Pharmacovigilance in Nigeria: a situational analysis at the start of the PAVIA project

24-28 September 2018

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List of abbreviations

ADR	Adverse Drug Reaction
aDSM	active Drug Safety Management And Monitoring
AE	Adverse Event
CAP	Chapter (Latin); used in legal documents
CEM	Cohort Event Monitoring
DOT	Directly Observed Treatment
EAC	East African Community
FMOH	Federal Ministry of Health
GOPD	General Outpatient Department
HCP	Health Care Professional
HIV	Human Immunodeficiency Virus
ICSR	Individual Case Safety Report
IHVN	Institute of Human Virology, Nigeria
IPAT	Indicator-based Pharmacovigilance Assessment Tool
LGTBLS	Local Government Tuberculosis and Leprosy Supervisor
MDR	Multi-Drug Resistant
M&E	Monitoring and Evaluation
NAFDAC	National Agency for Food and Drug Administration and Control
NETIMS	National Electronic TB Information Management System
NMRA	National Medicines Regulatory Authority
NTBLCP	National Tuberculosis and Leprosy Control Program
OPD	Outpatient Department
PHP	Public Health Program
PMDT	Programmatic Management of Drug-resistant Tuberculosis
PMS	Post-Marketing Surveillance
PSUR	Period Safety Update Report
PV	Pharmacovigilance
QPPV	Qualified Person responsible for Pharmacovigilance
SAE	Serious Adverse Event
SOP	Standard Operating Procedures
SPHAR-TI	Structured Pharmacovigilance and Training Initiative
SSA	Sub-Saharan Africa
STR	Shorter Treatment Regimen
TB	Tuberculosis
WHO	World Health Organization
XDR	Extensively Drug-Resistant

Table of contents

Acknowledgements 2
List of abbreviations 3
Table of contents 4
1. Introduction 6
1.1. PAVIA (Pharmacovigilance in Africa) 6
1.2. Pharmacovigilance 6
1.3. TB / aDSM 6
1.4. Nigeria country profile 7
1.5. Pharmacovigilance in Nigeria 9
2. Aim and objectives of the situational analysis 10
3. Methodology and team 10
3.1. Assessment strategy 10
3.2. PV indicator assessment tool 10
3.3. Assessment team 11
3.4. Documents reviewed 11
3.5. Sites assessed and stakeholders interviewed 12
3.6. Analysis of the indicator tool and interviews 13
3.7. Limitations 13
4. Results 13
4.1. Policy, law and regulations 13
4.1.1. National Drug Policy 13
4.1.2. Market authorization holders, importers, and private health care providers 14
4.1.3. Essential medicines 14
4.2. Systems, structure and stakeholder coordination 15
4.2.1. National pharmacovigilance unit 15
4.2.2. Role of non-governmental organizations 15
4.2.3. National budget for PV tasks 16
4.2.4. Pharmacovigilance training 16
4.2.5. National patient safety monitoring committee 18
4.2.6. Consumption and prescriptions of medicines 18
4.2.7. Mechanisms to disseminate PV information 18
4.3. Signal generation and data management 19
4.3.1. Collection of PV data: adverse event reporting, data flow and management 19
4.3.2. Reporting tools 25
4.4. Risk assessment and evaluation 26
4.4.1. Reporting of adverse events 26

4.4.2. Reporting and feedback 27
4.4.3. Data analysis and causality assessment 27
4.5 Risk management and communication 27
4.5.1. Management of adverse events 27
4.5.2. Risk management 27
4.5.3. Signal detection 28
4.5.4. Communication 28
5. Conclusions: Strengths and weaknesses of Nigeria's PV system 28
6. Recommendations and next steps 28
6.1. Respondents' recommendations 28
6.2. Visiting team's recommendations 29
6.3. Next steps 30
Annex 1. NMRA assessment tool 32
Annex 2. PHP assessment tool 45
Annex 3. PMDT sites assessment tool 49

1. Introduction

1.1. PAVIA (Pharmacovigilance in Africa)

In order for countries in Sub-Saharan Africa (SSA) to have more effective drug safety reporting mechanisms for new products introduced and to gain a better understanding of their safety profiles, PAVIA envisions to strengthen the PV systems in four SSA countries: Ethiopia, Nigeria, Eswatini and Tanzania. PAVIA's objectives are:
I) To strengthen governance of Pharmacovigilance (PV) systems, by strengthening regulatory and organizational structures and defining clear roles and responsibilities for all stakeholders.
II) To improve efficiency and effectiveness of national surveillance systems, by strengthening active (sentinel) surveillance of adverse drug reactions and implementation of tools and technologies for their detection, reporting, analysis and dissemination
III) To build capacity and skills to sufficiently conduct safety-monitoring activities throughout the country.
IV) To improve readiness of health systems within SSA, by improving performance assessment of PV systems allowing identification of enablers and barriers for implementation.

PAVIA's strategy is to strengthen national PV systems in a collaborative effort with Public Health Programs (PHPs), building up medicines safety surveillance activities in the context of the introduction of new drugs for Multidrug-Resistant-Tuberculosis. Capacity at the national PV Centre/ national medicines regulatory authority (NMRA) will be built gradually taking the PV activities for Tuberculosis as the "building and training ground" for a generic PV system including data collection, database entry, data analysis, signal identification and causality assessment. The results and lessons learned will be transferred by PAVIA to the PHP for HIV and malaria. Combined with identified enablers and barriers in addressing regional differences and needs, a blueprint will be developed that can guide other countries in strengthening their PV systems.

1.2. Pharmacovigilance

The World Health Organization (WHO) has defined PV as "the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other possible drug-related problems."[1] The aim of the PV system is to protect the public from medicines-related harm. Currently few low- and middle-income countries have a well-functioning PV system to support the timely identification, collection, and assessment of medicine-related adverse events.

1.3. TB / aDSM

Since 2013, after introduction of two new TB drugs (Bedaquiline and delamanid), WHO recommends active TB-drug safety monitoring and management (aDSM) when using one of these drugs. aDSM is defined as the active and systematic clinical and laboratory assessment of patients on treatment with new TB drugs (part of which have not yet received full approval from international Food & Drug/Medicinal Authorities), novel MDR-TB regimens or XDR-TB

[1] WHO 2009, The Importance of Pharmacovigilance. Safety Monitoring of medicinal products. Geneva.

regimens to detect, manage and report suspected or confirmed adverse drug reactions. The overall objectives of aDSM are to reduce risks from drug-related harms in patients on treatment for drug-resistant TB and to generate data to inform future policy updates on the use of such medicines.

aDSM is seen as an active and systematic way of patient monitoring to be incorporated in the programmatic management of patient with DR-TB. The WHO presents three different aDSM packages: in the core package, only serious adverse events (SAE) are to be reported. In the intermediate package, apart from the serious adverse events, also adverse events of special interest should be reported, and the advanced package targets all adverse events of clinical interest. Full cohort event monitoring is not deemed feasible for routine monitoring of DR-TB patients. However, depending on the information and setting, CEM might be considered for a limited period of time.

1.4. Nigeria country profile

The entity Nigeria is an expanse of land (923,768 km^2) in Sub-Saharan Africa, along its West Coast, and is located between Latitude 40 to 100 N and Longitude 30 to 140E. Along its Southern border is the Atlantic Ocean (Bight of Benin and Gulf of Guinea) and land borders with Cameroon on the East, Republic of Benin on the Western flank, and the Republics of Niger and Chad on the North West to North East respectively. It is the most populous nation in Africa with a projected estimate of 203,452,505 persons (July 2018) and a predominantly black population. The country is a federal republic with 36 States and one Federal Capital Territory, Abuja (Figure 1).[2]

Nigeria has sub-Saharan Africa's largest economy, with a GDP (purchasing power parity) of $1.121 trillion, ranking 24th in the world. However, its rank is only 166th with respect to the GDP per capita of $5,900. The unemployment rate was estimated at 12% in 2016. Despite economic growth in the past decade, poverty levels have remained high, with more than 62% of Nigerians still living in extreme poverty. The country's workforce is largely employed in agriculture. The current total health expenditure accounts for 3.6% of GDP; domestic general government spends only 0.6% of GDP on health.[1]

The public health sector in Nigeria consists of three levels: primary, secondary and tertiary. The Federal Government is responsible for policy development, regulation, overall stewardship and providing healthcare at the tertiary level (teaching hospitals and specialist hospitals), while state governments are responsible for secondary healthcare, and local government areas (LGAs) manage the primary healthcare sector.[3] The country has a vast private health sector, with private health expenditures accounting for 62% of the total health expenditure in 2010.[4] Also, there is a large informal sector. Some important health indicators are provided in Table 1[5].

[2] Source: CIA World Fact Book, 2018. http://www.aho.afro.who.int/profiles_information/index.php/Nigeria:Index

[3] Nigerian health sector; Market study report. PharmAccess, 2015. https://www.rvo.nl/sites/default/files/Market_Study_Health_Nigeria.pdf

[4] Nigeria Health Expenditure. Total versus Private [internet]. 2013. [cited 2013 Oct 11]. Available from: http://nigeria.opendataforafrica.org/msqivrf/nigeria-health-expenditure-total-vs-private

[5] Global Health Observatory. From: WHO country profiles. https://www.who.int/countries/swz/en/. Date accessed: 10 December 2018.

Table 1. Overview of important general health indicators[6,7].

Indicator	Value
Life expectancy at birth m/f (years, 2017)[10]	62.8/65.9
Infant mortality (per 1,000 live births, 2017)[10]	62.6
Under-five mortality (per 1,000 live births, 2017)[10]	103.2
Maternal mortality (100,000 live births, 2014)[11]	814
Total expenditure on health per capita (Intl $, 2014)[11]	217
Total expenditure on health as % of GDP (2014)[11]	3.7

Figure 1. Map of Nigeria. Source: https://en.wikipedia.org/wiki/Template:Nigeria_states_map.

Communicable diseases continue to be a major challenge for the country. Respiratory tract infections were the most common cause of death in 2017, followed by neonatal disorders, HIV/AIDS, malaria, diarrheal diseases, and tuberculosis.[8] Globally, Nigeria had the largest number of malaria cases and deaths in 2017 with estimated numbers of 53,700,000 (uncertainty interval, 36.3 x10^6-75.9x10^6) and 79,800 (62,500-97,000), respectively.[9] In 2017, 2.8% (uncertainty interval, 1.8-4.0) of the adult population was infected with HIV/AIDS. While the epidemic has passed its peak and since 2010, the number of new HIV

[6] IHME. http://www.healthdata.org/nigeria. Date accessed: 23 January 2019.
[7] WHO. https://www.who.int/countries/nga/en/. Date accessed: 10 December 2018.
[8] http://www.healthdata.org/nigeria. Date accessed: 12 Dec 2018.
[9] WHO, 2018. World Malaria Report 2018. Nigeria country profile. https://www.who.int/malaria/publications/country-profiles/profile_nga_en.pdf?ua=1

infections and AIDS-related death have decreased with 21% and 6%, respectively, the epidemic still is the second-largest in the world in terms of numbers of cases, and is disproportionally impacted by key populations (sex workers, men who have sex with men, and injecting drug users).[10] The estimated incidence rate of tuberculosis has remained stable over the past 15 years at just above 200 per 100,000 inhabitants being 219 (uncertainty interval, 143–311) per 100,000 in 2017.[11]

1.5. Pharmacovigilance in Nigeria

Pharmacovigilance activities in Nigeria date back to the 1980s with initial attempts of training of Ministry of Health officials, facilitated by the University of Benin where preliminary collection of adverse drug reactions (ADR) had started and an ADR Registry/Drug Poisons Information Unit was established.

The National Pharmacovigilance Centre (NPC) in Nigeria is part of the National Agency for Food and Drug Administration and Control (NAFDAC). The scope of PV activities in Nigeria includes the monitoring of adverse drug reactions (ADR), medication errors, interactions of medication, abuse/misuse of medicines and lack of effectiveness. NPC collects ADR reports on pharmaceutical products such as drugs, vaccines and biologicals as well as medical devices and cosmetics. There is a National Drug Safety Advisory Committee which provides expert advice on the safety of medicines. There are six Zonal PV centres, one in each of the six geopolitical zones of the country.

All medical products registered in Nigeria are monitored. NPC monitors the safety of medicines through active and passive surveillance. The reporting of ADRs is voluntary for health care professionals, but mandatory for marketing authorization holders (MAHs). The NPC maintains multilateral relationship with other NPC centres globally and a bilateral relationship with the Uppsala Monitoring Centre.

The main functions of the NPC include coordinating PV activities in Nigeria, establishing and maintaining a functional ADR data base, receiving, assessing, completing, analyzing and evaluating the ICRs sent in by health care professionals (HCPs), acknowledging reports received, disseminating information to HCPs and the general public, conducting causality assessment, and forwarding reports to the WHO database VigiBase. Other roles of the NPC include sending out alerts and medicine safety concerns, supporting the establishment of active PV units in healthcare institution, paying advocacy visits to decision makers and creating awareness on PV activities among HCPs and the general public.

NAFDAC, in collaboration with relevant stakeholders, in 2012 developed the Nigeria National PV Policy; NAFDAC Good Vigilance Practice Guideline 2016 and the Guideline for Reporting ADR by MAHs and HCPs.
The NPC in Nigeria became the 74th member of the WHO international drug monitoring program on the 9th of September 2004. PV activities in Nigeria have evolved from spontaneous reporting to active surveillance systems in the form of CEM in 2009. Active surveillance for monitoring the safety and effectiveness of medical products is increasingly recognized as a complement to spontaneous reporting commonly used in pharmacovigilance systems.

[10] UNAIDS, 2018. http://www.unaids.org/en/regionscountries/countries/swaziland. Date accessed: 10 December 2018.
[11] WHO Global Tuberculosis Report, 2018. https://www.who.int/tb/country/data/profiles/en/. Date accessed: 10 December 2018.

