

# Pharmacovigilance in Ghana: A Systems Analysis

Jude Nwokike  
Kwesi Eghan

April 2010



**USAID**  
FROM THE AMERICAN PEOPLE



Strengthening  
Pharmaceutical  
Systems



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## **Abstract**

The Strengthening Pharmaceutical Systems Program in collaboration with the Ghana Food and Drug Board and the National Malaria Control Program assessed the Ghana pharmacovigilance system using the indicator-based pharmacovigilance assessment tool. Basic structures for conducting pharmacovigilance activities are in place in Ghana. However, a need exists to develop a comprehensive pharmacovigilance system that should comprise more than adverse events data collection. It should include evaluation, minimization, and communication of risks. Several interventions were recommended for improving the regulations, organizational structures, and processes and for establishing a comprehensive pharmacovigilance system.

## **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.

## **Recommended Citation**

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## **Key Words**

pharmacovigilance, medicine safety, surveillance, capacity building

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## ACRONYMS AND ABBREVIATIONS

AA	artesunate-amodiaquine
ACT	artemisinin-based combination therapy
ADR	adverse drug reaction
AEFI	adverse event following immunization
ART	antiretroviral therapy
DTC	drug and therapeutics committee
FDB	Food and Drugs Board
GPP	good pharmacovigilance practice
HCW	health care worker
HF	health facility
HIV/AIDS	human immunodeficiency syndrome/acquired immune deficiency syndrome
ICP	institutional contact person
IPAT	Indicator-based Pharmacovigilance Assessment Tool
MAH	market authorization holder
MoH	Ministry of Health
MSH	Management Sciences for Health
NDIRC	National Drug Information Resource Center
NDP	National Drug Policy
PHP	public health programs
PMS	postmarketing surveillance
SMU	Safety Monitoring Unit
SOP	standard operating procedure
SPS	Strengthening Pharmaceutical Systems
TB	Tuberculosis
UMC	WHO Collaborating Center for International Drug Monitoring in Uppsala, Sweden
WHO	World Health Organization



## EXECUTIVE SUMMARY

A comprehensive pharmacovigilance system comprises more than adverse events data collection and should include risk evaluation, minimization, and communication. However, pharmacovigilance activities in many countries are fragmented and often do not address all components of a comprehensive pharmacovigilance and medicine safety system. Management Sciences for Health's Strengthening Pharmaceutical Systems (MSH/SPS) Program, in collaboration with the Ghana Food and Drug Board (FDB) and the National Malaria Control Program, assessed Ghana's pharmacovigilance system and used the results to develop recommendations for improving the safety of health products in Ghana.

The assessment was conducted using SPS's recently developed Indicator-based Pharmaceutical Assessment Tool (IPAT). Data were collected through the IPAT assessment questions, review of documents, and interviews of key informants.

### **Selected Assessment Results**

#### ***Policy, Law, and Regulation***

The Ghana National Drug Policy recognizes the need for pharmacovigilance and medicine information services and considers postmarketing surveillance and pharmacovigilance important aspects of medicines registration and selection in Ghana. However, the country lacks the legal provisions to enforce pharmacovigilance activities.

#### ***Systems, Structures, and Stakeholder Coordination***

The FDB's Safety Monitoring Unit is the national pharmacovigilance coordinating center. Ghana has developed basic structures for conducting pharmacovigilance activities, including a national pharmacovigilance unit with mandate and structure, designated persons for pharmacovigilance, functional information and technology infrastructure, and collaboration with the World Health Organization (WHO) Collaborating Center for International Drug Monitoring in Uppsala, Sweden (UMC). However, across all levels (national, public health programs, and health treatment facilities), lack of a dedicated pharmacovigilance budget, a safety bulletin, pharmacovigilance training for health care workers, a mechanism to coordinate activities, and pharmacovigilance guidelines or standard operating procedures was consistently reported.

#### ***Signal Generation and Data Management***

The assessment showed that adverse drug reaction (ADR) reporting forms are readily available at most levels of Ghana's health system. However, the scope of pharmacovigilance also covers therapeutic ineffectiveness, medication errors, and product quality, information about which can be collected using the existing ADR form, on a separate form, or as a part of the patient case file. The assessment showed that these other events are rarely reported and that respondents' knowledge or use of other reporting mechanisms is poor.

## **Risk Assessment and Evaluation**

Without collection, reporting, or analysis of adverse events data, signals of public health importance are missed and opportunities to learn about the safety and effectiveness of medicines during real-life use are lost. The assessment showed that adverse events data are poorly collected and analyzed. This finding has implications for the ability to generate signals and evaluate signals of public health importance. Several medicine safety projects and active surveillance studies have been conducted or are currently ongoing in Ghana. Studies related to malaria are in the majority, with five studies on the safety and effectiveness of medicines for the management of severe malaria alone.

## **Risk Management and Communication**

This assessment component targets efforts to mitigate the risk of medicine use, and based on the results, such efforts are still in the early stages across Ghana. Requesting safety information, responding to safety information, using bulletins to publish safety information, and communicating safety to health care workers and the community were not reported as routine at any level.

## **Recommendations**

Based on the assessment results and analysis, the following interventions need to be implemented to strengthen pharmacovigilance and develop a comprehensive medicine safety system—

- Establish a postmarketing surveillance directorate within the Ministry of Health (MoH).
- Revise relevant legislation to adequately address safety monitoring.
- Develop comprehensive national guidelines for pharmacovigilance.
- Improve stakeholder coordination.
- Strengthen the role of drug and therapeutics committees (DTCs) in pharmacovigilance.
- Implement interventions to improve adverse events reporting, such as the use of sentinel reporting sites, interactive PDF forms, cell phone text messaging, FDB phone contacts for manufacturers of products, and collation of adverse events entries in patient case files of public health programs.
- Enhance the use of spontaneous reporting to monitor product quality and treatment failure.
- Develop protocols and standard operating procedures (SOPs) and establish incidence registers.

- Integrate locally relevant pharmacovigilance topics in pre- and in-service training programs.
- Develop memoranda of understanding with universities and research institutions to conduct pharmacoepidemiological studies.
- Develop formal procedures to identify priority medicine safety research questions, and use findings to inform decision making.



## BACKGROUND

Many developing countries are confronted by formidable challenges in containing the spread of major communicable diseases that are responsible for high rates of morbidity and mortality. Some of these diseases, particularly those of public health importance, can be prevented or controlled through interventions deployed by public health programs. Such interventions include mass administration of medications as well as disease prevention and treatment using new essential medicines. Access to new essential medicines for malaria, HIV/AIDS, and tuberculosis (TB) has dramatically improved in many developing countries through the efforts of global health initiatives. With the increased access, lifesaving medicines are now available to many. The large population covered and the use of new medicines provide the potential for not only benefits to the local population but also harm. The possibility of harm is high—especially if adverse reactions are not monitored pursuant to a strategy aimed at good reporting and early detection, review, and management.<sup>1</sup>

### Definition and Scope of Pharmacovigilance

The WHO defines pharmacovigilance as the science and activities relating to the detection, assessment, understanding, and prevention of adverse reactions to medicines or any other medicine-related problems.<sup>2</sup> There is incomplete understanding of the safety of new medicines at the point of registration. Data on the safety of new medicines are mainly derived from pre-authorization clinical trials in controlled settings. Though data on safety are collected during clinical trials of new medicines, the limitations of clinical trials—including restricted exposure, narrow perspective, and short duration—make it imperative to monitor for safety and effectiveness when the product is used in large populations. Postmarketing surveillance (PMS) is crucial to quantify previously recognized ADRs, identify unrecognized adverse drug events, and evaluate the effectiveness of medicines in real-world situations as well as to decrease mortality and morbidity associated with adverse events.<sup>3</sup> The aims of pharmacovigilance are to—

- Improve patient care and safety in relation to the use of medicines and all medical and paramedical interventions
- Improve public health and safety in relation to the use of medicines
- Detect problems related to the use of medicines and communicate the findings in a timely manner

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<sup>1</sup> WHO. 2006. *The Safety of Medicines in Public Health Programmes: Pharmacovigilance an Essential Tool*. Geneva: WHO.

<sup>2</sup> World Health Organization. 2002. *The Importance of Pharmacovigilance: Safety Monitoring of Medicinal Products*. Geneva: WHO.

<sup>3</sup> 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.

- Contribute to the assessment of benefit, harm, effectiveness and risk of medicines, leading to the prevention of harm and maximization of benefit
- Encourage the safe, rational, and more effective (including cost-effective) use of medicines
- Promote understanding, education, and clinical training in pharmacovigilance and its effective communication to the public<sup>4</sup>

Overall, pharmacovigilance is important to ensure product stewardship and safeguard public health. The implementation of a comprehensive pharmacovigilance system requires efforts beyond data collection on adverse events and should include risk evaluation, minimization, and communication. Spontaneous ADR reporting and other forms of data collection for early warning on drug safety are part of the *risk identification* process. *Risk minimization* and *communication* are the preventive part of pharmacovigilance and include strategies for mitigating known risks, communication of drug safety information, and promotion of rational use of medicines. Pharmacovigilance activities in many countries are, however, fragmented and often do not address all components of a comprehensive pharmacovigilance and medicine safety system.

### **Need for Pharmacovigilance for Malaria and Other Public Health Programs**

The WHO recommends that pharmacovigilance should be an integral part of every public health program that uses medicines in order to optimize the use of scarce health resources and prevent potential tragedies.<sup>5</sup> Malaria contributes significantly to morbidity and mortality in Africa. Throughout Africa, extensive self-medication and presumptive treatment with antimalarials take place. Informal use of antimalarials, incorrect dosing, inappropriate treatment, and interactions of other medicines and coexisting illnesses (such as HIV/AIDS, TB, and malnutrition) could potentially increase the risk of adverse events.<sup>6</sup>

In Ghana, infection is hyperendemic and disproportionately affects the most vulnerable, including children, pregnant women, and the poor. In 2007, about one in every three outpatient attendance, one in every three hospital admissions, and 23.6 percent of all recorded deaths among children under five years of age were attributed to malaria. Malaria remains a huge burden for pregnant women in Ghana, contributing to 9.8 percent of deaths in pregnant women.<sup>7</sup> In 2004, Ghana adopted the use of artemisinin-based combination therapy (ACT) as recommended by the WHO as first-line therapy for the management of uncomplicated malaria. The chosen ACT for first-line treatment of malaria was artesunate-amodiaquine (AA). However, the deployment of AA was associated with several challenges, including ADRs, lack of other nationally recommended treatment options for those who could not tolerate AA, and safety

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<sup>4</sup> WHO. 2006. *The Safety of Medicines in Public Health Programmes*.

<sup>5</sup> Ibid.

<sup>6</sup> Talisuna, A., S. Staedke, and U. D'Alessandro. 2006. Pharmacovigilance of Antimalarial Treatment in Africa: Is It Possible? *Malaria Journal* 5:50 doi:10.1186/1475-2875-5-50. <http://www.malariajournal.com/content/5/1/50>.

<sup>7</sup> Ghana National Malaria Strategic Plan 2008–2015, June 2008 (draft).

concerns and perceptions among the population as captured by the mass media. These issues highlighted the need to explore other ACT medicines and led to the inclusion in 2009 of artemether-lumefantrine and dihydroartemisinin-piperaquine for those who could not tolerate AA.<sup>8</sup>

Similar challenges and concerns related to treatment-related adverse events have also been seen with the antiretroviral therapy (ART) program across several countries. The tolerability of some ART regimens, including stavudine, has recently been questioned and resulted in many treatment programs dropping stavudine as a backbone nucleoside reverse transcriptase inhibitor from their national guidelines. The WHO concluded that the cumulative toxicity of stavudine is unacceptable to patients and many health care providers. Newer, more patient-friendly but currently more expensive ART regimens should be considered.<sup>9</sup> Several adverse events have been recorded in ART programs in developing countries. The Forum for Collaborative HIV Research and the International Epidemiological Database to Evaluate AIDS (IeDEA) Pharmacovigilance Working Group survey identified anemia, rash, peripheral neuropathy, lipodystrophy, and hepatotoxicity as the top five adverse events related to the use of antiretrovirals in developing countries.<sup>10</sup> Adverse events can negatively affect patient adherence to treatment and overall ART treatment outcomes. Enhanced understanding of toxicities associated with use of antiretrovirals can facilitate the provision of more accurate information and expectations to patient regarding long-term toxicities and will improve advice given to patients by clinicians about timing of initial therapy, choice of regimen, and drug substitutions or discontinuations.<sup>11</sup> Monitoring treatment-related adverse events is also important in mass drug administration programs, particularly in mass administration of combination treatments as happens in the management of schistosomiasis, lymphatic filariasis, trachoma, and onchocerciasis.<sup>12</sup>

The challenges of adverse events and the need to monitor safety and effectiveness of medicines used in public health programs, their impact on adherence and treatment outcomes, and the implications for changes to the treatment guidelines can only be confronted by establishing and strengthening pharmacovigilance systems. In establishing sustainable pharmacovigilance systems in Africa, countries will need to critically assess the system that will be used for detection, assessment, evaluation of severity, and evaluation of relationship of adverse events.<sup>13</sup>

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<sup>8</sup> Republic of Ghana, Ministry of Health. Antimalaria Drug Policy for Ghana, 2nd revised version, January 2009.

<sup>9</sup> WHO. 2009. *Rapid Advice: Antiretroviral Therapy for HIV Infection in Adults and Adolescents*. Geneva: WHO.

<sup>10</sup> Bakare, N. 2008. Case Definition and Severity Grading for Treatment-Related Adverse Events. Presentation at the Forum for Collaborative HIV Research. 2nd International Workshop on HIV Treatment, Pathogenesis and Prevention Research in Resource-Poor Settings. Dakar, Senegal, May.

<sup>11</sup> Bissona, G., R. Gross, V. Miller, I. Weller, Ian, and A. Walker, on behalf of the Writing Group. 2003. Monitoring of Long-Term Toxicities of HIV Treatments: An International Perspective. *AIDS* 17: 2407–17.

<sup>12</sup> Alemayehu, D., E. N. Andrews, P. Glue, and C. A. Knirsch. 2010. Considerations for the Design and Conduct of a Pharmacovigilance Study Involving Mass Drug Administration in a Resource-Constrained Setting. *PLoS Neglected Tropical Diseases* 4(1): e564. doi:10.1371/journal.pntd.0000564.

<sup>13</sup> Talisuna, A., S. Staedke, and U. D'Alessandro. 2006. Pharmacovigilance of Antimalarial Treatment in Africa.

