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An Analysis of the Pharmacovigilance Landscape in Sub-Saharan Africa

Insights from five years of USAID National Supply Chain Assessments and beyond

July 2024 | Arthur Ostrega, Gabriela Simmons, and Julia Klebe with the support of the Chemonics' Supply Chain Practice team.

Abstract

This paper explores the state of pharmacovigilance (PV) systems in low-and-middle income countries and the effect on the health system and accessibility of quality health commodities in Africa. Despite several existing frameworks for strong PV and pharmaceutical management, operating an effective PV system remains a challenge in resource-limited settings. The paper provides an analysis of the status of PV practices in six countries in Sub-Saharan Africa (SSA) — Democratic Republic of Congo, Ghana, Guinea, Madagascar, Rwanda, and Uganda — across health facility levels, drawing from results of the USAID National Supply Chain Assessment conducted in these respective countries over the last five years. A key finding of this analysis is that PV system maturity level and capabilities decrease from central to service delivery point levels due to limitations of resources to support PV and gaps in collection and quality management of quality assurance sample testing at the warehouse level. The paper makes recommendations for addressing these challenges to strengthen PV practices in SSA, including engaging private sector service delivery points to increase adverse drug event reporting, prioritizing financing of PV practices, and supporting regional regulatory harmonization and data-sharing initiatives to improve regulatory standards for medicines and expedite registration of safe essential medicines.

Acknowledgments

This publication was produced by Arthur Ostrega, Gabriela Simmons, and Julia Klebe with the support of the Chemonics' Supply Chain Practice team. Mr. Ostrega, Ms. Simmons, and Ms. Klebe lead the Chemonics' Pharmaceutical Management Working Group within the Chemonics' Supply Chain Practice. We would like to thank reviewers who provided valuable knowledge and expertise to help shape this document: Barry Chovitz, Giuliana Canessa Walker, and Shiouchu (Judy) Wang.

Disclosure Statement

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Introduction

The purpose of this document is to provide recommendations for public health supply chain professionals on how to strengthen pharmaceutical management systems in low- and middle-income countries (LMICs) to improve access to quality health commodities in Sub-Saharan Africa (SSA). Chemonics has conducted an analysis of the status of pharmacovigilance (PV) practices in six countries in SSA — Democratic Republic of Congo (DRC), Ghana, Guinea, Madagascar, Rwanda, and Uganda — based on publicly available data within the results of countries that have conducted the USAID National Supply Chain Assessment (NSCA) within the last five years.

Pharmacist handling antiretroviral drugs supplied by the GHSC-PSM project in Kano, Nigeria.

Pharmacovigilance in Low- and Middle-Income Countries

PV refers to the science and activities relating to the detection, assessment, understanding, and prevention of adverse drug events (ADEs) or any other drug-related problem. This function is led by national regulatory authorities (NRAs) to enhance consumer care and ensure safety, as

well as to support public health programs by providing reliable, objective information for the effective assessment of the benefit-risk profile of medicines and vaccines (World Health Organization [WHO], 2023). PV systems include designing, rolling out, and enforcing the appropriate regulations, establishing processes and relevant informational technology collection and analytics, and training health professionals to respond to a drug's lifecycle. Post-market surveillance (PMS) of medicines is proactively led by the manufacturer while PV is led by NRAs.

Pharmacists sorting medicines in a stockroom in Zimbabwe.

PV is essential, given a 2023 United Nations Office on Drugs and Crime (UNODC) Transnational Organized Crime Threat Assessment — Sahel report (UNODC, 2023) that states, "fake medicines kill almost 500,000 sub-Saharan Africans a year." Ensuring access to safe, effective, and high-quality medicines in LMICs requires a strong pharmaceutical regulatory system, including PV surveillance, in which regulators, manufacturers, public and private distributors, community pharmacies, health facilities and community health workers, and consumers each have a role to play.