2. Aim and Objectives of the Situational Analysis

This report presents the situational analysis of the various aspects and needs of the PV systems in Nigeria at the start of the PAVIA project, including its strengths and gaps. The baseline situational analysis will be followed by a workshop with broader stakeholder involvement to discuss the findings, define the desired 'end state' per country and develop a PV plan to achieve this 'end state', including activities and priorities. A final assessment will be conducted at the end of the PAVIA project period, using the same methodologies as in the baseline situational analysis. The situation will be compared against the anticipated 'end state'. Lessons learned on how the true 'end state' was achieved will be defined, including how challenges were addressed and best practices identified. Also, challenges encountered that could not be overcome will be analysed for potential alternative approaches to address those in the future and in other settings. Lessons learned within PAVIA will be packaged in a practical blueprint for use in other Sub-Saharan African countries.

The aim of the baseline situational analysis was to get a good understanding about the strengths and weaknesses of the current PV system in Nigeria, as well as to get a good understanding on training needs that can be addressed by the PAVIA project.

3. Methodology and Team

3.1. Assessment strategy

The following strategy was used to assess the baseline situation:

1. PV indicators were assessed using a standardized assessment tool (see paragraph 3.2). For filling the list of indicators, documentation was reviewed if available. Additional information was provided through interviews with stakeholders.
2. Additional information regarding the current situation of the PV system was obtained through key informant interviews. This was in order to gain more insight in the PV system in the country, ascertain training needs, and get recommendations for the future from these key stakeholders.
3. Site visits to DR-TB treatment facilities were also conducted, to assess the current reporting of adverse events at health facility level and its barriers and facilitators.

3.2. PV indicator assessment tool

The status of PV was assessed using a slightly modified questionnaire based on the Indicator-based Pharmacovigilance Assessment Tool (IPAT)[12] and the WHO PV indicators[13], which has already been used by the Tanzanian Food and Drug Administration (TFDA). The following elements were addressed: health system, policies, laws and financing, PV processes, capacity and infrastructure including training needs, stakeholder environment and communication/ dissemination opportunities. The tool for assessment of the national medicine regulatory authority (NMRA) contains 58 indicators that address five PV

[12] 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.

[13] WHO 2009: pharmacovigilance indicators: a practical manual for the assessment of pharmacovigilance systems.

components: i) policy, law, and regulation; ii) systems, structures, and stakeholder coordination; iii) signal generation and data management; iv) risk assessment and evaluation; and v) risk management and communication. The indicator list for the public health programs (PHP) consists of 20 indicators addressing components two to five. The indicators are attached as Annex 1 and 2.

3.3. Assessment team

The assessment was conducted by a team consisting of national staff and international consultants. The team was split in two sub-teams on two of the three assessment days:

Team 1:

- Dr Edine Tiemersma, epidemiologist, KNCV Tuberculosis foundation, PAVIA WP4 lead
- Mr. Yohanna Avong, pharmacist and scientist, IHVN
- Dr Abiodun Abiola, medical doctor, Pharmacovigilance and Post Marketing Surveillance Directorate (PV/PMS), NAFDAC
- Ms Cassandra Aishatu Elagbaje, pharmacist, PV coordinator for PAVIA in Nigeria

Team 2:

- Dr Linda Harmark, pharmacist and epidemiologist, Lareb (Netherlands PV centre), PAVIA WP3 lead
- Prof Ambrose Isah, Consultant Physician/Clinical Pharmacologist, Departments of Medicine and Clinical Pharmacology and Therapeutics, University of Benin, PAVIA WP2 lead
- Dr Abimbola Opadeyi, Departments of Medicine and Clinical Pharmacology and Therapeutics, University of Benin
- Mr Ali Ibrahim, Pharmacist, Director PV/PMS, NAFDAC
- Mrs Helga Nosiri, Pharmacist, Deputy Director PV/PMS, NAFDAC

3.4. Documents reviewed

The following legal documents were reviewed by the team:

- The Decree establishing NAFDAC (1993; amended in 2004)
- National Health Policy (2004)
- National Drug Policy (formulated in 2003, revised 2005)
- National Pharmacovigilance Policy and Implementation Framework (2012)
- Counterfeit and Fake drugs and unwholesome processed foods (Miscellaneous Provisions) Act (1999 No.25: CAP C34)
- Essential Drug List Decree No. 43 1986 (Act CAP N1 2004)
- Essential Medicines List (6th edition, 2016)

Other documents reviewed were:

- Good Pharmacovigilance Practice Guidelines (2016)
- Good Distribution Practice Guidelines (2016)
- Guidelines for reporting by health care professionals (HCP) (2nd edition, 2008)
- Guidelines for MAH (2012)
- NAFDAC Annual Report (2017)
- National Strategic Health Development Plan (NSHDP) 2010-2015 (2010)
- National Health Information System Strategic Plan 2014-2018 (2014)
- National Quality Assurance Policy For Medicines and Other Health Products (2015)

- 2016 Health Budget
- Harmonized Guidelines for the Administration, Disbursement, Monitoring and Fund Management of the Basic Healthcare Provision Fund (2016)
- The National Strategic Plan for Tuberculosis Control 2015 – 2020: Towards Universal Access to Prevention, Diagnosis and Treatment (2014)
- Guidelines on the use of the shorter regimen and new drugs in the clinical and programmatic management of drug resistant tuberculosis and co-infections of Nigeria (an addendum to NTBLCP 2016 PMDT guidelines – 2nd edition) (2017)
- Guidelines on active tuberculosis drug safety monitoring and management (aDSM) (1st edition, May 2018)
- Standard operating procedure for completion of the aDSM form for reporting serious adverse event (SAE) (version 2.0, May 2018)
- National guidelines for HIV prevention treatment and care (2016)
- Avong et al., Doing no harm? Adverse events in a nation-wide cohort of patients with multidrug-resistant tuberculosis in Nigeria. PLoS One 2015; 10(3): e0120161.
- Avong et al., Addressing the under-reporting of adverse drug reactions in public health programs controlling HIV/AIDS, Tuberculosis and Malaria: A prospective cohort study. PLoS One 2018; 13(8):e0200810
- Avong et al., Integrating community pharmacy into community based anti-retroviral therapy program: A pilot implementation in Abuja, Nigeria. PLoS One 2018; 13(1): e0190286

3.5. Sites assessed and stakeholders interviewed

No site visits could be conducted (see paragraph 3.7).
The following stakeholders were interviewed:

- Dr Abdullahi Adamu from the National TB and Leprosy Referral and Training Centre in Zaria
- Pharmacist Ganiyu Abideen from Ibadan State TB and Leprosy Referral Centre
- Staff of IHVN: Dr Patrick Dakum (CEO); Mr Charles Mensah (COO); Pharmacist Avong Yohanna (Head of Pharmacy); Pharmacist Bola Joko Jatau (Senior Program Officer)
- Staff of NAFDAC/PV and PMS Directorate: Pharmacist Ali Ibrahim, Pharm. Helga Nosiri, Mrs. Tani Nimlan, Mrs Emmanuella Okoreafor, Mrs. Pauline Maikano, Dr. Jennifer Chukwumerije and Mr. Amadi Emmanuel
- Staff of NTBLCP: Pharmacist Tairu Alhassan, Dr. Victor Babawale
- Dr Sani Useni focal person of KNCV Tuberculosis Foundation Nigeria (via email)
- Representatives of the Pharmaceutical Industry including:
    - Mohammed Jalloh, Sanofi Country Safety Head
    - Ajiboye Temitope, GSK Pharma Regulatory Officer
    - Val Uche, GSK Pharma Safety Contact
    - Adikwu Ochayi, Swipha Medical Representative
    - Sameep Kapoor, Ranbaxy (SUN Pharma) Business Head

Due to an ongoing strike of Labour involving health workers, the Federal Ministry of Health (FMOH) could not be visited.
Some stakeholder interviews happened in larger groups, others with a small number of persons involved. During the interview sessions with NAFDAC and NTBLCP, the indicator tool was filled (Annex 1 and Annex 2); while during the interview with the representatives of two PMDT sites, a tool developed for the specifically for site visits was filled (Annex 3). In the other interviews were held in the form of guided discussions.

3.6. Analysis of the indicator tool and interviews

The indicator tool was used as a guide for structured interviews. Answers to the questions of the indicator tool as well as additional information provided by interviewees is described in the results section. At the end of the project the same set of indicators will be used and results will be compared to those obtained during the baseline assessment.

3.7. Limitations

There are some limitations to this assessment.
Due to the security conditions at the time of the mission and logistical challenges, unfortunately, no site visits could be conducted. Instead, designated staff from the two health centres selected for the assessment stayed one day longer in Abuja to answer questions of the assessment team. However, this limits the objectiveness of the findings for the TB treatment sites and also does not provide actual observations.
The FMOH could not be visited due to an ongoing strike action by Labour since Thursday 27 September.

4. Results

4.1. Policy, law and regulations

Twelve indicators were collected for this area (see Annex 1).

4.1.1. National Drug Policy

Nigeria has a Pharmacovigilance System with enabling legal provisions. The Health Policy document (2004) alludes to the provision of the National Drug Policy (2005), and the provision of medicines and vaccines as itemized in the Essential Medicines List. It further stipulates that surveillance be kept on the quality of food, drugs, cosmetics and other regulated products through effective monitoring of importation and distribution channels and enforcement of relevant regulations and development of a system of monitoring drugs' adverse effects.

The National Drug Policy (2003) was revised in 2005. This policy further underscores the importance of pharmacovigilance. It recognizes the inextricable relationship of medicines and adverse drug reactions and encourages the establishment of adequately equipped pharmacovigilance units nation-wide, to collect, evaluate and disseminate relevant information on adverse drug reactions and poisoning. It further notes that *"all drugs shall be regularly monitored with respect to their efficacy, safety, quality as well as adverse reactions to evaluate the need to change the conditions of their continuing registration or withdrawal from the market"*.

Also, the country has developed a Standalone Pharmacovigilance Policy document (2012) with explicit implementation strategies approved by the President in Council. The policy provides for a commitment to the pharmacovigilance goal with multi-stakeholder

engagement. Furthermore, the policy scope and thrust was specified. The roles and responsibilities of the stakeholders (their functions) were clearly spelt out.

There exists a National Medicines Regulatory Agency called the National Agency for Food and Drug Administration and Control (NAFDAC), established by Law (Decree 15 of 1993 (as amended) now cited as Act Cap N1 Laws of the Federal Republic of Nigeria 2004). The law mandates NAFDAC to ensure the quality, safety and efficacy of the above named regulated products, hence to conduct pharmacovigilance.
Following initial pharmacovigilance activities in a tertiary hospital, intense national activities commenced in 2003 with the establishment of the National Pharmacovigilance Centre located in NAFDAC. Nigeria was admitted as the 74th member of the WHO Program of International Drug monitoring in 2004.

4.1.2. Market authorization holders, importers, and private health care providers

Representatives from local and international pharmaceutical industries were interviewed by the assessors (see paragraph 3.5).
Essentially the existent legal provisions for pharmacovigilance in the pharmaceutical industry are in place as the National Medicine Regulatory Agency statutorily ensures best practices as in the US (FDA) and Europe (EMA). However, there are challenges in compliance especially for the local pharmaceutical industries. For MAH, the main aim is to build pharmacovigilance structures taking into account the local guidelines, which are described in the "NAFDAC Good Pharmacovigilance Practice Guidelines" (2016). For multinational companies it is easier to comply with these guidelines than for local companies as the guidelines are in line with the United States Food and Drug Authority and the European Medicines Agency guidelines and multinationals already have similar structures in other countries. However, the guideline was established in 2016 and not all MAHs have fully implemented all aspects described in the guideline yet. Although the legal basis is good, NAFDAC is not monitoring the MAH's compliance to the guideline.

The main problem is that the MAH receives only a low number of reports each year (the two multinational companies interviewed for this assessment received about 50 reports each in the last year) which makes it difficult for them to monitor the safety of their drugs on the market. To increase reporting, MAHs train their sales representatives in PV. MAHs also try to be accessible for HPCs and patients through phone lines and email if they want to report. However these two measures has not yet proven successful in increasing the reporting rate. Because of the lack of data, period safety update reports (PSURs), which are submitted to NAFDAC, often lack data specific to Nigeria, which reduces the value of the PSURs for the national regulator. Because of the lack of data, Nigerian Risk Management Plans are difficult to make since there is no possibility to adapt to the local situation (because this is unknown). The guidelines stipulate that a qualified person responsible for PV (QPPV) should be residing in the country. However, NAFDAC is worried about the PV competence of some of the QPPVs appointed by the MAHs. If the QPPVs are not truly qualified, it will be difficult for them to set up good MAH PV systems.
During the interviews, the MAHs expressed their desire to continue to have an open dialogue with NAFDAC. MAHs considered establishing a PV group within the Nigerian association for pharmaceutical companies which could then be the partner for NAFDAC to discuss matters relating to PV.

4.1.3. Essential medicines

There is an Essential Medicines List (6th edition 2016) currently in use (see paragraph 3.4). The first edition was introduced in 1986 backed by Decree 43 (now Act CAP N1 2004). This was an operational document for the Essential Drugs Programme which was used in the

provision of medicines supply. The list is used mainly in the public sector and adherence to the list at the various levels of the healthcare system is not optimal.

4.2. Systems, structure and stakeholder coordination

In this area, fifteen indicators were assessed at the level of the NMRA (Annex 1), and six indicators at the level of the PHPs (Annex 2).

4.2.1. National pharmacovigilance unit

The Directorate for Pharmacovigilance (PV) and Post marketing Surveillance (PMS) is one of 14 directorates within NAFDAC. The Directorate is led by a Director and within the Directorate there are 5 Deputy Directors, of which one is responsible for PV. In total 35 persons work at the Directorate, 5 of these are dedicated to PV. However, in practice, staff working in PMS also performs tasks belonging to PV.

The work processes of the Directorate are described in 17 SOPs which were recently updated works to ensure high quality of the work delivered by NAFDAC.