## What Is a Pharmacovigilance System?

A 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. The implementation of a comprehensive pharmacovigilance system requires efforts beyond adverse events data collection and should include risk evaluation, minimization, and communication. A framework for a comprehensive pharmacovigilance system should address functions for monitoring, detecting, reporting, evaluating, and documenting medicine safety using the people and structures or entities that have the authority to take appropriate action.<sup>14</sup> Good pharmacovigilance practice (GPP) describes all the elements of a robust pharmacovigilance system. GPP sets standards for the conduct, performance, monitoring, auditing, recording, analysis, and reporting of pharmacovigilance data that ensure the recorded data and reported information are credible and accurate, and that the rights, integrity, and confidentiality of patients and reporters are protected by all parties involved. The core elements of GPP are proactive and include the following—<sup>15</sup>

- Robust quality control system in pharmacovigilance operations and data safety management
- Quality assurance in pharmacovigilance operations and safety data management
- Good pharmacoepidemiological research practices
- Good systematic signal evaluation and assessment (signal generation) practice
- Good communication practice
- Thorough documented reviews
- Appropriate labeling
- Appropriate (in nature and timeliness) regulatory actions

The development, establishment, functioning, and sustainability of such a comprehensive medicine safety system require the building of institutional capacities. *Capacity building* is the creation of an enabling environment with appropriate policy and legal frameworks; institutional development, including community participation; human resources development; and strengthening of managerial systems.<sup>16</sup> Capacity building can be achieved through applying a

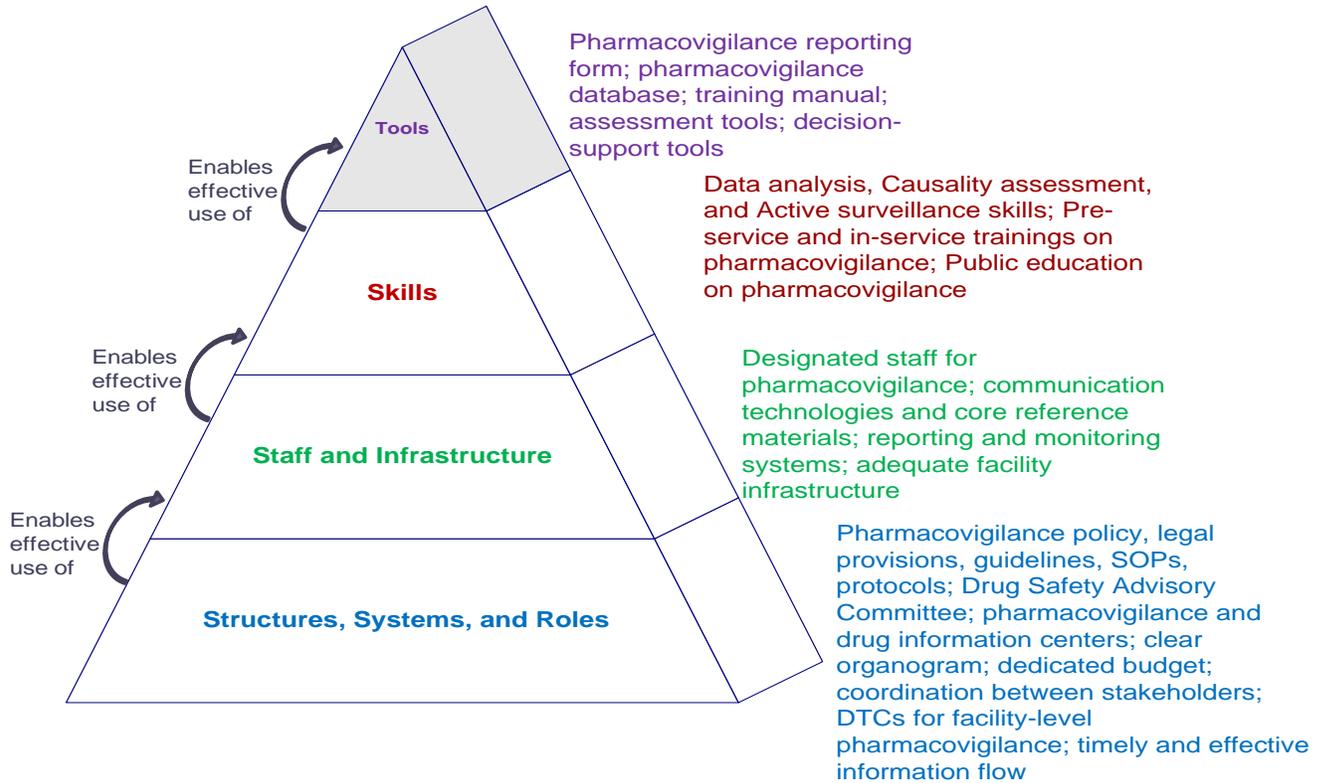
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<sup>14</sup> Strengthening Pharmaceutical Systems (SPS). 2009. *Supporting Pharmacovigilance in Developing Countries: The Systems Perspective*. Submitted to the U.S. Agency for International Development by the SPS Program. Arlington, VA: Management Sciences for Health.

<sup>15</sup> Alghabban, A. 2004. *Dictionary of Pharmacovigilance*. London: Pharmaceutical Press.

<sup>16</sup> Urban Environmental Management Web site. Urban Capacity Building, Defining Capacity Building. <http://www.gdrc.org/uem/capacity-define.html>.

four-tier hierarchy of capacity-building needs:<sup>17</sup> structures, systems, and roles; staff and infrastructure; skills; and tools. Figure 1 depicts the pharmacovigilance capacity-building pyramid that describes the related elements for achieving a fully functional and sustainable medicine safety system.



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

**Figure 1. Capacity-building model for pharmacovigilance**

<sup>17</sup> Potter, C., and R. Brough. 2004. Systemic Capacity Building: A Hierarchy of Needs. *Health Policy Planning* 19: 336–45.



# ASSESSMENT OF GHANA'S PHARMACOVIGILANCE SYSTEM

## Assessment Objectives

The U.S. Agency for International Development–funded MSH/SPS Program is an implementing partner under the Ghana Malaria Operational Plan for fiscal year 2009. MSH/SPS provides support to in-country stakeholders to improve the national pharmacovigilance and medication safety system. The MSH/SPS Program was requested to provide support to the Ghana Food and Drug Board, the National Malaria Control Program, and other public health programs and stakeholders in conducting a comprehensive assessment of the pharmacovigilance and medicine safety system in Ghana and, based on the assessment findings, developing options and recommendations for improving safety of health products in Ghana.

## Indicator-Based Pharmacovigilance Assessment Tool

Currently, no performance monitoring tool is available for assessing where a country stands in achieving a functional pharmacovigilance system. The Indicator-based Assessment Tool recently developed by MSH/SPS is useful for addressing this gap.<sup>18</sup> IPAT facilitates the diagnostic assessment of pharmacovigilance systems in developing countries. The tool supports evidence-based options analysis and development of relevant and feasible recommendations reflecting each country's local realities, existing regulatory capacity and priorities, identified system gaps, and resource availability. Additionally, the standardized and indicator-based approach included in the tool allows longitudinal measurement of progress after the recommended interventions are implemented. IPAT is a comprehensive performance metric to monitor and evaluate pharmacovigilance and the medicine safety system. 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 IPAT indicators are attached as Annex 1.

## Local Adaptation of IPAT

Key stakeholders in Ghana reviewed the IPAT before its use for the assessment. The reviewers made comments related to the individual indicators. For instance, reviewers requested addition of a new indicator to monitor for the existence of a policy for reporting of ADRs by health care providers. With regard to the component on systems, structures and stakeholder coordination, to reflect the local peculiarities, reviewers suggested that data collectors should ask whether an individual has been assigned responsibility for monitoring safety of medicines (Indicator 2.1). Changes were also recommended on the availability of a dedicated budget for pharmacovigilance activities (Indicator 2.5) and the role of DTCs in pharmacovigilance (Indicator 5.8). Reviewers

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<sup>18</sup> Strengthening Pharmaceutical Systems (SPS) Program. 2009. *Indicator-Based Pharmacovigilance Assessment Tool: Manual for Conducting Assessments in Developing Countries*. Submitted to the U.S. Agency for International Development by the SPS Program. Arlington, VA: Management Sciences for Health.

queried the practicality of updating national pharmacovigilance guidelines every five years (Indicator 2.7). Reviewers sought clarifications on some indicators, including the existence of protocols or SOPs for improving safety related to medicine use. They considered the availability of prepaid postage ADR forms as part of the core list of communication technologies to improve access to safety reporting (Indicator 2.9). Nursing schools were included in the indicator related to the preservice training curricula in pharmacovigilance (Indicator 2.12).

The IPAT was also independently reviewed by a local consultant and expert on pharmacovigilance. The consultant made several recommendations, including the need for greater emphasis on the roles of professional associations, industry, manufacturers, and the supply chain in pharmacovigilance. The consultant suggested reclassification of some “Core” and “Supplementary” indicators and clarifications on computation of some indicators. Reviewers’ comments will guide efforts to adapt the IPAT for routine use in monitoring the pharmacovigilance system in Ghana.

## **Assessment Methodology**

The assessment of the pharmacovigilance and medicine safety system in Ghana involved primarily the use of document review and structured interviews with IPAT to solicit responses.

- Documents reviewed included the National Drug Policy, 2004; Food and Drugs Law (PNDCL 3058), 1992; the Anti-Malaria Drug Policy for Ghana, 2009; the Guidelines for Product Safety Monitoring; National Drug Information Resource Center, medium-term program of work 2002–2006 and *National Drug Information Journal*, 2006 and 2009; *Annual Report of the Safety Monitoring Unit of FDB*, 2009; the Assessment of the pharmaceutical sector in Ghana, 2002; standard treatment guidelines, treatment policies, and guidelines of public health programs (PHPs), and documents from other MoH units, including the Pharmacy Council.
- Structured interviews were conducted using the assessment questions in IPAT. A total of 93 assessment questions were used for data collection. Three forms were used as data collection tools: a form dedicated to collecting data from the MoH and national-level respondents (including key informants), another for collecting data from PHPs, and the last for collecting data from health facilities (HFs).
- Additional feedback was collected from respondents to address other locally relevant issues or questions and to make recommendations toward the overall improvement of the pharmacovigilance and medicine safety system in Ghana.

## **Selection of Study Sites**

The assessment of the pharmacovigilance and medicine safety system in Ghana using the IPAT required selection of study sites at the national level, including the FDB and its national pharmacovigilance unit, pharmaceutical services, pharmaceutical companies, health professions,

university departments, and professional associations. Convenience sampling was used to ensure coverage and representation of each stakeholder in Ghana's pharmacovigilance system. Each PHP—including the HIV/AIDS, TB, malaria, immunization, and maternal and child health programs—was targeted for data collection. Representative samples were also selected from HFs, including 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 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.<sup>19</sup> Although the assessment used the preceding outline as a guide in identifying sites, ultimate site selection was informed by logistics challenges and availability of key respondents. Table 1 lists all the data collection sites visited.

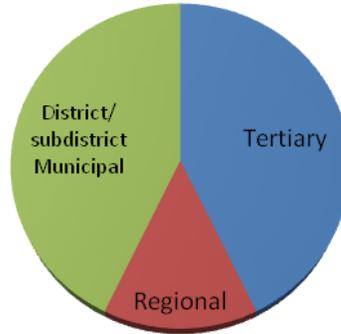
**Table 1. List of Sites Assessed**

Data Collection Sites	Number of Respondents
<b>MoH and National Level</b>	
FDB	4
National Drug Information Resource Center (NDIRC)	3
Universities	2
National opinion leaders	2
Pharmaceutical companies	2
<b>Public Health Programs</b>	
National Malaria Control Program	1
National Tuberculosis Control Program	1
Expanded Program on Immunization	1
National AIDS Control Program	1
<b>Health Facilities</b>	
<i>Tertiary health facilities</i>	
Korle-Bu Teaching hospital	2
Komfo Anokye Teaching Hospital	3
Tamale Teaching Hospital	1
<i>Regional health facilities</i>	
	2
Effia Nkwanta Hospital, Pharmacy department, Sekondi	1
Wa Hospital, Wa	1
<i>District/subdistrict/municipal health facilities</i>	
	6
Korle-Bu PolyClinic	1
Ridge Hospital	1
University of Cape Coast Hospital	1
University of Cape Coast Hospital, Pharmacy department	1
Essikadu Hospital, Pharmacy department, Sekondi	1
Cape Coast Municipal Hospital, Cape Coast	1

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<sup>19</sup> Ibid.

In some instances, data were collected from several units and respondents within the same site to ensure increased coverage and better understanding of the actual situation at that site. Figure 2 depicts the proportion of facilities covered from each level of health care delivery.



**Figure 2. Proportion assessed within each level of health facilities**

### **Limitations**

The assessment did not collect data from a representative number of health facilities, particularly lower-level ones. Hence, the situational analysis of the medicine safety system in treatment facilities may not be generalizable. Other limitations that may affect the findings from this assessment include nonverification of responses to assessment questions, conflicting feedback from respondents, reliance on the data collector's judgment, and imprecision in transforming responses to quantitative forms.

## ASSESSMENT FINDINGS, ANALYSIS, AND RESULTS

### Analysis Format

The findings from the assessment were analyzed by entering data into an Excel spreadsheet and transforming them into quantitative responses. Indicators with “Yes” responses were entered as 1 and those with “No” responses were entered as 0. For indicators with responses requiring numbers and percentages, a threshold was set based on what a minimally functional pharmacovigilance system should attain for those indicators. When thresholds are attained, the indicator is scored 1, and if not attained, it is scored as 0. The numbers are presented in descriptive statistics and then analyzed for trends. The charts developed from the findings are color coded with blue showing encouraging performance for that indicator while red shows poor performance.

Discussions of the findings from the analysis are presented under the headings of the five components of the pharmacovigilance and medicine safety system: policy, law, and regulation; systems, structures, and stakeholder coordination; signal generation and data management; risk assessment and evaluation; and risk management and communication.

### Policy, Law, and Regulation

Existence of a pharmacovigilance policy indicates that a country has accorded high-level attention and commitment to improving medicine safety and helps provide a broad direction to advance the cause. Similarly, existence of relevant legislation and regulations provides clear directions to ensure compliance by relevant parties and stakeholders and gives a legal basis for monitoring and action.