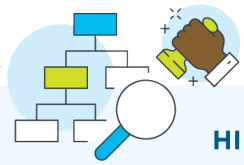
Medical products that circulate without regulatory oversight or market control measures may contain harmful substances, or not contain the active ingredients for which they have been

prescribed. They may have expired or may have deteriorated due to poor storage conditions, or they may be sold without prescription for purposes other than their medical use. For all these reasons, they may be ineffective and cause harm, including contributing to antimicrobial resistance (WHO, 2020). Additionally, most cases of ADEs go undetected, so the impact on patients' lives and the health system is likely higher than reported (Constant et. al., 2013).

There are several conceptual frameworks that detail how PV functions should be organized and are important technical reference documents for the field. These include USAID's Medicines, Technologies, and Pharmaceutical Services (MTaPS) Program's framework for a functional PV system. MTaPS uses the framework in the technical approaches to its work (MTaPS, 2022). The WHO also has a global benchmarking tool for regulatory systems strengthening that includes a module on PV (WHO, 2021). The tool is designed to be a periodic assessment tool for regulatory strengthening.

Another such conceptual framework for how a PV system should be organized to successfully execute its core functions is the European Medicines Agency's (EMA's) PV System Manual (Potts, 2021). The EMA PV System Manual lays out five key principles for monitoring and performing PV activities: (1) collect, manage, and analyze data in relation to the product safety-like inspections post-authorization studies, (2) review and assess, (3) decide and act through the coordination of decision-making committees, (4) provide safety communications, (5) and monitor implementation of proposed actions, for example, through an active database of products authorized in the European Union. In addition to the framework, the EMA manual includes a responsibility matrix for each task of the PV activities described above (see Exhibit 1 on the next page.)

Exhibit 1. EMA PV system in context of EMA quality system



HIERARCHY OF RULES AND EMA QUALITY SYSTEM

Legislation

- Regulation (EC) No 726/2004
- Directive 2001/83/EC
- Other legislations
- Implementing regulation (EU) No 520/2012

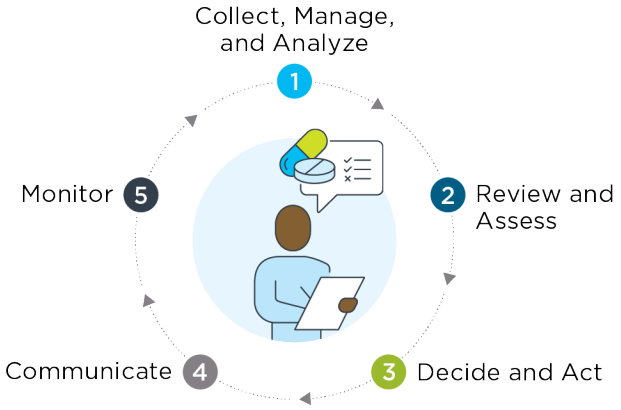
Policy

- Standards
- GVP and other guidelines
- Pharmacovigilance system manual
- (EMA) policies
- Business continuity plan/incident management plan
- Mandates/rules of procedure

People and Processes

- Job description
- Qualification
- Training files
- Standard operating procedures
- Working instructions

PROCESS DOMAINS (LIFECYCLE) FOR PHARMACOVIGILANCE TASKS



CORPORATE GOVERNANCE REQUIREMENTS

- Legal and regulatory compliance (quality system)
- Record management and transparency
- Business continuity and incident management
- Monitoring and risk-based audit
- Documented responsibilities, training, and qualification
- Data protection and access to documents

Despite the well-designed framework, challenges in implementation in resource-limited settings in SSA can be significant (both in an operational and financial sense) and compound the difficulties of operating an effective PV system. Key healthcare delivery challenges in the region include: a lack of public sector healthcare delivery facilities as well as a lack of skilled staff and resources; the poor quality of the healthcare system; and corruption, mismanagement, and low quality of education (Maritoux, 2000). In many SSA countries, PV does not receive a clear budget line in national budgets. Many countries link this funding to overall NRA funding, which is often insufficient. When examined further, some of the principal barriers reported by NRAs include lack of awareness of importance of PV by budget decision-makers, challenging legal environment, and no ability to generate revenue (Isah et. al., 2023).