There are 6 Zonal Pharmacovigilance Centres, located in tertiary institutions (primarily teaching hospitals). These include:

- Ahmadu Bello University Teaching Hospital (ABUTH) Zaria
- University of Benin Teaching Hospital (UBTH)
- University of Ilorin Teaching Hospital (UITH)
- Lagos University Teaching Hospital (LUTH)
- University of Maiduguri Teaching Hospital (UMTH)
- Federal Medical Centre (FMC) Owerri

The Zonal Pharmacovigilance Centres complement the work of the Directorate. The functions of the Zonal Pharmacovigilance Centres include:

a.) Distribution of ADR forms and collection of ICSRs from reporters, preliminary evaluation and submitting these promptly to the national centre for central evaluation and validation.
b.) Transmitting acknowledgements and feedback information to the reporters and also disseminating information from NAFDAC to the HCP and to the public as appropriate.
c.) Monitoring progress of PV activities at institutional levels.
d.) Supporting training and capacity building for PV.

The work at the Directorate is also supported by a National Drug Safety Committee. This committee consists of 12 members, of which 8 are external (with different competences such as clinical pharmacology and therapeutics, epidemiology, basic pharmacology, infectious diseases, internal medicine, pharmacy, etc.) and 4 are NAFDAC staff (4 Directors) with the Director PV/PMS acting as secretary. The current Chairman of the Committee is Professor Ambrose O. Isah. Due to limited funding the committee only met once in 2017. In case of emergency issues, remote review of cases can be done by the committee members.

4.2.2. Role of non-governmental organizations

IHVN is the most important partner for NAFDAC when it comes to provision of PV trainings (see paragraph 4.2.4). Other organizations implementing the United States President Emergency Plan for AIDS Relief (US PEPFAR) for the control of HIV/AIDS are also supporting PV activities through the training of healthcare workers and submission of ICSRs to NAFDAC.

The Global Fund for AIDS, Tuberculosis and Malaria (GFATM) is the most important donor fund that currently provides funding for PV activities. USAID provides funding for aDSM for DR-TB patients (all DR-TB patients on new drugs and regimens, plus (pre-) XDR-TB patients). This includes funding for technical assistance and consumables (e.g. printing of the aDSM form). IHVN supported (and supports) NAFDAC and the NTBLCP with developing the aDSM form and provision of aDSM trainings. KNCV has supported the NTBLCP with developing the aDSM plan as part of the new guidance related to the introduction of new anti-TB drugs and medicines, including the aDSM reporting form.

4.2.3. National budget for PV tasks

There is no direct funding for PV, but NAFDAC as a whole receives funding from the government. This budget is divided over the different directorates. At the moment there are problems with the budget release from the government. Receiving funding for PV capacity building is difficult.
To increase funding for PV, the Directorate also is looking into ways to obtain donor funding. An example of this is the collaboration with the malaria program, which was funded by the Global Fund to Fight Aids, Tuberculosis and Malaria. NAFDAC is also investigating the possibility to raise more registration service fees, but it is unclear if these would be paid directly to NAFDAC and if these can be retained within NAFDAC.

4.2.4. Pharmacovigilance training

Preservice training

Effectively, there is no preservice training specifically addressing pharmacovigilance in place.

In-service training

Routine NAFDAC trainings

NAFDAC provides trainings, which are still under construction and development. There is minimal impact of the current trainings on the quantity and quality of the submitted reports as there is little follow-up and no supportive supervision provided after the training due to limitation in human and financial resources. Due to the vastness of the country, frequent staff changes in health facilities (for different reasons, such as low salaries, government policies, political sensitivities), and limited budget and human resources, NAFDAC cannot train each (new) health care worker. Zonal PV centres also have a role in supporting NAFDAC's training and capacity building activities. Therefore, health care workers are expected to pass on the knowledge they gained during NAFDAC trainings to their fellow workers e.g. by organizing step-down trainings or on-the-job training. However, step-down trainings are not commonly organized – reasons mentioned were:

- logistical challenges (no training facilities, no funding);
- too little capacity of the staff original trained by NAFDAC in providing a training/the subject;
- little interest of fellow workers because of lack of status of the trained staff and/or the training (no special training venue, no certificate);
- even if (on-the-job) training was organized, staff may not feel trained, as it is less formal (no special training venue, no certificate).

A good exception is one hospital in Lagos that provides in-service trainings to each health care worker newly employed by the hospital. In general, interviewees have the impression that engagement in PV is best at the federal government level (teaching hospitals), and could be improved at State and Local government levels.

NTBLCP trainings

PV was part of the annual routine MDR-TB trainings (section Logistics) organized by the NTBLCP between 2012 and 2015. However, it was removed from this training as NTBLCP felt that provision of PV training was not their responsibility In September 2018, the first aDSM trainings were provided to the first six states (28 sites in 27 states). However, lower level trainings would be needed (see Box 1).

The on-going aDSM training targets clinicians at OPD clinics providing monthly follow-up to DR-TB patients on treatment, local government area (LGA) TB supervisors and TB state program staff. However, there is need for continuous awareness raising about occurrence, management and reporting of adverse events to all DOT providers managing DR-TB patients across the country. IHVN has started developing training materials on aDSM for lower cadre HPCs and conducted a small pilot including 20 lower cadre HPCs in a few States. These materials need to be further tested and may also need to be translated into local languages. Also, IHVN sees the need for also reaching DOT supporters (see Box 1).

Box 1. DR-TB treatment models in Nigeria

Currently there are two models for the treatment of (M)DR-TB: the first model includes hospital admission for the duration of the intensive phase (4 months for the shorter treatment regimen (STR) which is provided to all patients with MDR-TB who have no indication of additional resistance or intolerance to second-line injectable drugs or quinolones; 8 months* for patients on individualized regimens containing new drugs); while patients treated according to the second model receive ambulatory treatment supported by DOT providers at decentralized general OPDs.

There are 28 PMDT sites in 27 (out of a total of 36) states where DR-TB patients can be hospitalized. Ambulatory treatment can be provided by 238 general OPDs, which function as satellites to these 28 PMDT sites. Clinicians in these OPDs see all DR-TB patients in their catchment area once per month. For daily supervision and support, there are DOT supporters, which can be family or community members, or community health workers.

Each state has a consilium of DR-TB experts deciding which patients would benefit from hospital admission during the intensive phase of treatment. This depends on the treatment regimen provided, comorbidities, and age (for children, also the type of TB and diagnostic uncertainty are taken into account.

** since 8 months is too long to be acceptable for most patients, often patients are shifted to ambulatory care after having reached sputum culture conversion.*

SPHAR-TI training program

In 2016, IHVN , in collaboration with NAFDAC, conducted the Structured Pharmacovigilance and Training Initiative (SPHAR-TI), a practical modular PV course which was funded by the Special Programme for Research and Training in Tropical Diseases (TDR) of the WHO, UNICEF, UNDP, the World Bank and the WHO. The aim of SPAR-TI was to promote public health safety through the detection, reporting and monitoring of adverse drug reactions. The course started with a one-week intensive workshop (in March 2016), followed by nine months of mentoring and evaluation. All participants were expected to have submitted at least 20 accurately completed NAFDAC Yellow Forms by the end of the program. Those achieving this milestone received the Pharmacovigilance Certified Professional (PcP) certificate in January, 2017. The course was announced on several national platforms and in newspapers to provide equal opportunities for candidates throughout the country. All health staff directly interacting with patients with TB, HIV or malaria could apply. Fifty-five nurses, physicians and pharmacists from public hospitals and government institutions directly involved in HIV, TB and malaria control program participated in the course; 55 got a certificate. The tangible outputs of the course were:

- 2,937 health care workers trained by 55 trainees in so-called step-down trainings;

- 46 pharmacovigilance committees erected;
- And approximately 3,000 individual case safety reports (ICSR) submitted (vs. 805 ICSR submitted by non-trained health care workers). The Yellow forms could be sent straight to NAFDAC or scanned and sent through email using a Google email group. The latter reports were assessed by a team at IHVN for completeness and quality. Feedback about these reports was also provided per email.

The success of the project is explained by the team of IHVN as follows:

- Only those that see patients on daily basis were selected for the program;
- Experienced trainers with different areas of knowledge and expertise were providing the training;
- Readers and posters were provided to the trainees, both as job-aids and to be used during the step-down trainings;
- There were several clear milestones for the participants, and certificates were only handed out after completing all milestones in time;
- There was frequent contact with trainees;
- Reports could be submitted on paper via email;
- The program was a public-private partnership, in which the private (more resourceful) partner supported the tasks of the public partner.

The funding for this program stopped in 2017. Since then, NAFDAC and IHVN have continued providing trainings, but currently there is no (intensive) follow-up as there was for the SPHAR-TI program.

There were some limitations of the SPHAR-TI program:

- Although the ICSR sent to NAFDAC were assessed, including potential causative drugs, there was not feedback of the causality assessment to the research team or to the reporters;
- This was a donor-funded program, with a limited funding duration and scope. After the program stopped, though the Google mail group is still being used, a gradual decline in number of ICSRs submitted is seen;
- The training, in its existing model, was to be continued by NAFDAC. However, limitations in budget and staffing have hindered provision of follow-up as (intensive) as there was for the SPHAR-TI program.

4.2.5. National patient safety monitoring committee

There is no National patient safety monitoring committee in Nigeria.

4.2.6. Consumption and prescriptions of medicines

There is no available data on the prescription and consumption of drugs in Nigeria.
Non-authorized drugs can in principle not enter the country, unless used in a pilot study or research project within specific PHPs, as approved by the Minister of Health or even the President him/herself.

4.2.7. Mechanisms to disseminate PV information

The Deputy Director Food and Drug Information within the Directorate of PV and PMS is responsible for the communication plan. NAFDAC uses several means of communication:

- Public alerts are placed on NAFDACs website to inform HPCs and the general public. In 2017, 21 public alerts on pharmaceutical products were published;
- Zonal notifications are sent from NAFDAC to the zonal offices in order for surveillance activities to be carried out and reports to be submitted to the office of the Director of PV/PMS. In 2017, 28 zonal notifications were sent out;

- Dear Healthcare Provider Letters (DHCPLs) are letters sent out to healthcare providers to alert them of the pharmaceutical products to be vigilant of and monitor in their facilities. In 2017 38 DHCPL were issued.
- A quarterly newsletter published by the directorate of PV/PMS, although, in 2017 only one newsletter was published due to financial constraints;
- NAFDAC Consumer Safety publication, a magazine published bi-annually to inform the public and NAFDACs stakeholders on the agency's activities;
- publications of specific findings in international peer-reviewed journals.

4.3. Signal generation and data management

4.3.1. Collection of PV data: adverse event reporting, data flow and management

The reporting rate in Nigeria is low, in 2017, 2,173 reports were received by NAFDAC on a population of 190.6 million inhabitants in the same year[14] (1.14 reports per 100,000 population).

Marketing Authorization Holders

MAH receive only a low number of reports each year (two multinational companies had only received 50 reports each in the last year from HPCs). If a report is received, the information is entered into the MAH's (global) database. From there, the report is created, which the MAH's (local) office then submits to NAFDAC. NAFDAC does not share data collected through their spontaneous reporting system with the MAH. As a consequence, the MAH do not have an overview of all reports on their products.

Spontaneous reporting (passive surveillance) by clinicians

HPCs wishing to report an adverse event can use the so-called Yellow Form (Figure 3). This is a paper reporting system; no electronic reporting is possible. However, the form can be downloaded from the NAFDAC website, filled in, scanned and e-mailed to NAFDAC. The Google email group that was started during the SPHAR-TI project is still active and since NAFDAC is a member of this group, reports can still be scanned and submitted as attachment through this mail system. Reports can be sent directly to NAFDAC, or to the zonal PV center (that forwards the reports to NAFDAC on a quarterly basis), or to the health center's PV committee, that will forward the report to the zonal PV center, which in turn has to forward the report to NAFDAC (Figure 2).

Spontaneous reporting (passive surveillance) by the general public

The general public can contact NAFDAC through the Pharmacovigilance Rapid Alert System for Consumer Reporting (PRASCOR) system. In the PRASCOR system, consumers of medicines who experience an untoward effect are encouraged to send a prepaid short text message with the name of the medicine and the adverse reaction to a specific phone number. This message with the consumer's phone number is forwarded as an email alert to NAFDAC for follow-up. The reporter receives a tracking code and a phone call from staff of NADAC to find out more about the adverse event. If the follow up yields sufficient information, the PRASCOR alert will be made into an ICSR. In 2017, 4,300 PRASCOR alerts were received, of which 111 were transcribed to ICSRs. The number of alerts transcribed to ICSR was small because during the follow-up with reporter, relevant information needed to complete the mandatory phases was most often not provided by reporters, hindering transcription to ICSRs.

[14] CIA World Fact book. https://www.cia.gov/library/publications/the-world-factbook/rankorder/2119rank.html. Date accessed: 23 January 2019.

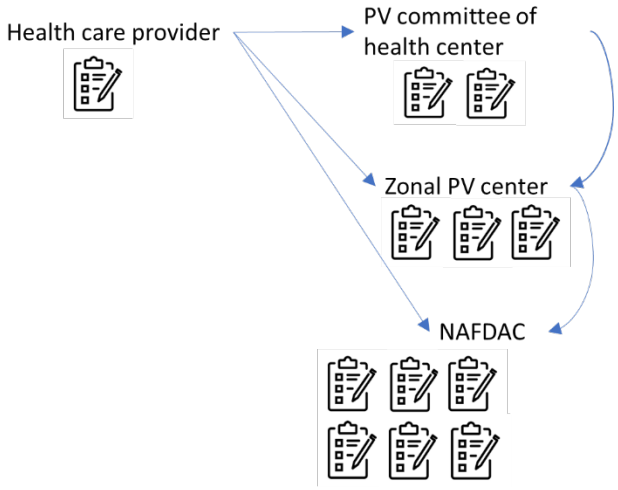


Figure 2. Report flow for Yellow forms, from reporter to NAFDAC.

