2.3; mean > 4.25 The responses have a standard deviation of less than 2.3 and mean score for the criteria of more than 4.25. Indicators falling in this category were modified and included as category 2.

Successful indicators from the first Delphi round were compiled and presented to the group in the second Delphi round. During the second round of consultations, respondents were requested to check *Include* or *Delete* or *Modify* for each indicator. They were also asked to recommend what the modified version should be for places where they checked *Modify*. Seven responses were obtained. For the analysis, indicators were included where four or more of the respondents asked for the indicator to be included and two or less asked for it to be deleted.

For the third and last Delphi consultation, respondents received a spreadsheet with three worksheets with the following instructions—

1. "Data collection template" contains detailed description of each indicator. You do not need to do anything in this sheet except read the indicators carefully for a better understanding of description, rationale, computation, and so on, for each indicator.

2. "Delphi 3" contains a line listing of each indicator grouped according to the component (as derived from the draft pharmacovigilance framework) and the outcome. Now that you clearly know what each indicator is meant to measure and how we propose to collect data, we now ask that you answer these two questions for each indicator:
    1. Recommend as Core (C) or Supplementary (S) indicator?
    2. What weight will you assign (in a scale of 1–10) to this indicator when substantially satisfied?

3. "Framework" contains the draft pharmacovigilance conceptual framework. You do not need to do anything but be informed of where the outcomes came from.

Eight responses were received from regular participants who were part of the first two consultations. A response was also received from a participant who missed the second round and a response from someone who had not been part of the consultation from the beginning. All together, there were three consultations, 12 respondents in eight countries, and 27 responses.

INDICATOR-BASED PHARMACOVIGILANCE ASSESSMENT TOOL

Objectives

The objective of the Indicator-Based Pharmacovigilance Assessment Tool, IPAT, is to serve as a performance monitoring tool for the diagnostic assessment of the pharmacovigilance and medicine safety system. The use of IPAT will guide the development of feasible interventions and recommendations to improve medicine safety. The recommendations resulting from the analysis of the data generated by IPAT reflect each country's local realities, existing regulatory capacity and priorities, identified system gaps, and resources available for conducting medicine safety activities. Additionally, the standardized and indicator-based approach included in the tool will allow longitudinal measurement of progress after the recommended interventions are implemented.

The assessment tool is modular and classified to guide the selection of the most relevant indicators for the every unit of the health system. This supports the idea that pharmacovigilance should be developed only to meet a country's level of development and key priorities. The tool focuses on significant issues related to health systems that are recognized as the key factors in the overall capacity and sustainability of a medicine safety system.

Limitations

IPAT has the following limitations—

- The sensitivity and specificity of the indicators are not established.
- Non-medication-related patient safety indicators are not included.

About the IPAT Manual

The IPAT indicators are classified as follows—

A. Components—The components represent the elements of a functional pharmacovigilance system, including—

   1. Policy, law, and regulation
   2. Systems, structures, and stakeholder coordination
   3. Signal generation and data management
   4. Risk assessment and evaluation
   5. Risk management and communication

   Indicators are numbered according to these components.

B. Core/Supplementary—Indicators are classified based on importance or how essential they are to a functional pharmacovigilance system. The most essential indicators are classified as *Core*, and others are classified as *Supplementary*.

C. Type of Indicator—Indicators are also classified based on the product or result they are measuring: structural, process, and outcome indicators.

- Structural: measures systems and physical infrastructures
- Process: measures how the pharmacovigilance system works
- Outcome: measures the final product of all the inputs into the pharmacovigilance activities

D. Data Collection Level—Indicators are classified according to the health system level where they are relevant and could be collected.

- Ministry of Health (MoH) headquarters, which represents any data that can be collected at the national level, including the medicines regulatory authority. Also, depending on the indicator, data can be collected from the national pharmacovigilance center, pharmaceutical services, pharmaceutical companies, health professions university departments and associations.

- Public Health Program (PHP) represents specialized health programs such as the HIV/AIDS, tuberculosis (TB), malaria, vaccination, and maternal and child health programs.

- Health facilities (HFs) include primary, secondary, and tertiary or referral hospitals that provide direct services to patients. The point of data collection at the health facility may be the drug and therapeutics committee (DTC), pharmacovigilance unit, quality assurance unit, patient safety or medication safety unit, infection control unit, and other similar units or departments of the clinic, health center, or hospital.

The indicator's data collection level classification can be used as a guide for determining which indicators are relevant to a particular unit of the health system. For example, the medicine regulatory authority will be interested in all indicators classified as MoH.

E. Recommended frequency of measurement—Indicators are classified according to the recommended frequency of data collection. For example, indicators related to policies and legislation are recommended to be collected every five years, allowing adequate time to review such documents and update them to current realities. Other indicators are recommended to be collected every year. Some of these indicators, particularly the structural ones, require subsequent monitoring that involves judgment of the current relevance of what is being measured.

Who Should Use IPAT?

This manual is designed for use by ministries of health, medicine regulatory authorities, public health programs, health facilities (e.g., DTCs, quality assurance units, and so on), development partners, and all stakeholders to measure relevant aspects that they support in ensuring medicine safety in a country. IPAT is designed to be modular, allowing each unit within the health system choose only relevant aspects of the tool, based on the data collection level classification, to monitor pharmacovigilance and medicine safety.

How to Use IPAT?

The final tool contains 43 indicators: 26 are core and 17 are supplementary indicators. These indicators address five pharmacovigilance and medicine safety system components: (a) policy, law, and regulation (4 indicators); (b) systems, structures, and stakeholder coordination (15 indicators); (c) signal generation and data management (6 indicators); (d) risk assessment and evaluation (8 indicators); and (e) risk management and communication (10 indicators). The frequency of administration of these indicators is either once every five years or once every year. To obtain a baseline assessment, users may have to administer the entire set of 43 indicators in the first year and in the subsequent year administer only the 33 annual indicators. After the baseline national assessment, a unit of the health system that is involved in medicine safety can use relevant IPAT indicators for routine monitoring and evaluation of the unit's services as related to medicine safety in subsequent years.

Sampling and Data Collection

Identification of samples for administering the tool should take into consideration each country's realities. The regulatory authority should be assessed. All the public health programs and other stakeholders involved in pharmacovigilance at the national level will also need to be assessed. The data collection tool for public health programs is attached as annex 6. A single indicator relates to the universities or academic institutions and to the health professions council and associations. Depending on the number of academic institutions that offer training for health professionals, a representative number can be chosen. The same applies for the pharmaceutical companies and marketing authorization holders (MAHs) operating in the country. The data collection tool for national drug authority (NDA), pharmacovigilance center, and other national-level institutions is attached as annex 7. For the indicators addressing safe use of medicines at the health facilities, 10–15 health facilities may need to be sampled to obtain representative data. The health facilities should represent all levels of health care delivery. The data collection tool for the assessment of health facilities is attached in annex 8.

Conclusions from Assessment Findings

For a country to be regarded as having a minimally functional pharmacovigilance and medicine safety system, it must achieve all the core indicators. Subsequently, achievement of the supplementary indicators can indicate the sophistication of development of the country's

medicine safety system. IPAT is a quality improvement tool, and users are encouraged to use it to benchmark progress over time.

SUMMARY OF INDICATORS

Indicator Number[a]	Indicator	Core/ Supplementary	Type of Indicator	Data Collection Level	Recommended Frequency of Measurement
Component 1. Policy, Law, and Regulation					
1.1	Existence of a policy document that contains essential statements on pharmacovigilance or medicine safety (stand alone or as a part of some other policy document)	Core	Structural	MoH, PHP	Every 5 years
1.2	Existence of specific legal provisions for pharmacovigilance in the national medicines legislation or similar legislation	Core	Structural	MoH	Every 5 years
1.3	Legal provisions require that the marketing authorization holder mandatorily report all serious ADRs to the national drug regulatory authority	Supplementary	Structural	MoH	Every 5 years
1.4	Legal provisions require the marketing authorization holder to conduct the same or similar postmarketing surveillance activities for products as required by stringent regulatory authorities	Supplementary	Structural	MoH	Every 5 years
Component 2. Systems, Structures, and Stakeholder Coordination					
2.1	Existence of a pharmacovigilance center or unit	Core	Structural	MoH, PHP, HF	Every 5 years
2.2	Pharmacovigilance center or unit has a clear mandate, structure, roles, and responsibilities	Core	Structural	MoH, PHP, HF	Every 5 years
2.3	Existence of a medicine information or pharmacovigilance service that provides ADR and drug safety–related question-and-answer services	Core	Structural	MoH, PHP, HF	Annually
2.4	A designated staff responsible for pharmacovigilance or medicine safety activities	Core	Structural	MoH, PHP, HF	Annually
2.5	Dedicated budget available for pharmacovigilance-related activities	Core	Structural	MoH, PHP, HF	Annually

Indicator Number[a]	Indicator	Core/ Supplementary	Type of Indicator	Data Collection Level	Recommended Frequency of Measurement
2.6	Existence of a national medicine safety advisory committee or a subcommittee with similar functions that has met at least once in the last year	Core	Structural	MoH	Annually
2.7	Existence of national pharmacovigilance guidelines updated within the last five years	Core	Structural	MoH	Every 5 years
2.8	Existence of protocols or SOPs for improving patient safety relating to medicine use	Core	Structural	MoH, PHP, HF	Annually
2.9	Existence of a minimum core list of communication technologies to improve access to safety reporting and provision of medicine information	Core	Structural	MoH, PHP, HF	Annually
2.10	Existence of an ADR or medicine safety bulletin (or any other health-related newsletter that routinely features ADR or medicine safety issues) published in the last six months	Core	Structural	MoH, PHP, HF	Annually
2.11	Percentage of predefined core reference materials available in the medicine information or pharmacovigilance center	Supplementary	Process	MoH, PHP, HF	Annually
2.12	Percentage of predefined core pharmacovigilance topics present in the preservice training curricula (disaggregated by medicine, pharmacy, nursing, and public health curricula)	Supplementary	Process	Universities, health profession council	Annually
2.13	Number of health care providers trained on pharmacovigilance and medicine safety in the last year	Supplementary	Process	MoH, PHP, HF	Annually
2.14	Platform or strategy exists for the coordination of pharmacovigilance activities at the national level	Core	Process	MoH	Annually
2.15	National pharmacovigilance center is a full or associate member of the WHO Collaborating Centre for International Drug Monitoring (UMC)	Supplementary	Structural	MoH	Every 5 years

Indicator Number[a]	Indicator	Core/ Supplementary	Type of Indicator	Data Collection Level	Recommended Frequency of Measurement
Component 3. Signal Generation and Data Management					
3.1	Existence of a system for coordination and collation of pharmacovigilance data from all sources in the country (e.g., health programs, immunization program, active surveillance studies)	Core	Process	MoH	Annually
3.2	Existence of a database for tracking pharmacovigilance activities	Core	Process	MoH	Annually
3.3	Existence of a form for reporting suspected ADRs	Core	Process	MoH, PHP, HF	Annually
3.4	Existence of a form for reporting suspected product quality issues (as a subset in the ADR form or as a separate form)	Core	Process	MoH, PHP, HF	Annually
3.5	Existence of a form for reporting suspected medication errors (as a subset in the ADR form or as a separate form)	Core	Process	MoH, PHP, HF	Annually
3.6	Existence of a form for reporting suspected treatment failure (as a subset in the ADR form or as a separate form)	Core	Process	MoH, PHP, HF	Annually
Component 4. Risk Assessment and Evaluation					
4.1	Number of medicine utilization reviews carried out in the last year	Supplementary	Process	MoH, PHP, HF	Annually
4.2	Pharmaceutical product quality survey conducted within the last five years	Supplementary	Process	MoH	Every 5 years
4.3	Incidence of medication errors quantified in the last year	Supplementary	Process	MoH, PHP, HF	Annually
4.4	Number of ADR reports received in the last year	Core	Process	MoH, PHP, HF	Annually
4.5	Number of active surveillance activities currently ongoing or carried out in the last five years	Core	Process	MoH, PHP, HF	Every 5 years
4.6	Percentage of patients in public health programs for whom drug-related adverse events were reported in the last year (disaggregated by type of adverse event, drug, severity, outcomes, and demographics)	Core	Process	MoH, PHP, HF	Annually

Indicator Number[a]	Indicator	Core/ Supplementary	Type of Indicator	Data Collection Level	Recommended Frequency of Measurement
4.7	Percentage of patients undergoing treatment within a public health program whose treatment was modified because of treatment failure or ADRs in the last year (disaggregated by treatment failure and ADRs)	Core	Process	MoH, PHP, HF	Annually
4.8	Percentage of patients in public health programs for whom drug-related, serious "unexpected adverse events" were reported in the last year	Supplementary	Process	MoH, PHP, HF	Annually
	Component 5. Risk Management and Communication				
5.1	Risk mitigation plans currently in place that are targeted at high-risk medicines	Supplementary	Outcome	MoH, PHP, HF	Annually
5.2	Prequalification schemes (e.g., WHO prequalification program and Pharmaceutical Inspection Co-operation Scheme) used in medicine procurement decisions	Supplementary	Outcome	MoH, PHP	Annually
5.3	Number of medicine safety information requests received and addressed in the last year	Supplementary	Outcome	MoH, PHP, HF	Annually
5.4	Percentage of planned issues of the medicine safety bulletin (or any other health-related newsletter that routinely features ADR or medicine safety issues) published in the last year	Supplementary	Outcome	MoH, PHP, HF	Annually
5.5	Number of medicine safety issues of local relevance identified from outside sources (e.g., from another country, or from regional or international sources) and acted on locally in the last year	Supplementary	Outcome	MoH, PHP, HF	Annually
5.6	Number of "Dear health care professional" letters or other safety alerts developed and distributed in the last year	Supplementary	Outcome	MoH, PHP, HF	Annually
5.7	Average time lag between identification of safety signal of a serious ADR or significant medicine safety issue and communication to health care workers and the public	Core	Outcome	MoH, PHP, HF	Annually

Indicator Number[a]	Indicator	Core/ Supplementary	Type of Indicator	Data Collection Level	Recommended Frequency of Measurement
5.8	Percentage of the sampled Drug and Therapeutics Committees that have carried out pharmacovigilance activities or addressed medicine safety issues in the last year	Core	Outcome	MoH, HF	Annually
5.9	Number of public or community education activities relating to medicine safety carried out in the last year	Supplementary	Outcome	MoH, PHP, HF	Annually
5.10	Percentage of medicines sampled in the last year that passed product quality tests	Core	Outcome	MoH, PHP, HF	Annually

a. The numbers for the core indicators are in **boldface** and those of the supplementary indicators are in *italic*.

DETAILED DESCRIPTION OF INDICATORS

Indicator Presentation Format

Heading	Definition
Indicator number and name	The number assigned to the indicator and its full name
Importance	Core or Supplementary represented by (C) or (S), respectively, following the indicator number
Purpose	A statement of the purpose or objective for collecting the indicator
Rationale and evidence	A statement of why the indicator is relevant and evidence on the validity for measuring the activity
Data collection	Detailed description of how data can be collected and analyzed
Collection level/frequency	*Which institution to visit for the collection of the data and how often*
Where to go	*Which office within the institution to go for the collection of the data*
Who to ask	*Potential respondents*
Assessment question	*Questions to address to the respondents*
What documents to review	*Which documents to request and review*
Computation	How to compute the results of the responses and document review and arrive at conclusions
Limitations and interpretation	A statement on the implications of the responses and the shortcomings of the conclusions derived through the assessment
Potential interventions	Description of interventions that can be implemented to support improvement in the indicator
Further information and references	Other relevant information to the indicator and related references

Note: Footnotes refer to sources listed in the **Further information and references** section of the indicator description.

Policy, Law, and Regulation

Indicator 1.1 (C)	**Existence of a policy document that contains essential statements on pharmacovigilance or medicine safety (stand alone or as a part of some other policy document)**
Purpose:	To determine whether a policy exists either within the National Medicines Policy (NMP) or as part of other MoH policy documents with a section that clearly addresses pharmacovigilance or medicine safety issues
Rationale and evidence:	A policy statement on pharmacovigilance or medicine safety is the guiding document and authority that mandates the need, scope, direction, and activities a country should carry out. The WHO identified key elements of pharmacovigilance that should be included in the NMP.[1] Other related policy documents, including those of PHPs and treatment guidelines may also contain such statements. Examples of "essential statements" on pharmacovigilance include commitment to monitor the safety and effectiveness of medicines, vaccines, or other health products used in PHPs, ADR reporting policies, and government commitment to fund or support pharmacovigilance activities.

Data collection

Collection level/frequency	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH, PHPs, HFs Every 5 years	NDA, Pharmacy Department, PHPs	Directors or heads of NDA, Pharmacy Department, PHPs, hospitals, or DTCs	1. Is there an approved national policy on pharmacovigilance or medicine safety? 2. Was the policy recently reviewed (in the last five years)?	NMP, National Pharmacovigilance Policy, MoH policy documents; other related policy documents	Check "**Yes**" if there are essential pharmacovigilance policy statements within the NMP or other policy documents and that policy statement was developed or reviewed within the last five years. Check "**No**" if there is no policy/policy statement on medicine safety and pharmacovigilance within the NMP and PHPs, or if the current one was not recently reviewed, or if key informants consider the current one no longer relevant.

Limitations	Policy statements on pharmacovigilance that are contained in the NMP and other MoH documents may be current within five years but not comprehensive, or more than five years old and still relevant. In interpreting this indicator, official commitments from units of the MoH, even if they are not policy declarations, can also be checked "Yes." However, no way exists to ensure that these statements are implemented.
Potential interventions	• Develop advocacy using WHO recommendations that pharmacovigilance elements should be included in the NMP as a reference. • Advocate that PHPs that conduct mass treatments should include essential statements on pharmacovigilance in their policy documents.
Further information and references	1. WHO. 2004. Pharmacovigilance: Ensuring the safe use of medicines. *WHO Policy Perspectives on Medicines* 9. http://apps.who.int/medicinedocs/pdf/s6164e/s6164e.pdf.