Methodology

The primary source of data (for this paper) for the analysis on PV in SSA is the publicly available results of USAID NSCA country reports conducted within the last five years. The NSCA is a publicly available survey tool designed to assess the capability and performance of a country's public health supply chain and provide a basis to inform country strategic planning and supply chain policies. The NSCA toolkit collects information through three primary methods: a supply chain system mapping exercise, the capability maturity model (CMM) questionnaire, and the collection of key performance indicators. The survey was developed through a collaborative input process between USAID, The Global Fund, UNICEF, and The Bill & Melinda Gates Foundation and implementing partners, such as Chemonics International, Management Sciences for Health, and John Snow Inc., and the tool represents the collective agreement of key questions, capabilities, and practices that the international health supply chain community believes are critical for effectively operating a health supply chain.

The CMM tool assigns a maturity level to each question (or response) included in the survey of either basic, intermediate, advanced, or state of the art. Those questions are scored and represent a specific proportion of the final score, as shown in Exhibit 2.

Exhibit 2. CMM maturity level definitions and examples

Level of Maturity (Contribution to total possible points)	Definition	Quality and PV Example
Basic (50%)	Must have capabilities and resources	Standard operating procedures (SOPs) for PV are available in this facility
Intermediate (30%)	Important, but not must-have	PV reporting tools and templates are available in this facility
Advanced (15%)	Nice-to-have	Samples are pulled from facility for quality control (QC) testing at least annually
State of the Art (5%)	As deployed by leading global logistics organizations	Facility staff are trained on action protocols based on PV results

Source: USAID NSCA Toolkit (ghsupplychain.org)

Final scores are tabulated and then presented by supply chain functional area and by facility type. A mix of levels is expected in the final result, recognizing that technologies or capabilities rarely advance in a linear fashion. Those scores are then interpreted at the country level, comparing scores between facility types. Responses to individual questions are also compared, where possible.

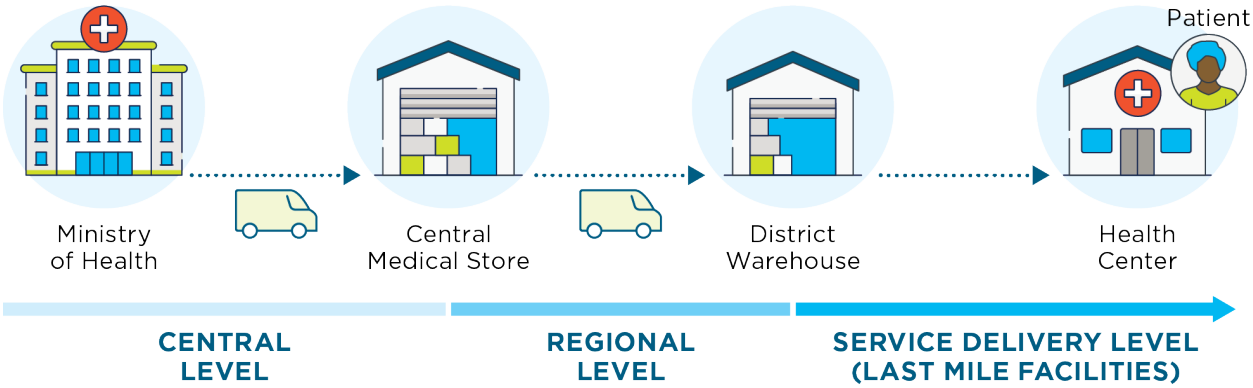
For the purpose of this analysis, we have chosen to focus on the results of the CMM questionnaire, which assesses supply chain effectiveness across 11 functional areas at all levels of the health system in a given country. Specifically, this analysis focuses on the "Quality and PV" functional area of the CMM tool, drawing from existing NSCA reports to generate insights and provide recommendations on how to improve PV systems.