Database

At NAFDAC, all ICSRs are entered into the national database (Excel). This local database houses all ADR reports. NAFDAC staff experiences problems with entering reports (which do still fulfil the minimum reporting requirements according to EU/CIOMS) in VigiFlow as these do not pass the validation rules, especially the start date of the reaction seems to be a mandatory field but this information is often missing. Since a large part of the reports cannot be uploaded to VigiBase as these are considered to be incomplete by VigiFlow, there is a need to store these in a local database, hence the existence of the Excel-file and double data entry.

The local database is not backed up on a regular basis which might cause loss of data if the computer on which it is stored crashes.

A problem with using VigiFlow is that internet access is very patchy. The PV/PMS Directorate buys additional bundles to ensure good internet access.

There are other challenges:

- Distribution of the paper forms is suboptimal because of limited funding available for printing (reportedly HPCs do not always get the number of forms they request) and logistical challenges due to the vast and difficult territory to be covered;
- Having a paper based system might potentially cause long reporting delays. Reportedly, to save transportation costs, some hospitals collect all forms to be submitted at once only a few times per year;
- Reporters wishing to submit their reports as an electronic attachment to email have to submit of the report at their own cost;
- Since the report can be submitted to three different entities, it is difficult for the reporter to know where to report;
- There is no tracking system to make sure that a report submitted by the reporter eventually reaches NAFDAC;
- Reportedly, not all HPCs preparing ADR reports do submit these reports – some of them wish to keep the reports for their own administration;
- Also, the SPHAR-TI project and the pharmacist interviewed indicate that there is lack of awareness about the importance of reporting.

After receipt, NAFDAC sends the reporter an acknowledgement of receipt. No further feedback is provided. In 2017, 2173 reports were received, the majority (81%) coming from pharmacists. Of these, 790 reports underwent causality assessment and 570 were submitted

to VigiBase. The cases submitted to VigiBase had an average completeness score of 0.87-0.91 in the first half of 2017.

Other PV projects

Drug safety program IHVN

The Institute of Human Virology Nigeria (IHVN) has a comprehensive drug safety programme, which runs in its network of hospitals treating HIV/AIDS and tuberculosis. This programme involves training of healthcare workers in PV, activating PV committees in hospitals, coordinating the collection and submission of ICSRs to NAFDAC and conducting operational research projects, with the aim of addressing health system challenges that are undermining the reporting of adverse drug reactions.

aDSM

Active Drug Safety Management and Monitoring (aDSM) guidelines, as well as the aDSM reporting form (Figure 5) and the SOP to fill this form, were developed by the NTBLCP with support of NAFDAC, the University of Benin, University College Hospital of Ibadan, IHVN KNCV Tuberculosis Foundation, WHO, and the Damian Foundation, in the spring of this year. This work was funded by USAID/CTB. The first HCPs were trained on aDSM in September 2018. Printing and distribution of the aDSM report forms is funded by USAID/CTB. So far, no aDSM reports have been submitted. The envisioned (paper) report flow uses the drug supply chain, and therefore involves multiple tiers (Figure 3a and 3b). As can be seen from Figure 3a and 3b, the flow for SAE report as provided in the aDSM guideline does slightly differ from the flow as outlined during discussions with the NTBLCP staff and other stakeholders (Figure 3b – note that this flow was confirmed during the debriefing by all stakeholders), illustrating that there may be a lack of clarity about reporting flows.

The NTBLCP sees aDSM reporting as its main responsibility, and therefore wants to assess all reports first, before these are submitted to NAFDAC.

A complication is that the main responsibility of actors involved in the report flow chain is controlling drug supplies, thus, making sure that all filled aDSM forms reach NAFDAC timely will not have primary priority. The limitation of this system is that the time lag between submission of an aDSM report and receipt at NAFDAC may be considerable, and can easily augment to several months. Another risk is that paper forms are lost between tiers. There is not yet a good M&E system to keep track of the number of aDSM reports submitted by treatment providers, and the number of reports that end up at NAFDAC.

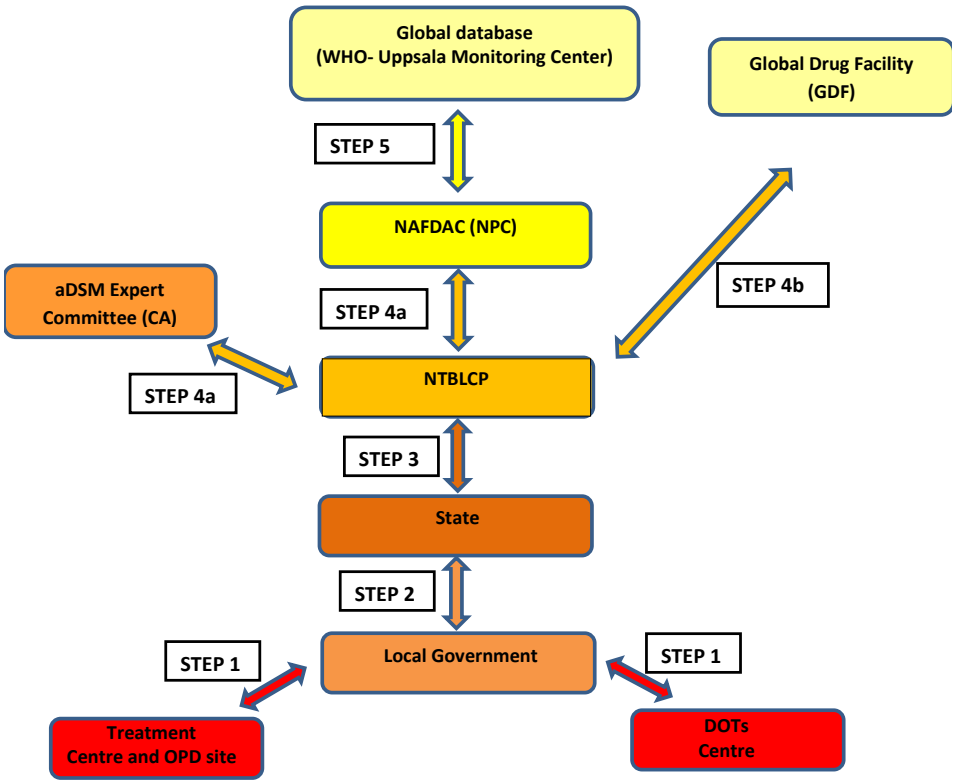


Figure 3a. Reporting flow for SAEs as provided in the aDSM guidelines of NTBLCP (2018)

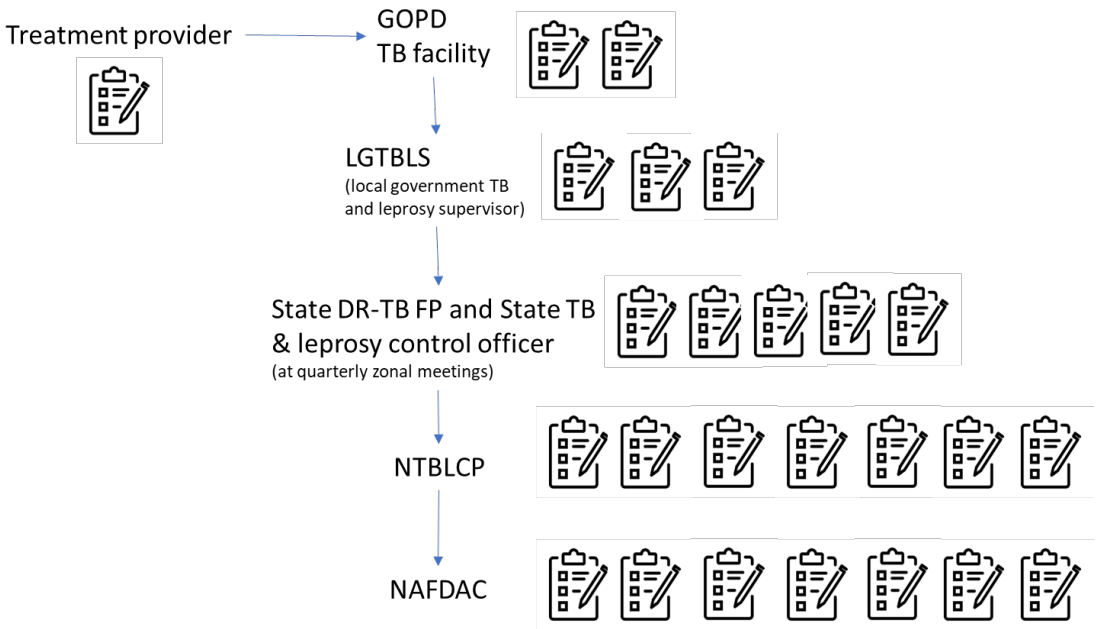


Figure 3b. Envisioned report flow of all aDSM forms in general, from reporter to NAFDAC.

The aDSM SOP prescribes that reports of SAEs reach the next level within 24 hours, but with five transfer steps, it can easily take 5 days before an SAE report reaches NAFDAC.

In future, the aDSM reports should be submitted electronically via NETIMS[15]. This is an e-TB Manager[16] - based electronic patient management system, in which PViMS[17] is currently being integrated. This integration is supported by MSH and expected to be ready by the end of September 2018. The system has an off-line mode, enabling to enter reports offline and upload them overnight.

NETIMS is currently being completed at national, state and local government level, i.e., not in the PMDT sites by the clinicians themselves. In addition, a mobile tablet/hand held device is available at 10 high TB burden facilities in each of the 37 states (total of 370) for direct data capture at facility level. However, it is known that not all available data is currently uploaded (estimated completeness is around 70%). This is probably because, while data entry can be done offline, uploading the entered data to the central database still requires internet, as does accessing the system.

Though IHVN is supporting aDSM, it has not been granted access to the electronic system by NTBLCP. Since the team did not meet with the experts who are currently developing the adverse event reporting module, and no computer was available at the NTBLCP to demonstrate NETIMS, the team has no good impression on how user-friendly the program is and what the internet connectivity needs are. An informant from KNCV Nigeria stated that the system is user-friendly, but requires a certain level of computer skills. It is unclear how the aDSM module performs. Also, it is not clear to the team how complete and timely the information in the system is. Although NTBLCP staff suggested that NAFDAC would receive PV reports through NETIMS (Figure 4), it seems not yet clear in what way information will be exchanged, as for reasons of patient confidentiality, NTBLCP cannot share the complete database with NAFDAC. Also it is unclear if the system is compatible with the format used by NAFDAC, which would enable electronic transfer of reports.

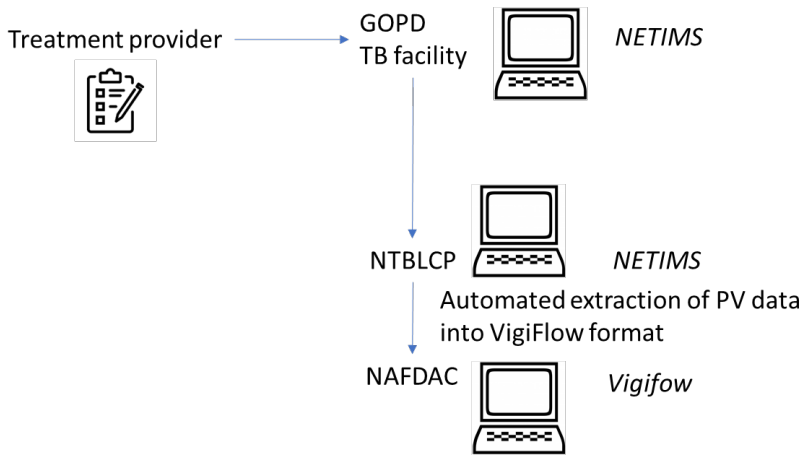
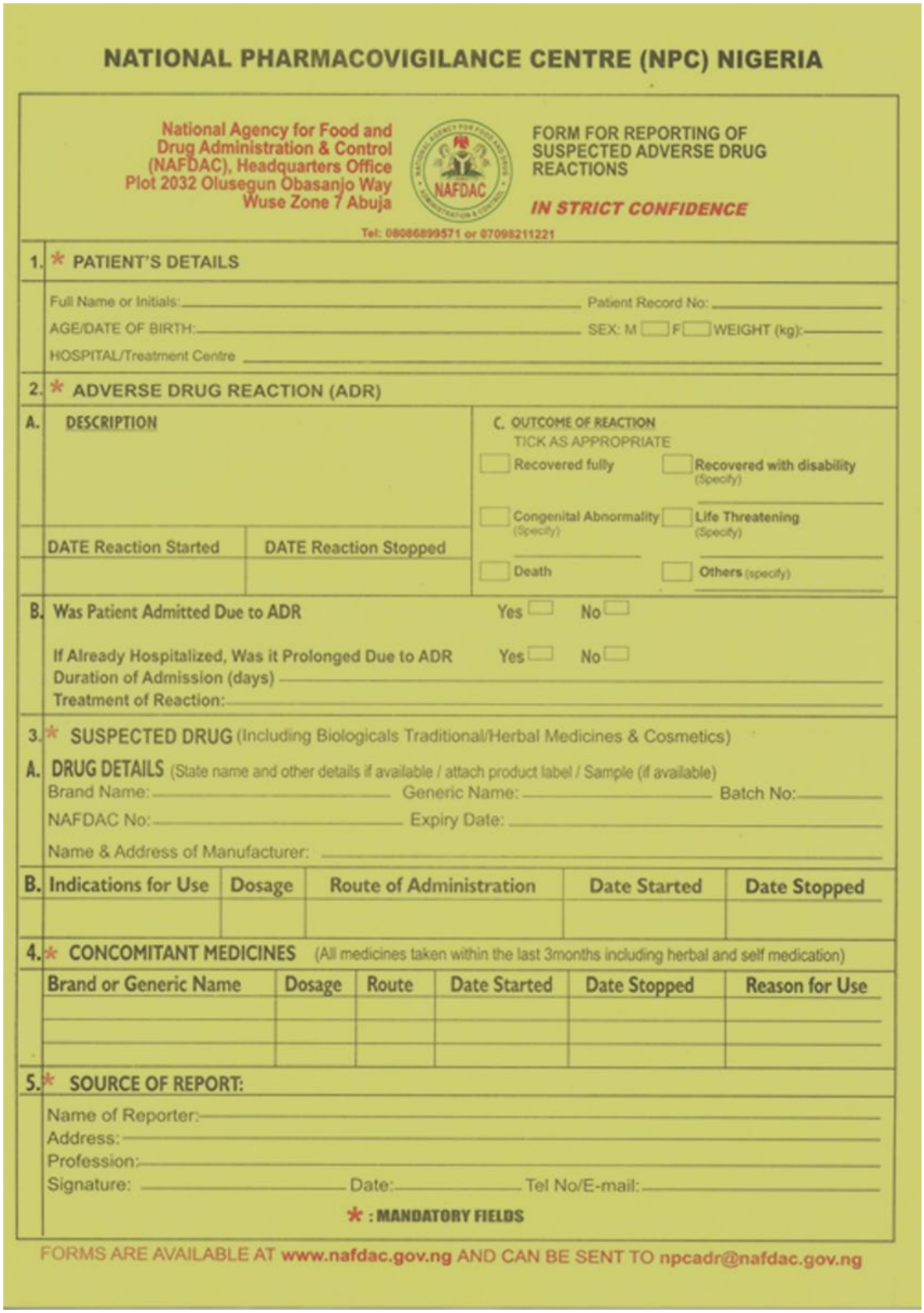


Figure 4. Suggested flow of electronic aDSM reports with NETIMS.