The assessment findings with regard to the policy, laws, and regulations for pharmacovigilance in Ghana showed that the necessary policy statement is in place. The Ghana National Drug Policy (NDP)<sup>20</sup> recognizes the need for pharmacovigilance and medicine information services and considers postmarketing surveillance and pharmacovigilance important aspects of medicine registration and selection in Ghana. The FDB, established by the Food and Drugs Act, 1992, PNDCL 3058,<sup>21</sup> is the national medicine regulatory authority for Ghana. The NDP entrusts the FDB with the responsibility for pharmacovigilance and for ensuring ethical standards in advertisement and promotion of medicines. The NDP states that the government shall ensure the establishment and maintenance of a National Drug Information Centre. The national policy envisaged that a pharmacovigilance center would be responsible for identifying risk factors for and mechanisms underlying ADRs occurring in Ghana.<sup>22</sup> The Ghana Food and Drugs Act, 1992,

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<sup>20</sup> Ministry of Health, Ghana. 2004. *Ghana National Drug Policy (Second Edition)*. Accra: Ministry of Health, Ghana. [http://www.who.int/countries/gha/publications/Ghana\\_National\\_DrugPolicy\\_2nd\\_Edition.pdf](http://www.who.int/countries/gha/publications/Ghana_National_DrugPolicy_2nd_Edition.pdf).

<sup>21</sup> PNDCL 3058, Food and Drugs Act, 1992.

<http://www.epa.gov.gh/ghanalex/acts/Acts/FOOD%20AND%20DRUGS%20BOARD.pdf>.

<sup>22</sup> Ministry of Health, Ghana, 2004. *Ghana National Drug Policy (Second Edition)*.

does not address pharmacovigilance. The law has no section specifically requiring the mandatory or voluntary reporting of adverse events.

The University of Ghana Medical School initiated pharmacovigilance activity in 1992 at the Centre for Tropical Clinical Pharmacology and Therapeutics, which also provided technical support to the FDB. National pharmacovigilance activities are now coordinated through the Safety Monitoring Unit (SMU) of the FDB. Table 2 shows the assessment findings of the current situation of pharmacovigilance policy, laws, and regulations in Ghana. Besides the national medicines policy, which contains essential statements on pharmacovigilance, the legal provisions that enforce pharmacovigilance activities were found lacking. In the PHPs, the national malaria control program (25 percent of all PHPs assessed) is the only one with clearly defined statements for monitoring safety of antimalarials used in the program.

**Table 2. Current Situation of Pharmacovigilance Policy, Laws, and Regulations**

<b>Indicator</b>	<b>Responses (%)</b>
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)	7 (100)
Policy statement on pharmacovigilance in public health programs	4 (25)
1.2 Existence of specific legal provisions for pharmacovigilance in the national medicines legislation or similar legislation	4 (0)
1.3 Legal provisions require the market authorization holder (MAH) mandatorily report all serious ADRs to the national drug regulatory authority	7 (0)
1.4 Legal provisions require the MAH to conduct postmarketing surveillance activities for products that have such requirement by stringent regulatory authorities	7 (14)
1.5 Existence of policy for reporting adverse drug reactions by health care providers	3 (0)

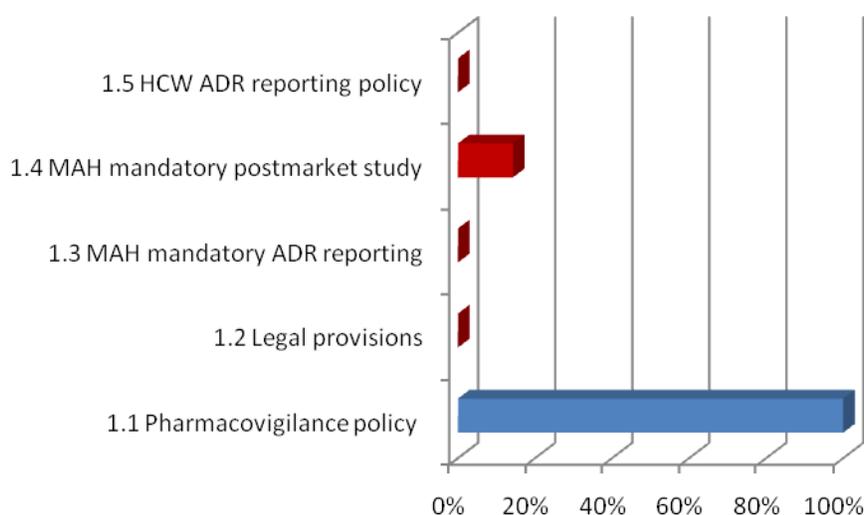
### ***Implication of Lack of Legislation***

The Ghana Food and Drugs Act did not place responsibility on the market authorization holder for product stewardship. This omission limits the capacity of the FDB to mandate postmarketing safety commitments of the licensee. Medicine laws in several other countries mandate the MAH to mandatorily report all adverse events related to the product they are licensed to market. In some countries, additional conditions are placed on the registration to ensure safe use and allow accumulation of real-life safety and effectiveness data on the product. These conditions may include the following—

- Provisional registration in the first few years, particularly for new chemical entities
- Requirement for the use of prominent warnings on medicine labels
- Requirement for mandatory reporting of all adverse events related to the product, including those that occurred outside the country where registration license was issued

- Requirement for postauthorization safety studies
- Requirement for routine and timely provision of all new information obtained that is related to the safety and effectiveness of the medicine
- Requirement for submission of periodic safety update reports

The lack of relevant laws and regulations reflects fundamental limitations for enforcing safety monitoring. The assessment asked whether policies and guidelines of PHPs contain statements on monitoring safety of medicines used in those programs. The antimalarial drug policy for Ghana is a model in that respect.<sup>23</sup>



Note: HCW = health care worker.

**Figure 3. Responses to the Policy, Law, and Regulation Indicators in the MoH assessment**

### Systems, Structures, and Stakeholder Coordination

The development of sustainable systems and their optimal functioning are critical to enable effective use of a pharmacovigilance and medicines safety system. Structures, systems, and roles provide a foundational basis for organized and systematic operationalization of pharmacovigilance activities. They enable or facilitate effective use of staff, skills, and tools. The Safety Monitoring Unit (SMU) of the FDB is the national coordinating center for pharmacovigilance activities in Ghana. Therefore, the SMU has the greatest responsibility to ensure that systems and structures are in place to guide implementation of a pharmacovigilance and medicines safety system in Ghana. The FDB has defined functions for the SMU.

<sup>23</sup> Republic of Ghana, Ministry of Health. Antimalaria Drug Policy for Ghana, 2nd revised version, January 2009.

The assessment provided some interesting responses, as seen in figures 4, 5, and 6, regarding the systems and structures that support pharmacovigilance in Ghana. All respondents at the national level (MoH) and review of the relevant documents confirmed that the following are in place—

- National pharmacovigilance unit has mandate and structure in place.
- Designated persons exist for pharmacovigilance.
- Functional information technology infrastructure exists.
- Preservice training on pharmacovigilance is being provided.
- Ghana’s pharmacovigilance center is collaborating in the WHO/UMC program for international medicine monitoring.

However, differences exist for some of these indicators that are also tracked at the PHP and HF levels. For example, only 50 percent of respondents at the HF level confirmed that their facilities have a pharmacovigilance mandate and structure; 46 percent confirmed that a designated staff member exists for pharmacovigilance or a staff member’s job description includes pharmacovigilance activities, and 77 percent considers functional information technology infrastructure available.

Some indicators were consistently poor across all the data collection points, and they include the following—

- Dedicated budget for pharmacovigilance
- Pharmacovigilance guidelines
- Protocol and SOPs
- Publication of safety bulletin/newsletter
- Pharmacovigilance training for health care workers (HCWs)
- Coordination of pharmacovigilance activities, including the mapping of stakeholders

For instance, the assessment indicated that a dedicated budget for pharmacovigilance activities seems to be more available at the national center than at the HFs: 75 percent and 43 percent of respondents from the PHPs and MoH, respectively, compared to 7 percent of respondents from the HFs.

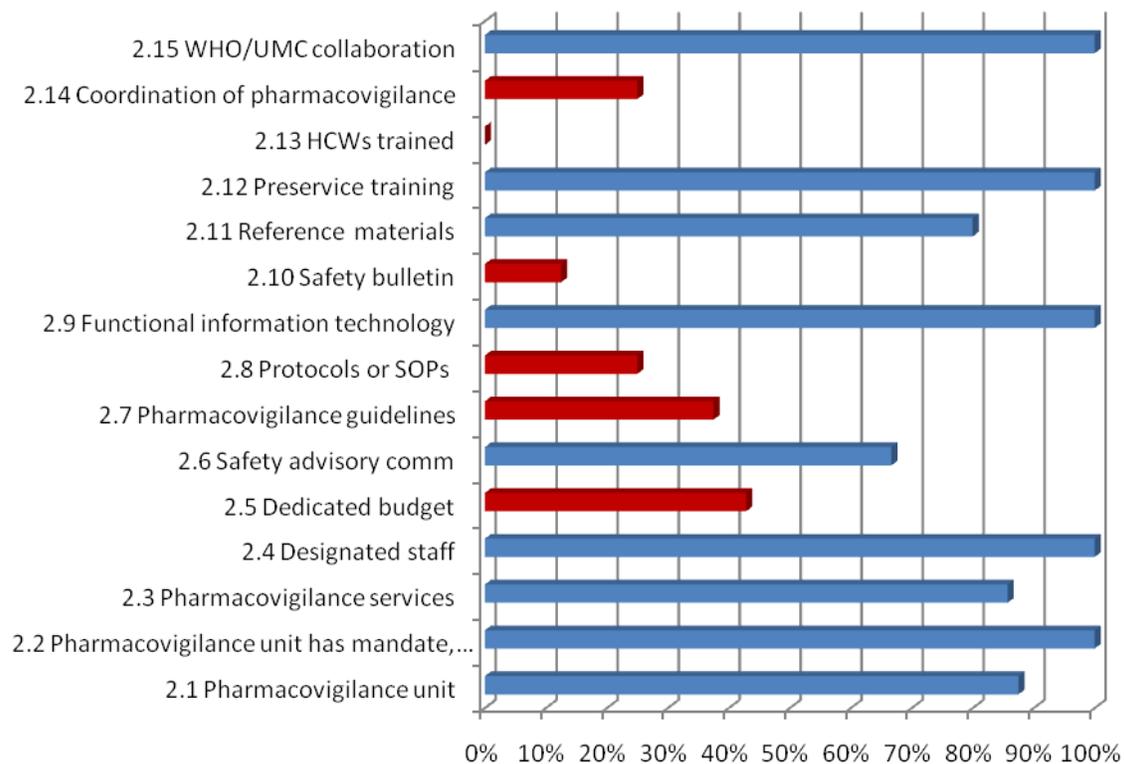
The assessment inquired about the availability of pharmacovigilance guidelines only from the MoH level; 62 percent of respondents did not agree that an adequate national pharmacovigilance guideline existed.

SOPs are necessary to standardize the provision of pharmacovigilance services. Only 25 percent of respondents from the MoH and PHPs agree that SOPs exist for pharmacovigilance activities, while none of the respondents from HFs acknowledged the existence of SOPs.

Periodic publication of safety bulletins either alone or as part of another bulletin or newsletter is one area in which the HFs are doing better than the national center; 54 percent of respondents think these publications are in place in their HFs whereas 13 percent at the national level acknowledge the routine publication of safety bulletins. Only the NDIRC publishes such bulletin at the national level.

Efforts to measure training as an indicator are usually guided by some form of target for the number of persons trained. The IPAT established a threshold for number of HCWs trained to ensure that facilities that do not meet those thresholds are not regarded as achieving optimal performance for pharmacovigilance training. At a minimum, 5 percent of professional HCWs (physicians, pharmacists, and nurses) should be trained in pharmacovigilance. Facilities that do not attain this threshold are therefore regarded as failing to provide training in pharmacovigilance. Using this target, only 33 percent of respondents from HFs and none at the national level met the training benchmark.

Only 25 percent of respondents at the MoH level acknowledge that strategies exist for coordination of pharmacovigilance activities. Even among those respondents, it was not possible to obtain a map of stakeholders working in medicine safety in Ghana.



**Figure 4. Responses to Systems, Structures, and Stakeholder Coordination Indicators in the MoH assessment**

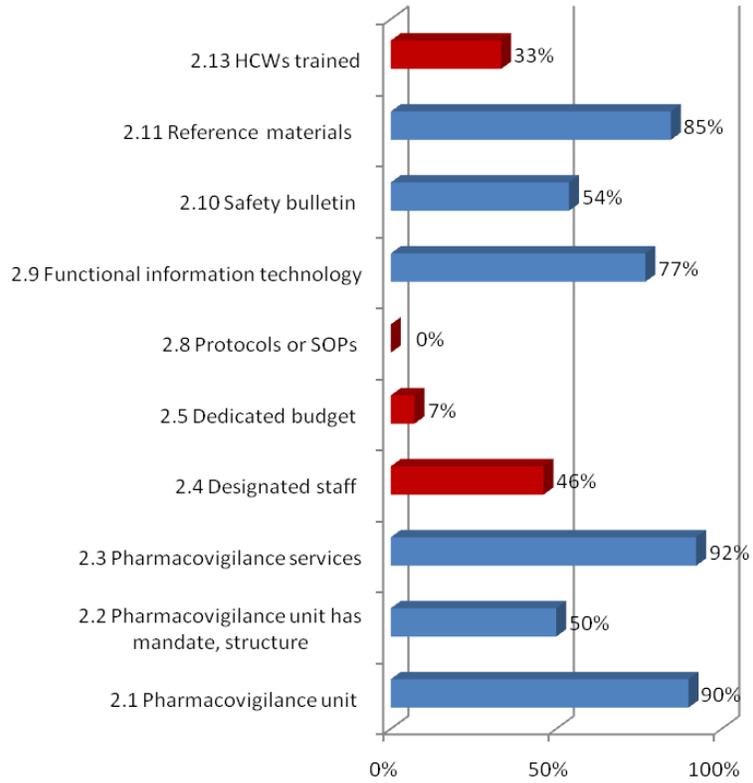


Figure 5. Responses to Systems, Structures, and Stakeholder Coordination Indicators in the HF assessment

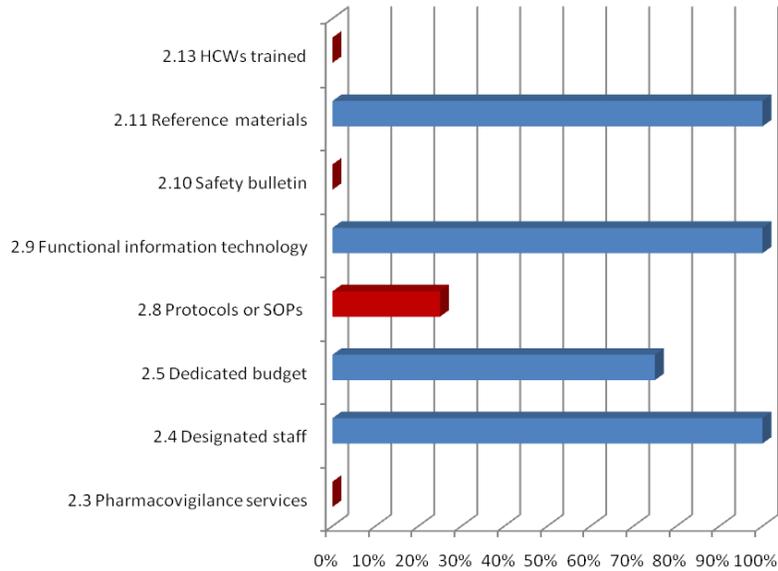


Figure 6. Responses to Systems, Structures, and Stakeholder Coordination Indicators in the PHP assessment

## **Implications of Weaknesses in Systems, Structure, and Stakeholder Coordination**

The blueprint that describes how pharmacovigilance is coordinated in a country is the national pharmacovigilance guidelines. The current guidelines for product safety monitoring<sup>24</sup> are particularly targeted at the industry and lack critical components that should be contained in a comprehensive national guideline for health product safety surveillance. The implications of the lack of this sort of guidelines can be seen in the inability to map and streamline stakeholders' contributions to pharmacovigilance. This lack has also contributed to the absence of structures within the PHPs and the treatment facilities for implementation and advancement of pharmacovigilance activities. The development and implementation of a comprehensive guideline will serve as a basis for structured and coordinated pharmacovigilance actions by various stakeholders. The lack of dedicated budget, SOPs, newsletters, and training in pharmacovigilance indicates inability and lack of capacity to consistently address medicine safety issues.