Chemonics complemented the PV data review from the NSCA results in the aforementioned countries with a literature review and an analysis of PV operational frameworks from leading medicines safety agencies, such as WHO and EMA.

Analysis and Findings

The analysis examines the status of PV system capabilities and maturity across six SSA countries (DRC, Ghana, Guinea, Madagascar, Rwanda, and Uganda), all of which have conducted NSCAs within the last five years. All reports analyzed include nationally representative data on the state of the PV system at the service delivery level as well as at warehouses and central level institutions. Exhibit 3 depicts the NSCA CMM scores for each country, by facility type. To simplify graphics, facilities have been standardized rather than using their official designation within their respective health systems.

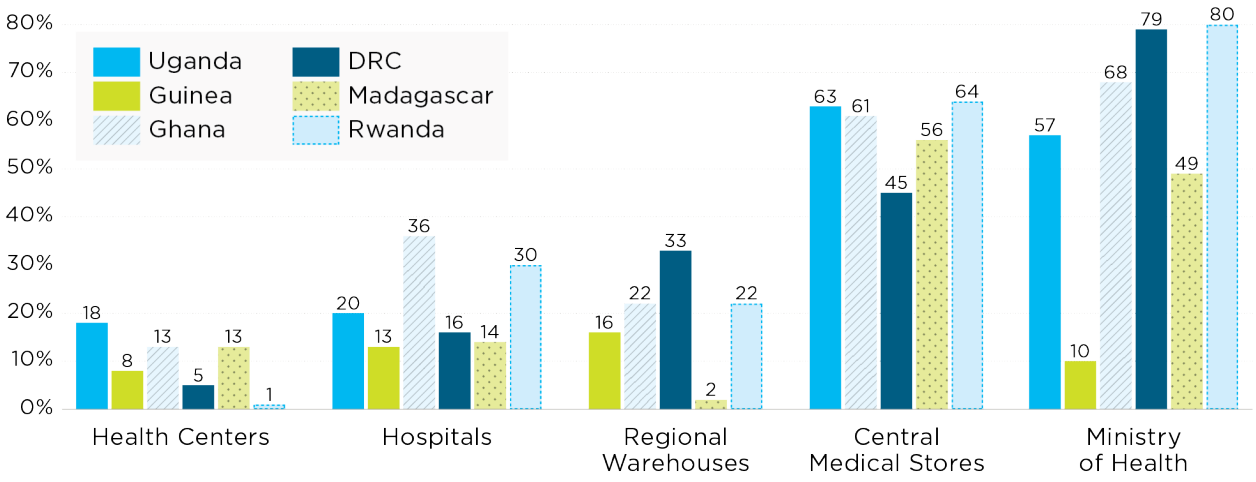
Exhibit 3. In-country supply chain levels included in the NSCA



Finding 1: PV system maturity and capability decreases, almost linearly, from the central level institutions (such as Ministry of Health, NRA or Food and Drug Authority) down to service delivery points.

In many ways, this trend is to be expected. In centrally managed health systems, capabilities need to be developed and codified at the central level first to ensure technical quality, validate appropriateness for context, and develop policy to guide implementation of any operational rules or reporting systems (Ampadu et al., 2018). As noted in the EMA PV system graphic (see Exhibit 1), the policies and legislation that define a PV system must be in place before it can realize any of its necessary functions. Only after norms and policies have been established can they be disseminated, trained on, and operationalized at the service delivery level. In a resource-limited environment in which ministries of health can struggle to finance even the procurement of essential medicines for their population, it is not uncommon to see PV go as an underfunded area of the health system (Elshafie et. al., 2018).