Indicator 1.2 (C)	**Existence of specific legal provisions for pharmacovigilance in the national medicines legislation or similar legislation**
Purpose:	To determine if current legislation for pharmaceuticals and other health products addresses aspects of pharmacovigilance
Rationale and evidence:	Laws and regulations are necessary to provide legal backing for pharmacovigilance and medicine safety activities. Regulations are derived from the legislation to guide the implementation of the law. Several regulatory authorities, such as the FDA and the EMEA have laws and regulations governing the safety of health products. The WHO recommends that key elements of pharmacovigilance should include the development of legislation and regulation for medicine monitoring.[1]

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH headquarters (HQ)	NDA, Pharmacy Department	Directors or heads of NDA and Pharmacy Department	1. Are there laws related to pharmacovigilance or medicine safety in the medicines act? 2. What is the specific act or section of the law or regulation that addresses pharmacovigilance?	Medicines and related substances control act (MRSCA), pharmaceutical legislation and regulations Other related laws and policy documents	Check "**Yes**" if specific requirements for pharmacovigilance or medicine safety are mentioned in the laws or the regulation. Check "**No**" if there is no such mention in any of the laws and regulations.

Limitations	The legislation may not address pharmacovigilance specifically and may use broad statements such as "all imported medicines must be safe and of good quality." Specific legislation for pharmacovigilance should go beyond such statements. Only draft legislation may be in place.
Potential interventions	Develop advocacy using the WHO recommendations that pharmacovigilance elements should include the development of legislation and regulation for medicine monitoring.
Further information and references	1. WHO. 2004. Pharmacovigilance: Ensuring the safe use of medicines. *WHO Policy Perspectives on Medicines* 9. http://apps.who.int/medicinedocs/pdf/s6164e/s6164e.pdf.

Indicator 1.3 (S)	**Legal provisions require that the marketing authorization holder mandatorily report all serious ADRs to the national drug regulatory authority**
Purpose:	To determine if specific laws or regulations exist that require MAHs to report ADRs
Rationale and evidence:	The MAH is responsible for reporting ADRs related to the use of a product for which the MAH has a license, wherever the product is marketed. Stringent regulatory authorities like the FDA[1] and EMEA[2] and the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)[3] guidelines require MAHs to report ADRs that occur in countries where their products are marketed. Specific requirements demand expedited reporting for serious ADRs.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH HQ	NDA, Pharmacy Department	Directors or heads of NDA and Pharmacy Department	1. Do laws or regulations require the MAH to report ADRs to NDA? 2. What is the specific act or section of the law or regulation that addresses mandatory reporting by the MAH?	MRSCA, pharmaceutical laws and regulations; other related laws and policy documents	Check "**Yes**" if there is a mention of specific requirements for the MAH to report all serious ADRs. Check "**No**" if no such mention occurs in any of the laws, regulations, or policy documents.

Limitations	The legislation may not distinguish between serious and nonserious ADRs.
Potential interventions	Advocate for revision of the legislation and regulations to include requirement for mandatory reporting of all serious ADRs by the MAH.
Further information and references	1. FDA. 2001. Draft Guidance for Industry: Postmarketing Safety Reporting for Human Drug and Biological Products Including Vaccines. http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Vaccines/ucm074850.htm. 2. ICH website, http://www.ich.org/cache/compo/276-254-1.html. 3. European Commission. EudraLex, Vol. 9, Pharmacovigilance Guidelines. http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol9_en.htm.

Indicator 1.4 (S)	**Legal provisions require the marketing authorization holder to conduct the same or similar postmarketing surveillance activities for products as required by stringent regulatory authorities**
Purpose:	To determine if the legislation/regulation of a country requires the MAH to provide similar postmarketing safety standards as required for the same product by stringent regulatory authorities
Rationale and evidence:	Some products with significant unresolved safety concerns or high-risk medicines are registered by stringent regulatory authorities such as the FDA and EMEA only on the condition that the MAH conduct postmarketing safety studies or risk minimization activities[1,2] for that product after registration. This indicator tries to identify if those same conditions are mentioned in developing-country legal provisions or if related conditions are placed on such products during registration in developing countries.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH HQ	NDA, Pharmacy Department	Directors or heads of NDA and Pharmacy Department	1. Are there laws or regulations requiring the MAH to conduct postmarketing safety activities? 2. What is the specific act or section of the law or regulation that addresses mandatory postmarketing safety activities for the MAH?	MRSCA, pharmaceutical laws and regulations, other related laws and policy documents	Check "**Yes**" if there is a mention in laws/regulations that some products may be registered with restricted conditions due to safety concerns. Review the list of products requiring risk management (see example from FDA in annex 1), and identify those that are also available and registered in the country. Confirm that they have some postmarketing study commitments tied to their registration. If so, check "**Yes**"; if not, check "**No**." Check "**No**" if there is no such mention in any of the legislation, regulations, or policy documents
Limitations	Computation requires the review of the national register and list of medicines requiring postmarketing surveillance activities from another regulatory authority.				
Potential interventions	Advocate for the revision of the legislation and regulations to include a requirement for mandatory postmarketing commitments for products that are locally available and required to have such commitments by stringent regulatory authorities.				
Further information and references	1. FDA. Postmarket Requirements and Commitments. http://www.accessdata.fda.gov/scripts/cder/pmc/index.cfm. 2. EMEA. 2005. Committee for medicinal products for human use (CHMP): Guidelines on risk management systems for medicinal products for human use. http://www.emea.europa.eu/pdfs/human/euleg/9626805en.pdf.				

Systems, Structures, and Stakeholder Coordination

Indicator 2.1 (C)	**Existence of a pharmacovigilance center or unit**
Purpose:	To identify the actual existence of a national and/or local center(s) or unit(s) specifically mandated to handle pharmacovigilance and medicine safety issues
Rationale and evidence:	According to the WHO, "ideally every country should have a pharmacovigilance centre."[1] A pharmacovigilance center may be within an MoH department, in a tertiary academic institution in a country, or in a health facility. Irrespective of where located, the pharmacovigilance center has a specific mandate to monitor safety of the use of medicines. In health facilities, any functional unit, including DTCs and quality assurance units, that addresses significant parts of a pharmacovigilance unit mandate is acceptable. This indicator does not recommend that each health facility must have a stand-alone pharmacovigilance center; the key functions of a pharmacovigilance center can be included in other existing committees or units within the health facility.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH, PHP, HF	MoH, NDA, Pharmacy Department, PHP, HF	Directors or heads of NDA, Pharmacy Department, PHP, HF	1. Is there a pharmacovigilance center, or any other body assigned responsibility for monitoring safety of medicines? 2. Does the pharmacovigilance center physically exist?	MRSCA and similar legislation, MoH memos for the establishment of the national pharmacovigilance center, establishment document for the national or local pharmacovigilance center Physical visit to the center	Check "**Yes**" if both of the following are true— • Official documents establish the existence of a pharmacovigilance center/unit. • A visit was made to the center/unit and it was found to be currently functioning. For HFs, check "**Yes**" if the documented mandate of the health facility unit or committee includes pharmacovigilance activities. Check "**No**" if these conditions are not met.
Limitations	Instances may exist where a pharmacovigilance center's operations are not clearly mentioned in the official documents.				
Potential interventions	Advocate and provide support for the establishment of a national pharmacovigilance center.				
Further information and references	1. WHO. 2004. Pharmacovigilance: Ensuring the safe use of medicines. *WHO Policy Perspectives on Medicines* 9. http://apps.who.int/medicinedocs/pdf/s6164e/s6164e.pdf. 2. *the* Uppsala Monitoring Centre (*the* UMC), WHO Collaborating Centre for International Drug Monitoring. 2000. *Safety Monitoring of Medicinal Products: Guidelines for Setting Up and Running a Pharmacovigilance Centre*. Geneva: WHO. http://apps.who.int/medicinedocs/en/d/Jh2934e/.				

Indicator 2.2 (C)	**Pharmacovigilance center or unit has a clear mandate, structure, roles, and responsibilities**
Purpose:	To confirm that the pharmacovigilance center has a formal organizational structure and setup
Rationale and evidence:	A pharmacovigilance center has the potential to function optimally if it has a clear mandate, organizational structure, roles, responsibilities, and reporting lines. When the pharmacovigilance activities are addressed as part of another unit or committee, an official mandate, roles, and responsibilities should be clearly assigned to that unit or committee.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH, PHP, HF	MoH, NDA, Pharmacy Department, PHP, HF	Directors or heads of NDA, Pharmacy Department, national or local pharmacovigilance center, PHP, HF	Is there a clear mandate, organizational structure, roles, responsibilities, and reporting lines for the pharmacovigilance center?	MRSCA, MoH memos for the establishment of the national pharmacovigilance center, establishment document for the national or local pharmacovigilance center	Check "**Yes**" if both of the following are true— • There is an official document with clear mandate, organizational structure, roles, responsibilities, and reporting lines for the pharmacovigilance center or unit/committee at the health facility. • These formal organizational details have been operationalized and are currently being implemented.

Limitations	Data collection may be challenging in instances where key respondents presume that clear mandates exist but they are not documented.
Potential interventions	Provide support for the development of a proposed mandate, structure, roles, and responsibilities for discussions with MoH.
Further information and references	1. *The* Uppsala Monitoring Centre (*the* UMC), WHO Collaborating Centre for International Drug Monitoring. 2000. *Safety Monitoring of Medicinal Products: Guidelines for Setting Up and Running a Pharmacovigilance Centre*. Geneva: WHO. http://apps.who.int/medicinedocs/en/d/Jh2934e/. 2. Strengthening Pharmaceutical Systems (SPS). *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. http://www.msh.org/projects/sps/Pharmaceutical-Management/Pharmacovigilance.cfm.

Indicator 2.3 (C)	**Existence of a medicine information or pharmacovigilance service that provides ADR and drug safety–related question-and-answer services**
Purpose:	To confirm that a general medicine information center or a specific pharmacovigilance center currently exists that provides ADR and medicine safety–related question-and-answer services
Rationale and evidence:	Provision of medicine information that includes query-response service contributes to rational use of medicines. Medicine safety alerts and warnings can be communicated through the same channel that provides overall medicine information services or through a service center specifically dedicated to pharmacovigilance.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH, PHP, HF	MoH, NDA, pharmacovigilance center, drug information center (DIC), PHP, HF	Directors or heads of NDA, Pharmacy Department, national or local pharmacovigilance center, DIC, PHP, HF	Does a general medicine information center or a specific pharmacovigilance center exist that provides query-response service on ADRs and medicine safety information?	Relevant publications and reports of Drug Information Center and Pharmacovigilance Center; database review	Check "**Yes**" if the following are true— • Key informant confirms that ADR and medicine safety–related question-answer service is currently being provided by the DIC or the pharmacovigilance center. • Relevant publications, reports, or database confirms that such a service is currently functional.

Limitations	The medicine information service may be separate from the pharmacovigilance center and services.
Potential interventions	Provide support for the medicine information and pharmacovigilance center(s) to provide medicine safety information services.
Further information and references	1. Namibia Medicines Regulatory Council website, http://www.nmrc.com.na/Downloads/tabid/1350/language/en-US/Default.aspx.

Indicator 2.4 (C)	**A designated staff responsible for pharmacovigilance or medicine safety activities**
Purpose:	To confirm that someone has a specific responsibility to address pharmacovigilance (This may be a component of the individual's overall job description.)
Rationale and evidence:	Having a staff specifically designated for pharmacovigilance or medicine safety activities will facilitate data collection and coordination. That individual may have pharmacovigilance as a full-time responsibility or as a part or subset of his or her overall responsibilities.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH, PHP, HF	MoH, NDA, national or local pharmacovigilance center, PHP, HF	Directors or heads of HIV, TB, malaria, and immunization programs; NDA; Pharmacy Department; national or local pharmacovigilance center; HF	1. Is there a staff member specifically responsible for pharmacovigilance or medicines safety? 2. Does the job description indicate that the person is charged with pharmacovigilance or medicine safety activities as a full-time function or as a part of other overall responsibilities?	Pertinent documents of pharmacovigilance center, HF, and HIV, TB, malaria, and immunization programs; organogram and job descriptions; key informants interview Job description	Check "**Yes**" if the following are true— • Key informant confirmed that someone is specifically responsible for ADR monitoring. • Job description cited and verified as containing responsibility for pharmacovigilance either as a sole responsibility or as a part of the overall job description.

Limitations	In health facilities, the drug safety activities may be part of the job description of the quality assurance unit. During data collection, particularly at health facilities, efforts should be made to speak to all persons who may already be charged with this responsibility.
Potential interventions	Provide support for the development of a job description, and advocate for the creation of a designated staff.
Further information and references	1. *The* Uppsala Monitoring Centre (*the* UMC), WHO Collaborating Centre for International Drug Monitoring. 2000. *Safety Monitoring of Medicinal Products: Guidelines for Setting Up and Running a Pharmacovigilance Centre*. Geneva: WHO. http://apps.who.int/medicinedocs/en/d/Jh2934e/.

Indicator 2.5 (C)	**Dedicated budget available for pharmacovigilance-related activities**
Purpose:	To identify whether funding is annually appropriated by MoH or donors for pharmacovigilance activities. Those budgetary allocations may not be provided directly to the center and can be from other MoH departments, but the *key is that the center has a yearly budget for its activities*.
Rationale and evidence:	For pharmacovigilance activities in a country to be sustained, government and donors should be convinced and willing to commit funds toward safety monitoring. Pharmacovigilance activities may be funded directly at the PHPs, or the programs may contribute to the budget of the national pharmacovigilance center. In whatever form, a dedicated annual budget should exist for issues related to pharmacovigilance. For HFs, a budget provided for a DTC, quality assurance, or other units or committees to address various issues that include pharmacovigilance is considered as fulfilling this indicator.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH, PHP, HF	MoH, NDA, pharmacovigilance center, PHP, HF	Directors or heads of NDA, Pharmacy Department, and national, or local pharmacovigilance center, PHPs, HFs	1. Is there an annual budgetary allocation for pharmacovigilance activities or for the Pharmacovigilance Center? 2. In the last fiscal year, what funds were provided by the MoH and donors toward the functioning and implementation of pharmacovigilance activities?	MRSCA and related laws and regulations; NDA documents; national or local pharmacovigilance center documents Budget allocation documents	Check "**Yes**" if both of the following are true— • Key informants confirm availability of budgets for pharmacovigilance activities. • MoH or donor money funded some or all of the pharmacovigilance activities in the last fiscal year. For HF, check "**Yes**" if HF supports resources required for the functioning of the unit or committee with mandate that includes pharmacovigilance activities.

Limitations	There may be instances where the center is part of a larger MoH unit that has responsibility for several other activities. It may therefore not be possible to confirm that specific funding is made available for pharmacovigilance activities.
Potential interventions	• Provide support for the costing of funding and resources required for supporting pharmacovigilance-related activities. • Advocate for dedicated funding of pharmacovigilance activities.
Further information and references	1. *The* Uppsala Monitoring Centre (*the* UMC), WHO Collaborating Centre for International Drug Monitoring. 2000. *Safety Monitoring of Medicinal Products: Guidelines for Setting Up and Running a Pharmacovigilance Centre.* Geneva: WHO. http://apps.who.int/medicinedocs/en/d/Jh2934e/.

Indicator 2.6 (C)	**Existence of a national medicine safety advisory committee or a subcommittee with similar functions that has met at least once in the last year**
Purpose:	To verify that an advisory committee to the NDA exists and that such a committee meets and provides advice on medicine safety to the NDA and the pharmacovigilance center
Rationale and evidence:	A national medicine safety advisory committee (that is functional) provides expert technical advice to the regulatory authorities and pharmacovigilance centers on the safety of medicines in use in a country.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH, PHP	MoH, NDA, pharmacovigilance center	Directors or heads of NDA, Pharmacy Department, and national or local pharmacovigilance center	1. Does a national drug safety advisory committee or subcommittee with the responsibility to provide technical advice on the safety of medicines to the regulatory authority exist? 2. Has the national medicine safety advisory committee or subcommittee met in the last year?	MRSCA and related laws and regulations, NDA documents, national or local pharmacovigilance center establishing documents National medicine safety advisory (sub)committee meeting minutes	Check "**Yes**" if both of the following are true— • Official document constituting a national medicine safety advisory (sub)committee exists. • Records of the national medicine safety advisory (sub)committee confirm meeting(s) within the last year.

Limitations	A committee may exist that addresses medicine safety–related issues in a sporadic manner without safety issues being clearly documented as part of the committee's mandate.
Potential interventions	• Provide support for developing terms of reference for a medicine safety advisory committee. • Advocate for the establishment of such a committee or for the addition of the proposed terms of reference to the role of an existing committee.
Further information and references	1. *The* Uppsala Monitoring Centre (*the* UMC), WHO Collaborating Centre for International Drug Monitoring. 2000. *Safety Monitoring of Medicinal Products: Guidelines for Setting Up and Running a Pharmacovigilance Centre.* Geneva: WHO. http://apps.who.int/medicinedocs/en/d/Jh2934e/.

Indicator 2.7 (C)	**Existence of national pharmacovigilance guidelines updated within the last five years**
Purpose:	To confirm that national guidelines are in place that provide standards for the implementation of pharmacovigilance activities (spontaneous reporting/active surveillance, provision of drug information, roles an responsibilities of stakeholders, lines of reporting, information flow, etc.)
Rationale and evidence:	National guidelines for ADR reporting and medicine safety monitoring provide standards and directions on definitions, approaches, and processes for pharmacovigilance in a country. Where national pharmacovigilance guidelines exist, they help harmonize understanding and approaches for medicine safety monitoring.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH HQ	MoH, NDA, pharmacovigilance center	Directors or heads of NDA, Pharmacy Department, and national or local pharmacovigilance center	1. Does a national guideline for pharmacovigilance or a related document exist? 2. Has the national pharmacovigilance guideline been updated in the last five years?	MRSCA, national pharmacovigilance guidelines, related MoH guidelines and documents	Check "**Yes**" if an official guideline document exists and if it has been updated in the last five years.

Limitations	Some countries may have guidelines that are meant only for the purposes of educating reporters on how to file an ADR report without addressing all issues related to pharmacovigilance in a country.
Potential interventions	Develop (or revise existing documents to make them into full-fledged) national guidelines for pharmacovigilance and medicine safety services.
Further information and references	Kingdom of Saudi Arabia, Saudi Food and Drug Authority, Drug Sector, Procedure for the SFDA on the undertaking of Pharmacovigilance activities, http://www.sfda.gov.sa/NR/rdonlyres/6C8CDBB2-730A-4A5B-8841-C9188BE30D03/0/PMSResponsibilities.pdf.