## **Signal Generation and Data Management**

The pharmacovigilance process involves signal detection, signal evaluation, and risk management.<sup>25,26</sup> Signal detection is achieved through the reporting of suspected adverse events. It is the first step in a comprehensive pharmacovigilance process. A rigorous data management system is usually required for adverse event reporting and signal detection. The development of a unified data management system that receives and collates pharmacovigilance data from all sources in a country will help coordinate and maximize data use, synthesis, and interpretation as well as comprehensive and effective results dissemination, communication, and response.

The assessment findings show that adverse event reporting forms are readily available in most levels of Ghana's health system, as shown in figures 7, 8, and 9. Within the facilities assessed, 86 percent of respondents acknowledged that ADR forms are available at the national level, 75 percent at the PHPs, and 77 percent at the HFs. At the national level, the FDB uses the WHO VigiFlow database for submitting ADR reports to the WHO/UMC. A review of the SMU annual reports and a survey conducted by the WHO in Ghana showed a consistent picture of ADR form availability. The WHO survey indicated that 81 percent of respondents are "aware of ADR forms." However, that survey also indicated that only 50 percent of respondents consider the ADR forms as "widely disseminated." In developing countries, the most frequent medicine-related problems are counterfeit and substandard products, and treatment failure (some of which may be as a result of the poor-quality products). The scope of pharmacovigilance includes therapeutic ineffectiveness, medication errors, and product quality.<sup>27</sup> Ineffectiveness is a reportable

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<sup>24</sup> Food and Drugs Board. Guidelines for Product Safety Monitoring.

<http://www.fdbghana.gov.gh/pdf/drugs/Guideline%20for%20Safety%20Monitoring.pdf>.

<sup>25</sup> Bisson, G., R. Gross, V. Miller, et al. 2003. Monitoring of Long-Term Toxicities of HIV Treatments: An International Perspective. *AIDS* 17(17): 2407–17.

<sup>26</sup> 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.

<sup>27</sup> Ibid.

event in pharmacovigilance.<sup>28</sup> Treatment failure and suspected poor product quality can be reported using the existing ADR form, a separate form or a subset of another form, or the patient case file. The assessment identified that reporting of such events is poor across all the surveyed levels. As seen in figure 7, at the MoH level, only 40 percent of respondents think that forms exist for reporting these events. The situation is worse at the PHP and the HF levels (figures 8 and 9, respectively) where only 25 percent and 29 percent, respectively, acknowledge the existence of forms for reporting product quality problems. The results are worse for medication errors and treatment failure, where none of the respondents at the PHP are aware of the existence of such forms and only 36 percent and 29 percent in the treatment facilities are aware of forms for reporting medication errors and treatment failures, respectively. The FDB acknowledges that no dedicated forms exist for these aspects of adverse events; reporters are expected to use the existing ADR form for reporting product quality defects, suspected counterfeits, and medication errors. At the national level, only 29 percent of respondents think a system exists for the collation of nationwide pharmacovigilance data into a data warehouse.

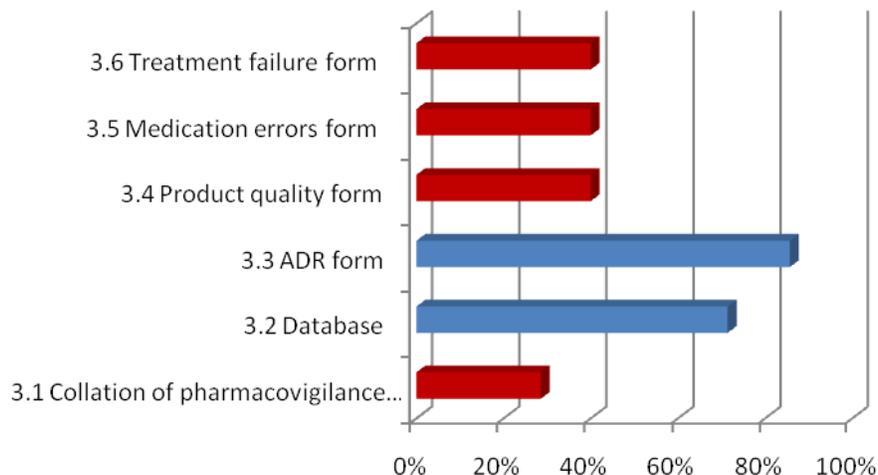
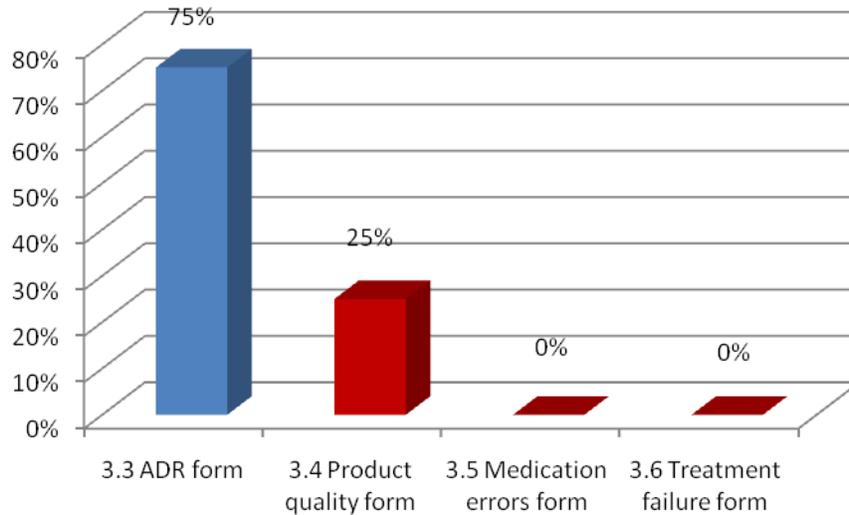
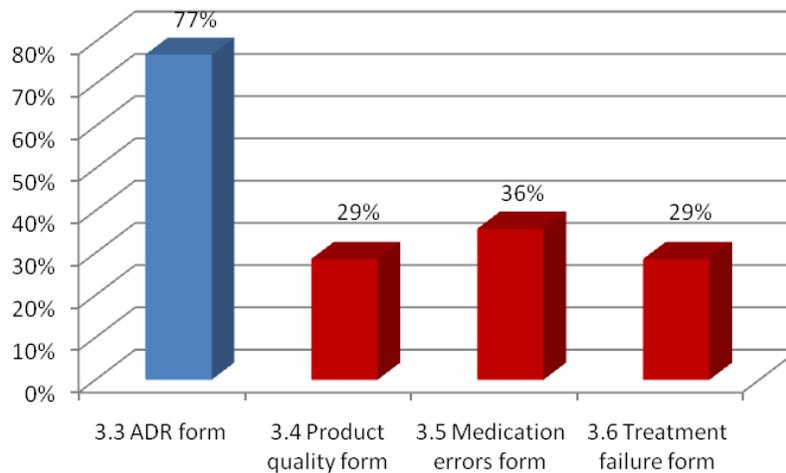


Figure 7. Responses to Signal Generation and Data Management Indicators in the MoH assessment

<sup>28</sup> Meyboom, R.H.B., 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* 23(2): 95–99.



**Figure 8. Responses to Signal Generation and Data Management Indicators in the PHP assessment**



**Figure 9. Responses to Signal Generation and Data Management Indicators in the HF assessment**

***Implications of Lack of Adequate Systems for Signal Generation and Data Management***

In many countries, signal generation relies on sensitized HCWs and stakeholders who report suspected adverse events. With the poor availability of forms or other tools for reporting such suspected adverse events as treatment failure and poor product quality, one can conclude that postmarketing surveillance activities in Ghana are impaired. The result is low reporting rates and late recognition of adverse events. Collection of data on treatment failure can potentially be integrated into routinely collected clinical data, but this is currently not happening. Therefore, opportunities for using the same data collection system to address multiple safety issues are lost.

## **Risk Assessment and Evaluation**

Risk assessment is triggered by the generation of signals. A *signal* is information that arises from one or multiple sources that 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.<sup>29</sup> When signals are generated from pharmacovigilance activities, it is imperative to assess and evaluate them—particularly signals that have significant public health importance. The periodic review of the number and types of medicine-related adverse events through passive surveillance (spontaneous reporting) as well as evaluation of significant safety issues through active surveillance are fundamental attributes of any comprehensive pharmacovigilance and medicine safety system. Active approaches to surveillance are particularly valuable for public health programs, such as HIV/AIDS, TB, and malaria programs, and can provide useful information for decisions involving revision of treatment guidelines.

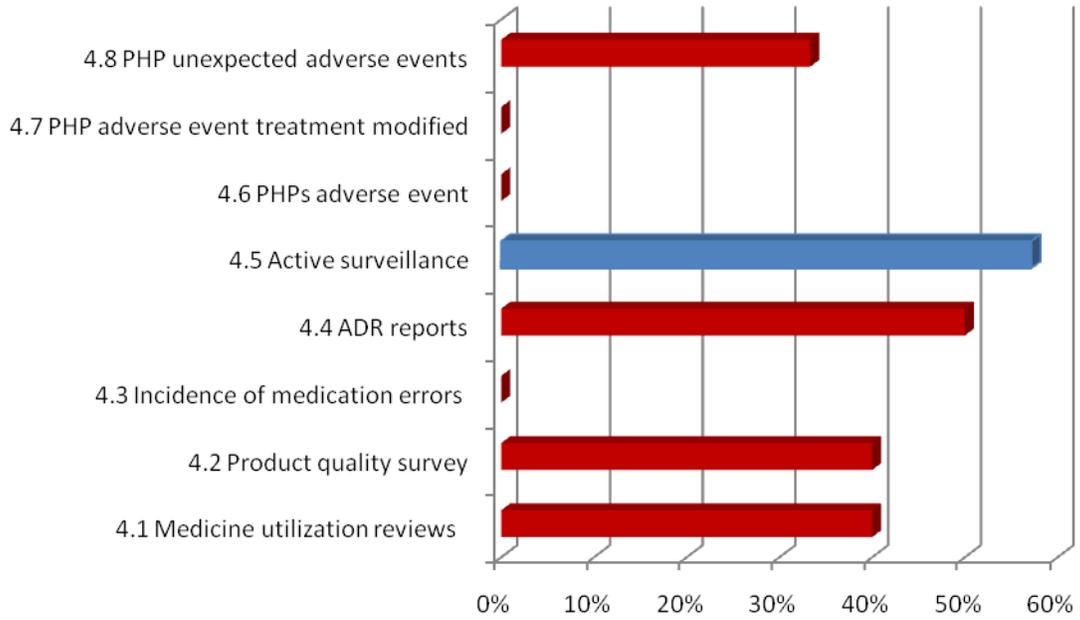
Signals can be generated only when adverse events are reported. Several indicators in IPAT address the reporting of adverse events. It may be inaccurate to consider a pharmacovigilance system functional merely because one or two reports are sent in a year. In many developing countries, the ADR reporting guidelines require reporting of all serious adverse events and, in some instances, the reporting of all ADRs related to new medicines or medicines used for mass drug administration or public health programs. IPAT recommends the use of thresholds to determine whether the number of reported adverse events meets that expected from a minimally functional system. For example, using a threshold of 100 reports per million population per year, Ghana will be expected to generate about 2,300 reports per year, and a health facility with about 50,000 people in its catchment area will be expected to generate a minimum of 5 reports per year to meet the threshold. For adverse events following immunization (AEFI), reporting rates can be calculated using vaccine distribution data. Though varied across vaccine types, an analysis of AEFI reports for 27 vaccines in 10 years showed an overall dose-based reporting rate of 11.4 reports per 100,000 net doses distributed.<sup>30</sup> The numbers of reports received in Ghana are shown on table 3.

The assessment showed some encouraging developments with regard to the conduct of active surveillance studies for the evaluation of the safety and effectiveness of medicines. However, poor reporting of adverse events was identified at the national MoH level. The situation was particularly bad, with no formal reporting of adverse events including those leading to treatment modification and incidences of medication errors. Other poorly ranked indicators include the reporting of unexpected adverse events, ADR reporting rates, product quality surveys, and medicine utilization reviews.

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<sup>29</sup> Hauben, M., and J. Aronson. 2009. Defining “Signal” and Its Subtypes in Pharmacovigilance Based on a Systematic Review of Previous Definitions. *Drug Safety* 32(2): 99–110.

<sup>30</sup> Centers for Disease Control and Prevention. 2003. Surveillance for Safety after Immunization: Vaccine Adverse Event Reporting System (VAERS)—United States, 1991–2001. *Morbidity and Mortality Weekly Report* 52(SS-1). <http://www.cdc.gov/mmWR/PDF/ss/ss5201.pdf>.



**Figure 10. Responses to Risk Assessment and Evaluation Indicators in the MoH assessment**

Table 3 analyzes the SMU 2009 annual report for the unit's activities. Using some estimated expected rates of reporting based on review of international literature, spontaneous reporting, including product quality reports, is particularly lacking.