Exhibit 4. NSCA quality assurance (QA) and PV maturity scores, by facility type, by country



Finding 2. Within the QA/PV module at the health facility level, the lack of reporting forms and SOPs for PV is pervasive.

The analysis shows that a major weakness at the health facility level is the availability (or lack) of formal guidance (in the form of SOPs) and data transmission mechanisms (in the form of ADE reporting forms). Exhibit 5 shows that the availability of key inputs, technical guidance, and reporting forms is quite low. As noted in the EMA PV framework, collection and management of

PV data is the first critical step to completing the PV lifecycle. Without these critical resources, the PV system cannot function as intended.

Exhibit 5. Key PV capabilities in place at the health facility level

Capability or Resource	DRC	Ghana	Guinea	Madagascar	Rwanda	Uganda
National availability of SOPs for PV	5%	10%	15%	6%	8%	--*
National availability of reporting forms for PV	11%	47%	31%	66%	24%	51%
Facilities reporting sharing PV data with central level authorities	--*	--*	25%	46%	19%	28%

* These data points were not retrievable from publicly available NSCA reports at the time of publication.

Finding 3: Systematic approach to QA at the warehouse level is needed.

Complementing the active reporting of events at the service delivery level of ADEs from drug administration, effective PV systems also employ other methods of active monitoring as part of a holistic QA program. A common method employed is taking samples of medicines throughout their journey through the in-country supply chain to ensure medicines are of sufficient quality to be used for patients, a process known as PMS. Sampling medicines is another input to step 1 of the EMA framework (collect, manage, and analyze), further highlighting the challenge of launching effective PV systems within these countries.

Exhibit 6. Key PV capabilities in place at the health facility level

Capability or Resource	DRC	Ghana	Guinea	Mada-gascar	Rwanda	Uganda
Proportion of regional warehouses that take samples of pharmaceuticals for quality testing	37%	20%	0%	0%	13%	--**
Proportion of regional warehouses that reported having QA/QC SOPs on-hand during the day of the visit	63%	40%	29%	0%	10%	--**
Proportion of regional warehouses that keep Certificates of Analysis and Certificates of Conformance for medicines received from domestic sources	--*	10%	0%	--*	13%	--**
Proportion of regional warehouses that keep Certificates of Analysis and Certificates of Conformance for medicines received from international sources	--*	0%	0%	--*	13%	--**

* These data points were not available from publicly accessible reports at the time of publication.

** Uganda does not operate regional warehouses but rather has several Central Medical Stores institutions conducting last mile delivery.

As the NSCA results reveal, the collection of samples from regional warehouses for QA testing is a rare practice. The SOPs and guidelines for QA/QC which support that process are also infrequently found within these subnational institutions. Even more infrequent is the important record-keeping practice of maintaining Certificates of Analysis and Certificates of Conformance for products received both domestically and internationally. This documentation is critical in case of a recall of medicines or need to validate a particular batch or lot of medicines that are in circulation within the health system. For this analysis, the regional level had the greatest data availability from publicly accessible reports to enable cross-country comparisons. While Central

Medical Stores are a more traditional repository for storing QA documents from suppliers, all entities listed in this table (except Uganda) perform some degree of procurement at the regional warehouse level, domestically and internationally, and would be expected to store those documents.

Finding 4: State of QA and PV policy is well established at the central level.

As referenced in the beginning of this analysis, all the countries included have demonstrated strengths in their central level capabilities for PV and QA. As demonstrated in Exhibit 7, all countries included have a QA testing lab that they use for pharmaceutical testing, though not all of them have international accreditation for their labs. Many countries across SSA have a national drug regulatory authority of some kind. These institutions are the champions of strong pharmaceutical management guidance and implementing PV frameworks through system design. Policy frameworks and system conceptual designs have been elaborated for all these countries but, as evidenced earlier, their dissemination and implementation by frontline healthcare workers is yet to be realized in many of these settings and needs to be a priority area of focus moving forward (Stegmann et. al., 2022).