Indicator 2.8 (C)	**Existence of protocols or SOPs for improving patient safety related to medicine use**
Purpose:	To verify whether the pharmacovigilance center has standardized routine activities in standard operating procedures (SOPs)
Rationale and evidence:	Protocols and SOPs are critical in ensuring consistent quality in the provision of services and implementation of interventions to improve patient safety.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH, PHP, HF	MoH, NDA, PHP, HF	Directors or heads of NDA, Pharmacy Department, national or local pharmacovigilance center, and health facilities	1. Are SOPs present for pharmacovigilance activities? 2. Are the SOPs written and signed by relevant persons, documented, and officially adopted?	NDA, national or local pharmacovigilance center, and health facility documents	Check "**Yes**" if any formal protocols or SOPs exist for improving patient safety relating to medicine use.
Limitations		SOPs for reporting ADRs and other medicine safety–related duties may be included in other SOPs, such as pharmaceutical services dispensing SOPs or standard treatment guidelines.			
Potential interventions		Develop (or revise existing SOPs and protocols to make them into full-fledged) national SOPs for pharmacovigilance and medicine safety services.			

Indicator 2.9 (C)	**Existence of a minimum core list of communication technologies to improve access to safety reporting and provision of medicine information**
Purpose:	To confirm that communication technologies are in place to improve the provision of information and access to reporting (Minimum core list of communication technologies will be used.)
Rationale and evidence:	Communication technologies are important for a functional system that provides safety reporting and medicine information services. These technologies facilitate access to services and resources for the optimal and efficient functioning of a pharmacovigilance center.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH, PHP, HF	MoH, NDA, pharmacovigilance center, DIC, PHP, HF	Directors or heads of NDA, Pharmacy Department, and national or local pharmacovigilance center, DIC, PHP, HF	1. Are basic communication technologies available to facilitate safety reporting and provision of medicine information? 2. Are they functional and currently being used for safety reporting and provision of information?	Operating procedure documents of the pharmacovigilance center, DIC; review of information technology resources	Check "**Yes**" if the following are true— • Key informant confirms communication technologies are available. • Basic communication technologies are functional and currently in use compared to the *minimum core list for medicine information services* (example provided in annex 2).

Limitations	The procured resources may not contain the basic set referenced but may contain additional resources the center considers important to their duties.
Potential interventions	• Develop or revise existing core list of resources. • Provide support for the procurement of the resources that are lacking.
Further information and references	1. USP DQI. 2007. *Ensuring the Quality of Medicines in Resource-Limited Countries: An Operational Guide*. Rockville, MD: United States Pharmacopeia Convention. www.usp.org/worldwide/dqi/resources/technicalReports.

Indicator 2.10 (C)	**Existence of an ADR or medicine safety bulletin (or any other health-related newsletter that routinely features ADR or medicine safety issues) published in the last six months**
Purpose:	To confirm that a medicine information bulletin is currently being published
Rationale and evidence:	ADR or medicine information bulletins are used as a key communication tool for informing health care providers and consumers about significant medicine safety issues. Dedicated bulletins or other newsletters that include a regular feature on pharmacovigilance can cover and disseminate medicine safety information.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH, PHP, HF	MoH, NDA, pharmacovigilance center, PHP, HF	Directors or heads of NDA, Pharmacy Department, national or local pharmacovigilance center, PHP, HF	1. Does an ADR bulletin or a medicine information bulletin that regularly features pharmacovigilance topics exist? 2. Has the bulletin been published within the last six months?	Publications of NDA, national or local pharmacovigilance center, pharmaceutical services Last issue of the bulletin or newsletter	Check "**Yes**" if the following are true— • Key informant confirms the existence of a bulletin (stand alone or as part of another bulletin/newsletter that regularly addresses a pharmacovigilance-related subject). • The last edition/issue of the bulletin/newsletter was published within the last six months and included topic(s) relating to pharmacovigilance.

Limitations	The bulletin production cycle may not allow for clear determination that publication is routine.
Potential interventions	Develop or revise publication cycle and provide support for the enhancement of current publication.
Further information and references	1. *The Namibian Medicines Watch*, http://www.nmrc.com.na/Downloads/tabid/1350/language/en-US/Default.aspx.

Indicator 2.11 (S)	**Percentage of predefined core reference materials available in the medicine information or pharmacovigilance center**
Purpose:	To confirm that core resources for providing ADR and medicine safety–related information services are in place (A list of minimum resources for running such a center is used.)
Rationale and evidence:	Provision of medicine information including both proactive and query-response services is critical to ensure rational use of medicines. Medicine safety alerts and warnings can be communicated through the same channel that provides general medicine information services or through a center that is dedicated to pharmacovigilance. To provide up-to-date and accurate information, the center needs to have recent editions of at least a core set of reference materials.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH, PHP, HF	MoH, NDA, pharmacovigilance center, DIC, PHP, HF	Directors or heads of NDA, Pharmacy Department, national or local pharmacovigilance center, DIC, PHP, HF	Are basic reference materials and related resources available?	Resources present at the national or local pharmacovigilance center, DIC	Check "**Yes**" if the following are true— • Key informant confirms that ADR and medicine safety services are currently being provided. • Pharmacovigilance-related core reference materials are available and in use at the center that provides ADR and medicine safety information. • Using the *List of Basic DIC Resources* (example included in annex 2) as a checklist, identify which of these resources are available in the center. Express the recourses available in the center as percentage of the total number recommended in the list of basic DIC resources.

Limitations	Where no dedicated office exists for medicine information and pharmacovigilance services, the reference material may not be accessible at only one specific location or office.
Potential interventions	Develop or revise the existing inventory of reference materials to include the recommended all resources included in the basic list of DIC resources.
Further information and references	1. USP DQI. 2007. *Ensuring the Quality of Medicines in Resource-Limited Countries: An Operational Guide*. Rockville, MD: United States Pharmacopeia Convention. www.usp.org/worldwide/dqi/resources/technicalReports.

Indicator 2.12 (S)	**Percentage of predefined core pharmacovigilance topics present in the preservice training curricula (disaggregated by medicine, pharmacy, nursing, and public health curricula)**
Purpose:	To identify the extent of coverage of pharmacovigilance and medicine safety topics in training curricula for health professionals
Rationale and evidence:	Teaching pharmacovigilance and medicine safety in courses such as those in medicine, pharmacy, and nursing can help entrench the knowledge, skills, and competency among future health workers while they are still undergoing preservice training.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
Universities, health professionals' councils, and professional associations	Universities offering training courses for health professionals, health professionals' councils, pharmacovigilance center	Relevant authorities of universities and health professionals' councils; pharmacovigilance center staff	1. Is the pharmacovigilance and medicine safety curriculum taught in medical, pharmacy, and other related programs as a stand-alone unit or as part of the pharmacotherapy course? 2. What specific topics relating to pharmacovigilance and medicine safety are covered in the curriculum?	NDA, national pharmacovigilance center documents, medical/pharmacy university pharmacovigilance or pharmacotherapy curriculum	List of core topics in pharmacovigilance and medicine safety is provided. Check "**Yes**" if the following are true— • Key informant confirms pharmacovigilance topics are taught (a) current curriculum was reviewed and contains topics mentioned by the key informants. • Using the *List of Core Pharmacovigilance Topics* (b) (example included in annex 2), calculate value = (a)/(b) × 100. • More than 70% of the included topics are covered by the curriculum.

Limitations	Different aspects of the curriculum may be offered at different programs and schools.
Potential interventions	Develop or revise existing curriculum to include most parts of the list of core pharmacovigilance topics, and provide support for the adoption of these topics in health profession training programs.
Further information and references	1. Amin, A. A., L. Nzumbu, G. Tetteh, J. Pandit, S. Kangethe, and M. Thuo. 2008. *SPS Technical Assistance in the Development of a Pharmacovigilance Curriculum Package in Kenya: July–November 2008.* Submitted to the U.S. Agency for International Development by the Strengthening Pharmaceutical Systems (SPS) Program. Arlington, VA: Management Sciences for Health. http://pdf.usaid.gov/pdf_docs/PNADN945.pdf.

Indicator 2.13 (S)	**Number of health care providers trained on pharmacovigilance and medicine safety in the last year**
Purpose:	To determine the number of health care providers trained on pharmacovigilance within the last year
Rationale and evidence:	In-service trainings are important in advancing and maintaining appropriate knowledge and skills of health care workers. Because of the evolving nature of the medicine safety field, health care providers require regular and refresher continuing education on pharmacovigilance.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH, PHP, HF, training centers for health professionals, and professional associations	MoH, NDA, pharmacovigilance center, PHP, HF, training centers for health professionals, and professional associations	Directors or heads of NDA, Pharmacy Department, and national or local pharmacovigilance center, DIC, PHP, HF, and training centers for health professionals	How many health care professionals on staff have received training in pharmacovigilance in the last year?	Documents of NDA, pharmacovigilance center, and DIC; training reports of training centers for health professionals	• Enter value if key informant confirms that health care providers were trained and that the trainings attended were formal pharmacovigilance trainings. Value entered should be the number of staff members who underwent such trainings during the last two years. • Sample of health care workers can also be interviewed and "Percentage of health care workers sampled who have been trained" calculated. Enter "**Yes**" if more than 5% of professional health care workers (Physicians, Pharmacists, Nurses) have been trained in pharmacovigilance.

Limitations	This indicator can also be measured as "Percentage of health care workers sampled who have been trained." This alternative will require sampling health care workers. Staff members may have attended trainings that were not specifically planned as pharmacovigilance trainings but that may contain elements addressing toxicities, their management, and other safety -related issues of that PHP. A minimum of 5% is recommended as an acceptable value to ensure that this indicator is useful for advancing training in pharmacovigilance.
Potential interventions	Provide support for the training of health care workers on pharmacovigilance-related topics that were not covered in their previous trainings.
Further information and references	Ideally, all health care providers should be trained on pharmacovigilance. However, this is not realistic. No globally accepted threshold exists of the number of health care workers who should be trained in pharmacovigilance.

Indicator 2.14 (C)	**Platform or strategy exists for the coordination of pharmacovigilance activities at the national level**
Purpose:	To identify whether a platform exists for the coordination of pharmacovigilance activities across all stakeholders and players
Rationale and evidence:	Pharmacovigilance involves multiple stakeholders (e.g., health care providers, drug manufacturers and traders, consumers, drug regulatory authority, public health programs, donors and international bodies, academia and training institutes, professional associations). Proper coordination is required to ensure that no gaps exist and that communication and opportunities for leveraging resources are exploited. Where stakeholders are identified and their roles clearly spelled out, a greater opportunity exists for addressing all components of a medicine safety system.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH	MoH, NDA, pharmacovigilance center	Directors or heads of NDA, Pharmacy Department, PHPs, and pharmacovigilance center	Do you have a platform or a forum for coordination of pharmacovigilance activities across all stakeholders?	Documents of NDA and other relevant bodies	Check "**Yes**" if— • Key informant confirms that a formal platform (map of stakeholders, regular meetings, organogram or reporting lines, sharing of notes, etc.) exists for the coordination of pharmacovigilance activities. • A pharmacovigilance and medicine safety stakeholders' map is in place that describes what each partner does.
Limitations	This indicator may require further discussions in each country to agree on what defines coordination of activities beyond what has been recommended here.				
Potential interventions	Develop or revise stakeholders' map.				
Further information and references	1. Strengthening Pharmaceutical Systems (SPS). *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. http://www.msh.org/projects/sps/Pharmaceutical-Management/Pharmacovigilance.cfm.				

Indicator 2.15 (S)	**National pharmacovigilance center is a full or associate member of the WHO Collaborating Centre for International Drug Monitoring (UMC)**
Purpose:	To confirm that the national pharmacovigilance center participates in global international drug monitoring through the WHO/UMC Center
Rationale and evidence:	Participation in international drug monitoring activities and sharing of information will ensure that new safety alerts are shared and acted on in a timely and coordinated manner.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH	MoH, NDA, national pharmacovigilance center	Directors or heads of NDA, Pharmacy Department, and national pharmacovigilance center	1. Is the national pharmacovigilance center a full member or associate member of the WHO Collaborating Centre for International Drug Monitoring? 2. Is there documentation to show membership?	MoH memos; documents of NDA and national pharmacovigilance center	Check "**Yes**" if the following are true— • Key informant confirms that the national pharmacovigilance center is a full or associate member of WHO/UMC • Documentation exists to confirm such membership

Limitations	A country that remains an associate member for many years will achieve this indicator even though efforts are not being made to become a full member.
Potential interventions	Provide support for country preparations and application for full membership in the international drug monitoring program.
Further information and references	1. *The* Uppsala Monitoring Centre (*the* UMC), WHO Collaborating Centre for International Drug Monitoring. 2000. *Safety Monitoring of Medicinal Products: Guidelines for Setting Up and Running a Pharmacovigilance Centre.* Geneva: WHO. http://apps.who.int/medicinedocs/en/d/Jh2934e/.

Signal Generation and Data Management

Indicator 3.1 (C)	**Existence of a system for coordination and collation of pharmacovigilance data from all sources in the country (e.g., health programs, immunization program, active surveillance studies)**
Purpose:	To identify whether spontaneous ADR reports and other pharmacovigilance data from all sources are housed in the national pharmacovigilance center or some other coordinating location
Rationale and evidence:	Public health programs collect pharmacovigilance data, but most of the time these data are not processed further or transmitted to the pharmacovigilance center. This indicator determines the existence of efforts to coordinate pharmacovigilance data collection at one site on the national level.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH	MoH, NDA, national pharmacovigilance center	Directors or heads of HIV, TB, malaria, and immunization programs; NDA; Pharmacy Department; and national pharmacovigilance center	1. Does a system exist for the collation of all pharmacovigilance data from all sources, including the health programs, to one database at the national pharmacovigilance center or some other coordinating location? 2. Was this central database found to contain data transmitted from various sources, including PHPs?	NDA, national or local pharmacovigilance center documents; HIV, TB, malaria, and immunization program documents; database	Check "**Yes**" if the following are true— • Key informant confirmed that a system or strategy exists for collation of ADR and other pharmacovigilance data at the national pharmacovigilance center or some other coordinating location. • The central database was found to contain ADR and other pharmacovigilance data sent or obtained from various sources.
Limitations	Coordination of data from all sources may happen in a sporadic manner. This kind of instance should not be regarded as existence of a system for coordination of data, because it may have been done as a one-off to satisfy a need that arose.				
Potential interventions	Provide support to country to develop an ADR data warehouse that will contain disparate data from all sources.				
Further information and references	1. Strengthening Pharmaceutical Systems (SPS). *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. http://www.msh.org/projects/sps/Pharmaceutical-Management/Pharmacovigilance.cfm.				

Indicator 3.2 (C)	**Existence of a database for tracking pharmacovigilance activities**
Purpose:	To identify whether the pharmacovigilance center has developed a local database to track center activities and inventories
Rationale and evidence:	Pharmacovigilance centers that have access to the WHO web-based tool (VigiFlow) for submitting ADR reports to WHO/UMC. Centers may also require local databases for tracking center activities (e.g., publishing drug bulletin, trainings), for tracking workload (e.g., following up for missing data in an ADR form, replying to medicine safety information request), and for keeping inventory of center resources.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH	MoH, NDA, pharmacovigilance center	Directors or heads of NDA, Pharmacy Department, national or local pharmacovigilance center, PHP	1. Does a local database exist for tracking center activities and workload? 2. Is there any manual or electronic tool in use to facilitate center activities?	NDA documents, national or local pharmacovigilance center documents and database, other pertinent documents	Check "**Yes**" if a local database for tracking center activities was found to exist and to be in use.
Limitations		Some of the databases in use may be personal and not standardized or validated.			
Potential interventions		Provide support to the pharmacovigilance center to identify essential work processes that may require the use of a database, and provide those essential databases.			

Indicator 3.3 (C)	**Existence of a form for reporting suspected ADRs**
Purpose:	To confirm the existence of a form for collecting suspected ADR from health care workers and others as stipulated in the guidelines
Rationale and evidence:	An ADR form is critical for spontaneous reporting. This indicator identifies the existence of a form used for ADR reporting from health care professionals and MAHs. Stringent regulatory authorities require MAHs to develop written procedures for ADR reporting, including expedited reporting of serious ADRs and submission of periodic safety update reports. This indicator identifies whether ADR forms are available for routine reporting from health care professionals and MAHs.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH, pharmaceutical companies, PHP, HF	MoH, NDA, pharmacovigilance center, pharmaceutical companies, PHP, HF	Directors or heads of NDA, Pharmacy Department, and national or local pharmacovigilance center, pharmaceutical companies, PHP, HF	1. Does a form exist for spontaneous reporting of suspected ADRs? 2. Was a copy of the ADR form presented?	MRSCA and related laws and regulations, NDA documents, national or local pharmacovigilance center establishing documents Sample of ADR reports sent to the national or local pharmacovigilance center	Enter "**Yes**" if the following are true— • Key informant confirms that ADR forms are readily available at known locations for health workers. • ADR forms were found to be available when these locations were visited.

Limitations	Confirmation that ADR forms exist and are used routinely is better verified through health facility audits to observe the forms being used.
Potential interventions	Provide support to develop or revise the ADR form to ensure that it is consistent with international standards.
Further information and references	1. FDA, MedWatch Online Voluntary Reporting Form, https://www.accessdata.fda.gov/scripts/medwatch/. 2. Namibia Medicines Regulatory Council, Adverse Medicine reaction reporting form, http://www.nmrc.com.na/PVSystem/FormforHCW/tabid/1348/language/en-US/Default.aspx. 3. Kenya Pharmacy & Poisons Board, Reporting a Suspected Adverse Drug Reaction, http://www.pharmacyboardkenya.org/index.php?id=46.

Indicator 3.4 (C)	**Existence of a form for reporting suspected product quality issues (as a subset in the ADR form or as a separate form)**
Purpose:	To confirm the existence of a separate form or a field in the regular ADR form for recording suspected product quality problems by health care workers and other stakeholders
Rationale and evidence:	The monitoring of product quality can be enhanced by spontaneous reporting. Fields for product quality can be included in the standard ADR form, or a special form can be developed for this purpose.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH, pharmaceutical companies, PHP, HF	MoH, NDA, pharmacovigilance center, pharmaceutical companies, PHP, HF	Directors or heads of NDA, Pharmacy Department, national or local pharmacovigilance center, pharmaceutical companies, PHP, HF	1. Does a separate form or subset of a regular ADR form exist for reporting suspected poor product quality problems? 2. Was a copy of such a form presented?	MRSCA and related laws and regulations, NDA documents, national or local pharmacovigilance center documents Sample of product quality reports sent to the national or local pharmacovigilance center	Enter "**Yes**" if the following are true— • Key informant confirms that a separate product quality form or the regular ADR form with a field for reporting product quality problems is readily available at known locations for health workers. • This form was found to be available when these locations were visited.
Limitations		In some countries, the difference between consumer product quality reporting forms and those used by inspectors may not be clear.			
Potential interventions		Provide support to develop a product quality complaint form or to include fields on product quality in the general ADR form.			
Further information and references		1. FDA, Drug Quality Reporting System, http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm082071.htm.			