**Table 3. Analysis of SMU 2009 Annual Report**

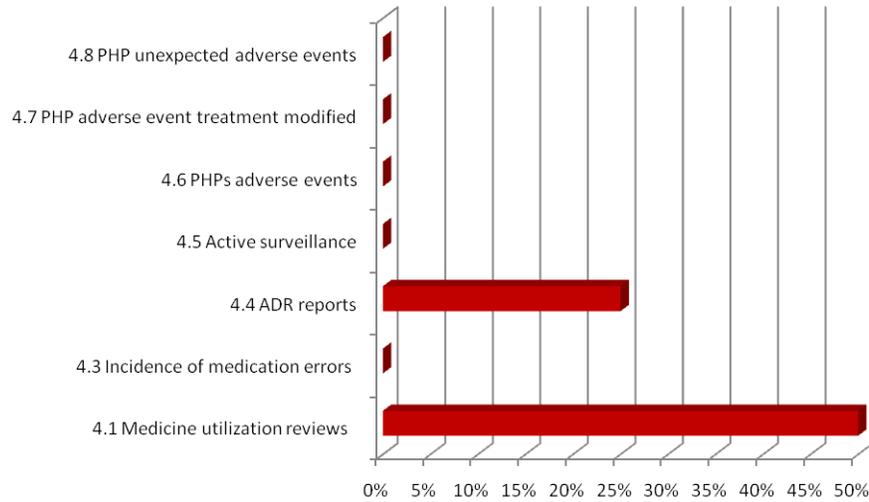
Type of Report	Observed	Expected	Percent	Comments
Spontaneous reports (x100)	1.55	23	7	Using 100 reports per million population
AEFI	15	22	68	Using 11.4 reports per 100,000 net doses distributed and assuming 200,000 doses distributed
Product quality reports (x10)	0.2	14.8	1	Using data from <i>Pharmaceutical Counterfeiting: Understanding the Extent of a New Transnational Crime</i> , average of China, India, Brazil for 2007 <sup>31</sup>
International safety reports	13	38	34	Using the <i>WHO Pharmaceuticals Newsletter</i> <sup>32</sup> (included all 2009 issues for products that are available in Ghana)
Safety communications (Dear Doctor/Health Care Professional letters)	8	20	40	Using the <i>WHO Pharmaceuticals Newsletter</i> (included all 2009 issues for products that are available in Ghana)

The same situation of poor reporting is seen from the responses obtained from the PHPs and the treatment facilities, as can be seen from figures 11 and 12. Responses to the indicator on active surveillance (Indicator 4.5) were varied, from 57 percent at the national MoH level to 36 percent within the PHPs and 0 percent at the HFs. This result may be caused by respondents' lack of information about active surveillance studies being carried out in the country.

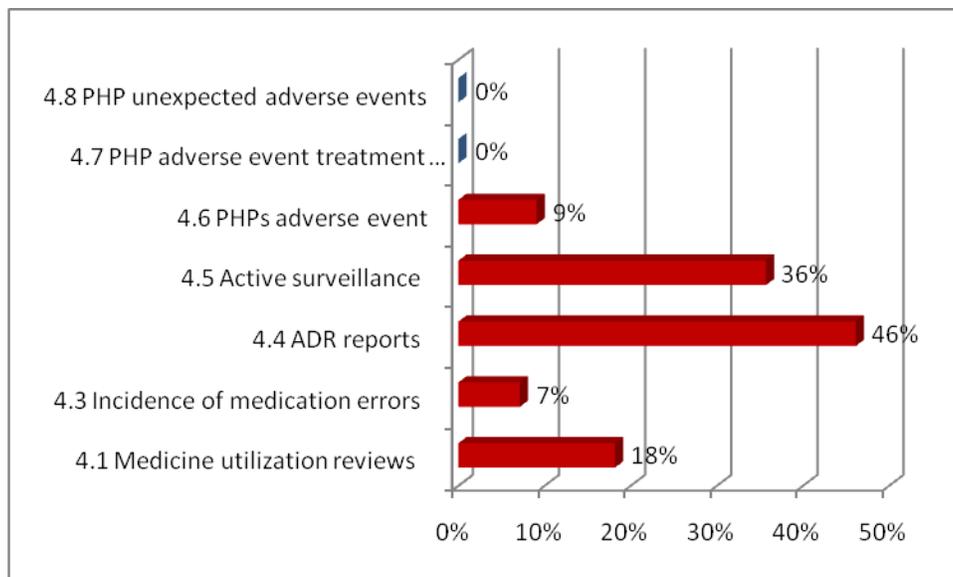
<sup>31</sup> Kubic, T. 2010. Pharmaceutical Counterfeiting: Understanding the Extent of a New Transnational Crime. *The Police Chief*, April.

[http://policechiefmagazine.org/magazine/index.cfm?fuseaction=display\\_arch&article\\_id=1574&issue\\_id=82008](http://policechiefmagazine.org/magazine/index.cfm?fuseaction=display_arch&article_id=1574&issue_id=82008).

<sup>32</sup> *WHO Pharmaceuticals Newsletter*. <http://www.who.int/medicines/publications/newsletter/en/>.

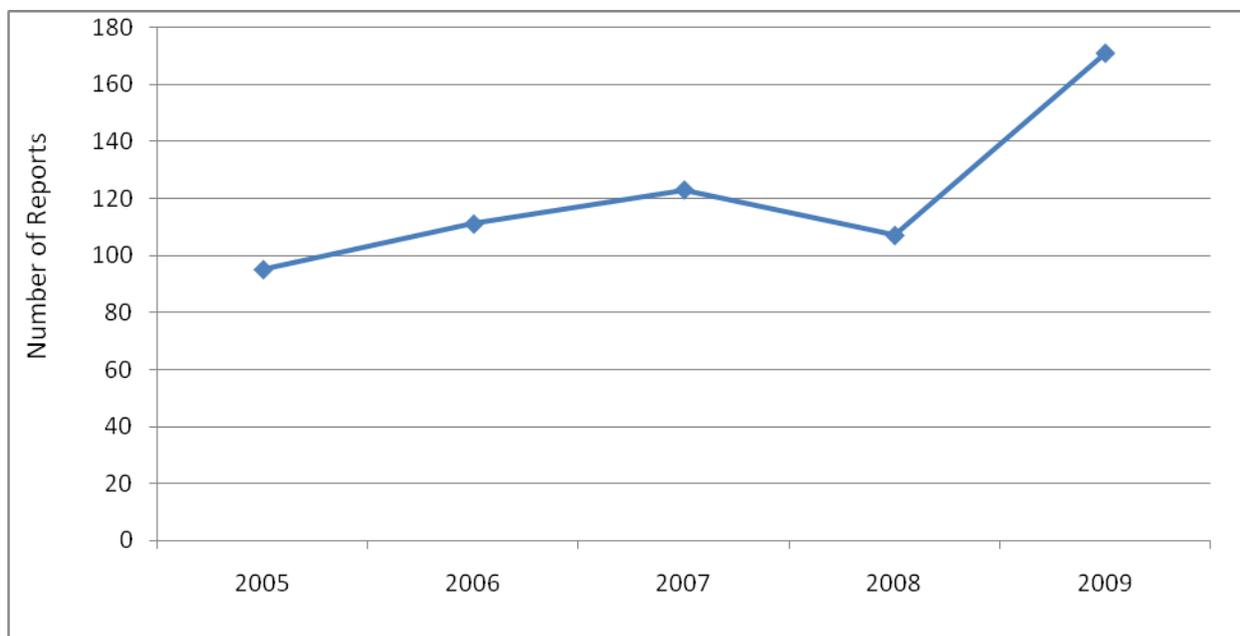


**Figure 11. Responses to Risk Assessment and Evaluation Indicators in the PHP assessment**



**Figure 12. Responses to Risk Assessment and Evaluation Indicators in the HF assessment**

Though the reporting rate is seemingly poor, some improvement has occurred in adverse event reporting generally. As can be seen from figure 13, adverse event reporting has increased from 95 reports nationwide in 2005 to 171 reports in 2009. However, improved efforts are needed in strengthening ADR reporting by all stakeholders across the country.



**Figure 13. Gradual increase in adverse event reporting from 2005 to 2009**

Table 4 was developed based on the analysis of a report from the Centre for Tropical Clinical Pharmacology & Therapeutics of the University of Ghana Medical School and the FDB.<sup>33</sup> Several research organizations and health facilities are involved in conducting medicine safety studies and projects in Ghana. The studies were categorized according to medicine safety projects and the public health program areas they are addressing. No doubt some of the institutions listed for active surveillance are merely serving as sites for conducting the same study. However, several active surveillance studies have been conducted or are currently ongoing (figure 14). Studies related to malaria are in the majority, with five studies on medicines for the management of severe malaria alone, as shown in figure 15.

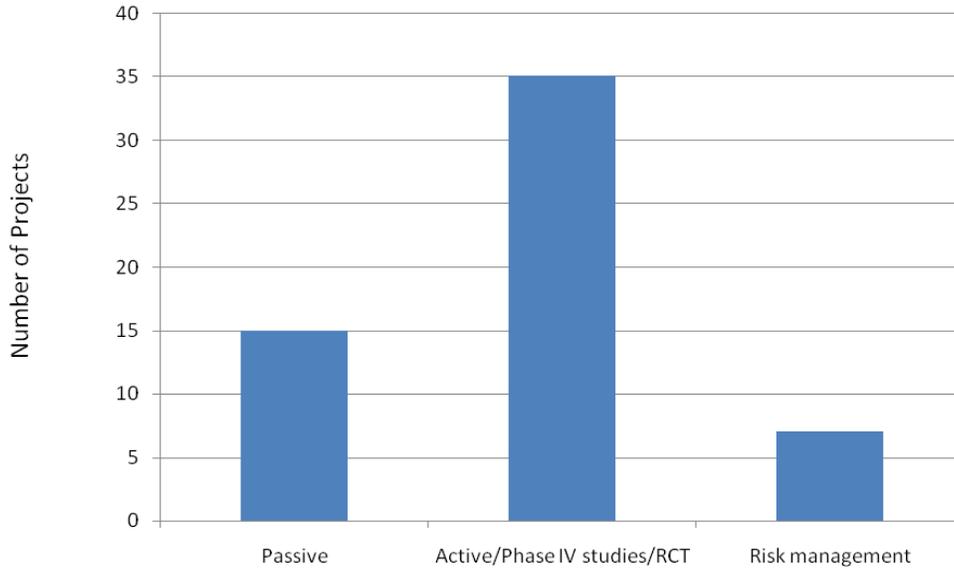
### ***Implications of Limitations in Risk Assessment and Evaluation***

The poor collection and analysis of adverse events has implications for the ability to generate signals and evaluate signals of public health importance. When such risk evaluation efforts are not undertaken, opportunities to learn about the safety and effectiveness of medicines during real-life use is lost. From the assessment, it was apparent that opportunities for the collection of longitudinal data on significant ADRs experienced by patients receiving antiretroviral medicines are not being exploited. Subsequently, opportunities to use such new knowledge to inform treatment guidelines decisions are also not utilized.

<sup>33</sup> Sabblah, G., et al. 2009. Situational Analysis of Pharmacovigilance in Ghana Centre for Tropical Clinical Pharmacology & Therapeutics, University of Ghana Medical School Food and Drugs Board, Ghana.

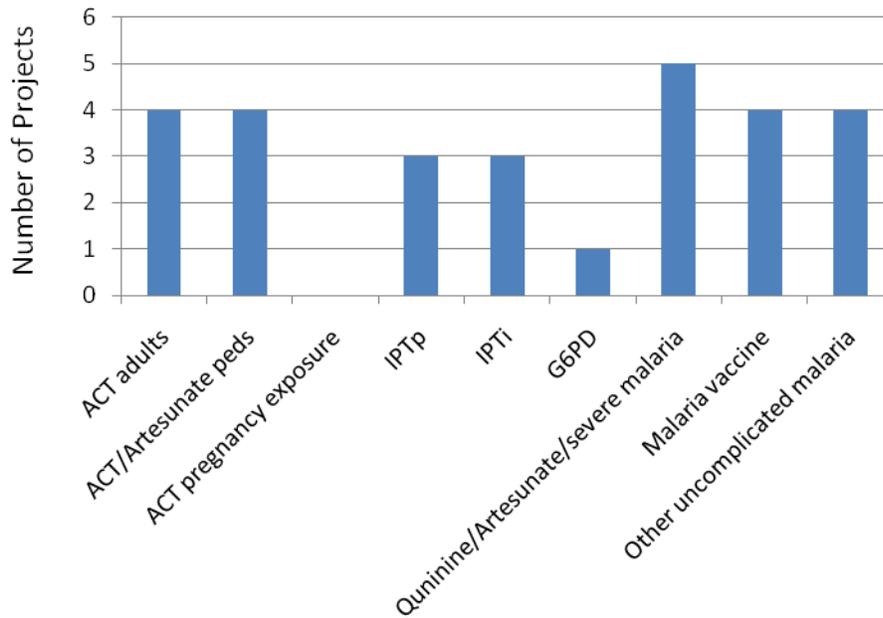
**Table 4. Projects Related to Safety and Effectiveness of Medicines Conducted by Research Facilities in Ghana**

Research Facility	Medicine Safety Projects				PHP Area				
	Number of Projects	Passive	Active/Phase IV Studies	Risk Management	HIV/AIDS	Malaria	TB	Immunization/Vaccination	Mass Drug Administration
Centre for Pharmacovigilance, Centre for Tropical Clinical Pharmacology and Therapeutics (CTCPT), University of Ghana Medical School	8	8		2	2	3		2	1
UNICEF, Ghana	1	1				1			
Police Hospital, Accra	2	1	1	1					
St. Martins De Porres Mission Hospital, Somanya	1	1		1					
Atua Government Hospital	1	1		1					
Koforidua Regional Hospital	1	1		1					
Onchocerciasis Research Centre (OCRC), Hohoe	5		5						5
School of Nursing, College of Health Sciences, Kwame Nkrumah University of Science and Technology (KNUST), Kumasi	1	1				1			
School of Medical Sciences, KNUST, Kumasi	8		8			7		1	
Dangbe West Health Research Centre, Dodowa	2	1	1			2			
Kintampo Health Research Centre, Kintampo	8		8	1		7			1
Navrongo Health Research Centre, Navrongo	12		12			10		3	1
Centre for Scientific Research into Plant Medicine, Mampong									
<b>Total</b>	<b>50</b>	<b>15</b>	<b>35</b>	<b>7</b>	<b>2</b>	<b>31</b>	<b>0</b>	<b>6</b>	<b>8</b>



RCT = randomized controlled trial.