[15] National Electronic TB Information Management System

[16] e-TB Manager, developed by MSH, is a web or desktop-based tool for managing all the information needed by national TB control programs. It integrates data across all aspects of TB control, including information on suspected cases, patients, medicines, laboratory testing, diagnosis, treatment, and outcome. In most countries, it is used for management of DR-TB cases. See http://siapsprogram.org/wp-content/uploads/2016/12/TechBrief-Tools-eTB-Manager-10-14-16.pdf for more information.

[17] PViMS (PharmacoVigilance Monitoring System) is a web-based application for clinicians, regulatory bodies, and implementing partners to monitor the safety of medicines. PViMS enables the implementation of active surveillance activities in low- and middle-income countries (LMICs) by addressing the entire data collection, data analysis and reporting process.P ViMS has the ability to export case safety data in E2B interface and is health level 7 (HL7) compliant. See http://siapsprogram.org/wp-content/uploads/2017/02/PViMSbrochure-10-14-16.pdf for more information.



NATIONAL PHARMACOVIGILANCE CENTRE (NPC) NIGERIA

National Agency for Food and Drug Administration & Control (NAFDAC), Headquarters Office
Plot 2032 Olusegun Obasanjo Way
Wuse Zone 7 Abuja

Tel: 08086899571 or 07098211221

FORM FOR REPORTING OF SUSPECTED ADVERSE DRUG REACTIONS

IN STRICT CONFIDENCE

1. * PATIENT'S DETAILS

Full Name or Initials: _____ Patient Record No: _____

AGE/DATE OF BIRTH: _____ SEX: M ☐ F ☐ WEIGHT (kg): _____

HOSPITAL/Treatment Centre _____

2. * ADVERSE DRUG REACTION (ADR)

A. DESCRIPTION

DATE Reaction Started	DATE Reaction Stopped

C. OUTCOME OF REACTION
TICK AS APPROPRIATE

☐ Recovered fully ☐ Recovered with disability (Specify) _____

☐ Congenital Abnormality (Specify) _____ ☐ Life Threatening (Specify) _____

☐ Death ☐ Others (specify) _____

B. Was Patient Admitted Due to ADR Yes ☐ No ☐

If Already Hospitalized, Was it Prolonged Due to ADR Yes ☐ No ☐

Duration of Admission (days) _____

Treatment of Reaction: _____

3. * SUSPECTED DRUG (Including Biologicals Traditional/Herbal Medicines & Cosmetics)

A. DRUG DETAILS (State name and other details if available / attach product label / Sample (if available)

Brand Name: _____ Generic Name: _____ Batch No: _____

NAFDAC No: _____ Expiry Date: _____

Name & Address of Manufacturer: _____

B. Indications for Use	Dosage	Route of Administration	Date Started	Date Stopped

4. * CONCOMITANT MEDICINES (All medicines taken within the last 3months including herbal and self medication)

Brand or Generic Name	Dosage	Route	Date Started	Date Stopped	Reason for Use

5. * SOURCE OF REPORT:

Name of Reporter: _____

Address: _____

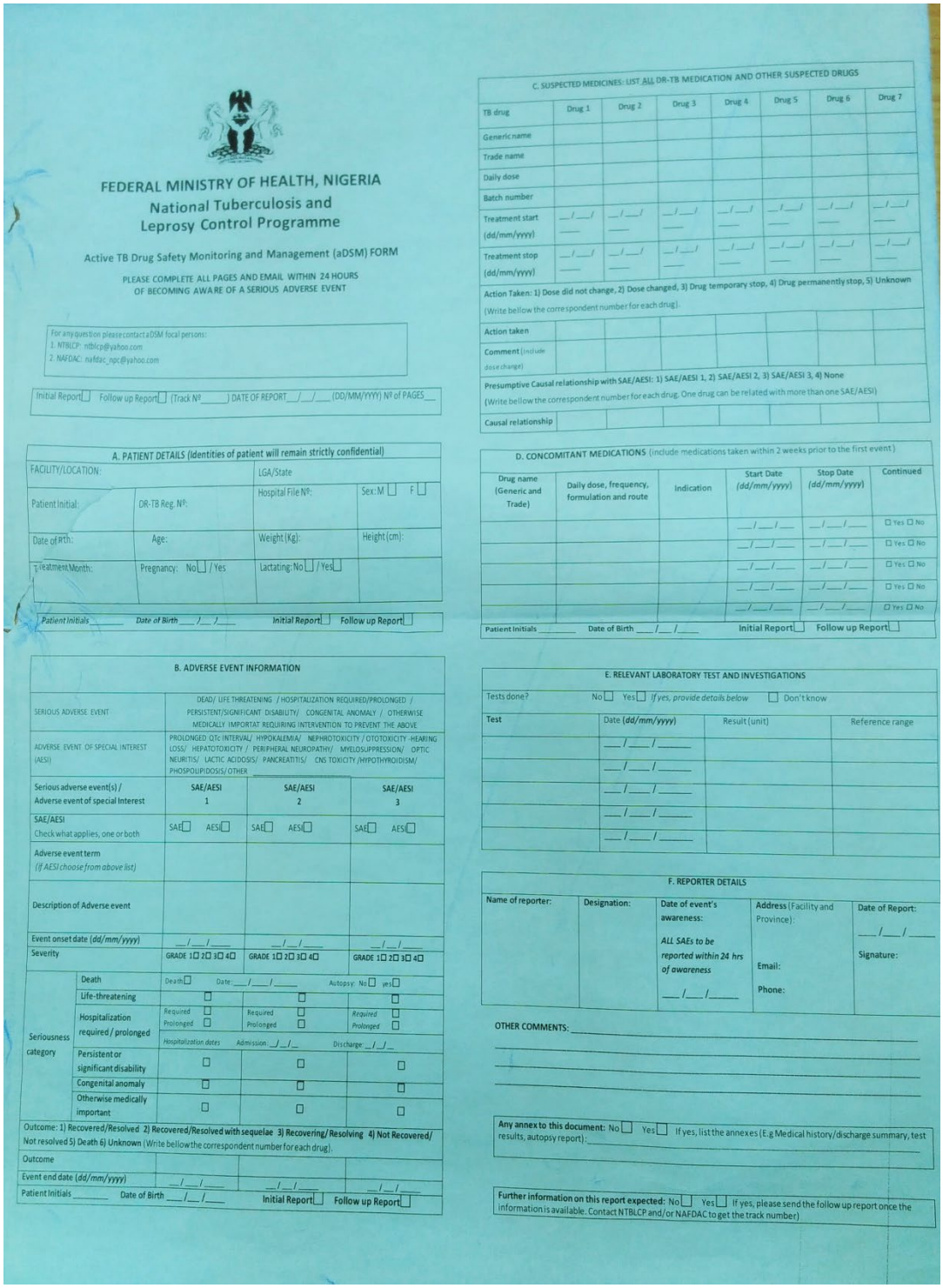
Profession: _____

Signature: _____ Date: _____ Tel No/E-mail: _____

*** : MANDATORY FIELDS**

FORMS ARE AVAILABLE AT **www.nafdac.gov.ng** AND CAN BE SENT TO **npcadr@nafdac.gov.ng**

Figure 5. NAFDAC's Yellow Form used for the reporting of adverse events.



FEDERAL MINISTRY OF HEALTH, NIGERIA
National Tuberculosis and
Leprosy Control Programme

Active TB Drug Safety Monitoring and Management (aDSM) FORM

PLEASE COMPLETE ALL PAGES AND EMAIL WITHIN 24 HOURS
OF BECOMING AWARE OF A SERIOUS ADVERSE EVENT

For any question please contact aDSM focal persons:
1. NTBLCP: ntblcp@yahoo.com
2. NAFDAC: nafdac_npc@yahoo.com

Initial Report☐ Follow up Report☐ (Track Nº_____) DATE OF REPORT__/__/___ (DD/MM/YYYY) Nº of PAGES__

A. PATIENT DETAILS (Identities of patient will remain strictly confidential)

FACILITY/LOCATION:		LGA/State	
Patient Initial:	DR-TB Reg. Nº:	Hospital File Nº:	Sex: M☐ F☐
Date of Birth:	Age:	Weight (Kg):	Height (cm):
Treatment Month:	Pregnancy: No☐ / Yes☐	Lactating: No☐ / Yes☐	

Patient Initials _____ Date of Birth ___/___/___ Initial Report☐ Follow up Report☐

B. ADVERSE EVENT INFORMATION

SERIOUS ADVERSE EVENT	DEAD/ LIFE THREATENING / HOSPITALIZATION REQUIRED/PROLONGED / PERSISTENT/SIGNIFICANT DISABILITY/ CONGENITAL ANOMALY / OTHERWISE MEDICALLY IMPORTAT REQUIRING INTERVENTION TO PREVENT THE ABOVE		
ADVERSE EVENT OF SPECIAL INTEREST (AESI)	PROLONGED QTc INTERVAL/ HYPOKALEMIA/ NEPHROTOXICITY / OTOTOXICITY -HEARING LOSS/ HEPATOTOXICITY / PERIPHERAL NEUROPATHY/ MYELOSUPPRESSION/ OPTIC NEURITIS/ LACTIC ACIDOSIS/ PANCREATITIS/ CNS TOXICITY /HYPOTHYROIDISM/ PHOSPOLIPIDOSIS/OTHER _____		
Serious adverse event(s) / Adverse event of special Interest	SAE/AESI 1	SAE/AESI 2	SAE/AESI 3
SAE/AESI Check what applies, one or both	SAE☐ AES☐	SAE☐ AESI☐	SAE☐ AES☐
Adverse event term (If AESI choose from above list)			
Description of Adverse event			
Event onset date (dd/mm/yyyy)	__/__/____	__/__/____	__/__/____
Severity	GRADE 1☐ 2☐ 3☐ 4☐	GRADE 1☐ 2☐ 3☐ 4☐	GRADE 1☐ 2☐ 3☐ 4☐
Seriousness category: Death	Death☐ Date: ___/___/____ Autopsy: No☐ yes☐		
Life-threatening	☐	☐	☐
Hospitalization required / prolonged	Required ☐ Prolonged ☐	Required ☐ Prolonged ☐	Required ☐ Prolonged ☐
Hospitalization dates	Admission: __/__/__	Discharge: __/__/__	
Persistent or significant disability	☐	☐	☐
Congenital anomaly	☐	☐	☐
Otherwise medically important	☐	☐	☐
Outcome: 1) Recovered/Resolved 2) Recovered/Resolved with sequelae 3) Recovering/Resolving 4) Not Recovered/ Not resolved 5) Death 6) Unknown (Write bellow the correspondent number for each drug).			
Outcome			
Event end date (dd/mm/yyyy)	__/__/____	__/__/____	__/__/____

Patient Initials _____ Date of Birth ___/___/___ Initial Report☐ Follow up Report☐

C. SUSPECTED MEDICINES: LIST ALL DR-TB MEDICATION AND OTHER SUSPECTED DRUGS

TB drug	Drug 1	Drug 2	Drug 3	Drug 4	Drug 5	Drug 6	Drug 7
Generic name							
Trade name							
Daily dose							
Batch number							
Treatment start (dd/mm/yyyy)	__/__/____	__/__/____	__/__/____	__/__/____	__/__/____	__/__/____	__/__/____
Treatment stop (dd/mm/yyyy)	__/__/____	__/__/____	__/__/____	__/__/____	__/__/____	__/__/____	__/__/____
Action Taken: 1) Dose did not change, 2) Dose changed, 3) Drug temporary stop, 4) Drug permanently stop, 5) Unknown (Write bellow the correspondent number for each drug).							
Action taken							
Comment (Include dose change)							
Presumptive Causal relationship with SAE/AESI: 1) SAE/AESI 1, 2) SAE/AESI 2, 3) SAE/AESI 3, 4) None (Write bellow the correspondent number for each drug. One drug can be related with more than one SAE/AESI)							
Causal relationship							

D. CONCOMITANT MEDICATIONS (include medications taken within 2 weeks prior to the first event)

Drug name (Generic and Trade)	Daily dose, frequency, formulation and route	Indication	Start Date (dd/mm/yyyy)	Stop Date (dd/mm/yyyy)	Continued
			__/__/____	__/__/____	☐ Yes ☐ No
			__/__/____	__/__/____	☐ Yes ☐ No
			__/__/____	__/__/____	☐ Yes ☐ No
			__/__/____	__/__/____	☐ Yes ☐ No
			__/__/____	__/__/____	☐ Yes ☐ No

Patient Initials _____ Date of Birth ___/___/____ Initial Report☐ Follow up Report☐

E. RELEVANT LABORATORY TEST AND INVESTIGATIONS

Tests done? No☐ Yes☐ If yes, provide details below ☐ Don't know

Test	Date (dd/mm/yyyy)	Result (unit)	Reference range
	___/____/_____		
	___/____/_____		
	___/____/_____		
	___/____/_____		
	___/____/_____		

F. REPORTER DETAILS

Name of reporter:	Designation:	Date of event's awareness: ALL SAEs to be reported within 24 hrs of awareness ___/___/_____	Address (Facility and Province): Email: Phone:	Date of Report: ___/___/____ Signature:

OTHER COMMENTS: _____

Any annex to this document: No☐ Yes☐ If yes, list the annexes (E.g Medical history/discharge summary, test results, autopsy report): _____

Further information on this report expected: No☐ Yes☐ If yes, please send the follow up report once the information is available. Contact NTBLCP and/or NAFDAC to get the track number)

Figure 6. Final draft of the aDSM form.