Indicator 3.5 (C)	**Existence of a form for reporting suspected medication errors (as a subset in the ADR form or as a separate form)**
Purpose:	To confirm the existence of a form or a field in the regular ADR form for recording medication error information from health care workers and other stakeholders
Rationale and evidence:	Medication errors are preventable and can cause patient harm. The monitoring of suspected medication error can be enhanced by spontaneous reporting. Fields for medication error can be included in the standard ADR form, or a special form can be developed for this purpose.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH, pharmaceutical companies, PHP, HF	MoH, NDA, pharmacovigilance center, pharmaceutical companies, PHP, HF	Directors or heads of NDA, Pharmacy Department, national or local pharmacovigilance center, pharmaceutical companies, PHP, HF	1. Does a separate form or a subset of the regular ADR form exist for reporting medication error? 2. Was a copy of such form presented?	MRSCA and related laws and regulations, NDA documents, national or local pharmacovigilance center documents Sample of medication error reports sent to the national or local pharmacovigilance center	Enter "**Yes**" if the following are true— • Key informant confirms that a separate medication error form or the regular ADR form with a field for reporting medication error is readily available at known locations for health workers. • Such a form was found to be available when these locations were visited.
Limitations		Medication error reporting may be part of sentinel event monitoring or a quality assurance program; data collectors should recognize this and interview these units.			
Potential interventions		Provide support to develop a medication error form or to include fields on medication error in the general ADR form.			
Further information and references		1. National Coordinating Council for Medication Error Reporting and Prevention website, http://www.nccmerp.org/. 2. Institute for Safe Medication Practices website, http://www.ismp.org/default.asp.			

Indicator 3.6 (C)	**Existence of a form for reporting suspected treatment failure (as a subset in the ADR form or as a separate form)**
Purpose:	To confirm the existence of a separate form or a field in the regular ADR form for recording suspected treatment failure from health care workers and other stakeholders
Rationale and evidence:	Monitoring of treatment failure can be enhanced by spontaneous reporting. Fields for treatment failure can be included in the standard ADR form, or a special form can be developed for this purpose.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH, PHP, pharmaceutical companies, HF	MoH, NDA, pharmacovigilance center, pharmaceutical companies, PHP, HF	Directors or heads of NDA, Pharmacy Department, and national or local pharmacovigilance center; pharmaceutical companies; PHP; HF	1. Does a form or subset of a regular ADR form exist for reporting suspected treatment failure? 2. Was a copy of such form presented?	MRSCA and related laws and regulations, NDA documents, national or local pharmacovigilance center documents Sample of suspected treatment failure reports sent to the pharmacovigilance center	Enter "**Yes**" if the following are true— • Key informant confirms that treatment failure recording form or a regular ADR form with a defined field for reporting suspected treatment failure is readily available at known locations for health workers. • Such a form was found to be available when these locations were visited.
Limitations		Therapeutic ineffectiveness or treatment failure may already be reported in patient case files. During data collection, records must be reviewed to see if a specific field exists for reporting reasons for treatment switches or treatment failure specifically.			
Potential interventions		Provide support to develop treatment failure form or to include fields on treatment failure in the general ADR form or in the patient case file.			
Further information and references		1. Meyboom, R. H., M. Lindquist, A. K. Flygare, C. Biriell, and I. R. Edwards. 2000. The value of reporting therapeutic ineffectiveness as an adverse drug reaction. *Drug Safety: An International Journal of Medical Toxicology and Drug Experience* 23(2):95–9.			

Risk Assessment and Evaluation

Indicator 4.1 (S)	**Number of medicine utilization reviews carried out in the last year**
Purpose:	To identify whether drug distribution and consumption data is collected, aggregated, and used to improve medicine safety and rational use
Rationale and evidence:	Medicine use evaluations are criteria-based programs to enhance appropriate medicine use that obtain information to identify problems and provide means of correcting those problems. This indicator tries to find out if a medicine utilization review study or a drug use survey has been carried out within the last year.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH, PHP, HF	MoH, PHP, HF	Directors or heads of NDA, Pharmacy Department, pharmacovigilance center, DIC, PHP, and HF; chairperson or secretary of sampled DTCs	1. Has a medicine utilization review study and/or a drug use survey been carried out in the last year? 2. Was a report of the medicine utilization review study circulated or published?	Documents of NDA, Central Medical Stores (CMS), Pharmacy Department, and pharmacovigilance or drug information center	Check "**Yes**" if the following are true— • A medicine utilization review/study or a drug use survey has been carried out in the last year. • Report of the study was circulated or published.

Limitations	Challenges exist in determining what to regard as a medicine utilization study, medicine use survey, and medicine utilization evaluation.
Potential interventions	• Provide support for the development of protocols for the initiation of medicine utilization evaluation studies. • Provide support for the implementation of the protocol.
Further information and references	1. Rational Pharmaceutical Management. 1997. *Guidelines for Implementing Drug Utilization Review Programs in Hospitals.* Arlington, VA: Management Sciences for Health. http://erc.msh.org/mainpage.cfm?file=2.6.1.htm&language=english&module=drugs. 2. National Prescribing Service Limited. NPS drug use evaluation (DUE) programs. http://www.nps.org.au/health_professionals/drug_use_evaluation_due_programs.

Indicator 4.2 (S)	**Pharmaceutical product quality survey conducted within the last five years**
Purpose:	To identify whether periodic survey of product quality is carried out
Rationale and evidence:	A survey to determine the quality of pharmaceutical products in circulation can provide valuable information on the prevalence of poor-quality products and can be the first signal to guide efforts at targeted evaluation of the source of the problem and the design of interventions.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH, PHP	MoH, NDA, quality surveillance laboratory (QSL), pharmacovigilance center, PHP	Directors or heads of NDA, QSL, Pharmacy Department, pharmacovigilance center, PHP	1. Has a survey on the quality of health products in circulation in the country been carried out in the last 5 years? 2. Was a report generated on the result of the survey?	Documents of NDA, QSL, and CMS and other relevant bodies	Check "**Yes**" if the following are true— • Key informants reports that a product quality survey has been carried out in the last 5 years. • A report of the survey was generated and is available for review.

Limitations	Determining the quality of the survey may be challenging.
Potential interventions	Provide support for developing a survey protocol for assessment of in-country product quality.
Further information and references	1. USP DQI. 2007. *Ensuring the Quality of Medicines in Resource-Limited Countries: An Operational Guide*. Rockville, MD: United States Pharmacopeia Convention. www.usp.org/worldwide/dqi/resources/technicalReports.

Indicator 4.3 (S)	**Incidence of medication errors quantified in the last year**
Purpose:	To identify the incidence of medication errors in the last year
Rationale and evidence:	It is estimated that 70 percent of all ADRs are possibly preventable. When the prevalence of preventable ADRs is known, interventions can be developed to reduce them.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH, PHP, HF	MoH, NDA, pharmacovigilance center, DIC, PHP, HF, DTC	Directors or heads of NDA, Pharmacy Department, national or local pharmacovigilance center, DIC, PHP, HF, DTC	Has a study been done in the last year to determine the level of medication errors?	Documents of NDA, PHP, pharmacovigilance center, DIC, and other relevant bodies; study reports	Check "**Yes**" if the following are true— • Key informants report that a survey of the incidence of medication error has been carried out in the last year. • A report of the survey was generated and is available for review.

Limitations	Formal studies may not be conducted; hospital managers may provide numbers that may not have proper documentation. During data collection, consensus must be reached on the level of documentation that is required for this indicator.
Potential interventions	Provide support for the development of a survey protocol for assessment of in-country incidence of medication errors.
Further information and references	1. Institute for Safe Medication Practices. ISMP Self-Assessments, http://www.ismp.org/selfassessments/default.asp.

Indicator 4.4 (C)	**Number of ADR reports received in the last year**
Purpose:	To identify the number of ADR reports received by the center in the last year
Rationale and evidence:	Spontaneous reporting is very important for obtaining safety signals and for hypothesis generation. This indicator identifies the number of reports that have been submitted to the pharmacovigilance center in the last year.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH, pharmaceutical companies, PHP, HF	MoH, NDA, national or local pharmacovigilance center, pharmaceutical companies, PHP, HF	Directors or heads of NDA, Pharmacy Department, pharmacovigilance center, pharmaceutical companies, and DIC	1. What is the number of ADR reports received in the last year? 2. Are these reports complete and committed to ADR databases?	Documents of NDA, and pharmacovigilance center ADR report register or database	Check "**Yes**" if any of the following is true— • Key informant shows a register for documenting the ADR reports that are received by the center. • There is a minimum of 100 reports per million population per year
Limitations	Some of the reports received may not be complete and may not have been entered in the register or database.				
Potential interventions	Develop strategies for improving spontaneous reporting.				
Further information and references	Several thresholds have been proposed; however, no consensus exists on the minimum acceptable number of reports per year from a country to demonstrate a minimally functional pharmacovigilance system.				

Indicator 4.5 (C)	**Number of active surveillance activities currently ongoing or carried out in the last five years**
Purpose:	To identify if whether active surveillance studies and related activities have been initiated or conducted within the last five years
Rationale and evidence:	Active surveillance studies such as cohort event monitoring, prescription event monitoring, and pregnancy exposure registry may be going on in a country as a result of the regulatory requirements for introducing a new medicine or in an effort to address unresolved safety concerns, for example, safety in pregnancy.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH, pharmaceutical companies, PHP, HF	MoH; NDA; pharmacovigilance center; HIV, TB, malaria, and immunization programs; pharmaceutical companies; HFs	Directors or heads of NDA; Pharmacy Department; HIV, TB, malaria, and immunization programs; pharmacovigilance center; pharmaceutical companies; F	1. Has any active surveillance study been initiated or carried out in the last five years? 2. Does any documentation report on ongoing or completed active surveillance studies?	Documents of NDA; Pharmacy Department; HIV, TB, malaria, and immunization programs; and pharmacovigilance center	Enter value if the following are true— • Key informant confirms that active surveillance activities have been carried out within the last five years. • Documentation exists of the completed or ongoing active surveillance activities. Document the number of such activities. Enter "**Yes**" if at least one active surveillance study is currently ongoing or was completed in the last five years.

Limitations	Studies for this indicator should be formal active surveillance studies that have protocols and were approved by in-country authorities.
Potential interventions	Provide support for the initiation of active surveillance activities.
Further information and references	1. International Society of Pharmacoepidemiology (ISPE) Commentary. 2008. Guidelines for good pharmacoepidemiology practices (GPP). *Pharmacoepidemiology and Drug Safety* 17: 200–8. http://www.pharmacoepi.org/resources/ispe_guidelines_2008.pdf.

Indicator 4.6 (C)	**Percentage of patients in public health programs for whom drug-related adverse events were reported in the last year (disaggregated by type of adverse event, drug, severity, outcomes, and demographics)**
Purpose:	To determine the proportion of the population exposed to medicines by the public health programs that experienced drug-related adverse events
Rationale and evidence:	Public health programs such as HIV/AIDS, TB, malaria, and the Expanded Program on Immunization should be able to document the proportion of patients who experienced drug-related adverse events compared to the total number of patients who were exposed to the medicine. This indicator presumes at least 1 percent of patients in mass treatment programs will experience some form of adverse event. If that much is not recorded, adverse event documentation can be assumed to be suboptimal.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
PHP, HF	PHP, pharmacovigilance center, HF	Directors and managers of public health programs; chairperson or secretary of the sampled DTCs	1. Do you document patients who experience drug-related adverse events? 2. Among all patients treated in the last year, what percentage experienced adverse events?	PHP, pharmacovigilance center, and HF records	Denominator is the total number of patients who underwent treatment within the public health program in the last year (a). Transcribe the number of PHP patients who had drug-related adverse events in the last year (b). Enter a value: (b)/(a) × 100 Enter "**Yes**," if the result is 1% and above.

Limitations	Data may be contained in individual patient files but not collated nationally.
Potential interventions	Provide support for the development of a system for reporting, collating, and aggregating adverse event data from mass treatment programs
Further information and references	1. WHO. 2006. *The Safety of Medicines in Public Health Programmes: Pharmacovigilance an Essential Tool*. Geneva: WHO. http://apps.who.int/medicinedocs/documents/s14085e/s14085e.pdf.

Indicator 4.7 (C)	**Percentage of patients undergoing treatment within a public health program whose treatment was modified because of treatment failure or ADRs in the last year (disaggregated by treatment failure and ADRs)**
Purpose:	To determine the proportion of patients whose treatment was modified because of treatment failure or ADR
Rationale and evidence:	Public health programs such as HIV/AIDS, TB, malaria, and the Expanded Program on Immunization should be able to document patients who experienced treatment failure and adverse events compared to the total number of patients exposed to the medicine. Because toxicity or treatment failure–related switches surely occur in PHPs, no documentation shows a weak pharmacovigilance system rather than no event.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH, PHP, HF	MoH, PHP, HF	Directors and managers of public health programs; chairperson or secretary of sampled DTCs	1. Do you document patients who had treatment failure or ADR? 2. What percentage of the patients treated in the last year had treatment failure or ADR?	Health facility patient records and guidelines	Denominator is the total number of patients treated within the public health program in the last year (a). Transcribe the number of patients whose treatment was modified because of treatment failure or ADR (b). Enter a value: (b)/(a) × 100 Enter "**Yes**," if the result is more than 1%.

Limitations	Data may be contained in individual patient files but not collated nationally.
Potential interventions	Provide support for the development of a system for reporting, collating, and aggregating toxicity and treatment failure–related switches.
Further information and references	1. WHO. 2006. *The Safety of Medicines in Public Health Programmes: Pharmacovigilance an Essential Tool*. Geneva: WHO. http://apps.who.int/medicinedocs/documents/s14085e/s14085e.pdf.

Indicator 4.8 (S)	**Percentage of patients in public health programs for whom drug-related, serious "unexpected adverse events" were reported in the last year**
Purpose:	To determine the number of patients who experienced previously unknown and new adverse drug events
Rationale and evidence:	Previously unknown and serious adverse events should be reported, and their causality to the medicine the patient was exposed to needs to be determined. ICH defines serious ADRs as any untoward medical occurrence at any dose that results in death, is life threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability or incapacity, or is a congenital anomaly or birth defect.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH, PHP, HF	MoH, PHP, HF	Directors and managers of public health programs; chairperson or secretary of sampled DTCs	1. Do you document patients who experienced new, unknown adverse events? 2. How many patients experienced such new and serious unknown adverse events in the last year?	PHP records and health facility patient records	Check if the public health program has a register or documentation that includes recording of new, unknown adverse drug events. Identify from the records the number of patients who had serious "unexpected adverse events" in the last year. Enter "**Yes**" if this is routinely documented (It is expected that the computed value may range from 0 to 0.1% unexpected and previously unknown serious adverse events in the treated population.)

Limitations	Unexpected events may be lumped into all other reports received by the pharmacovigilance center.
Potential interventions	Develop a protocol to build the capacity of the pharmacovigilance center for determining "expectedness" and requirements for expedited reporting of serious adverse events.
Further information and references	Unusual ADRs may occur at a frequency of less than 0.1%; however, any report documented may be an indication that efforts are made to monitor for such events. 1. ICH. 1994. Clinical safety data management: Definitions and standards for expedited reporting E2A. http://www.ich.org/LOB/media/MEDIA436.pdf. 2. ICH. 2003. ICH Harmonised Tripartite Guideline: Post-Approval Safety Data Management: Definitions and Standards for Expedited Reporting E2D. http://www.ich.org/LOB/media/MEDIA631.pdf.

Risk Management and Communication

Indicator 5.1 (S)	**Risk mitigation plans currently in place that are targeted at high-risk medicines**
Purpose:	To identify whether risk management plans (either formal ones or in the form of restricted prescription rights) exist or are planned for high-risk products
Rationale and evidence:	The U.S. Institute of Medicine estimates that at least 1.5 million preventable adverse drug events occur within the health system each year.[1] The majority of ADRs can be prevented when clear plans exist for avoiding serious known risks of medicine. Some medicines are considered as high-alert or high-risk agents[2] because they bear heightened risk of causing significant patient harm when used in error. This indicator tries to identify whether any efforts are made from the national level or from the hospital management level (or DTC) to mitigate the impact of high-risk medicines.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH, PHP, HF	NDA, Pharmacy Department, PHP, HF, DTC	Directors or heads of NDA and Pharmacy Department; chairperson or secretary of DTC	1. Is any form of effort made to control the use of high-risk medicines because of concerns about their safety when used incorrectly?	MRSCA, pharmaceutical laws and regulations, MoH memos; DTC work plans and meeting notes	Check "**Yes**" if the following is true— Key informant confirms that plan exists to mitigate or restrict or supervise the use of high-risk medicines because of safety concerns.
			2. What are the existing and proposed activities to mitigate risk of such high-risk medicines?	Pharmacy Department's practices for the release of high-risk medicines; other related hospital documents	Confirm that the plan is documented in writing and that it has been put into action.

Limitations	Obtaining documentation to ensure that some risk mitigation practices are standard may be a challenge.
Potential interventions	Provide support for the development or revision of existing risk mitigation plans into consolidated and standardized procedures that are widely implemented.
Further information and references	1. Institute of Medicine of the National Academies. 2007. *Preventing Medication Errors. Washington, DC:* National Academies Press. 2. Institute for Safe Medication Practices. ISMP's List of High-Alert Medications. http://www.ismp.org/Tools/highalertmedications.pdf.

Indicator 5.2 (S)	**Prequalification schemes (e.g., WHO prequalification program and Pharmaceutical Inspection Co-operation Scheme) used in medicine procurement decisions**
Purpose:	To identify whether opportunities provided by internationally recognized authorities, such as the WHO through the prequalification program and the Pharmaceutical Inspection Cooperation Scheme (PIC/S), are used to inform procurement of quality and safe products
Rationale and evidence:	When countries lack the capacity for manufacturing site inspection and for determining the quality of products they intend to procure, they can rely on prequalification certification issued by internationally recognized authorities such as the WHO through the prequalification program and the PIC/S.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH, PHP	MoH, NDA, QSL, PHP	Directors or heads of NDA, QSL, Pharmacy Department, and PHP; also HFs if they procure commodities directly	1. Are prequalification reports from WHO and PIC/S considered prior to procurement? 2. Does the procurement policy stipulate that prequalification reports should be used to guide procurement?	NDA, QSL, CMS, and PHP documents Compare latest procurement with WHO list of prequalified medicines and suppliers	Check "**Yes**" if the following are true— • Key informants confirm prequalification reports are used. • Procurement policy or guidelines recommend prequalification to complement site inspections. • In the last procurement, manufacturing sites and suppliers that were not inspected were preapproved because the manufacturing site or the product is prequalified by the WHO and/or PIC/S.