Figure 14. Breakdown of medicine safety projects



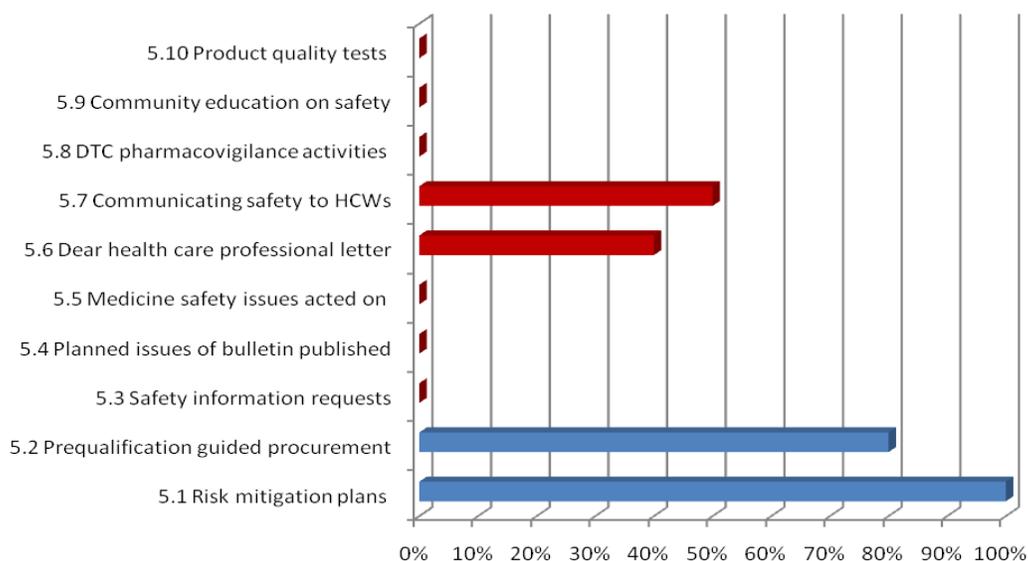
Note: peds = pediatrics; IPTp and IPTi = intermittent preventive treatment of malaria in pregnancy and in infants; G6PD = glucose-6 phosphate dehydrogenase.

Figure 15. Studies in special patient populations

## Risk Management and Communication

Increasingly, the need to use pharmacovigilance data to improve safe use of medicines is being emphasized.<sup>34,35</sup> The focus is on preventing or minimizing risk rather than merely identifying and managing harm after it has already occurred. The IPAT used in the Ghana assessment has several indicators addressing risk management and communication. These indicators focus on the recognition of the role of prevention in pharmacovigilance. If effectively implemented, such preventive approaches have significant potential to reduce the incidences of harm caused by medication use.

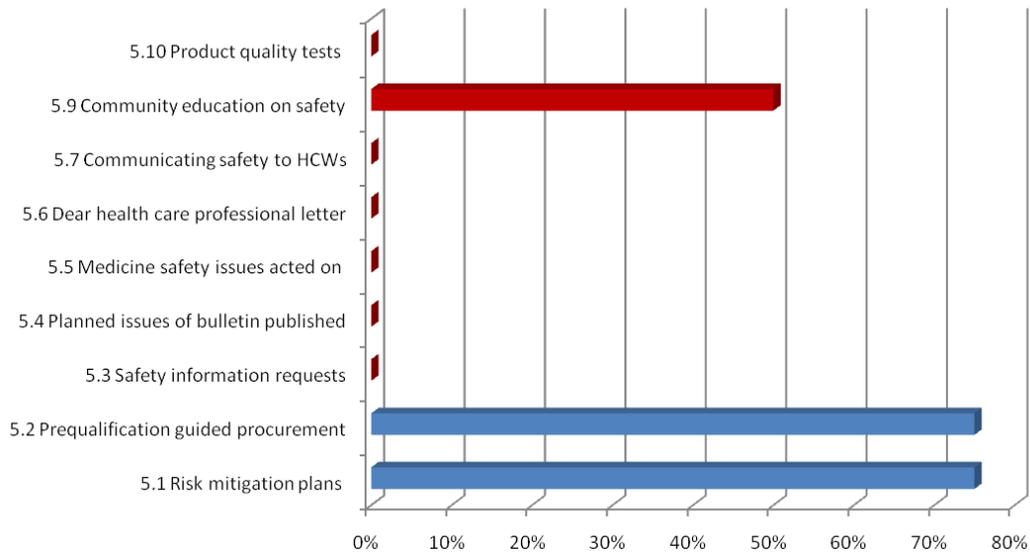
Figures 16, 17, and 18 depict the feedback received about risk management and communication activities in Ghana. Overall, efforts at mitigating the risk of medicinal products are clearly still in their early stages across all levels in Ghana. The assessment used a broad definition for risk mitigation activities with a view to ensuring that ongoing efforts that have the potential to reduce risk are identified and encouraged. Therefore, elements of risk mitigation plans were identified across all the levels assessed. However, safety communication activities, including requests for safety information, using bulletins to publish safety information, responding to safety information once received, and communicating safety to HCWs and the community, all fared poorly across all levels assessed. At HFs, the assessment identified that only 36 percent of the sampled DTCs had conducted or were conducting ongoing pharmacovigilance-related activities.



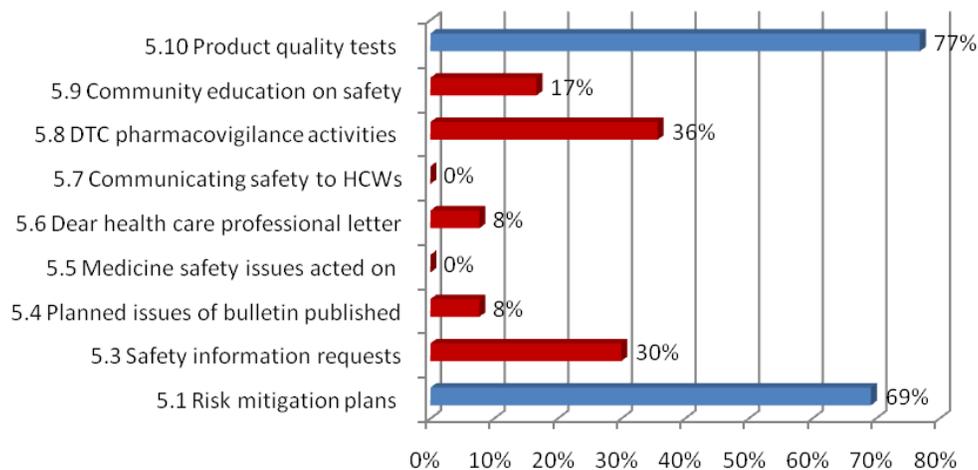
**Figure 16. Responses to Risk Management and Communication Indicators in the MoH assessment**

<sup>34</sup> U.S. Food and Drug Administration. FDA Safe Use Initiative: Collaborating to Reduce Preventable Harm from Medications. <http://www.fda.gov/Drugs/DrugSafety/ucm187806.htm>.

<sup>35</sup> 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 17. Responses to Risk Management and Communication Indicators in the PHP assessment**



**Figure 18. Responses to Risk Management and Communication Indicators in the HF assessment**

### ***Implications of Limitations in Risk Management and Communication***

Risk management and communication is a component of pharmacovigilance with high impact in preventing harm from the use of medicines. The assessment findings indicate that opportunities for improving medicine harm prevention practices are lost. For instance, regulatory authorities in developed countries are currently concerned about the misuse of over-the-counter pain relievers, particularly those containing multiple analgesics. The assessment did not find this issue addressed in Ghana, notwithstanding the ready availability of over-the-counter products such as

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No-Spalgin (codeine phosphate 8 mg, drotaverine hydrochloride 40 mg, paracetamol 500 mg), Molfen (ibuprofen 400 mg, paracetamol 325 mg), Navran (diclofenac 50 mg, paracetamol 650 mg). The national medicine register contains many products that require some form of risk management. Although these products are available in the market, no strategies are in place to ensure safe use of the products. Information that is already known about safety of most medicines to improve patient outcomes is not used. This situation greatly affects the quality of patient care.

## **Respondents' Recommendations**

During the assessment, respondents were asked to offer other suggestions and recommendations that they consider are useful for improving Ghana's pharmacovigilance and medicine safety system. Some of the respondents who offered recommendations addressed several issues. Some of the responses are quoted in table 5. Recommendations are categorized into themes according to the five components of the pharmacovigilance system. All responses were not included in this table.

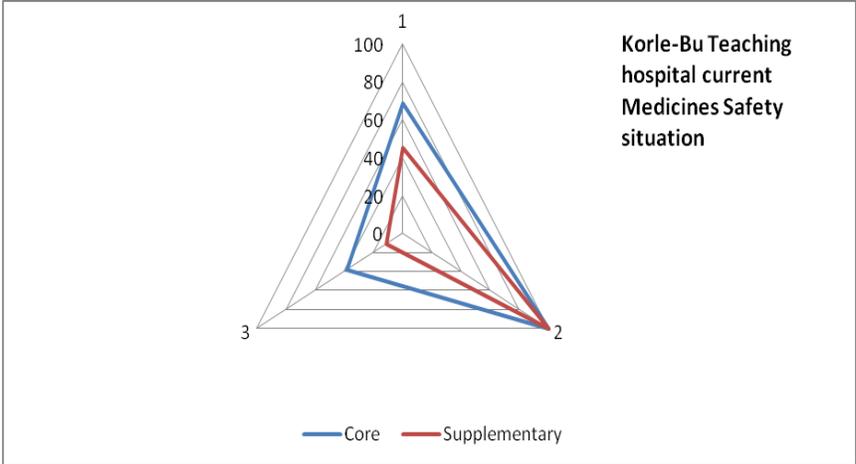
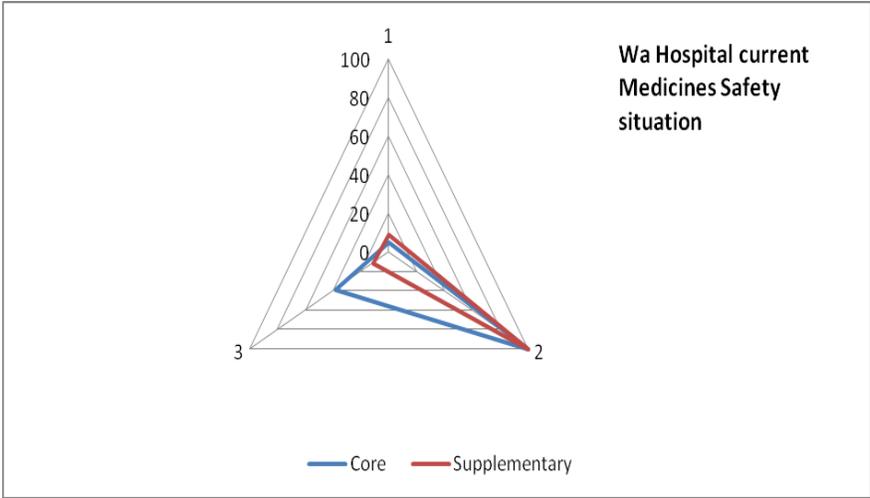
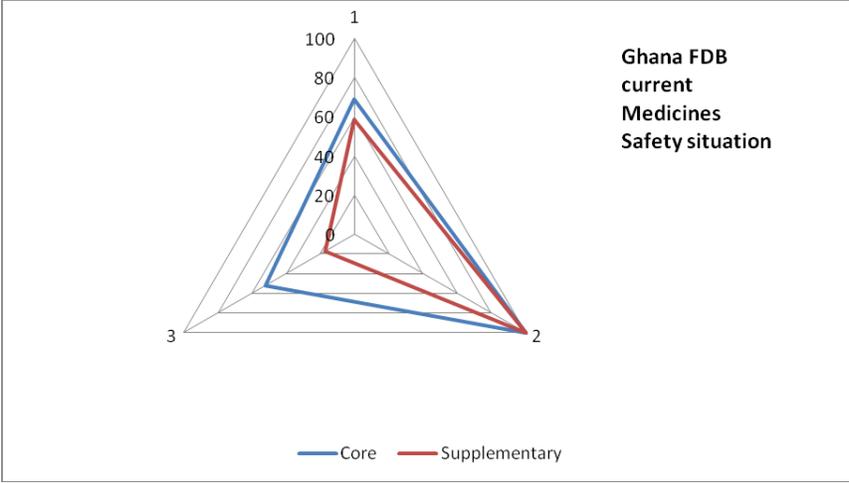
## **Pictorial Representation of the Pharmacovigilance Situation in Selected Institutions**

When the current situation of the pharmacovigilance system in an institution is represented pictorially, for example using radar diagrams (and subsequently tracked longitudinally), the visualization is anticipated to assist in recognizing improvements as they occur. Samples of such representations for the FDB, Wa Hospital, and the Korle-bu Hospital are shown in figure 19. These figures are constructed by converting the responses to the assessment questions and the indicators (disaggregated as core and supplementary) to "Yes/No" and using weighted scoring. For instance, the "Yes" responses to core indicators are scored 2 each and supplementary indicators scored 1. A functional pharmacovigilance and medicine safety system should answer "Yes" on all the 26 core indicators. Hence, it will have a score of 52, which is equivalent to 100 percent. Such a system will show the blue lines at the outer tips of the axes of the chart in the figures. Likewise, when the 17 supplementary indicators are met, a score of 17 will have the dark red line at the outermost part of the chart. The blue and dark red lines in the figures therefore show the current situation of the pharmacovigilance system with regard to the core and supplementary indicators, respectively.