Exhibit 7. Key quality assurance capabilities in place at the central level

Capability or Resource	DRC	Ghana	Guinea	Madagascar	Rwanda	Uganda
Utilization of a laboratory to conduct quality testing	✓(internal)	✓(internal)	✓(external)	✓(external)	✓(internal)	✓(external)
QA laboratory possesses WHO-accreditation	✓	✓	X	X	✓	--*
Existence of national policies for PV and QA	✓	✓	✓	✓	✓	✓

* These data points were not available from publicly accessible reports at the time of publication.

Conclusions and Recommendations

The analysis of six SSA countries of NSCA reports on PV system capabilities highlight one key trend — PV system maturity level and capabilities decrease from central level as they transition down to service delivery points. Looking more closely into the data, two critical challenges were identified as key reasons for this, which call for strategic solutions.

Firstly, at the service level, resources, technical guidance, and reporting forms for PV are in limited supply. Without these resources and guidance, the PV system cannot function as intended; a PV manual and responsibility matrix are the first steps to an accountable and successful PV system, as modeled by the EMA framework. This deficiency not only undermines the system's effectiveness but also poses a risk to patient safety.

Secondly, at the warehouse level, there is a gap in the collection and quality management of QA sample testing. Collection of product samples and data related to product safety across the product life cycle is the first step to a successful PV framework, as modeled by the EMA framework. Without this data, the efficient monitoring and reporting of ADEs is at risk.

Addressing these challenges is imperative to ensure a functional PV system, and it calls for resource allocation and strategic partnerships to address the challenges to enhance its capabilities and efficiency.

- **Recommendation 1:** Engage private sector service delivery points to increase ADE reporting and PMS sample collection for decision-making. Private sector entities, such as logistics providers and pharmaceutical companies could facilitate the sharing of resources/expertise and collection and management of data. Outsourcing data collection and management with QC tasks to private firms with expertise in these areas can help alleviate the resource constraints and ensure more efficient and accurate data management to detect patient adverse events.
- **Recommendation 2:** Advocate and prioritize financing of PV, an area that historically has been underfunded, but plays a critical role in ensuring the health outcomes that national health systems are so focused on achieving. The EMA PV framework emphasizes the need for this, noting the existence of the hierarchy of rules of the EMA quality system as an essential framing and support for how the PV system should be operationalized.
- **Recommendation 3:** Support regional regulatory harmonization efforts already underway to improve regulatory standards for medicines and expedite registration of safe essential medicines. The East African Community (EAC) launched its Medicines Regulatory Harmonization initiative in 2012, which led to improved regulatory capacity in

EAC Partner States and the adoption of regional policy frameworks (Ndomondo-Sigonda, 2021). This experience should serve as the foundation for the African Medicines Agency (AMA). The AMA is expected to lead efforts to improve access to quality, safe medical products in Africa; however, effectiveness will depend on all 55 African Union countries signing on to the initiative. In January 2024, the EMA announced that it received a grant specifically to support AMA implementation through sharing models and learnings. This collaboration will be critical in ensuring the AMA's success.

- **Recommendation 4:** Encourage data standardization and information-sharing on ADEs and falsified medical products to ensure patient safety at regional and continental level. The adoption of GS1 standards or National Product Catalogs helps ensure globally unique, standardized identification of medical products and can allow for efficient reverse logistics when cases of expired or fraudulent products are identified on the market. Regulatory harmonization can also help encourage regional PV data-sharing as product recalls and market withdrawals can have multi-country impacts as suppliers expand across the involved countries.

Call to Action

Have other findings and/or recommendations for public health professionals? Interested in learning more about this analysis? Please reach out to the supplychainteam@chemonics.com. Thank you.

Pharmacist dispensing medicine at a clinic in Ethiopia.

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