Limitations	Countries may include these considerations in their procurement decisions without necessarily having a formal procurement policy that clearly states that prequalification must be considered. If health facilities procure medicines directly, then this indicator can also be used.
Potential interventions	Provide support to review registration and procurement policy processes to ensure that use of prequalification is included and used for improving regulatory and procurement decisions.
Further information and references	1. WHO prequalification program website, http://apps.who.int/prequal/default.htm. 2. Pharmaceutical Inspection Co-operation Scheme website, http://www.picscheme.org/pics.php. 3. FDA/PEPFAR tentatively approved ARVs, http://www.fda.gov/internationalprograms/fdabeyondourbordersforeignoffices/asiaandafrica/ucm119231.htm.

Indicator 5.3 (S)	**Number of medicine safety information requests received and addressed in the last year**
Purpose:	To identify the number of medicine information requests received and addressed by the pharmacovigilance center in the last year
Rationale and evidence:	User satisfaction increases and confidence in the pharmacovigilance center improves when ADR or medicine safety information requests from clients are processed and responded to in a timely manner. This indicator gives a general idea about the use of the available service and the center's responsiveness. A number of 100 requests per million population per year has been recommended as a threshold for a minimally functional center.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH, PHP, HF	MoH, NDA, Pharmacovigilance Center, Drug Information Center, PHP, HF	Directors or heads of NDA, Pharmacy Department, national or local pharmacovigilance center, Drug Information Center, PHP, HF	1. What is the number of pharmacovigilance-related information requests received in the last year? 2. How many of these requests were addressed?	Documents of NDA, national or local pharmacovigilance center, Drug Information Center Register or database	Enter value if the following are true— • Key informant provides the number of pharmacovigilance-related information requests received in the last year. • Check the number of requests that were addressed and logged. • Enter "**Yes**" if 100 requests per million population received per year.

Limitations	During data collection, it should be ensured that formally documented information requests that were formally responded to and documentation of response can be counted.
Potential interventions	• Provide support for the development of a tracking system for documenting information requests and the responses. • Provide support for the development of strategies for improving subscription to the services of the center by health care workers, patients, and the public.
Further information and references	1. Therapeutics information and pharmacovigilance center: Namibia's approach to monitoring medicines safety, PowerPoint presentation, http://www.hivimplementers.com/pdfs/Session%2057/57_2078_Nwokike.pdf. 2. Shankar, R., et al. The drug information center at the Manipal teaching hospital—going beyond drug information. http://www.nxtbook.com/nxtbooks/dia/druginformationjournal1107/index.php?startpage=88&qs=Drug+information+centers.

Indicator 5.4 (S)	**Percentage of planned issues of the medicine safety bulletin (or any other health-related newsletter that routinely features ADR or medicine safety issues) published in the last year**
Purpose:	To identify whether regular issues of the bulletin are produced as originally planned
Rationale and evidence:	Many medicine information and pharmacovigilance centers may be able to initiate a drug bulletin, but most experience challenges in the longer run in meeting their publication schedules and at times completely cease publishing due to various constraints. This indicator helps track whether the bulletin is appearing as planned. For a bulletin or newsletter to be considered minimally functional, this tool recommends that at least 70 percent of planned issues must be published.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH	MoH, NDA, pharmacovigilance center, DIC	Directors or heads of NDA, Pharmacy Department, national pharmacovigilance center, DIC	1. What is the planned frequency of publication of the bulletin (dedicated solely to pharmacovigilance or including a regular feature on topics relating to pharmacovigilance)? 2. What percentage of the planned issues was actually published in the last year?	Work-plans and establishing documents for the DIC and national or local pharmacovigilance center; published bulletins	Enter value if the following is true— • Key informant provides confirmation that a publication schedule exists for the bulletin (dedicated solely to pharmacovigilance or including a regular feature on topics relating to pharmacovigilance). Check for issues of the bulletin published within the last year— • Compute the value as follows: (Number of issues published in the last year/Total number of issues planned for publication in the last year) ×100. • Enter "**Yes**" if result is more than 70%.

Limitations	The publication schedule may be so far spread out that assessment always turns up 100 percent; for instance, bulletins that are scheduled to be published only once a year.
Potential interventions	• Provide support to identify factors associated with failure to publish planned issues. • Provide technical assistance to establish a realistic publication schedule and improve the efficiency of the bulletin.
Further information and references	1. International Society of Drug Bulletins and WHO. 2005. *Starting or Strengthening a Drug Bulletin: A Practical Manual*. http://apps.who.int/medicinedocs/en/d/Js8111e/3.html. 2. *The Namibian Medicines Watch,* http://www.nmrc.com.na/Downloads/tabid/1350/language/en-US/Default.aspx.

Indicator 5.5 (S)	**Number of medicine safety issues of local relevance identified from outside sources (e.g., from another country, or from regional or international sources) and acted on locally in the last year**
Purpose:	To identify whether medicine safety issues of local relevance that are identified from outside sources, such as through global safety literature scanning, stimulate any form of local attention and plans for further evaluation
Rationale and evidence:	When a medicine safety issue of local relevance is identified through outside sources, such information provides an alert that should be further studied or acted on to ensure that related experiences from other places are used for improving local safety. Ideally, all global safety alerts of local relevance should be acted on (regulatory decision, communicated to health care workers, etc.); however, this tool recommends that at least 70 percent of such alerts should be communicated by a minimally functional system.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH, PHP, HF	MoH, NDA, pharmacovigilance center, DIC, PHP, HF	Directors or heads of NDA, Pharmacy Department, national or local pharmacovigilance center, DIC	1. Is a system in place for monitoring for new safety reports from outside sources? 2. How many medicine safety issues of local relevance identified from outside sources were acted on locally in the last year?	NDA and pharmacovigilance center activity reports; DIC activity reports; other relevant documents	Enter value if the following are true— • Key informant confirms that a system exists for monitoring new safety reports from outside sources. • A register or some other form of documentation exists that confirms the type and number of actions or steps taken locally to address the safety issues in the last year. • Compute the value as follows— o Make a *list of safety alerts from FDA/EMEA in the last year.* o Using this list as a checklist, identify the number of safety alert actions taken by local bodies in the last year. o (Number of safety alerts acted on locally/Total number of relevant alerts in the last year) × 100 • Enter "**Yes**" if the result is more than 70%.

Limitations	Poor documentation of previous actions may hinder data collection.
Potential interventions	Provide support for the development of a system for routine scanning of global safety literature and establish how to communicate such alerts to regulators and consumers.
Further information and references	The conditions for the determination that such a safety alert is of local relevance includes that the medicine or health product involved in the safety alert is registered in the country and in the national essential medicines list. Publication of such safety alerts in the medicine information and pharmacovigilance bulletin is also acceptable evidence that the alert was acted on locally. 1. *The Namibian Medicines Watch,* http://www.nmrc.com.na/Downloads/tabid/1350/language/en-US/Default.aspx.

Indicator 5.6 (S)	**Number of "Dear health care professional" letters or other safety alerts developed and distributed in the last year**
Purpose:	To identify whether and how many regulatory alert letters were sent out in the last year (Distribution can be confirmed through review of documents.)
Rationale and evidence:	When new medicine safety issues arise either from spontaneous reports or from global safety literature scanning, relevant information and alert letters should immediately be sent to health care professionals to alert them of the safety concerns. Ideally, such alerts should be sent for all essential medicines in the country's essential medicines list. This tool recommends a threshold of 70 percent for a minimally functional system.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH, PHP, HF	MoH, NDA, Pharmacy Department, PHP, pharmacovigilance center, DIC, HF, DTC	Directors or heads of NDA, Pharmacy Department, pharmacovigilance center, DIC, DTC	1. How many "Dear Health care professional" letters or any other type of regulatory safety alert letters were developed and distributed in the last year?	NDA and pharmacovigilance center documents, MoH memos	Enter number of letters if both of the following are true— • Key informants confirm that regulatory alert letters were sent to health care professionals within the last year • Find and verify the number of such alerts sent in the last year. (A *list of regulatory alert letters from FDA/EMEA in the last year concerning products that are registered in-country* can be used to benchmark the need for regulatory safety alert letters.)
			2. Is the inventory of the regulatory alert letters and the distribution list available for review?	Inventory of official communications from NDA, pharmacovigilance center, or DTC to health care professionals	Enter "**Yes**" if 70% of alerts for medicines in the essential medicines list had "Dear health care professional" letter.

Limitations	Other communications and memos within the MoH or the health facility may be regarded as a "Dear Health Professional" letter.
Potential interventions	Provide support for the development or revision of a standard format and strategy for the communication of "Dear Health Care Professional" letters.
Further information and references	1. U.S. Food and Drug Administration. MedWatch: The FDA Safety Information and Adverse Event Reporting Program, http://www.fda.gov/Safety/MedWatch/default.htm. 2. U.S. Food and Drug Administration. FDA Patient Safety News, http://www.fda.gov/psn.

Indicator 5.7 (C)	**Average time lag between identification of safety signal of a serious ADR or significant medicine safety issue and communication to health care workers and the public**
Purpose:	To identify how fast serious ADR signals and significant safety issues are communicated to health care workers and to the public
Rationale and evidence:	New signals of serious ADR or significant safety issues should be communicated to health care workers and the public as soon as the signals are generated. Safety signals and significant safety issues can be generated either locally or through scanning the global literature for safety reports. Once these reports are obtained, locally relevant ones that are significant to in-country clinical practice and public health should be immediately communicated to health workers and the public. This indicator helps determine how fast such reports are communicated. The tool recommends that such communications should happen within three weeks of the publication of that alert in global literature.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH	MoH, NDA, pharmacovigilance center, DIC	Directors or heads of NDA, Pharmacy Department, pharmacovigilance center, DIC	1. Are safety signals and significant safety issues promptly communicated to health workers and the public? 2. How long does it usually take from when a safety signal or significant safety issue is identified to when it is communicated to the health workers and the public?	NDA, MoH memos; pharmacovigilance center documents; drug information bulletin and related publications; ADR register; relevant documents	Enter value if the following are true— • Key informant confirms that safety signals and significant safety issues are promptly communicated to health workers. • A register or some other form of documentation of safety signals or medicine safety updates with dates is available. Compute the value as follows— • Using a *list of recent safety warnings* with dates, identify when in-country warnings were communicated. • (Average time lag from receipt to communication of safety report/Total number of reports communicated) × 100 • Enter "**Yes**" if 70% of all locally relevant safety warnings were communicated within three weeks.
Limitations	It may be challenging to obtain data on when the safety signal was published and when it was communicated locally.				
Potential interventions	Provide support for the development of a system for routine scanning of global safety literature and establish how to track when such safety issues have been communicated locally.				
Further information and references	1. U.S. Food and Drug Administration. MedWatch: The FDA Safety Information and Adverse Event Reporting Program, http://www.fda.gov/Safety/MedWatch/default.htm.				

Indicator 5.8 (C)	**Percentage of the sampled Drug and Therapeutics Committees that have carried out pharmacovigilance activities or addressed medicine safety issues in the last year**
Purpose:	To identify how much of DTC activities address safety of medicines
Rationale and evidence:	Drug and Therapeutic Committees are critical for implementing efforts to improve medicine safety within health facilities. Interventions designed to improve medicine safety should include the participation of DTCs in the area. DTCs should have medicine safety as part of their terms of reference, and all DTCs ideally should carry out pharmacovigilance-related activities. The tool recommends that at least 70 percent of DTCs should address pharmacovigilance.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
HF DTCs	HF DTCs	Chairperson or secretary of sampled DTCs	1. Within the last year, has the DTC carried out pharmacovigilance activities or addressed medicine safety issues? 2. Does documentation exist to show the number of DTC meetings or activities that addressed medicine safety issues?	Meeting notes of sampled DTCs; pharmacovigilance or drug information center documents; PHP activity reports	Determine the number of HF DTCs to be interviewed through sampling (a). Enter a value if the following are true— • Through key informant interviews and document verification, identify the number of DTCs that carried out pharmacovigilance-related activities or addressed medicine safety issues within the last year (b). • Compute the of [(b)/(a)] × 100. • Enter "**Yes**" if 70% of DTCs have carried out pharmacovigilance activities in the last year.

Limitations	Some DTC safety-related activities may not be well documented.
Potential interventions	• Provide support for the development or revision of the terms of reference of DTCs to ensure that pharmacovigilance and medicine safety activities are included and highlighted. • Develop strategies for training DTCs on how to identify and develop interventions to address medicine safety issues within their health facilities.
Further information and references	1. Strengthening Pharmaceutical Systems (SPS). *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. http://www.msh.org/projects/sps/Pharmaceutical-Management/Pharmacovigilance.cfm.

Indicator 5.9 (S)	**Number of public or community education activities relating to medicine safety carried out in the last year**
Purpose:	To determine the number of medicine safety–related public and community education activities carried out within the last year
Rationale and evidence:	Public health education on medicine safety is important to ensure patients and caregivers are well informed on safety and effectiveness of the medicines they use. At least one formal community education activity on medicine safety should be carried out every year. Examples of community education activities include community drug safety campaigns, radio talk shows, public health outreach campaigns, and other outreach programs.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH, PHP, HF	MoH, NDA, national pharmacovigilance center, PHP, HF, consumer-related nongovernmental organizations or associations	Directors or heads of NDA, Pharmacy Department, pharmacovigilance center, DIC, PHP, HF, nongovernmental organizations, and consumer associations	How many public and community education activities on ADRs and medicine safety topics have been carried out in the last year?	Documents of NDA, pharmacovigilance center, and DIC; training reports	Enter value if the following are true— • Key informant confirms public or community education activities on ADR and medicine safety topics were carried out in the last year. • Evidence of those activities was provided. Enter "**Yes**" if at least one community education activity was carried out.

Limitations	Some challenges could arise in establishing that the community education activity was planned to formally address medicine safety–related issues.
Potential interventions	Provide support for the development and piloting of a medicine safety community education event.
Further information and references	1. National Prescribing Service Limited. NPS health promotion campaigns. http://www.nps.org.au/news_and_media/campaigns.

Indicator 5.10 (C)	**Percentage of medicines sampled in the last year that passed product quality tests**
Purpose:	To determine the extent of problems in product quality
Rationale and evidence:	When poor-quality products are identified, remedial actions should be taken to ensure that they are no longer in circulation. This indicator determines the extent of product quality problems among the medicines circulating in the country. When tracked longitudinally, the indicator also helps quantify whether the problem has increased or decreased over time.

Data collection

Collection level	***Where to go***	***Who to ask***	***Assessment questions***	***What documents to review***	***Computation***
MoH, PHP, HF	MoH, NDA, national pharmacovigilance center, PHP, HF	Directors or heads of NDA, Pharmacy Department, pharmacovigilance center, QSL, PHP, HF	How many products have been withdrawn from the market in the last year because of product quality concerns?	Documents of NDA, QSL, and CMS; QSL register of quality analysis and other documents	Denominator is the total of all quality analyses conducted by the lab in the last year. Test done with the Minilab and subsequently with a confirmatory test is counted as only one test. Enter a value if the following are true— • Key informants provide the value. • Percentage calculated using the following formula: (Number of samples that failed the test/Total number of samples tested in the last year) × 100. • Enter "**Yes**" if the result is more than 80%.
Limitations	There may not have been proper sampling; products tested may have just been those suspected and sent to the laboratory.				
Potential interventions	Provide support for developing a protocol for regular sampling and testing of medicines in the country and compilation of the reports.				
Further information and references	1. USP DQI. 2007. *Ensuring the Quality of Medicines in Resource-Limited Countries: An Operational Guide*. Rockville, MD: United States Pharmacopeia Convention. www.usp.org/worldwide/dqi/resources/technicalReports.				

PRESENTATION OF ASSESSMENT FINDINGS

At the completion of an assessment of the pharmacovigilance and medicine safety system in a country, findings from the assessment must be collated, analyzed, and reported back to stakeholders. An example of how to collate data obtained from the assessment of health facilities using the IPAT indicators is presented in annex 8. It is important, as is the case in all measurements, to see how an assessment measured up to expectations. To enable countries to make a sense of their situation, some guidelines are provided. This tool recommends that a functional pharmacovigilance and medicine safety system must meet, as a bare minimum, all the core indicators of the IPAT. Irrespective of how this is scored or recorded, a review of the current situation should make clear that this bare minimum is achieved. A country that meets all the core indicators can be regarded as having a basic functional pharmacovigilance and medicine safety system. Depending on the country's level of development, the achievement of the supplementary indicators may also be critical to attain the regulatory and safety system needs in that country. Countries that have met all the core indicators should develop plans and targets for achieving the rest of the supplementary indicators.

Examples of How to Present Findings

The findings from a pharmacovigilance and medicine safety assessment using IPAT can be presented in several formats. In the first format, numerical values can be used to depict findings from the assessment. If all the responses are recorded as "Yes" or "No" (the indicators that have numbers and percentages have recommended thresholds, when those thresholds are met, it is regarded as "Yes" and when they are not met, as "No"). Each "Yes" on a core indicator is given a score of 2; each supplementary indicator that is achieved is given a score of 1, resulting in a total possible score of 52 for the core indicators and 17 for the supplementary indicators. This presentation allows visual recognition of improvements over time, for instance when presented as a radar chart. However, the presentation of the findings from the assessment in this format was not tested for sensitivity. Figure 6 provides an example for Country A.