**Table 5. Respondents' Recommendations for Improving the Pharmacovigilance System in Ghana**

Theme	Respondents' Recommendations
<p><b>Policy, Law, and Regulation</b></p>	<p>“Currently there are no legislations which could be enforced. So there is a need to translate policy into regulations and legislative instruments.”</p> <p>“Efforts should be made to draw up clear policies that will enable premarketing safety information handled by TAC [technical advisory committee] for clinical trials to be translated to the postmarketing safety monitoring and safety data.”</p> <p>“For the industry, reporting adverse events has to be a law.”</p> <p>“Factor in cost of managing product safety issues to registration fees. Some of the funds out of this should go to NDIRC as they participate in managing/preventing drug safety issues.”</p>
<p><b>Systems, Structures, and Stakeholder Coordination</b></p>	<p>“The current guidelines on safety monitoring are not comprehensive and would not bind any stakeholders to be active participant in the pharmacovigilance system. There should be a data and safety monitoring board which would be independent of all clinical trial committees. That committee will protect the integrity of clinical trial study.”</p> <p>“The national guideline is not comprehensive. Only touches on pharmacovigilance in industry and not on stakeholders. Need to expand to cover other stakeholders. This should cover all studies, product safety studies (both pre and post-market surveillance).”</p> <p>“Pharmacovigilance has not caught on well within the general system. Also there is a need to create systems for ADR reporting, postmarketing surveillance, and quality monitoring etc., which would be more useful locally to generate data. This may work better than allocating specific funds for generation of such data so that even when there are no funds, the system will work.”</p> <p>“Priorities to improve pharmacovigilance systems: review and revise MOU between FDB and UGMS. Review current safety monitoring guideline to capture details of all stakeholders, activities.”</p> <p>“Dedicate time in the current medical training curriculum. Pharmacovigilance is only taught 2 hours in the entire 4-year course. The current TACs need training and orientation; only few members have detailed training.”</p> <p>“Technical expertise is required by the safety monitoring unit to manage data entered to Vigiflow and to do data mining. More efforts and resources are needed to follow up poor quality reports.”</p> <p>“There is lack of coordination between the major stakeholders in pharmacovigilance. A number of people are doing safety monitoring research that other stakeholders do not know.”</p> <p>“Need for FDB to make representation on NDIRC, TAC for enhanced communication. The option of making NDIRC part of SMU system should be reconsidered.”</p> <p>“Challenge of getting FDB product register. Need for a system/routine procedure that will forward update drug register to NDIRC? This could even include products pending registration.”</p>

Theme	Respondents' Recommendations
<b>Signal Generation and Data Management</b>	<p>“Data collected by young professionals should be published as motivation.”</p> <p>“Need to consider making ADR reporting form an interactive PDF form that would be made available to the centre to use when necessary.”</p> <p>“There is a need undertake far more training for people to understand the definitions on the ADR forms. Need to update ADR form so treatment failure section stands out.”</p> <p>“ICPs [institutional contact persons] need to be formally recognized by their facilities and may have to be remunerated.”</p> <p>“Confidentiality of ADR reporting and the anonymity of the reporter should be ensured at all times to enhance continual reporting. Need for training of health professionals on the essence of reporting ADRs.”</p> <p>“Need for FDB to supply cabinets for storage of ADR forms in various facilities/wards to make them more accessible.”</p>
<b>Risk Assessment and Evaluation</b>	<p>“Institutions should be given benchmarks that will form the bases for awards or incentives after a period: e.g., number of active studies carried out by an institution per year, number of reports received from a hospital per year, relevant drug registry developed by an institution per year.”</p> <p>“A part of medicine registration fee should be dedicated to pharmacovigilance, especially for training.”</p>
<b>Risk Management and Communication</b>	<p>“A distribution or e-mail list should be made so stakeholders will receive regular safety information intended for the public that will come to FDB. This same list could be given to WHO/UMC so information from the center could also be forwarded to stakeholders to serve as a motivation.”</p> <p>“Emphasis on ADR prevention and its reporting. Health workers should be encouraged to report medication errors.”</p> <p>“Outsourcing could help. For example, the NDIRC could help in reviewing ADR reports. There could be lots of synergy with NDIRC—it is currently underutilized.”</p> <p>“Consider the option of outsourcing or collaboratively undertaking, vetting, and reviewing of adverts and promotional materials to or with the NDIRC since they have underutilized technical expertise and capacity in pharmacy and communication.”</p>



**Figure 19. Radar charts of current situation of pharmacovigilance system in a sample of three institutions**

## RECOMMENDATIONS FOR IMPROVING PHARMACOVIGILANCE IN GHANA

### Establish the Directorate of Postmarketing Surveillance

The FDB is advised to initiate discussions immediately toward the establishment of a directorate of PMS under the Drug Evaluation and Registration Department of the FDB. The proposed directorate will consist of medicine information services, pharmacovigilance, and quality surveillance units. The proposed PMS directorate should ultimately comprise the current SMU of the FDB, the NDIRC, and the Drug Post-Market Surveillance Unit.

The NDIRC is currently set up directly under the Research and Development Department of the MoH; however, its mandate, current resources, and staffing can be very helpful to the FDB not just for PMS activities but also for the provision of support services in reviewing the summary of product characteristics, labeling, and promotional materials for the initial registration of health products. Therefore, the NDIRC can provide useful services for the FDB drug evaluation department with regard to review of advertising and promotional materials submitted for use by regulated industries.

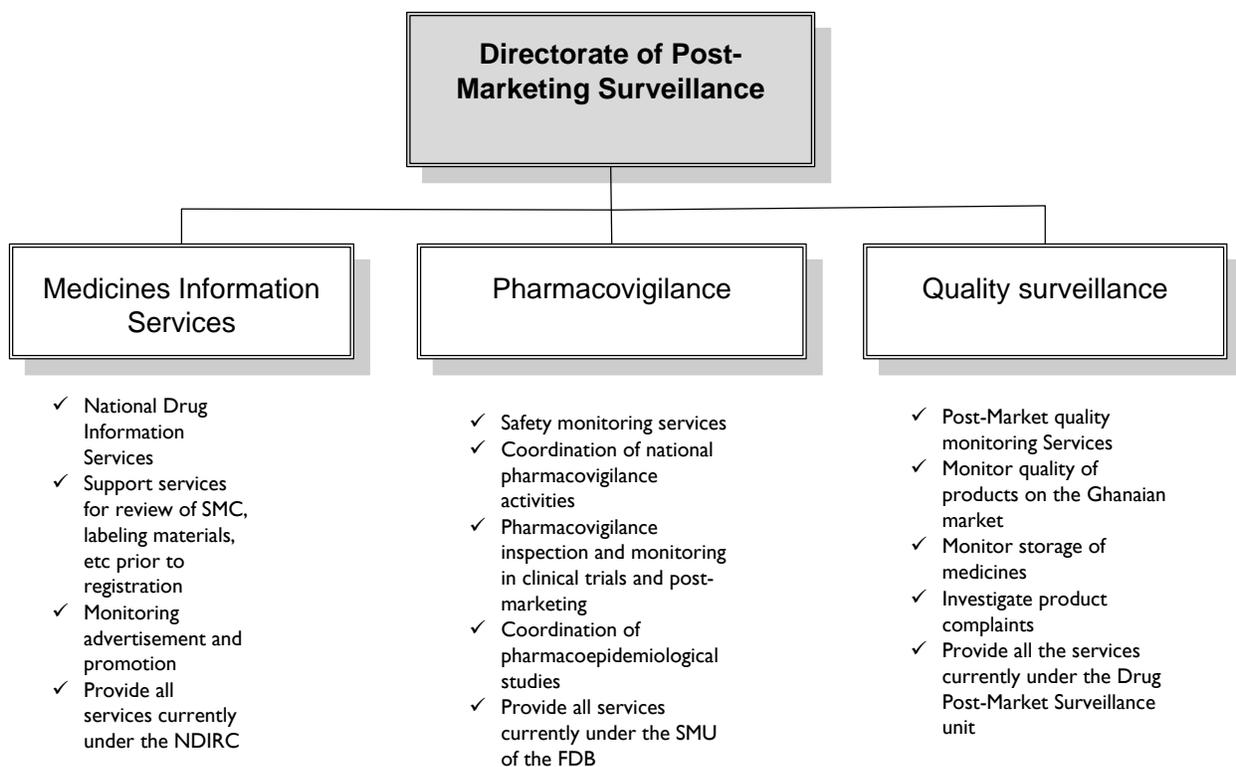
Currently, the FDB's guidelines for product safety monitoring recommend that such advertising materials should be submitted for review and approval prior to use. The assessment found that a backlog of more than one year exists in the review of such materials submitted for approval. Regulated industries therefore do not take the recommendation seriously, and most do not submit their promotion materials for prior approval. Those that do submit their materials use them before approvals are obtained. These delayed approvals are not unconnected to lack of capacity within the current FDB for review and approval of promotional materials, whereas the NDIRC already has relevant resources and staffing that can enable it provide this service for the FDB. The review and approval of advertising and promotional materials is a potential source of revenue for the proposed directorate and the FDB in general.

According to the WHO, the overall objective of a National Regulatory Authority for medical products is to ensure that all medicines (drugs, vaccines, biological, and medical devices) are of assured quality, safety, and efficacy and are accompanied by appropriate information to promote their rational use.<sup>36</sup> Establishing the PMS will enable the FDB to achieve this goal. Several countries have similar structures where the medicine information and pharmacovigilance activities are carried out under the same unit and within the National Regulatory Authority.<sup>37</sup> Figure 20 presents the structure and key responsibilities of the units under the proposed directorate of PMS.

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<sup>36</sup> WHO. 2003. Aide-Memoire: Strengthening National Regulatory Authorities. <http://whqlibdoc.who.int/hq/2003/a80815.pdf>.

<sup>37</sup> The Drug Administration and Control Authority of Ethiopia has a Planning, Drug Information Establishment and Distribution Department that is responsible for both drug information and pharmacovigilance. Others are the National Drug Authority of Uganda and the Namibia Medicines Regulatory Council.



**Figure 20. Proposed structure for the directorate of PMS of the FDB**

### **Revise Relevant Legislation to Adequately Address Safety Monitoring**

The Food and Drugs Law (PNDCL 3058) of 1992 is deficient in that it lacks provisions on pharmacovigilance. Modern practices from competent regulatory authorities, such as mandatory reporting requirements for the MAH, conditional registration of new medicines, and postmarketing safety commitments, are not included in the current legislation. The current legislation should be immediately amended to include relevant provisions that address the role of the MAH in safety monitoring. In addition, regulations should be developed so that rules are consistent with the legislation described to enhance compliance by MAH and the regulated industries.

### **Develop Comprehensive National Guidelines for Pharmacovigilance**

The assessment and respondents’ recommendations highlighted the need to develop comprehensive pharmacovigilance guidelines that will be useful for all stakeholders. The essential components of such comprehensive guidelines for health product safety surveillance may include—

- Policy and legal provisions for pharmacovigilance
- Scope of pharmacovigilance and medicine safety surveillance activities
- Stakeholders' roles and responsibilities
- Notification system
- Methods for health product safety surveillance
  - Spontaneous reporting
  - Active surveillance
    - Guidelines for conducting active surveillance studies
- Medicine information, communicating safety and effectiveness
  - Guidelines for ethical promotion of health products
  - Comparative effectiveness
- Benefit-harm assessment
  - Postlicense responsibilities of medicinal product MAH
  - Risk minimization
- Monitoring and evaluation

The FDB should be tasked to initiate efforts to develop such comprehensive national guidelines for safety monitoring activities. The development of the guidelines can be supported by development partners and involve stakeholders in pharmacovigilance in Ghana.

### **Coordinate Stakeholders**

The responsibility for pharmacovigilance should be shared among multiple stakeholders, including drug regulators, the pharmaceutical industry, the WHO, PHPs, academic researchers, donor organizations, the health care delivery sector, and the public and patients.<sup>38</sup>

Pharmacovigilance is an overarching issue requiring that all stakeholder participation be encouraged and welcomed for successful implementation. However, the experience in many countries is that such interactions among stakeholders have been limited and fragmented. A common understanding and coordinated functioning by these interrelated bodies is imperative for strengthening the pharmacovigilance system.

Implementing the recommendations of this assessment provides an opportunity to clearly define the roles and responsibilities of different stakeholders as well as to create a platform that enables effective coordination among these stakeholders. The first step in establishing such coordination is to develop a comprehensive mapping of all players. Currently, several pharmacovigilance-

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<sup>38</sup> Pirmohammed, M., K. N. Atuah, A. N. O. Dodoo, and P. Winstanley. 2007. Pharmacovigilance in Developing Countries. *BMJ* 335:462.

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related activities are going on without the knowledge of key figures within the ministry. Such stakeholder mapping is shown in figure 21 and will enhance the identification of opportunities for synergies. Besides the MoH, other bodies such as the U.S. President's Emergency Plan for AIDS Relief, the President's Malaria Initiative, the Global Fund to Fight AIDS, Tuberculosis and Malaria, the U.S. Centers for Disease Control and Prevention, the U.S. Agency for International Development, and the WHO are leveraging funding for pharmacovigilance. As these various streams of funding and actions move forward, maintaining effective coordination to achieve results that are complementary and synergistic will be important. It is recommended that the FDB should develop a comprehensive mapping document to describe pharmacovigilance stakeholders and their roles and responsibilities. This process will help identify gaps, plan and improve coordination, and advance efforts on pharmacovigilance and medicine safety monitoring.

*Recommendations for Improving Pharmacovigilance in Ghana*

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 laws	Development/ review/ monitoring compliance with 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
<b>International</b>																
WHO/UMC																
<b>National</b>																
Ministry of Health																
FDB																
Technical Advisory Committee																
FDB SMU																
NDIRC																
PHPs																
Manufacturers, Importers, Wholesalers, Distributors																
NGOs (MSH/SPS)																
Universities/Research Institutions																
<b>Regional</b>																
Regional center/Institutional contacts																
Wholesalers, Distributors																
Others																
<b>Local</b>																
Hospitals/Clinics (Providers)																
Hospitals (DTCs)																
PHPs at the health centers and clinics																
Retailers																
Community and Consumers																
Consumer organizations																
Others																

**Figure 21. Sample map of stakeholders and their roles in pharmacovigilance in Ghana**

## Strengthen the Role of DTCs in Pharmacovigilance

The DTCs should be revitalized and used as a vehicle for strengthening pharmacovigilance at the treatment facilities. The DTCs are well positioned to address medicines safety issues in the treatment facilities. A previous survey in Ghana had recommended that DTCs should be strengthened to coordinate pharmacovigilance programs at facility level.<sup>39</sup> Also, a respondent during the assessment mentioned that currently using the institutional contact person (ICP) is not an efficient way to entrench pharmacovigilance in health facilities because the ICPs are inadequately motivated and at times are transferred out of the facility. It is therefore recommended that DTCs should play a major role in championing pharmacovigilance in treatment facilities. The role of the DTC has been highlighted in figure 22, adapted from the current notification system in Ghana.