4.3.2. Reporting tools

NAFDAC accepts the Yellow Form for the spontaneous reporting of adverse events (see Figure 5).

The NTBLCP has developed the aDSM form for the reporting of SAE and adverse events of special interest (Figure 6). This paper form is currently available as a final draft version, and is used in trainings. Reportedly, two small changes are still needed to finalize the form. The NTBLCP will also submit all information regarding SAEs to the Global Drug Facility using this aDSM form.

Also, the immunization programme has developed its own form, and this programme's staff collects and assesses the information themselves.
Both the NTBLCP and the immunization program do share their reports with NAFDAC.
The malaria and HIV program each have developed their own ADR reporting forms. Information is sent on their forms to NAFDAC, which is transcribed on the spontaneous reporting form (Yellow Form) at NAFDAC.

4.4. Risk assessment and evaluation

In this area, twelve indicators were assessed at the level of the NMRA (Annex 1), and eight indicators at the level of the PHPs (Annex 2).

4.4.1. Reporting of adverse events

Spontaneous reporting

In Ibadan Chest Referral Centre, the pharmacist is expected to fill the forms on behalf of nurses and clinicians, and will thus be called by them whenever there is an adverse event that they feel needs to be reported. The pharmacist also reviews clinical files, to check if there are adverse events that were not reported, and then fills a form. He feels that both the yellow form and the aDSM form will be needed on-site as *"the aDSM form is needed for reporting SAE and AE* (adverse event) *of special interest[18], while the yellow form is needed to report any other potential ADRs"*. This pharmacist was trained in SPHAR-TI and seems to be very motivated to reporting AEs. So far, the AEs are reported on paper forms which are then scanned and submitted via email. However, scanning of reports at the pharmacist's own personal expense.
Also reporting is generally seen as a burden as it is time consuming, PV activities are not mentioned in the health care workers' job description, and there are no direct incentives to health care workers to report adverse events (see also the next paragraph about feedback).
To increase PV reporting amongst HCPs, more advocacy is needed. This can be done in several ways:

- Integrating PV as a specific topic into the existing routine monthly clinical review meetings;
- Adding one or more PV-indicators to NTBLCP's quarterly report template;
- Developing modules on adverse event occurrence, management and reporting for lower cadre staff (including DOT officers)

aDSM

The interviewees from the PMDT centers mentioned that the aDSM form contains a lot of clinical jargon and it might thus be less well understood (and filled) by lower cadre health workers, like the DOT officers, who are the main HCPs in charge of ambulatory DR-TB patient management.
Also, DOT officers who directly supervise the patients in health facilities, report on regular basis about their patient(s) to the OPD clinician assigned at local government level who is responsible for paper documentation and online reporting to higher levels (state and national). Information may get lost on the (oral) transfer of information between the DOT officer and the OPD clinician.

[18] These are 13 (groups of) AE that the WHO in its aDSM guidance document recommends to be reported if the "intermediate" aDSM package is chosen by the country.

4.4.2. Reporting and feedback

Currently, NAFDAC sends acknowledgements of receipt, but does not provide any feedback on the contents of the reports (quality, completeness, accepted or rejected, number of reports on similar adverse events/diseases/drugs, etc.).
During the SPHAR-TI program, IHVN got feedback on the number of reports received and the number of reports accepted and rejected; however, the result of causality assessment was not shared with IHVN nor with the reporter.

4.4.3. Data analysis and causality assessment

The process for causality assessment is lined out by NAFDAC. Reports are selected for causality assessment if the case is complete, i.e., contains enough information to allow causality assessment. The causality assessment is done by the PV staff. There are four multidisciplinary teams consisting of doctors, pharmacists and someone with experience of causality assessment, performing the causality assessment. Causality assessment is performed twice a week on Tuesdays and Thursdays. For more complex cases, external expertise is available.

4.5 Risk management and communication

In this area, ten indicators were assessed at the level of the NMRA (Annex 1), and five indicators at the level of the PHPs (Annex 2).

4.5.1. Management of adverse events

Since no site visits were conducted, the team could not observe (from observing clinicians/nurses with patients, or from patient files) how adverse events are managed. According to the clinician from Zaria TB & Leprosy referral centre, there is good awareness among clinicians and nurses about adverse events and how to manage these. Patients are actively questioned and investigated for adverse events. Ancillary drugs are available free of charge for the patients.
According to the pharmacist of Ibadan chest referral center, he himself and his assistant pharmacist visit all TB patients admitted to the hospital (currently 29 patients) on daily basis, to ask them about their wellbeing. He also reviews clinical files, to check if there are adverse events that were not reported, and asks nurses to contact him in case of adverse events. Clinicians and nurses expect the pharmacist to report. Ancillary drugs are available free of charge for the patients. The pharmacist indicates that not all adverse events are reported by clinicians and nurses. To raise awareness about PV in health care facilities, the interviewees suggest that PV could be integrated into the existing routine monthly clinical review meetings as a specific section.
The new guidelines for the treatment of DR-TB with the shorter treatment regimen and new drugs clearly describes which adverse events occur frequently and how to manage them. It also includes an annex with a scheme prescribing when to do what (laboratory) tests.

4.5.2. Risk management

In relation to risk management of a medicinal product, it is specified in the NAFDAC Good Vigilance Practice Guideline of 2016 in section 3.6 that the MAH is responsible for:

- Ensuring that it constantly monitors the risk of its medicinal product(s) and report this as required by the Agency.
- Taking all appropriate action to minimize risks of its medicinal product(s) and maximize the benefits including ensuring the accuracy of all information produced

by the company in relation to its medicinal product(s) and actively updating and promptly communicating it when new information becomes available.

4.5.3. Signal detection

Due to the low number of reports in the country, no signals of adverse drug reactions were identified last year. However, one signal of substandard quality was identified.

4.5.4. Communication

In the field of communication, NAFDAC communicates through their websites, the zonal pharmacovigilance centers and DHCPLs. However it is unknown in how far these communications reach the intended user. The PV newsletter is not sent as frequently as agreed as there are not enough resources to produce it. See paragraph 4.2.7 for more information.

5. Conclusions: Strengths and Weaknesses of Nigeria's PV system

The Nigerian pharmacovigilance system has grown since its conceptualization and entry into the WHO Programme for International Drug Monitoring in the last two to three decades.
The strengths of this system include its visibility with basic infrastructure distributed around the country by regionalization/zonalisation and growing availability of resource persons, the presence of a standing National Drug Safety Advisory Committee and a strong legal/policy framework. This is enhanced by the standalone National Pharmacovigilance Policy approved by the country's President in Council which to a significant extent demonstrates government's support and goodwill.

The weakness of the PV System is the lack of awareness amongst HCPs and the public as is reflected by the low reporting rate of adverse drug reactions to NAFDAC. Failure to address the numerous factors hindering reporting of adverse events such as the filling of yellow ADR forms being time consuming, process and fears of litigation are of importance. The opportunity now provided the growing awareness about the potential harmful effects among health care professionals and the presence of focused efforts like the PAVIA project and other grant awarding bodies as well as the WHO should be latched on to provide the leverage for promoting pharmacovigilance. The major threats to the strengthening of the pharmacovigilance system remain those of funding and the mobility of staff to other sectors of the economy.

6. Recommendations and Next Steps

6.1. Respondents' recommendations

Some respondents had clear recommendations to make PV work in Nigeria. These included:

1) Nigerian government should make specific funding allocation available for PV, with clear recommendations on how the government should fund PV.

2) Nigerian government should assign health care workers as PV focal person in each health facility.
3) Donor agencies should see PV as an activity that needs funding. Especially those donors funding treatment should feel responsible for funding PV. Specific grants should become available for funding PV activities.
4) Nigerian government should develop a clear strategy to retain knowledge and experience built in trainings and subsequent application of these is retained within health care facilities.
5) The FMOH should increase the funding allocation for PV related activities and thus show that PV has an important place within NAFDAC.
6) Nigerian government should make PV reporting mandatory for HCPs. The National Medical Association (NMA), the major professional clinical society of Nigeria, could be helpful here with accreditation provisions and has already expressed willingness to collaborate with PAVIA.
   Other steps could be taken to increase reporting willingness, e.g.:
   a. Recommending that HCPs have PV reporting included in their job descriptions
   b. Including PV indicators into the routine quarterly reporting template.
7) Strengthen the ongoing support system for state representative of National Food and Drug Regulatory Agency and Control (FAFDAC) to periodically visit selected OPD clinics and ensure implementation of aDSM.

There were also visions about PAVIA's role in the country:

- Assisting with developing and providing trainings (PAVIA may be able to further strengthen the capacity of the IHVN trainers);
- Offering blended learning to lower-cadre of health care;
- Facilitation of the collection of PV forms.

6.2. Visiting team's recommendations

Policy, law and regulations

- Advocacy to ensure that PV legislation gets through the National Assembly.
- Implementation of Policy provisions and attainment of goals considering the set time frame.
- Need to implement and revise the documents as appropriate and in a timely manner.
- Urgent need to address issues regarding staff guaranteeing job satisfaction and security.

Systems, structures and stakeholder coordination

- Appropriate funding should be provided for PV with a clear budget line and funds released timely for identified PV activities.
- The PV system with the Network including healthcare facilities, Public Health programmes should be enabled to perform their roles.
- Government to assign specific PV-focal persons and support creation of PV committees in health facilities responsible for awareness raising, assistance with filling PV forms, collection and assessment of filled PV forms, and forwarding PV forms to the designated authority.
- The Pharmaceutical industry and Traditional medicines sector should be adequately engaged and made to comply with set provisions.
- Capacity building with training of HCPs taking care of patients should be prioritized.
- Donor agencies should be motivated to fund PV activities.

- The role of the zonal centers should be more clearly defined and all logistic and financial support provided.

Methodology of data collection

- This recommendation is best presented in a diagram (Figure 7).

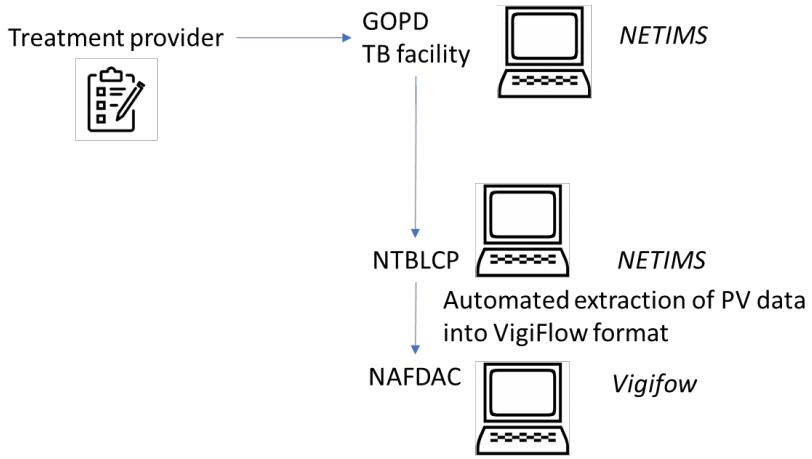


Figure 7. Suggested flow of adverse event reports within the NTBLCP and to NAFDAC using NETIMS (when ready for use).

Data collection tools

- Electronic data collection tools should be considered.
- The logistics and processes around distributing and collecting reports could be streamlines to ensure quality and efficiency.

Data management

- Local database should be backed up on a regular basis to prevent loss of data.
- Introducing the new E2B-R3 compatible VigiFLow should be considered as this version of VigiFlow does have any validation rules. VigiFlow could then act as the local database which would make double data entry redundant.
- There is urgent need to provide an efficient internet service for PV function.

Adverse event reporting

- HCPs should be better and more actively educated (both in pre- and in-service trainings about the importance of reporting adverse events. PHPs can play a crucial role in improving the commitment of HCPs active in their programmes to increase the number of ICSRs submitted.

Data analysis, causality assessment and signal generation

- It is important to build capacity in the area of signal detection.
- It is important to have a database and data analysis tools that support signal detection.
- It is important to monitor the process put in place for signal detection and to evaluate it.

6.3. Next steps

Next steps, timelines and responsibilities were outlined and agreed upon with all key stakeholders present during the debriefing meeting (stakeholders were present from the NTBLCP, NAFDAC, IHVN, and KNCV Tuberculosis Foundation).