Indicators	Score	Country A	Max	
1.1	Core	2	2	
1.2	Core	2	2	
1.3	Supplementary	1	1	
1.4	Supplementary	0	1	
2.1	Core	0	2	
2.2	Core	0	2	
2.3	Core	2	2	
2.4	Core	2	2	
2.5	Core	0	2	
2.6	Core	0	2	
2.7	Core	0	2	
2.8	Core	0	2	
2.9	Core	0	2	
2.10	Core	2	2	
2.11	Supplementary	1	1	
2.12	Supplementary	0	1	
2.13	Supplementary	0	1	
2.14	Core	0	2	
2.15	Supplementary	0	1	
3.1	Core	0	2	
3.2	Core	0	2	
3.3	Core	2	2	
3.4	Core	2	2	
3.5	Core	2	2	
3.6	Core	0	2	
4.1	Supplementary	0	1	
4.2	Supplementary	0	1	
4.3	Supplementary	0	1	
4.4	Core	0	2	
4.5	Core	0	2	
4.6	Core	0	2	
4.7	Core	2	2	
4.8	Supplementary	0	1	
5.1	Supplementary	0	1	
5.2	Supplementary	0	1	
5.3	Supplementary	0	1	
5.4	Supplementary	0	1	
5.5	Supplementary	1	1	
5.6	Supplementary	1	1	
5.7	Core	0	2	
5.8	Core	0	2	
5.9	Supplementary	1	1	
5.10	Core	0	2	
	Core	35	100	52
	Supplementary	29	100	17

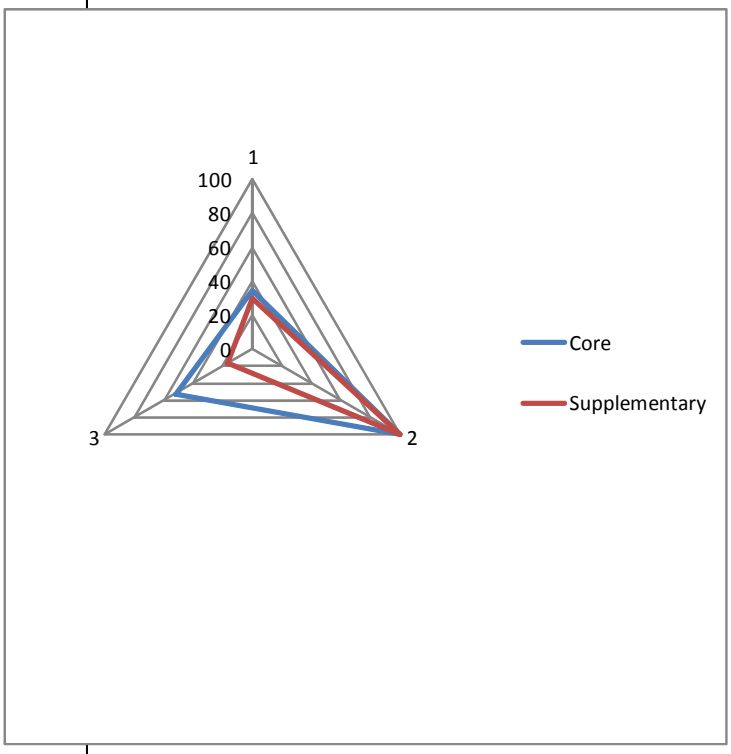
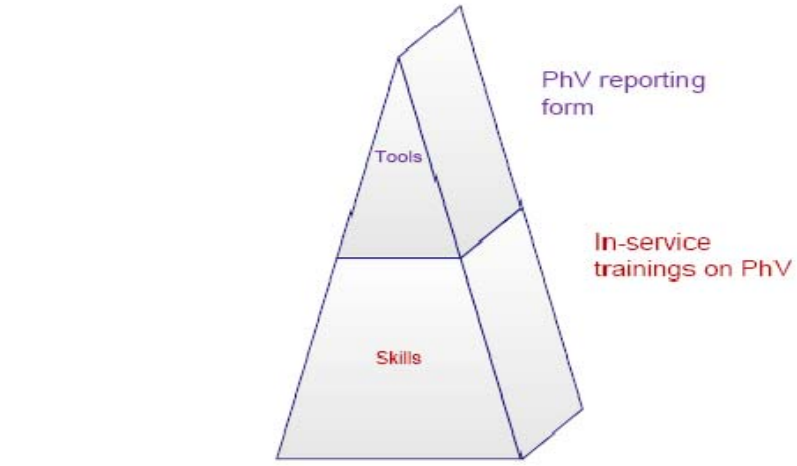


Figure 6. Example of a radar chart

Alternatively, assessment findings can be presented in a pharmacovigilance capacity-building framework format, as shown in figure 7. Aspects of the capacity-building pyramid that were identified as not achieved from the assessment are deleted from the notes beside the pyramid, allowing for a diagram that contains only aspects currently attained. Like the presentation in figure 6, this presentation allows visual recognition of what has been achieved and what is lacking in building capacity for a pharmacovigilance and medicine safety system.



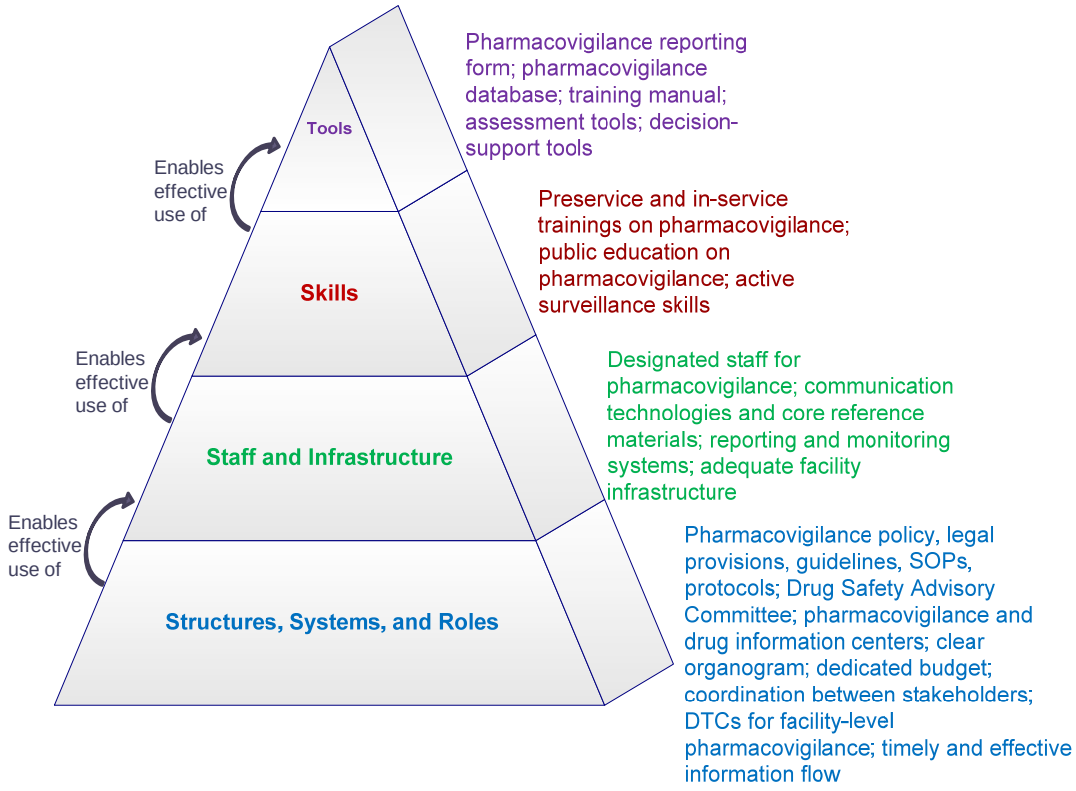


Figure 7. Example (Country A current situation of capacity building for pharmacovigilance)

Other findings of the assessment, for example, the coordination of stakeholders, can be presented in similar formats. The assessment provides an opportunity for the mapping all stakeholders and their roles in pharmacovigilance and medicine safety activities. Such a map is needed for the identification of gaps and opportunities for leveraging resources for improving medicines safety activities. An example of such a map is presented in table 2.

Table 2. Mapping of Pharmacovigilance Stakeholders

Stakeholders	Policy, Law, and Regulation			Systems, Structures, and Stakeholder Coordination				Signal Generation and Data Management			Risk Assessment and Evaluation			Risk Management and Communication		
	Development/ review of Policies	Development/ review of law	Development/ review/ monitoring compliance to regulation	Strengthening systems	Strengthening organizational structures	Stakeholder coordination	Evaluation and decision making	Systems for signal generation	ADR reporting	Data management	Systems for risk assessment	Active surveillance	Other risk evaluation efforts	Risk management strategies	Consumer involvement	Risk communication
International																
WHO/UMC																
National																
National Advisory Committees																
National EML and STG Committees																
National Regulatory Authority																
Pharmacovigilance and Medicine Information Center																
Public Health Programs																
Manufacturers, Importers, Wholesalers, Distributors																
Poisons Center																
NGOs																
Research Institutions																
Regional																
Regional Pharmacovigilance and medicines information center																
NGOs																
Wholesalers, Distributors																
Others																
Local																
Hospitals/ Clinics (Providers)																
Hospitals (Drug and Therapeutics Committees)																
Public Health Programs at the Health Centers and Clinics																
Retailers																
Community and Consumers																
NGOs																
Others																

IMPLEMENTATION OF ASSESSMENT USING IPAT

A national assessment of the pharmacovigilance and medicine safety system in a country will require detailed work planning and allocation of adequate resources. The workplan should include such details as identification of stakeholders who are to participate in the assessment, in-country leads, projection of cost of assessment, prior notice to facilities that will be visited, identification of data collectors, and the like. Planning for a national assessment will also require the development of a detailed itinerary that takes into consideration the availability of key informants to meet with the data collectors. The first draft of IPAT was field-tested in Rwanda. During the assessment, an itinerary was developed and agreed on with in-country stakeholders before the development of other aspects of the assessment plan (the trip report of the Rwanda assessment is referenced below).[30] Data collectors for the assessment should be trained. Experience shows that such training requires about three hours for health professionals. More time may be required for nonprofessional health care workers.

At the end of the Rwanda assessment, the resulting data were collected, input to a master sheet, and analyzed. Several lessons were learned from this first real-life use of the tool. For example, the first IPAT draft had a visual analogue scale included to enable respondents to decide if the indicators were feasible and relevant in their environment. Many respondents were not able to answer using this scale and were not able to specify if they consider an indicator feasible for collection in their environment. Also, many of the indicators had a "No" response or were not being collected because Rwanda had not formally established a national pharmacovigilance center. Plans for implementation of the proposed National Pharmacovigilance and Medicine Information Center (NPMIC) have been finalized; however, the Pharmacy Task Force and the DTC had been addressing pharmacovigilance-related activities. The conduct of the assessment at this point provided the much-needed baseline on which to benchmark subsequent improvement, particularly with the implementation of plans for the setup of the NPMIC. Some of the recommendations from the results of the assessment included the following—

- Finalize/approve the pharmacovigilance-related policy, legal provisions, and guidelines.
- Establish the NPMIC as early as possible.
- Prepare an initial core group of in-country experts and trainers by providing them a training-of-trainers course on pharmacovigilance.
- Establish a multidisciplinary "Medicine Safety Committee" to assist the NPMIC on technical matters.

[30] Nwokike, J., and M. Joshi. 2009. *Assessment of 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.

- Strengthen the National Pharmacovigilance Working Committee to enable it to advance pharmacovigilance activities.

Several other recommendations were made with respect to critical immediate next steps to be taken to ensure that pharmacovigilance and medicine safety systems are developed and sustained in Rwanda. A systems analysis of the situation of the pharmacovigilance system in Rwanda is referenced here.[31]

The tool was also field-tested in South Africa. During the field test, it was agreed that at this stage opinion leaders should be consulted as a first step to enquire about the relevance and feasibility of the indicators in the South African context. Several health facilities and key opinion leaders were interviewed. They found the indicators very relevant and feasible for collection in South Africa. They also recommended that the scope of the indicators be expanded to cover more areas related to the roles of the pharmaceutical industry in postmarketing safety. It was also recommended that the indicators be revised in a workshop and the final sets of indicators used for a national assessment to explore South Africa's current status in monitoring safety of health products from the role of the regulatory authority to the safe use of medicines at the health facilities.

After the field-test experiences, it was agreed that the final version of IPAT will not include the visual analogue scale. It was thought that eliminating the visual analogue scale will help reduce respondents' burden and improve the opportunities for self-administration of the tool in developing countries. The full report of the South Africa review of IPAT is available and referenced here.[32]

[31] Nwokike, J., and M. Joshi. 2009. *Pharmacovigilance in Rwanda: A Systems Analysis.* Submitted to the U.S. Agency for International Development by the Strengthening Pharmaceutical Systems (SPS) Program. Arlington, VA: Management Sciences for Health.

[32] Banoo, S., J. Nwokike, and M. Joshi. 2009. *Assessment of Pharmacovigilance and Medicine Safety System in South Africa 2nd–7th of June 2009: Trip Report*. Submitted to the U.S. Agency for International Development by the Strengthening Pharmaceutical Systems (SPS) Program. Arlington, VA: Management Sciences for Health.

ANNEX 1. FDA LIST OF PRODUCTS REQUIRING RISK MANAGEMENT

Pioglitazone hydrochloride and metformin hydrochloride tablets	Metoclopramide hydrochloride orally disintegrating tablets	Ustekinumab injection	Sacrosidase oral solution
Pioglitazone and metformin (extended-release tablets)	Dronedarone tablets	Pancrelipase delayed-release capsules	Budesonide and formoterol inhalation aerosol
Pioglitazone hydrochloride tablets	Rimabotulinumtoxin B injection	Propoxyphene tablets	Olanzapine and fluoxetine capsules
Fluticasone propionate and salmeterol xinafoate inhalation powder	Norfloxacin tablets	Pioglitazone hydrochloride and glimepiride tablets	medication guide
Fluticasone propionate and salmeterol xinafoate inhalation powder	Romiplostim for subcutaneous injection	Morphine sulfate and naltrexone hydrochloride extended-release capsules	Testosterone gel
Zolpidem tartrate oral spray	Zonisamide capsules	Etanercept for subcutaneous injection	Topiramate tablets and sprinkle capsules
Buproprion hydrobromide (extended-release tablets)	Fentanyl buccal soluble film	Alvimopan capsules	Bosentan tablets
Rosiglitazone maleate and metformin hydrochloride tablets	Sodium phosphate, dibasic anhydrous and sodium phosphate, monobasic, monohydrate tablets	Abacavir sulfate and lamivudine tablets	Sumatriptan succinate and naproxen sodium tablets
Rosiglitazone maleate and glimepiride tablets	Peginterferon alfa-2b, Redipen single-dose delivery system and Rebetol Ribavirin	Interferon beta-1b	Fenofibric acid delayed-release capsules
Moxifloxacin tablets and I.V. solution	Eltrombopag tablets	Gemifloxacin tablets	Abacavir sulfate, lamivudine, and zidovudine
Rufinamide tablets	Ciprofloxacin extended-release tablets	Telbivudine oral solution	Telbivudine tablets
Onabotulinumtoxin A injection	Metoclorpramide hydrochloride orally disintegrating tablets	Interferon alfacon-1	Venlafaxine hydrochloride extended-release tablets
Diclofenac potassium oral solution	Ramelteon tablets	Lopinavir and ritonavir oral solution	Telavancin injection
Certolizumab pegol lyophilized powder for solution for subcutaneous injection	Vigabatrin tablets and oral solution	Levetiracetam tablets, extended-release tablets, oral solution, and injection	Lacosamide injection

Ciprofloxacin tablets, oral suspension, I.V. solution, and extended-release tablets	Tolvaptan tablets	Lamictal (lamotrigine) tablets, chewable dispersible tablets, orally disintegrating tablets, and extended-release tablets	Nevirapine tablets and oral suspension
Colchicine tablets	Golimumab injection	Mefloquine hydrochloride tablets	Pazopanib tablets
Pregabalin capsules	Pancrelipase delayed-release capsules	Olanzapine tablets	Tetrabenazine tablets
Metoclopramide oral solution	Abacavir sulfate tablets and oral solution	Levofloxacin tablets, injection, and oral solution	Omalizumab injection

ANNEX 2. REFERENCE LISTS FOR DATA COLLECTION

List of Recent Safety Warnings

Suicidal ideation with SSRIs and other antidepressants
Suicidal risk with antiepileptics
Heparin-like contaminant
Cough and cold medications in children less than two years of age
Fatal hypersensitivity reactions (HSR) caused by abacavir therapy
Risk of muscle injury, rhabdomyolysis, which can lead to kidney failure or death, when simvastatin is used with amiodarone
Conventional and atypical antipsychotics are associated with an increased risk of mortality in elderly patients treated for dementia-related psychosis
Rosiglitazone and MI
Marketing of unapproved, injectable colchicine
Increased risk of developing tendinitis and tendon rupture in patients taking fluoroquinolones for systemic use
Neuropsychiatric events associated with the use of Tamiflu, in patients with influenza
Data Collection on Adverse Events of Anti-HIV Drugs Study. Data analyses from this study indicate a higher risk of heart attack in patients infected with HIV-1 who were taking Ziagen (abacavir) or Videx (didanosine) as part of their drug therapy

List of Basic DIC Resources

Books and Databases
National medicines policy, medicines and related substances act, essential medicines list, register of medicines registered in the country, all other medicine-related policies, regulations, and guidelines
All MoH standard treatment guidelines
Martindale: The Complete Drug Reference, 35th edition, 2006
Goodman & Gilmans The Pharmacological Basis of Therapeutics
FirstDataBank (including Evaluations of Drug Interactions and others), http://www.firstdatabank.com/
The Pharmaceutical Codex: Principles and Practice of Pharmaceutics (British Pharmaceutical Codex), 12th edition, 1994
The WHO International Pharmacopoeia, 4th edition, 2006
Stockley, I.H. *Drug Interactions: A Source Book of Adverse Interactions, Their Mechanisms, Clinical Importance and Management*, 5th edition (Hardcover)
Pharmacoepidemiology, 4th edition, Brian L.I. Strom (Editor) ISBN: 978-0-470-86681-8
Stephens' Detection of New Adverse Drug Reactions, 5th edition. Editor(s): Dr John Talbot, Dr Patrick Waller Print ISBN: 9780470845523 Online ISBN: 9780470014196
Meyler's Side Effects of Drugs, 15th Edition. The International Encyclopedia of Adverse Drug Reactions and Interactions, 6 volumes (Meyler's Side Effects of Drugs)
Treatment of Human Poisoning (Ellenhorn's Medical Toxicology: Diagnosis and Treatment of Human Poisoning)

Journals
The Lancet
British Medical Journal
New England Journal of Medicine
Annals of Internal Medicine
Annals of Pharmacotherapy
Drug and Therapeutics Bulletin
Pharmacological Reviews
American Journal of Health System Pharmacy
Journal of Clinical Pharmacy and Therapeutics
Clinical Pharmacology and Therapeutics
The International Journal of STD and AIDS
British National Formulary
Drug Safety http://www.ingentaconnect.com/content/adis/dsf
Pharmacoepidemiology and Drug Safety http://www3.interscience.wiley.com/journal/5669/home
Prescrire International http://www.prescrire.org/signature/productions/international.php
WHO Drug Information http://www.who.int/medicines/publications/druginformation/en/
WHO Pharmaceutical Newsletter http://www.who.int/medicines/publications/newsletter/en/
The International Journal of Risk & Safety in Medicine http://www.iospress.nl/loadtop/load.php?isbn=09246479
The Journal of the American Medical Association