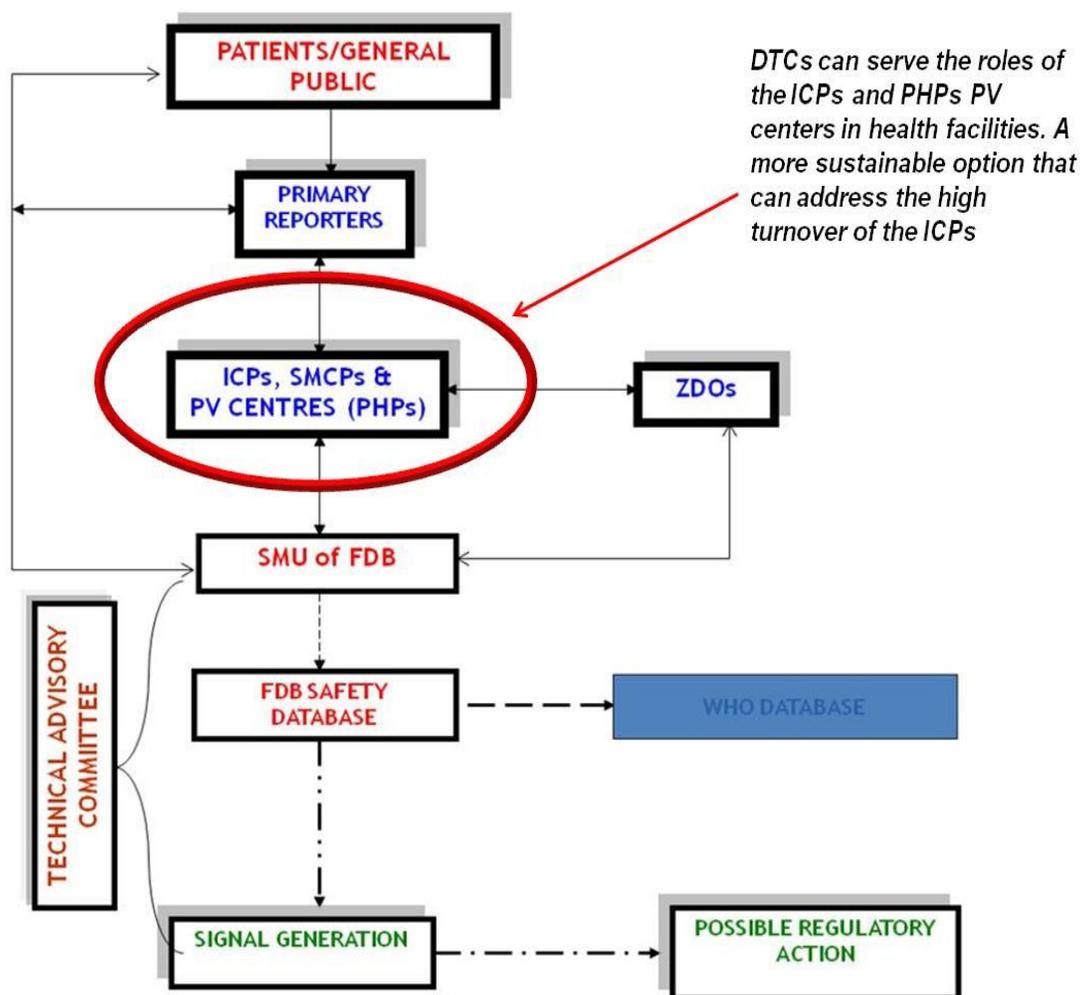


Figure 22. Ghana adverse event notification system and the potential role for DTCs

<sup>39</sup> Owusu-Antwi, F., and E. Andrews Annan. 2010. WHO, NPO Accra Ghana. Pharmacovigilance Systems Review Meeting feedback from the field. Presentation made at the preassessment workshop Accra, Ghana, January 19.

## **Improve Reporting of Adverse Events**

For immediate gains in strengthening pharmacovigilance in Ghana, simple and cost-effective strategies should be put in place to improve adverse events reporting. Some of these strategies include the following—

- Provide support to selected sentinel sites for improving reporting. Preference should be accorded to sites with computers and Internet connections, sites that currently have high reporting rates, and sites with functional DTCs.
- Implement simple information and technology strategies to improve reporting.
  - Interactive PDF forms: These interactive PDF forms can be loaded on computers at sentinel health facilities. The forms can be completed electronically, saved, and sent through the cell phone general packet radio service system to the FDB. Interactive PDF forms also have features for capturing completed forms in Excel spreadsheets.
  - Cell phone text messaging: Cell phones are widely deployed in Ghana and can be a good tool for postmarketing safety surveillance. Consumers can send reports of adverse events suspected to be related to medicines they used or reports of products of suspicious quality. These reports can be sent through prepaid lines that the FDB can support. The current effort in Ghana using cell phones to tackle fake medicines is a good example.<sup>40</sup>
  - Collaboration with pharmaceutical companies and other stakeholders to enhance their participation in adverse event reporting: For instance, the FDB can request all manufacturers of antimalarials to include SMU phone numbers on the packaging and request consumers to call or send text messages when they have a reaction or treatment failure.
- Develop online forms that when sent from sites with an Internet connection and received at the FDB can automatically populate spreadsheets prior to entry into VigiFlow. The Saudi Food and Drug Authority uses such online ADR forms.<sup>41</sup>
- Improve reporting within the PHPs. PHPs such as the antiretroviral therapy program have improved the collection of longitudinal data on patients undergoing treatment. Some of these programs collect data on patient responses to the medicines prescribed. Strategies should be put in place to collate these routinely collected data and make them available to the SMU. The SMU should also consider developing some indicators and requesting the PHPs to adopt these indicators and to routinely report them to the FDB. In South Africa, efforts have been made to ensure that the antiretroviral therapy program adopts pharmacovigilance indicators for monitoring safety of medicines.<sup>42</sup>

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<sup>40</sup> mPedigree: The use of SMS messaging to report fake medicines in Ghana. <http://mpedigree.net/>.

<sup>41</sup> Kingdom of Saudi Arabia, Saudi Food & Drug Authority, Adverse Drug Reaction reporting form (ADR) for healthcare professionals. <http://www.sfda.gov.sa/Services/ADR/Forms/DrugADR1.aspx>.

<sup>42</sup> Department of Health. 2004. *Monitoring and Evaluation Framework for the Comprehensive HIV and AIDS Care, Management, and Treatment Program for South Africa*. <http://www.doh.gov.za/docs/reports/2004/hivaids-care/monitorevaluation.pdf>.

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## Enhance the Use of Spontaneous Reporting for Monitoring Product Quality and Treatment Failure

During the assessment, respondents mentioned concerns about poor product quality as a major issue in Ghana. Many respondents highlighted cases of treatment failure but were unaware that the current ADR form can also be used for product quality and treatment failure complaints. Such reports can generate signals. Currently, FDB efforts exist to improve product quality surveillance activities, particularly using support from the United States Pharmacopeia's Promoting Quality of Medicines program of the U.S. Agency for International Development. Poor-quality antimalarials are a huge issue in Ghana and other developing countries in Africa.<sup>43</sup> The cornerstone of routine surveillance for poor product quality is the use of the adverse event reporting form to signal suspected cases of substandard products.

It is recommended that the FDB adopt risk-based surveillance that focuses on product quality complaints generated through the spontaneous reports. Products involved in these reports can be screened with Minilab. Subsequently, confirmatory tests may be carried out if warranted. When products are found to be substandard and have caused harm, then case-control studies should be carried out to determine risk and to characterize and quantify adverse events associated with the product of poor quality.

## Develop Protocols and SOPs and Establish Incident Registers

Efforts should be made immediately to develop and implement standards and procedures for risk management and communication activities. These interventions can go a long way in facilitating safe use of medicines and in improving treatment outcomes. The development and use of SOPs for improving safe and rational use of medicines and strategies for harm prevention related to high-risk medicines should be given a priority. In addition, risk management tools should be developed for medicines that have the potential for self-medication, for example, ACTs and other antimalaria medicines.

The DTCs should be challenged by the FDB to develop SOPs on topics related to safe use of medicines. Examples of such SOPs may include—

- Dispensing high-risk medicines
- Interventions for correcting prescription errors
- Adverse events incidence reporting and mitigation
- Medication guides and patient information leaflet
- Counseling patients on side effects to expect from their medicines
- Adherence counseling
- Risk registers
- Prevention and management of adverse events<sup>44</sup>

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<sup>43</sup> Maponga, C., and C. Ondari. 2003. *The Quality of Antimalarials: A Study in Selected African Countries*. WHO/EDM/PAR/2003.4. Geneva: WHO. <http://apps.who.int/medicinedocs/pdf/s4901e/s4901e.pdf>.

<sup>44</sup> Fomundam, H., and C. Mathews. 2009. *Antiretroviral Therapy in South Africa: A Pocket Guide on Prevention and Management of Side Effects and Drug Interactions*. 2nd ed. National Department of Health, South Africa.

The FDB should immediately develop plans for the implementation of simple risk management and communication activities.<sup>45</sup> Public education on responsible and informed self-medication and attention to medicine safety are equally vital for a comprehensive approach to supporting the medicine safety system. It is also recommended that the FDB strengthen efforts at using the mass media and information, education, and communication materials in advocating safe use of medicines in Ghana.

### **Integrate Locally Relevant and Contextualized Pharmacovigilance Topics in Pre- and In-Service Training Programs**

Presently, only one of three medical schools in Ghana undertakes some level of pharmacovigilance training as part of its preservice training. A similar situation exists in the pharmacy and nursing schools. The FDB should collaborate with the Pharmacy Council, the Medical Council, and the Dental Council, which have oversight authority for curriculum development and approval, to ensure that fundamental topics in pharmacovigilance (including regulatory pharmacovigilance, risk identification and evaluation, patient safety management, and communication) are introduced into the curricula of these schools.

### **Develop Memoranda of Understanding with Universities and Research Institutions for Pharmacoepidemiological Studies**

Regulatory authorities in many countries are not directly responsible for conducting pharmacoepidemiological studies. However, competent regulatory authorities from developed countries routinely use findings from such studies to inform their regulatory decisions. In some instances, formal relationships exist between the regulatory authority and the academic institutions for the provision of this type of support. The FDB should develop memoranda of understanding with prequalified academic institutions and mobilize them to conduct pharmacoepidemiological studies on high-priority safety and effectiveness topics.

### **Develop Formal Processes for Identifying Priority Medicine Safety Research Questions and How to Use Findings to Inform Decisions**

The FDB should liaise with other stakeholders and develop formal processes for the identification of priority safety research questions for health products marketed in Ghana. Such processes when ratified can be used to improve efficiency and ensure that limited resources for research in safety and effectiveness of health products are not squandered by nonpriority studies or by studies that lack adequate methodological rigor and sample size and therefore will not be useful for making evidence-based regulatory decisions.

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<sup>45</sup> For instance, the U.S. Food and Drug Administration has simple information, education, and communication materials. Consumer Education: Ensuring Safe Use of Medicine. <http://www.fda.gov/Drugs/ResourcesForYou/ucm079529.htm>.

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## CONCLUSION

The widespread use of new essential medicines has highlighted the need for improving systems for monitoring the safety and effectiveness of those medicines. The assessment of the pharmacovigilance system in Ghana identified that basic structures exist for improving the pharmacovigilance system. However, processes and outcomes that mark well-functioning pharmacovigilance systems are lacking. The assessment and analysis of the pharmacovigilance system has highlighted those limitations. The opportunities for improving health product safety monitoring in Ghana are anchored on the leadership role of the FDB, the willingness for partnership from stakeholders, and the population's concerns about adverse events related to adverse drug reactions, poor product quality, and treatment failure. These opportunities can be exploited to implement the recommendations set out in this report.

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## ANNEX 1. SUMMARY OF INDICATORS

Indicator Number <sup>a</sup>	Indicator	Core/ Supplementary	Type of Indicator	Data Collection Level	Recommended Frequency of Measurement
<b>Component 1. Policy, Law, and Regulation</b>					
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
<b>Component 2. Systems, Structures, and Stakeholder Coordination</b>					
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

<b>Indicator Number<sup>a</sup></b>	<b>Indicator</b>	<b>Core/ Supplementary</b>	<b>Type of Indicator</b>	<b>Data Collection Level</b>	<b>Recommended Frequency of Measurement</b>
<b>2.6</b>	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
<b>2.7</b>	Existence of national pharmacovigilance guidelines updated within the last five years	Core	Structural	MoH	Every 5 years
<b>2.8</b>	Existence of protocols or SOPs for improving patient safety relating to medicine use	Core	Structural	MoH, PHP, HF	Annually
<b>2.9</b>	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
<b>2.10</b>	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
<b>2.11</b>	Percentage of predefined core reference materials available in the medicine information or pharmacovigilance center	Supplementary	Process	MoH, PHP, HF	Annually
<b>2.12</b>	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
<b>2.13</b>	Number of health care providers trained on pharmacovigilance and medicine safety in the last year	Supplementary	Process	MoH, PHP, HF	Annually
<b>2.14</b>	Platform or strategy exists for the coordination of pharmacovigilance activities at the national level	Core	Process	MoH	Annually
<b>2.15</b>	National pharmacovigilance center is a full or associate member of the WHO Programme for International Drug Monitoring	Supplementary	Structural	MoH	Every 5 years

*Annex 1. Summary of Indicators*

<b>Indicator Number<sup>a</sup></b>	<b>Indicator</b>	<b>Core/ Supplementary</b>	<b>Type of Indicator</b>	<b>Data Collection Level</b>	<b>Recommended Frequency of Measurement</b>
<b>Component 3. Signal Generation and Data Management</b>					
<b>3.1</b>	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
<b>3.2</b>	Existence of a database for tracking pharmacovigilance activities	Core	Process	MoH	Annually
<b>3.3</b>	Existence of a form for reporting suspected ADRs	Core	Process	MoH, PHP, HF	Annually
<b>3.4</b>	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
<b>3.5</b>	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
<b>3.6</b>	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
<b>Component 4. Risk Assessment and Evaluation</b>					
<b>4.1</b>	Number of medicine utilization reviews carried out in the last year	Supplementary	Process	MoH, PHP, HF	Annually
<b>4.2</b>	Pharmaceutical product quality survey conducted within the last five years	Supplementary	Process	MoH	Every 5 years
<b>4.3</b>	Incidence of medication errors quantified in the last year	Supplementary	Process	MoH, PHP, HF	Annually
<b>4.4</b>	Number of ADR reports received in the last year	Core	Process	MoH, PHP, HF	Annually
<b>4.5</b>	Number of active surveillance activities currently ongoing or carried out in the last five years	Core	Process	MoH, PHP, HF	Every 5 years
<b>4.6</b>	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 <sup>a</sup>	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

*Annex 1. Summary of Indicators*

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<b>Indicator Number<sup>a</sup></b>	<b>Indicator</b>	<b>Core/ Supplementary</b>	<b>Type of Indicator</b>	<b>Data Collection Level</b>	<b>Recommended Frequency of Measurement</b>
<b>5.8</b>	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
<i>5.9</i>	Number of public or community education activities relating to medicine safety carried out in the last year	Supplementary	Outcome	MoH, PHP, HF	Annually
<b>5.10</b>	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*.

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