Activity	When	Who
Full baseline situational analysis report ready	End Oct	Full core team
Baseline situational analysis report approved by head of NMRA (DG NAFDAC)	End Nov	Head of NMRA
Full report disseminated as paper/pdf to all key stakeholders	Mid Dec	PV coordinator
Stakeholder meeting to start PV roadmap drafting process	Early Mar	All key stakeholders
Full PV roadmap developed based on input stakeholders	End Mar	In country PAVIA team
Presentation of draft PV roadmap to key stakeholders	Early April	In country PAVIA team
PV roadmap finalized	End April	In country PAVIA team
Final PV roadmap endorsed by Minister of Health	April/May	

To keep track of the PAVIA activities in Nigeria, a monthly call on the first Wednesday of every month at 10 AM local time is proposed, including all project partners and NTBLCP in the country, as well as the executive board of PAVIA.

Annex 1. NMRA assessment tool

Indi-cator #	Indicator	Assessment Questions	Answer	Notes & additional comments	Information source
Component 1. Policy, Law, and Regulation					
1.1	Existence of a policy document that contains essential statements on pharmacovigilance or safety of medicines, health products and technologies (stand alone or as a part of some other policy document)	Is there a national policy on pharmacovigilance or medicine safety, or a more general medicines policy that contains essential statements?	Yes	There exists a standalone Pharmacovigilance policy document	National Pharmacovigilance Policy and Implementation Framework (2012)
		When was the policy last reviewed? *Date* (DD/MM/YYYY)	___ /___ /_____	Not done. The policy document was launched in 2012 and is yet to be revised	
1.2	Existence of specific legal provisions for pharmacovigilance in the national medicines legislation or similar legislation	Are there legal provisions for pharmacovigilance or medicine safety in the medicines act or law?	Yes	The National Health Policy, Drug Policy and Pharmacovigilance Policy all allude to PV. The NAFDAC ACT also has provisions for enforcement which may be applicable to PV. Also Counterfeit and Fake drugs and unwholesome processed foods (Miscellaneous Provision) ACT.	• Decree establishing NAFDAC • National Health Policy • National Drug Policy • National Pharmacovigilance Policy and Implementation Framework • Counterfeit and Fake drugs and unwholesome processed foods (Miscellaneous Provisions) Act
1.3	Legal provisions for Marketing Authorization Holders to monitor and report the safety and quality of their products	Is it mandatory by law or regulations for MAHs to			
		- conduct post marketing safety activities?	No		
		- report adverse drug reactions/medicine safety related issues?	Yes	Policy provision	Nigerian National Pharmacovigilance Policy and Implementation Framework
		- regularly submit periodic safety update reports (PSUR) or periodic benefit-risk evaluation reports (PBRER)? *If yes, specify the required time intervals*	Yes	Policy provision	Nigerian National Pharmacovigilance Policy and Implementation Framework
1.4	Existence of legal provisions empowering the national regulatory authority to require Marketing Authorization Holders to submit proof of their proactive pharmacovigilance	Does the national regulatory authority have the power to require MAH to submit any of the following documents prior to product licensing?			
		I. Pharmacovigilance plan	Yes		
		II. Risk management plan	Yes		

	planning as part of an application for product licensing	III. Risk minimization/mitigation plan	Yes		
		Are MAHs required to adapt the plans to the particular risk situation of the population in the country?	Yes / No	This may be dependent on the report of the review of submission made	
1.5	Existence of national pharmacovigilance guidelines developed or reviewed within the past 5 years	Does a national guideline for PV (or a related document) exist?	Yes		NAFDAC Good Pharmacovigilance Practice Guidelines 2016
		Has the national PV guideline been developed or reviewed within the past 5 years?	Yes / No	The national guideline was developed in 2016 (i.e., 2 years ago) and has not yet been reviewed.	
		When were the guidelines last reviewed? *Date*	___ /___ /_____	Not applicable	
1.6	Regulations and guidelines encourage distributors, importers exporters, health-care institutions, other stakeholders and consumers to report ADR and/or AE to the MAH and/or NRA	Do regulations and guidelines encourage distributors, importers exporters, health- care institutions, other stakeholders and consumers to report ADR and/or AE to the MAH and/or NRA	Yes		Nigerian National Pharmacovigilance Policy and Implementation Framework
1.7	The legal provisions and/or regulations allow NRA to require manufacturers and/or MAHs to conduct specific studies on safety and effectiveness under specific conditions	Does the national regulatory authority have the mandate to require manufacturers and/or marketing authorization holders to conduct and present results from specific studies addressing identified safety concerns?	Yes		Nigerian National Pharmacovigilance Policy and Implementation Framework
1.8	Legal provisions, regulations and/or guidelines require manufacturers and/or marketing authorization holders to designate a Qualified Person responsible for vigilance.	Do legal provisions, regulations and/or guidelines require manufacturers and/or marketing authorization holders to designate a Qualified Person responsible for vigilance?	Yes		Nigerian National Pharmacovigilance Policy and Implementation Framework
1.9	Existence of updated National Essential Medicines List that was reviewed with consideration of medicine safety information	Is there an essential medicines list in use?	Yes		Essential Medicines List (6th edition, 2016)
		Does the essential medicines list selection committee consult medicine safety information?	Yes		
		When was the list last reviewed? *Date*	in 2016	Month and year unavailable.	
1.10	Existence of a medicines regulatory authority or agency	Is there a drug regulatory authority or agency?	Yes	Established 1 October 1992	

1.11	Existence of official records of licensed medicinal products	Is there an official source of information on medicinal products that are licensed for use in the country?	Yes	but not publicly available	
1.12	Accreditation of private health facilities includes requirements for the existence of a pharmacovigilance system	Does the public authority responsible for accreditation of private health facilities require that a pharmacovigilance system is in place?	No		
Component 2. Systems, Structures, and Stakeholder Coordination					
2.1	Existence of a national pharmacovigilance centre with a clear mandate and structure	Is there a National PV centre or any other body assigned the responsibility of monitoring safety of medicines?	Yes		
		Is there a clear mandate and organizational structure for the pharmacovigilance centre?	Yes	In the organogram the structure of NAFDAC is presented with the place of the Directorate of Pharmacovigilance and Post Marketing Surveillance. In the annual report 2017 the tasks and responsibilities of the directorate are described	Organogram via https://www.nafdac.gov.ng/wp-content/uploads/Publications/Others/NAFDAC-UPDATED-ORGANOGRAM_2018.pdf, Tasks and responsibilities https://www.nafdac.gov.ng/wp-content/uploads/Publications/Others/NAFDAC-UPDATED-ORGANOGRAM_2018.pdf
2.2	The pharmacovigilance centre has designated, qualified human resources to carry-out its functions	How many staff members (full-time equivalent) does the PV centre or system have who are specifically responsible for carrying out its functions (technical and administrative)?		The whole directorate has 35 staff members (28 Abuja and 7 in Lagos). The staff dedicated to PV is 5, all based in Abuja	Although there seems to be a division in staff between PV and PMS, PMS staff also help with certain PV tasks
2.3	Existence of a dedicated financial provision or statutory budget for the pharmacovigilance centre	Is there an annual budgetary allocation for PV activities or for the PV Centre?	Yes	There is no direct funding for PV, but NAFDAC as a whole receive funding from the government. NAFDAC then divides the budget between the different directorates. At the moment there are problems with the budget release from the government. Receiving funding for PV capacity building is difficult.	
		In the last fiscal year, how many funds were allocated by the government and donors for pharmacovigilance activities? *Please specify the amount & currency*		In the last year the Government assigned 75 million Naira (USD 180,000) to NAFDAC, of which only 30 million was released last year. To increase funding for PV, the directorate also search for donor funding, an example of this is the collaboration with malaria program. They are also investigating in raising more registration service fees, but it is unclear if these would be	

				paid directly to NAFDAC and also be retained within NAFDAC. So in principle there are three forms of funding government/donors/registration, service fees	
2.4	Existence of a functional national medicine safety advisory committee	Does a national medicine safety advisory committee exist with the responsibility to provide technical advice on the safety of medicines to the regulatory authority?	Yes	National Drug Safety Committee, The committee consists of 12 members, of which 8 are external (with different competences such as clinical pharmacology, epidemiology, pharmacology etc.) and 4 internal NAFDAC staff (4 directors) with the Director PV/PMS acting as secretary.	see list of the members of the committee
		Has the national medicine safety advisory committee met at least twice in the previous calendar year?	No	No, only one meeting in the last year as there is no adequate funding for the committee. In case of emergency issues, remote review of cases can be done by the committee members.	
2.5	Existence of standard operating procedures (SOPs) for conducting pharmacovigilance activities	Does the NMRA / PV centre have SOPs for pharmacovigilance activities?	Yes	17 SOP, with the last time it was reviewed 30/6/2018. The review frequency is once every two years or more frequent if needed. Staff are trained in the content of the SOPs and the effect of the training is assessed.	See list for the 17 SOPs present
		When were the SOPs last reviewed? *Date.*	30/06/ 2018		
2.6	Existence of a source of data on consumption and prescription of medicines	Are there any sources of information on sales or consumption of medicines on a national, regional or local level?	No	No	
		Are they publicly available?	n/a	n/a	
2.7	Existence of a library or other reference source for drug safety information	Does the PV centre has access to a library or electronic sources providing up-to-date information on medicine safety and the progress of scientific knowledge in the domain?	No	In the past they has accessed to Ebscohost but this has been cut off because of funding. At the moment internet and information from other regulatory authorities are used as the main sources of PV information. There is a wish to get access to Ebscohost again.	
2.8	Existence of a mechanism to disseminate pharmacovigilance information (including one or more of the following: newsletters, information bulletin, website or phone line for dissemination of pharmacovigilance information)	Is there a communication plan in place to disseminate PV information?	Yes	The Deputy Director Food and Drug Information is responsible for this. DHPCs, issues with safety and quality of medicines, newsletters, consumer safety publications and alarm notices. The DG NAFDAC is responsible for the content of the communications	
		Is there a newsletter or information bulletin for dissemination of PV information?	Yes		

		How many issues of the medicine safety bulletin are supposed to be published per year		4 per year	
		How many issues of the medicine safety bulletin were published in the previous calendar year?		1	
		Is there a website for dissemination of PV information?	Yes	NAFDAC website, every directorate have their own section on the website	
		Is there a publicly advertised phone line to receive and provide medicine safety and PV information?	Yes	PRASCOR is used for contacts with the general public. Members of the general public sends an SMS with the name of the drug and the kind of reaction experienced to NAFDAC and this is followed up by NAFDAC staff.	SOP for PRASCOR
		Are findings published in national/international journals?	Yes	New methodologies such as PRASCOR have been published internationally	
		Is there another mechanism for dissemination of PV information? *Please describe the mechanism in Notes*	Yes	Focus group discussions, community group discussions and advocacy to health facilities, clinical meetings in hospitals, professional associations	
2.10	Existence of harmonized pharmacovigilance curricula for key healthcare workers - **In-Service**	Is there a pharmacovigilance training module, manual, or curriculum for **in-service** training of health care workers?	Yes	There is a training module for in service training	Training module available on memory stick Linda
2.11	Number of healthcare workers trained in pharmacovigilance in the previous calendar year through in-service training program	How many healthcare workers has the centre/program trained on PV in the previous calendar year (through **in-service** training)?			
		a. Health professionals			
		b. Community health workers			
		How many training events/sessions were conducted in the previous calendar year?			
		a. For health professionals			
		b. For community health workers			
2.12	Adoption and use of harmonized web-based pharmacovigilance training tools	Are web-based PV training tools available?			
		a. For health professionals	No		
		b. For the general public	No		

2.13	Existence of a functioning platform, mechanism or strategy for the coordination of pharmacovigilance activities - **National Level**	Does a platform, mechanism or strategy for the coordination of pharmacovigilance activities (such as PV technical working group, forum or regularly scheduled meetings) exist among **national stakeholders**?	Yes	In theory yes, in practice no because of limited funds. One of one interactions are possible as are interactions with MAHs	
		Have the key **national stakeholders** convened at least once in the previous calendar year?	No		
2.16	Submission of AE reports by health-care facilities in the previous year	From how many health facilities were AE reports received in the previous calendar year?	Data not available		
		How many health facilities are there in the country?	Approx. 815 government Facilities	PV awareness and reporting rates are low	
		How many health facilities submitted >10 reports to the PV centre in the previous calendar year?	Data not available		
2.17	Evidence of consideration of safety data when developing and updating standard treatment guidelines	When developing standard treatment guidelines is evidence on safety data being described and taken into consideration?	Yes		
2.18	National PV centre is a full or associate member of the WHO Program for International Drug Monitoring	Is the national pharmacovigilance centre a full or associate member of the WHO Program for International Drug Monitoring?	Full member	09/09/2004	
Component 3. Signal Generation and Data Management					
3.1	Existence of a national database for pharmacovigilance information	Does a central database exist for managing PV data?	Yes	Local database, not E2B compatible and VigiFlow (E2B compatible). Local database houses all ADR reports, it is an Excel sheet. Incomplete reports and complete reports are stored in the local database. Complete reports are entered into Vigiflow. As a large part of the reports are considered to be incomplete, there is a need to store these as well. They experience problems with entering incomplete reports (who do still fulfil the minimum reporting requirements according to EU/CIOMS) in VigiFlow as these do not pass the validation rules, especially the start date of the reaction seem to be a mandatory	

				field. A problem with using VigiFlow is that internet access is very patchy, PV buys additional bundles to ensure good internet access.	
		Does the central database contain data from various PV sources and methods (including PHPs?)	Yes	Central database only contains spontaneous reports from different sources, including PHPs such as TB. In the past CEM studies have been conducted in Nigeria but for these studies CEM flow was used which was then developed and maintained by the UMC.	
		Is there a dedicated computer for pharmacovigilance activities?	Yes	2 computer. Staff also use their personal laptops for work purposes. The local database is available on one computer.	
		Does the computer have internet access?	Yes	2 computers have internet access	
		Is data stored on a cloud/server? *Please specify*	No	The local database is saved on a dedicated computer only. VigiFlow is a on a server in Uppsala.	
		Is there a back-up system? *Please specify*	Yes	Back up is made once a year of the dedicated computer with the local database.	
3.2	Evidence of a process or mechanism for sharing information with other regulatory functions, other regulatory agencies and global databases	Has information in the database been shared (either electronically or via report) with other regulatory functions, other regulatory agencies and/or global databases?	Yes	Through VigiFlow with the members of the Program for International Drug Monitoring. Information is also shared with other directorates within NAFDAC and upon request also with other countries such as Ghana.	
3.3	Existence of a standard adverse event (AE) reporting form and subset indicators	Is there a standard AE reporting form?	Yes		
		How is the reporting form offered? (e.*g.* paper form, web, app)		Paper, is also available for download at the NAFDAC website.	
		Are there relevant fields in the standard AE form (or a separate form) to report:			
		- adverse drug reactions?	Yes	Standard AE reporting form	
		- Suspected medication errors?	No	Standard AE reporting form	
		- therapeutic ineffectiveness?	No	Standard AE reporting form	
		- misuse, abuse and/or dependence on medicines?	No	Standard AE reporting form	
		- suspected/ observed poor quality issues?	No	Standard AE reporting form, if received through the yellow form the reports are forwarded to	