List of Basic Communication Technologies for Safety Reporting and Medicine Information Services

Phone (both fixed and mobile)
Fax
Internet
E-mail address
Local database for logging in calls and requests
Overhead projector
Desktop computers (minimum of 2)
Laptop computer (minimum of 1)

List of Key Topics

Modules	Sessions	Contents
Fundamental Topics		
1. Regulatory pharmacovigilance	Overview of national medicine policy and regulatory system	• National medicines policy • Legislations and regulations related to medicines and health products • Pharmacovigilance as described in the medicine policy in the legislations
	History and overview of pharmacovigilance	• History of medicine regulation • History of pharmacovigilance • Evaluating safety throughout the life cycle of a medicine
	Overview of national guidelines for medicine safety surveillance	• National pharmacovigilance guidelines • Roles and responsibilities of stakeholders in pharmacovigilance • ADR notification system • List of tools used in medicine safety
2. Risk identification	Definitions and classification of adverse events	• Definitions in pharmacovigilance • Classifications and types of ADR, medication error, and poor product quality • Adverse events predisposing factors
	Adverse event reporting	• Spontaneous reporting • Keys areas of the adverse event notification form • Strengths and limitations of spontaneous reporting • Sources of spontaneous reports
	Causality assessment and signal generation	• Causation and hypothesis generation • Causality assessment • Signals, their sources and characteristics • Strengths and weaknesses of methods used to identify safety signals
3. Risk evaluation	Active surveillance	• Active surveillance method • Active sentinel surveillance system • Drug event monitoring • Registries • Record linkage studies • Descriptive studies (drug utilization studies)
	Comparative observational studies	• Cohort studies • Case-control studies • Targeted clinical investigations

Modules	Sessions	Contents
4. Patient safety, risk management, and communication	Medication error and patient safety	• Types and causes of medication errors • Sentinel event reporting • Strategies for reducing medication error
	Medicine information and risk communication	• Sources of information on medicines • Hierarchy of evidence • Use of information technology in risk communication • Systems and strategies for providing information on medicines
	Risk management strategies	• Principles of risk management • Scope and objectives of risk management • Risk management strategies
Electives: Pharmacovigilance in Public Health Programs		
5 (a). HIV/AIDS	ARVs and opportunistic infection medicines	• Medicines used in the national guidelines for the management of opportunistic infections and HIV/AIDS • Burden of ARV-related morbidity and mortality • Measures to reduce ARV-related morbidity • Improving adverse event reporting in antiretroviral therapy program
5 (b). TB	Anti-TB medicines	• Medicines used in the national guidelines for the management of TB • Burden of anti-TB medicines adverse events • Measures to reduce adverse events related to anti-TB medicines • Improving adverse event reporting in the national TB program
5 (c). Malaria	Antimalaria medicines	• Medicines used in the national guidelines for the management of malaria • Burden of antimalaria medicines adverse events • Measures to reduce adverse events related to malaria medicines • Improving adverse event reporting in the national malaria program
5 (d). Pharmacovigilance in pediatrics, vaccine/immunization	Vaccines and mother and child health products	• Vaccines used in the national immunization guidelines • Burden and challenges of monitoring adverse events in pediatrics, vaccines, and family planning health products • Adverse events following immunization and measures to reduce vaccine-related adverse events • Improving adverse event reporting in the national malaria program

ANNEX 3. STAKEHOLDER IDENTIFICATION WORKSHEET

(Data collected used for filling out Table 2. Mapping of Pharmacovigilance Stakeholders)

Stakeholder Category	Relevant In-Country Stakeholders	Current Pharmacovigilance-Related Focus Areas/Activities (and Contact Persons, and Other Comments)
Government (e.g., MoH, regulatory body, public health program)		
Donors (U.S. government; multilateral, bilateral, global partnerships)		
Nongovernmental organizations, faith-based organizations, private voluntary organizations (local and international)		
Health professionals		
Health Professionals Associations (medical, pharmaceutical, nursing, etc.)		

Stakeholder Category	**Relevant In-Country Stakeholders**	**Current Pharmacovigilance-Related Focus Areas/Activities (and Contact Persons, and Other Comments)**
Patients, consumers, and consumer groups		
Medicine and poison information centers		
Pharmaceutical industry		
Academia (training institutes, universities, etc.)		
News media and journalists		
Pharmacovigilance centers, laboratory services		

ANNEX 4. HIGH-ALERT MEDICINES

Institute for Safe Medication Practices, ISMP List of High-Alert Medications[33]

Classes/Categories of Medications
adrenergic agonists, IV (e.g., epinephrine, phenylephrine, norepinephrine)
adrenergic antagonists, IV (e.g., propranolol, metoprolol, labetalol)
anesthetic agents, general, inhaled and IV (e.g., propofol, ketamine)
antiarrhythmics, IV (e.g., lidocaine, amiodarone)
antithrombotic agents (anticoagulants), including warfarin, low-molecular-weight heparin, IV unfractionated heparin, Factor Xa inhibitors (fondaparinux), direct thrombin inhibitors (e.g., argatroban, lepirudin, bivalirudin), thrombolytics (e.g., alteplase, reteplase, tenecteplase), and glycoprotein IIb/IIIa inhibitors (e.g., eptifibatide)
cardioplegic solutions
chemotherapeutic agents, parenteral and oral
dextrose, hypertonic, 20% or greater
dialysis solutions, peritoneal and hemodialysis
epidural or intrathecal medications
hypoglycemics, oral
inotropic medications, IV (e.g., digoxin, milrinone)
liposomal forms of drugs (e.g., liposomal amphotericin B)
moderate sedation agents, IV (e.g., midazolam)
moderate sedation agents, oral, for children (e.g., chloral hydrate)
narcotics/opiates, IV, transdermal, and oral (including liquid concentrates, immediate and sustained-release formulations)
neuromuscular blocking agents (e.g., succinylcholine, rocuronium, vecuronium)
radiocontrast agents, IV
total parenteral nutrition solutions

Specific Medications
colchicine injection***
epoprostenol (Flolan), IV
insulin, subcutaneous and IV
magnesium sulfate injection
methotrexate, oral, non-oncologic use
opium tincture
oxytocin, IV
nitroprusside sodium for injection
potassium chloride for injection concentrate
potassium phosphates injection
promethazine, IV
sodium chloride for injection, hypertonic (greater than 0.9% concentration)
sterile water for injection, inhalation, and irrigation (excluding pour bottles) in containers of 100 mL or more

****Although colchicine injection should no longer be used, it will remain on the list until shipments of unapproved colchicine injection cease in August 2008. For details, please visit:* www.fda.gov/bbs/topics/NEWS/2008/NEW01791.html.

Background

Based on error reports submitted to the USP-ISMP Medication Errors Reporting Program, reports of harmful errors in the literature, and input from practitioners and safety experts, ISMP created and periodically updates a list of potential high-alert medications. During February-April 2007, 770 practitioners responded to an ISMP survey designed to identify which medications were most frequently considered high-alert drugs by individuals and organizations. Further, to assure relevance and completeness, the clinical staff at ISMP, members of our advisory board, and safety experts throughout the US were asked to review the potential list. This list of drugs and drug categories reflects the collective thinking of all who provided input.

[33] Institute for Safe Medication Practices. ISMP's List of High-Alert Medications. http://www.ismp.org/Tools/highalertmedications.pdf.

ANNEX 5. PHARMACOVIGILANCE-RELATED SWOT/BEEM ANALYSIS

Strengths	**Building** on them
Weaknesses	**Eliminating** them
Opportunities	**Exploiting** them
Threats	**Minimizing** them

ANNEX 6. DATA COLLECTION TOOL FOR PUBLIC HEALTH PROGRAMS

Data collection form for PHP Indicators (data should be collected from the antiretroviral therapy, TB, malaria, vaccination, and maternal and child health programs)					
Relevant Indicators (31 Indicators)		**1.1, 2.1, 2.2, 2.3, 2.4, 2.5, 2.8, 2.9, 2.10,** *2.11, 2.13,* **3.3, 3.4, 3.5, 3.6,** *4.1, 4.3*, **4.4, 4.5, 4.6, 4.7,** *4.8, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6,* **5.7**, *5.9,* **5.10**			
Country					
Name of Public Health Program (ART/TB/Malaria/Vaccination/MCH)					
Name of Respondent					
Name of Data Collector					
Data of Data Collection					
Indicator No.	**Indicator**	**Assessment Questions**	**Computation**	**Overall Answer to the Indicator (Yes/No and Value Where Applicable)**	
1.1	Existence of a policy document that contains essential statements on pharmacovigilance or medicine safety (stand alone or as a part of some other policy document)	1. Is there an approved national policy on pharmacovigilance or medicine safety?			
		2. Is the policy recently reviewed (in the last five years)?			
2.1	Existence of a pharmacovigilance center or unit	1. Is there a Pharmacovigilance Center, or any other body assigned with the responsibility for monitoring safety of medicines?			
		2. Does the Pharmacovigilance Center physically exist?			

2.2	Pharmacovigilance center or unit has a clear mandate, structure, roles, and responsibilities	1. Are there a clear mandate, organizational structure, roles, responsibilities, and reporting lines for the Pharmacovigilance Center?			
2.3	Existence of a medicine information or pharmacovigilance service that provides ADR and drug safety–related question-and-answer services	1. Does a general drug information center or a specific pharmacovigilance center exist that provides query-response service on ADR and medicine safety information?			
2.4	A designated staff responsible for pharmacovigilance or medicine safety activities	1. Is there a staff specifically responsible for pharmacovigilance or medicines safety?			
		2. Job description indicates that the staff is charged with pharmacovigilance or medicines safety activities as a full-time function or as a part of other overall responsibilities.			
2.5	Dedicated budget available for pharmacovigilance-related activities	1. Is there an annual budgetary allocation for pharmacovigilance activities or for the Pharmacovigilance Center?			
		2. In the last fiscal year what funds were provided by the MoH and donors toward the functioning and implementation of pharmacovigilance activities?			
2.8	Existence of protocols or SOPs for improving patient safety relating to medicine use	1. Are SOPs present for pharmacovigilance activities?			
		2. Are the SOPs written and signed by relevant persons, documented, and officially adopted?			

2.9	Existence of a minimum core list of communication technologies to improve access to safety reporting and provision of medicine information	1. Are there basic communication technologies available to facilitate safety reporting and provision of medicine information?			
		2. Are they functional and currently being used for safety reporting and provision of information?			
2.10	Existence of an ADR or medicine safety bulletin (or any other health-related newsletter that routinely features ADR or medicine safety issues) published in the last six months	1. Does an ADR bulletin or a medicine information bulletin exist that regularly features pharmacovigilance topics?			
		2. Has the bulletin been published within the last six months?			
2.11	Percentage of predefined core reference materials available in the medicine information or pharmacovigilance center	1. Are basic reference materials and related resources available?			
2.13	Number of health care providers trained on pharmacovigilance and medicine safety in the last year	1. How many staff health care professionals have received trainings in - pharmacovigilance in the last year?			
3.3	Existence of a form for reporting suspected ADRs	1. Does a form exist for spontaneous reporting of suspected ADRs?			
		2. Was a copy of the ADR form presented?			
3.4	Existence of a form for reporting suspected product quality issues (as a subset in the ADR form or as a separate form)	1. Does a separate form or subset of a regular ADR form exist for reporting suspected poor product quality problem?			
		2. Was a copy of such a form presented?			

3.5	Existence of a form for reporting suspected medication errors (as a subset in the ADR form or as a separate form)	1. Does a separate form or a subset of the regular ADR form exist for reporting medication error?			
		2. Was a copy of such form presented?			
3.6	Existence of a form for reporting suspected treatment failure (as a subset in the ADR form or as a separate form)	1. Does a form or subset of a regular ADR form exist for reporting suspected treatment failure?			
		2. Was a copy of such form presented?			
4.1	Number of medicine utilization reviews carried out in the last year	1. Has a medicine utilization review study and/or a drug use survey been carried out in the last year?			
		2. Was a report of the medicine utilization review study circulated or published?			
4.3	Incidence of medication errors quantified in the last year	1. Has a study been done in the last year to determine the level of medication errors?			
4.4	Number of ADR reports received in the last year	1. What is the number of ADR reports received in the last year?			
		2. Are these reports complete and committed to ADR databases?			
4.5	Number of active surveillance activities currently ongoing or carried out in the last five years	1. Has any active surveillance study been initiated or carried out in the last five years?			
		2. Are there documentations to show the report of ongoing or completed active surveillance studies?			

4.6	Percentage of patients in public health programs for whom drug-related adverse events were reported in the last year (disaggregated by type of adverse event, drug, severity, outcomes, and demographics)	1. Do you document patients that experience drug-related adverse events?			
		2. Among all patients treated in the last year, what percentage experienced adverse events?			
4.7	Percentage of patients undergoing treatment within a public health program whose treatment was modified because of treatment failure or ADRs in the last year (disaggregated by treatment failure and ADRs)	1. Do you document patients who had treatment failure or ADR?			
		2. What percentage of the patients treated in the last year had treatment failure or ADR?			
4.8	Percentage of patients in public health programs for whom drug-related, serious "unexpected adverse events" were reported in the last year	1. Do you document patients that experienced new, unknown adverse events?			
		2. How many patients experienced such new and serious unknown adverse events in the last year?			
5.1	Risk mitigation plans currently in place that are targeted at high-risk medicines	1. Is there any form of effort to control the use of high-risk medicines because of concerns about their safety when used incorrectly?			
		2. What are the existing and proposed activities to mitigate risk of such high-risk medicines?			

5.2	Prequalification schemes (e.g., WHO prequalification program and Pharmaceutical Inspection Co-operation Scheme) used in medicine procurement decisions	1. Are prequalification reports from WHO and PIC/S considered prior to procurement?			
		2. Does the procurement policy stipulate that prequalification reports should be used to guide procurement?			
5.3	Number of medicine safety information requests received and addressed in the last year	1. What is the number of pharmacovigilance-related information requests received in the last year?			
		2. How many of these requests were addressed?			
5.4	Percentage of planned issues of the medicine safety bulletin (or any other health-related newsletter that routinely features ADR or medicine safety issues) published in the last year	1. What is the planned frequency of publication of the bulletin (dedicated solely to pharmacovigilance or including a regular feature on topics relating to pharmacovigilance)?			
		2. What percentage of the planned issues was actually published in the last year?			
5.5	Number of medicine safety issues of local relevance identified from outside sources (e.g., from another country, or from regional or international sources) and acted on locally in the last year	1. Is there a system for monitoring for new safety reports from outside sources?			
		2. How many medicine safety issues of local relevance identified from outside sources were acted on locally in the last year?			

5.6	Number of "Dear health care professional" letters or other safety alerts developed and distributed in the last year	1. How many "Dear health care professional" letters or any other type of regulatory safety alert letters were developed and distributed in the last year?			
		2. Is the inventory of the regulatory alert letters and the distribution list available for review?			
5.7	Average time lag between identification of safety signal of a serious ADR or significant medicine safety issue and communication to health care workers and the public	1. Are safety signals and significant safety issues promptly communicated to health workers and the public?			
		2. How long does it usually take from when a safety signal or significant safety issue is identified to when it is communicated to the health workers and the public?			
5.9	Number of public or community education activities relating to medicine safety carried out in the last year	1. How many public and community education activities on ADR and medicine safety topics have been carried out in the last year?			
5.8	Percentage of the sampled Drug and Therapeutics Committees that have carried out pharmacovigilance activities or addressed medicine safety issues in the last year	1. How many products have been withdrawn from the market in the last year because of product-quality concerns?			

ANNEX 7. DATA COLLECTION AT MOH AND NATIONAL LEVEL

Data Collection Form for MoH Indicators **(Depending on the indicator, data can be collected from NDA, National Pharmacovigilance Center, pharmaceutical services, pharmaceutical companies, health professions university departments and associations)**	
Relevant Indicators (42 Indicators)	**1.1, 1.2,** *1.3, 1.4,* **2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 2.10,** *2.11, 2.12, 2.13,* **2.14,** *2.15,* **3.1, 3.2, 3.3, 3.4, 3.5, 3.6,** *4.1, 4.2, 4.3,* **4.4, 4.5, 4.6, 4.7,** *4.8, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6,* **5.7, 5.8,** *5.9,* **5.10**
Country	
Name of Organization (regulatory authority/pharmacovigilance center, pharmaceutical company, university, association, etc.)	
Name of Respondent	
Name of Data Collector	
Data of Data Collection	

Indicator No.	**Indicator**	**Assessment Questions**	**Computation**	**Overall Answer to the Indicator (Yes/No and Value Where Applicable)**	
1.1	Existence of a policy document that contains essential statements on pharmacovigilance or medicine safety (stand alone or as a part of some other policy document)	1. Is there an approved national policy on pharmacovigilance or medicine safety?			
		2. Is the policy recently reviewed (in the last five years)?			
1.2	Existence of specific legal provisions for pharmacovigilance in the national medicines legislation or similar legislation	1. Are there laws related to pharmacovigilance or medicine safety in the Medicines Act?			
		2. What is the specific act or section of the legislation or regulation that addresses pharmacovigilance?			

1.3	Legal provisions require that the marketing authorization holder mandatorily report all serious ADRs to the national drug regulatory authority	1. Are there laws or regulations requiring the MAH to report ADRs to the NDA?			
		2. What is the specific act or section of the legislation or regulation that addresses mandatory reporting by the MAH?			
1.4	Legal provisions require the marketing authorization holder to conduct the same or similar postmarketing surveillance activities for products as required by stringent regulatory authorities	1. Are there laws or regulations requiring the MAH to conduct postmarketing safety activities?			
		2. What is the specific act or section of the legislation or regulation that addresses mandatory postmarketing safety activities for the MAH?			
2.1	Existence of a pharmacovigilance center or unit	1. Is there a Pharmacovigilance Center or any other body assigned with the responsibility for monitoring safety of medicines?			
		2. Does the Pharmacovigilance Center physically exist?			
2.2	Pharmacovigilance center or unit has a clear mandate, structure, roles, and responsibilities	1. Is there a clear mandate, organizational structure, roles, responsibilities, and reporting lines for the Pharmacovigilance Center?			
2.3	Existence of a medicine information or pharmacovigilance service that provides ADR and drug safety–related question-and-answer services	1. Does a general drug information center or a specific pharmacovigilance center exist that provides query-response service on ADR and medicine safety information?			

2.4	A designated staff responsible for pharmacovigilance or medicine safety activities	1. Is there a staff specifically responsible for pharmacovigilance or medicine safety?			
		2. Job description indicates that the staff is charged with pharmacovigilance or medicine safety activities as a full-time function or as a part of other overall responsibilities?			
2.5	Dedicated budget available for pharmacovigilance-related activities	1. Is there an annual budgetary allocation for pharmacovigilance activities or for the Pharmacovigilance Center?			
		2. In the last fiscal year what funds were provided by the MoH and donors toward the functioning and implementation of pharmacovigilance activities?			
2.6	Existence of a national medicine safety advisory committee or a subcommittee with similar functions that has met at least once in the last year	1. Does a national drug safety advisory committee or subcommittee with the responsibility to provide technical advice to the regulatory authority on the safety of medicines exist?			
		2. Has the national drug safety advisory committee or subcommittee met in the last year?			
2.7	Existence of national pharmacovigilance guidelines updated within the last five years	1. Does a national guideline for pharmacovigilance or a related document exist?			
		2. Has the national pharmacovigilance guideline been updated in the last five years?			
2.8	Existence of protocols or SOPs for improving patient safety relating to medicine use	1. Are SOPs present for pharmacovigilance activities?			
		2. Are the SOPs written and signed by relevant persons, documented, and officially adopted?			

2.9	Existence of a minimum core list of communication technologies to improve access to safety reporting and provision of medicine information	1. Are there basic communication technologies available to facilitate safety reporting and provision of medicine information?			
		2. Are they functional and currently being used for safety reporting and provision of information?			
2.10	Existence of an ADR or medicine safety bulletin (or any other health-related newsletter that routinely features ADR or medicine safety issues) published in the last six months	1. Does an ADR bulletin or a medicine information bulletin exist that regularly features pharmacovigilance topics?			
		2. Has the bulletin been published within the last six months?			
2.11	Percentage of predefined core reference materials available in the medicine information or pharmacovigilance center	1. Are basic reference materials and related resources available?			
2.12	Percentage of predefined core pharmacovigilance topics present in the preservice training curricula (disaggregated by medicine, pharmacy, nursing, and public health curricula)	1. Is a pharmacovigilance and medicine safety curriculum taught in medical, pharmacy, and other related programs as a stand alone or as part of the pharmacotherapy course?			
		2. What specific topics relating to pharmacovigilance and medicine safety are covered in the curriculum?			
2.13	Number of health care providers trained on pharmacovigilance and medicine safety in the last year	1. How many staff health care professionals have received trainings in pharmacovigilance in the last year?			
2.14	Platform or strategy exists for the coordination of pharmacovigilance activities at the national level	1. Do you have a platform or a forum for coordination of pharmacovigilance activities across all stakeholders?			

2.15	National pharmacovigilance center is a full or associate member of the WHO Collaborating Centre for International Drug Monitoring (UMC)	1. Is the national pharmacovigilance center a full member or associate member of the WHO Collaborating Centre for International Drug Monitoring?			
		2. Is there documentation to show membership?			
3.1	Existence of a system for coordination and collation of pharmacovigilance data from all sources in the country (e.g., health programs, immunization program, active surveillance studies)	1. Is there a system developed for the collation of all pharmacovigilance data from all sources including the health programs to one database at the national pharmacovigilance center or some other coordinating location?			
		2. Was this central database found to contain data transmitted various sources, including public health programs?			
3.2	Existence of a database for tracking pharmacovigilance activities	1. Does a local database exist for tracking center activities and workload?			
		2. Is there any manual or electronic tool in use to facilitate center activities?			
3.3	Existence of a form for reporting suspected ADRs	1. Does a form exist for spontaneous reporting of suspected ADR?			
		2. Was a copy of the ADR form presented?			
3.4	Existence of a form for reporting suspected product quality issues (as a subset in the ADR form or as a separate form)	1. Does a separate form or subset of a regular ADR form exist for reporting suspected poor product quality problem?			
		2. Was a copy of such a form presented?			
3.5	Existence of a form for reporting suspected medication errors (as a subset in the ADR form or as a separate form)	1. Does a separate form or a subset of the regular ADR form exist for reporting medication error?			
		2. Was a copy of such form presented?			

3.6	Existence of a form for reporting suspected treatment failure (as a subset in the ADR form or as a separate form)	1. Does a form or subset of a regular ADR form exist for reporting suspected treatment failure?			
		2. Was a copy of such form presented?			
4.1	Number of medicine utilization reviews carried out in the last year	1. Has a medicine utilization review study and/or a drug use survey been carried out in the last year?			
		2. Was a report of the medicine utilization review study circulated or published?			
4.2	Pharmaceutical product quality survey conducted within the last five years	1. Has a survey on the quality of health products in circulation in the country been carried out in the last five years?			
		2. Was a report generated on the result of the survey?			
4.3	Incidence of medication errors quantified in the last year	1. Has a study been done in the last year to determine the level of medication errors?			
4.4	Number of ADR reports received in the last year	1. What is the number of ADR reports received in the last year?			
		2. Are these reports complete and committed to ADR databases?			
4.5	Number of active surveillance activities currently ongoing or carried out in the last five years	1. Has any active surveillance study been initiated or carried out in the last five years?			
		2. Is there documentation to show the report of ongoing or completed active surveillance studies?			

4.6	Percentage of patients in public health programs for whom drug-related adverse events were reported in the last year (disaggregated by type of adverse event, drug, severity, outcomes, and demographics)	1. Do you document patients who experience drug-related adverse events?			
		2. Among all patients treated in the last year, what percentage experienced adverse events?			
4.7	Percentage of patients undergoing treatment within a public health program whose treatment was modified because of treatment failure or ADRs in the last year (disaggregated by treatment failure and ADRs)	1. Do you document patients who had treatment failure or ADR?			
		2. What percentage of the patients treated in the last year had treatment failure or ADR?			
4.8	Percentage of patients in public health programs for whom drug-related, serious "unexpected adverse events" were reported in the last year	1. Do you document patients who experienced new, unknown adverse events?			
		2. How many patients experienced such new and serious unknown adverse events in the last year?			
5.1	Risk mitigation plans currently in place that are targeted at high-risk medicines	1. Is there any form of effort to control the use of high-risk medicines because of concerns about their safety when used incorrectly?			
		2. What are the existing and proposed activities to mitigate risk of such high-risk medicines?			
5.2	Prequalification schemes (e.g., WHO prequalification program and Pharmaceutical Inspection Co-operation Scheme) used in medicine procurement decisions	1. Are prequalification reports from WHO and PIC/S considered prior to procurement?			
		2. Does the procurement policy stipulate that prequalification reports should be used to guide procurement?			

5.3	Number of medicine safety information requests received and addressed in the last year	1. What is the number of pharmacovigilance-related information requests received in the last year?			
		2. How many of these requests were addressed?			
5.4	Percentage of planned issues of the medicine safety bulletin (or any other health-related newsletter that routinely features ADR or medicine safety issues) published in the last year	1. What is the planned frequency of publication of the bulletin (dedicated solely to pharmacovigilance or including a regular feature on topics relating to pharmacovigilance)?			
		2. What percentage of the planned issues was actually published in the last year?			
5.5	Number of medicine safety issues of local relevance identified from outside sources (e.g., from another country, or from regional or international sources) and acted on locally in the last year	1. Is there a system for monitoring for new safety reports from outside sources?			
		2. How many medicine safety issues of local relevance identified from outside sources were acted on locally in the last year?			
5.6	Number of “Dear health care professional” letters or other safety alerts developed and distributed in the last year	1. How many “Dear health care professional” letters or any other type of regulatory safety alert letters were developed and distributed in the last year?			
		2. Is the inventory of the regulatory alert letters and the distribution list available for review?			

5.7	Average time lag between identification of safety signal of a serious ADR or significant medicine safety issue and communication to health care workers and the public	1. Are safety signals and significant safety issues promptly communicated to health workers and the public?			
		2. How long does it usually take from when a safety signal or significant safety issue is identified to when it is communicated to the health workers and the public?			
5.8	Percentage of the sampled Drug and Therapeutics Committees that have carried out pharmacovigilance activities or addressed medicine safety issues in the last year	1. Within the last year has the DTC carried out pharmacovigilance activities or addressed medicine safety issues?			
		2. Is there documentation to show the number of DTC meetings or activities that addressed medicine safety issues?			
5.9	Number of public or community education activities relating to medicine safety carried out in the last year	1. How many public and community education activities on ADR and medicine safety topics have been carried out in the last year?			
5.10	Percentage of medicines sampled in the last year that passed product quality tests	1. How many products have been withdrawn from the market in the last year because of product quality concerns?			

ANNEX 8. DATA COLLECTION AT HEALTH FACILITIES

Data Collection Form for Health Facilities Pharmacovigilance Indicators					
Relevant Indicators (30 Indicators)	**2.1, 2.2, 2.3, 2.4, 2.5, 2.8, 2.9, 2.10,** *2.11, 2.13,* **3.3, 3.4, 3.5, 3.6,** *4.1, 4.3,* **4.4, 4.5, 4.6, 4.7,** *4.8, 5.1, 5.3, 5.4,* **5.5,** *5.6, 5.7,* **5.8,** *5.9,* **5.10**				
Date					
Name of Health Facility					
Facility Type (Health center or clinic/District Hospital/Tertiary or Referral Hospital					
Data Collector's Name					
Indicator No.	**Indicator**	**Assessment Questions**	**Computation**	**Overall Answer to the Indicator (Yes/No and Value Where Applicable)**	
2.1	Existence of a pharmacovigilance center or unit	1. Is there a Pharmacovigilance Center or any other body assigned with the responsibility for monitoring safety of medicines?			
		2. Does the Pharmacovigilance Center physically exist?			
2.2	Pharmacovigilance center or unit has a clear mandate, structure, roles, and responsibilities	1. Is there a clear mandate, organizational structure, roles, responsibilities, and reporting lines for the Pharmacovigilance Center?			
2.3	Existence of a medicine information or pharmacovigilance service that provides ADR and drug safety–related question-and-answer services	1. Does a general drug information center or a specific pharmacovigilance center exist that provides query-response service on ADR and medicine safety information?			

2.4	A designated staff responsible for pharmacovigilance or medicine safety activities	1. Is there a staff specifically responsible for pharmacovigilance or medicine safety?			
		2. Job description indicates that the staff is charged with pharmacovigilance or medicine safety activities as a full-time function or as a part of other overall responsibilities?			
2.5	Dedicated budget available for pharmacovigilance-related activities	1. Is there an annual budgetary allocation for pharmacovigilance activities or for the Pharmacovigilance Center?			
		2. In the last fiscal year what funds were provided by the MoH and donors toward the functioning and implementation of pharmacovigilance activities?			
2.8	Existence of protocols or SOPs for improving patient safety relating to medicine use	1. Are SOPs present for pharmacovigilance activities?			
		2. Are the SOPs written and signed by relevant persons, documented, and officially adopted?			
2.9	Existence of a minimum core list of communication technologies to improve access to safety reporting and provision of medicine information	1. Are there basic communication technologies available to facilitate safety reporting and provision of medicine information?			
		2. Are they functional and currently being used for safety reporting and provision of information?			
2.10	Existence of an ADR or medicine safety bulletin (or any other health-related newsletter that routinely features ADR or medicine safety issues) published in the last six months	1. Does an ADR bulletin or a medicine information bulletin that regularly features pharmacovigilance topics exist?			
		2. Has the bulletin been published within the last six months?			

2.11	Percentage of predefined core reference materials available in the medicine information or pharmacovigilance center	1. Are basic reference materials and related resources available?			
2.13	Number of health care providers trained on pharmacovigilance and medicine safety in the last year	1. How many staff health care professionals have received trainings in pharmacovigilance in the last year?			
3.3	Existence of a form for reporting suspected ADRs	1. Does a form exist for spontaneous reporting of suspected ADR?			
		2. Was a copy of the ADR form presented?			
3.4	Existence of a form for reporting suspected product quality issues (as a subset in the ADR form or as a separate form)	1. Does a separate form or subset of a regular ADR form exist for reporting suspected poor product quality problem?			
		2. Was a copy of such a form presented?			
3.5	Existence of a form for reporting suspected medication errors (as a subset in the ADR form or as a separate form)	1. Does a separate form or a subset of the regular ADR form exist for reporting medication error?			
		2. Was a copy of such form presented?			
3.6	Existence of a form for reporting suspected treatment failure (as a subset in the ADR form or as a separate form)	1. Does a form or subset of a regular ADR form exist for reporting suspected treatment failure?			
		2. Was a copy of such form presented?			
4.1	Number of medicine utilization reviews carried out in the last year	1. Has a medicine utilization review study and/or a drug use survey been carried out in the last year?			
		2. Was a report of the medicine utilization review study circulated or published?			

4.3	Incidence of medication errors quantified in the last year	1. Has a study been done in the last year to determine the level of medication errors?			
4.4	Number of ADR reports received in the last year	1. What is the number of ADR reports received in the last year?			
		2. Are these reports complete and committed to ADR databases?			
4.5	Number of active surveillance activities currently ongoing or carried out in the last five years	1. Has any active surveillance study been initiated or carried out in the last five years?			
		2. Is there documentation to show the report of ongoing or completed active surveillance studies?			
4.6	Percentage of patients in public health programs for whom drug-related adverse events were reported in the last year (disaggregated by type of adverse event, drug, severity, outcomes, and demographics)	1. Do you document patients who experience drug-related adverse events?			
		2. Among all patients treated in the last year, what percentage experienced adverse events?			
4.7	Percentage of patients undergoing treatment within a public health program whose treatment was modified because of treatment failure or ADRs in the last year (disaggregated by treatment failure and ADRs)	1. Do you document patients who had treatment failure or ADR?			
		2. What percentage of the patients treated in the last year had treatment failure or ADRs?			
4.8	Percentage of patients in public health programs for whom drug-related, serious “unexpected adverse events” were reported in the last year	1. Do you document patients who experienced new unknown adverse events?			
		2. How many patients experienced such new and serious unknown adverse events in the last year?			

5.1	Risk mitigation plans currently in place that are targeted at high-risk medicines	1. Is there any form of effort to control the use of high-risk medicines because of concerns about their safety when used incorrectly?			
		2. What are the existing and proposed activities to mitigate risk of such high-risk medicines?			
5.3	Number of medicine safety information requests received and addressed in the last year	1. What is the number of pharmacovigilance-related information requests received in the last year?			
		2. How many of these requests were addressed?			
5.4	Percentage of planned issues of the medicine safety bulletin (or any other health-related newsletter that routinely features ADR or medicine safety issues) published in the last year	1. What is the planned frequency of publication of the bulletin (dedicated solely to pharmacovigilance or including a regular feature on topics relating to pharmacovigilance)?			
		2. What percentage of the planned issues was actually published in the last year?			
5.5	Number of medicine safety issues of local relevance identified from outside sources (e.g., from another country, or from regional or international sources) and acted on locally in the last year	1. Is there a system for monitoring for new safety reports from outside sources?			
		2. How many medicine safety issues of local relevance identified from outside sources were acted on locally in the last year?			
5.6	Number of “Dear health care professional” letters or other safety alerts developed and distributed in the last year	1. How many “Dear health care professional” letters or any other type of regulatory safety alert letters were developed and distributed in the last year?			
		2. Is the inventory of the regulatory alert letters and the distribution list available for review?			

5.7	Average time lag between identification of safety signal of a serious ADR or significant medicine safety issue and communication to health care workers and the public	1. Are safety signals and significant safety issues promptly communicated to health workers and the public?			
		2. How long does it usually take from when a safety signal or significant safety issue is identified to when it is communicated to the health workers and the public?			
5.8	Percentage of the sampled Drug and Therapeutics Committees that have carried out pharmacovigilance activities or addressed medicine safety issues in the last year	1. Within the past year has the DTC carried out pharmacovigilance activities or addressed medicine safety issues?			
		2. Is there documentation to show the number of DTC meetings or activities that addressed medicine safety issues?			
5.9	Number of public or community education activities relating to medicine safety carried out in the last year	1. How many public and community education activities on ADR and medicine safety topics have been carried out in the last year?			
5.10	Percentage of medicines sampled in the last year that passed product quality tests	1. How many products have been withdrawn from the market in the last year because of product quality concerns?			

Health Facilities Data Collation Example									
Indicator Number	Core (Yes=2, No=0); Suppl (Yes=1, No=0)	Health Facility A	Health Facility B	Health Facility C	Health Facility D	Health Facility E	Health Facility F	Total (average score: = sum) (HF A–E)/6 = x	% HF achieving indicator = 100x/2
2.1		2	2	0	2	2	0	1.33	66.7
2.2									
2.3									
2.4									
2.5									
2.8									
2.9									
2.10									
2.11									
2.13									
3.3									

3.4									
3.5									
3.6									
4.1									
4.3									
4.4									
4.5									
4.6									
4.7									
4.8									
5.1									
5.3									
5.4									
5.5									

5.6									
5.7									
5.8									
5.9									
5.10									
								Total score for minimally functional health facility	38
								Total maximum score	49

ANNEX 9. GLOSSARY

Adverse drug reaction – A response to a drug that is noxious and unintended and that occurs at doses normally use in humans for the prophylaxis, diagnosis, or therapy of disease or for the modification of physiological function.

Causality assessment – Determination of whether a reasonable possibility exists that the product is etiologically related to the adverse experience.

Drug utilization review studies – Studies that investigate the appropriateness of drug use, designed to detect and quantify drug use problems.

Effectiveness – A study of whether, in real-world settings, a drug achieves the effect intended.

Efficacy – A study under ideal conditions to determine if a drug can bring its desired effect.

Medication error – A medication error is any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. Such events may be related to professional practice, health care products, procedures, and systems, including prescribing; order communication; product labeling, packaging and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use.

Medicines safety system – the coordinated and interdependent functioning of activities to improve benefits and reduce harm related to the use of medicines by the public through the efficient mobilization of various stakeholders and resources at all levels and in all sectors

Pharmacoepidemiology – Study of the use and the effects of drugs in large numbers of people.

Pharmacovigilance – The science and activities relating to the detection, evaluation, understanding, and prevention of adverse reactions to medicines or any other medicine-related problems.

Postmarketing safety surveillance – The study of drug use and drug effects after release onto the market.

Signal – Information that arises from one or multiple sources (including observations and experiments), which suggests a new potentially causal association, or a new aspect of a known association, between an intervention and an event or set of related events, either adverse or beneficial, which would command regulatory, societal, or clinical attention, and is judged to be of sufficient likelihood to justify verificatory and, when necessary, remedial actions.

Spontaneous reporting systems – Maintained by regulatory bodies to collect unsolicited clinical observations that generally originate outside of a formal study.