				PMS and stored in a separate database, they are not stored as ICSR in the ICSR database	
		- adverse events following immunization?	Yes	separate form, AEFI reports are sent by the health care professionals to the immunization program and the immunization program sends them in batches to the PV centre	
		- medical devices and diagnostics?	No	Standard AE reporting form	
3.4	Existence of a form or mechanism for the public to report AEs (Patient reporting system)	Is there a standard reporting form for the general public to report AEs?	Yes	it is the same form as the standard reporting form. The general public can also send a text message to the PRASCOR service and if follow up shows that this could be reported as an ADR, the normal ADR form will be filled in.	
3.5	Existence of electronic AE reporting system that complies with international reporting format standards	Is there an electronic AE reporting system?	No	There is a need for an electronic reporting form, both from reporters and NAFDAC. It will decrease the workload for both partners and increase the timeliness for receiving reports. Many Nigerians have internet service through their smart phone, so an app would be a good choice, HCPs are willing to use their own data bundle to submit reports.	
		If yes, please provide technical details.	n/a		
		Is the system compliant with the international reporting standards (E2B)?	n/a		
3.6	A process is in place for collection, recording and analysis of ADR reports	Is there a process in place for collection, recording and analysis of ADR reports?	Yes	are described in the SOPs	
Component 4. Risk Assessment and Evaluation					
4.1	Number of registered products with a PV plan and/or a risk management strategy	How many registered products with a pharmacovigilance plan and/or a risk management strategy from market authorization holders exist in the country?	58		GVP Module: Guideline on Good Pharmacovigilance Practice (GVP) module V11-Periodic Safety Update Report.
4.2	Total number of AE reports received in the previous calendar year (also expressed as number of AEs per 100 000 persons in the population). And number of reports of sub-indicators	What is the total number of AE reports received in the previous calendar year? Of the total, what is the number of reports of:	2173 (1.1682 IN 100 000)		NPC Database (Local Database)
		- ADR?		NOT CATEGORIZED.	

		- suspected medication errors?		NOT CATEGORIZED.	
		- therapeutic ineffectiveness?		NOT CATEGORIZED.	
		- suspected misuse, abuse, dependence?		NOT CATEGORIZED.	
		- AEFI?		From this year reports are forwarded from the immunization program to NAFDAC, causality assessment of vaccine reports is done by the immunization program.	
		- medical devices and diagnostics?		NOT CATEGORIZED.	
		- suspected counterfeit / substandard drugs?		NOT CATEGORIZED.	
		What is the total population of the country?		186,000,000	
4.3	Number and percentage of total AE reports received by the national pharmacovigilance center in the previous calendar year from:	What is the number of AE reports received by the national pharmacovigilance centre in the previous calendar year from:	2,173		NPC Database (Local Database)
	- Marketing Authorization Holders	- Marketing Authorization Holders		NOT DIFFERENTIATED	
	- PHPs	- PHPs		NOT DIFFERENTIATED, NAFDAC has within their own organization a focal person for every program. Within the immunization program they have a technical team that look at the reports before they are submitted to NAFDAC, NAFDAC staff are part of the technical team. With the Malaria program there has been close collaboration in the field of PV.	
	- Health care providers	- Health care providers		NOT DIFFERENTIATED but pharmacists and medical doctors are the main reporters	
	- Patients	- Patients		NOT DIFFERENTIATED, through PRASCOE patients are also an important source of information	
	-Distributors	-Distributors		NOT DIFFERENTIATED	
	-Suppliers	-Suppliers		NOT DIFFERENTIATED	
4.4	Number and percentage of total AE reports received that are entered in the national database in the previous calendar year	What is the total number of AE reports received that have been entered in the national database in the previous calendar year?	2173	Total AE reports of 2173 were received and entered into the NPC database. That represents 10.03% of the cumulative AE reports on the NPC database (21,656)	NPC Database (Local Database)

4.6	Number and percentage of total AE reports acknowledged and/or issued feedback in the previous calendar year	What is the total number of AE reports acknowledged/issued feedback in the previous calendar year?		Total AE reports of 2173 were received and acknowledged but no feedback were issued. That represents 10.03% of the cumulative AE reports received and acknowledged (21,656). If you report more than 5 reports you get a special acknowledgement. The results of the causality assessment is not communicated with the reporters.	NPC Database (Local Database)
4.7	Number and percentage of AE reports subjected to causality assessment in the previous calendar year	What is the total number of AE reports subjected to causality assessment in the previous calendar year?	790	Total AE reports subjected to causality assessment last year is 790. If a case is complete, i.e. contains enough information to allow causality assessment, causality assessment is performed. The causality assessment is done by the PV staff. For causality there are 4 multidisciplinary teams consisting of doctors, pharmacists and someone with experience of causality assessment. Causality assessment is performed twice a week, Tuesdays and Thursdays. For more complex cases, external expertise is available.	Internal Records
4.8	Number and percentage of AE reports submitted to VigiBase in the previous calendar year	How many of the AE reports received at the national PV centre were submitted to Vigibase in the previous calendar year?	570	570 (5.5%) according to the VigiBase	VigiBase
4.9	Average completeness score of quarterly reports submitted to VigiBase in the previous four quarters (= one year)	What was the average completeness score of quarterly reports submitted to Vigibase in the previous calendar year? *Consult quarterly reports from VigiGrade for completeness scores of submitted reports*	First quarter 0.87 and Second quarter 0.91	According to VigiBase Completeness score for 2017, First quarter 0.87 and Second quarter 0.91	VigiBase
4.10	Number of active surveillance activities initiated, ongoing or completed during the previous three years	How many active surveillance studies have been conducted in the last three years (36 months)?	None		
		Indicate what type (e.g. cohort event monitoring, targeted spontaneous reporting, etc.) and stage of completion (e.g. initiated, on-going or completed) for each study. *Request research protocol*	None		

4.11	Number and percentage of total AE reports received at the national pharmacovigilance center in the previous calendar year from healthcare providers by type of provider	What is the number of AE reports received in the previous calendar year submitted by:			
		- doctors?	90		
		- nurses or midwifes?	96		
		- pharmacists?	1769		
		- manufacturers and pharmaceutical companies?	not available	most AE reports lack adequate information.	
		- dentists?	nil		
		- the general public?	94		
		What is the total number of AE reports received in the previous calendar year?	2173		
4.12	Evidence of supervision visits to marketing authorization holders by NMRA that address PV	Does the NMRA conduct supervision visits of MAHs that address PV?	No		
		How many supervision visits have been conducted in the previous calendar year?	None		
Component 5. Risk Management and Communication					
5.1	Number of regulatory actions taken in the previous calendar year as a consequence of national pharmacovigilance activities. *Request documentation to verify*	How many regulatory actions were taken in the previous calendar year as a consequence of pharmacovigilance activities that resulted in:			
		- product label changes (variation)?	None		
		- safety warnings on medicines to health professionals?	28	28 DHCPLs were issued	Annual report 2017
		- safety warnings on medicines to the general public?	21	Posted on the NAFDAC website	Annual report 2017
		- withdrawals of medicines?	None		
		- treatment guideline/policy changes?	None		
		- other restrictions on use of medicines?	None	a number of the safety warnings concerns recalls	
5.2	Number of signals detected in the past 5 years by the pharmacovigilance centre	How many signals were detected in the past 5 years by the pharmacovigilance centre?	None		
		If any signals were detected, which ones and how were they identified?	n/a		

5.3	Average time lag between identification of safety signal of a serious ADR or significant medicine safety issue generated nationally and communication to health care workers and the public	How long does it take from when a safety signal or significant safety issue is identified to when it is communicated to health workers and the public? *Please answer in days for each signal identified in the previous calendar year.*		NOT DONE	
5.4	Number of suspected product quality issues detected through the pharmacovigilance system	What is the number of suspected product quality issues detected through the pharmacovigilance system in the previous calendar year?	1	oxytocin due to break in cold-chain, (poor storage)	
5.5	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 previous calendar year	How many issues of the medicine safety bulletin are supposed to be published per year?	four(4)		
		How many issues of the medicine safety bulletin were published in the previous calendar year?	1		
5.6	Number of products voluntarily withdrawn by marketing authorization holders because of safety concerns in the previous calendar year	How many products were voluntarily withdrawn by marketing authorization holders because of safety concerns in the previous calendar year?	None		
5.7	Number and percentage of medicine safety information requests addressed in the previous calendar year	How many requests for information about medicine safety were received in the previous calendar year?	None	The state and zonal office will be the primary point of information. This question is answered with none, since there is no system to document the queries.	
		Of the total received, how many requests for medicine safety information were addressed in the previous calendar year?			
5.8	Number of summaries of product characteristics updated by MAH because of safety concerns in the previous year		5		From PMS data
5.9	Number of medicine safety issues of local relevance identified from outside sources (e.g., from another country, from region or international	How many medicine safety issues identified from outside sources were acted on locally in the previous calendar year?	31	31	Internal records

	sources) and acted on locally in the previous calendar year				
5.10	Number of public or community education activities relating to medicine safety carried out in the previous calendar year	How many public or community education activities relating to medicine safety were carried out in the previous calendar year?	Number is not certain, but activities were conducted	Examples of activities are: media chat about malaria, Radio spots on national network promote the use of PRASCOE, NAFDAC safety consumer club, NUS collaboration graduates from the university, coming to the camp, forming a club to use as a network	

Annex 2. PHP assessment tool

Indicator #	Indicator	Assessment Questions	Answer	Notes & additional comments	Information source
Component 2. Systems, Structures, and Stakeholder Coordination					
P2.1	PV activities included within the strategic and/or annual operational plans of PHPs	Are PV activities included within the strategic and/or annual operational plans of public health programs?	Yes	Very briefly described	Strategic page 153, objective 9.5.12, Strategic plan 2015-2020
P2.2	Existence of a dedicated financial provision or statutory budget for the PHPs	Is there an annual budgetary allocation for PV activities for the PHP?	No	No budget line for pharmacovigilance, GF has given some support for the implementation of aDSM, training, USAID through MSH has sponsored the development of TB manager	
		In the last fiscal year, how many funds were allocated by the MOH and donors for PV activities? *Please enter the amount and specify the currency*		It is unclear how much has been spent on the implementation of aDSM	
P2.3	Existence of a mechanism to disseminate PV information (including one or more of the following: newsletters, information bulletin, website or phone line for dissemination of pharmacovigilance information)	Is there a mechanism in place to disseminate PV information?	No	Structure is present to reach the health facilities so it could be used for PV purposes. The structures in place are quarterly zonal review meetings, state programme managers, focal persons in the facilities can be mailed, what's app groups	
		Is there a newsletter or information bulletin for dissemination of PV information?	No		
		Is there a website for dissemination of PV information?	No		
		Is there a publicly advertised phone line to receive and provide medicine safety and PV information?	No	Only a toll free number for case finding	
		Is there another mechanism for dissemination of PV information? *Please describe the mechanism*	No		
P2.4	Number of healthcare workers trained in pharmacovigilance in the previous calendar year through in-service training	How many healthcare workers has the centre/program trained on PV in the previous calendar year (through **in-service** training)?	Formal PV training: 0	Formal PV training has not been given to HCP, but 29 NAFDAC staff consisting of Pharmacists, Biochemist, Lab technicians, from 3 states (Gombe, Kwara and Kano) were trained on PV. aDSM training on Anti-TB Medication has been given	
		- Clinicians / nurses	150	150 participants have participated in aDSM training from all over the country. Not all 150 General Patient Sites where patient come once a month have been	

				trained yet, even though they should be conducting aDSM	
		- Community health workers	0		
		How many training events/sessions were conducted in the previous calendar year?	Not available		
P2.5	National treatment guidelines or protocols in use within the public health programs that consider pharmacovigilance	Do the treatment guidelines or protocols in use in the PHP provide instruction for PV activities?	Yes		
P2.6	Evidence of consideration of safety data when developing and updating standard treatment guidelines or treatment policies	When developing standard treatment guidelines is evidence on safety data being described and taken into consideration?	Yes		
Component 3. Signal Generation and Data Management					
P3.1	PHPs use the national, standard ADR/AE reporting form	Does the PHP use the national, standard ADR/AE reporting form? *Request a copy of all existing reporting forms.*	Yes	a separate a DSM form has been developed. NO special GDF form, but will use the Nigerian a DSM form	
Component 4. Risk Assessment and Evaluation					
P4.1	Number and percentage of ADR/AE reports received by PHPs that were submitted to the national PV centre in the previous calendar year	What is the number of AE reports received by the PHP in the previous calendar year?	1,210	reports are printed in triplet copies	copies of the reports
		What is the number of AE reports submitted by the PHP to the national PV centre in the previous calendar year?	156	The pharmacovigilance forms are printed in 3 copies	Facilities copies of the report
P4.2	Total number of ADR reports per 1000 individuals exposed to medicines in the PHP in the previous calendar year.	How many individuals received medicines under the PHP in question during the previous year?	109,637	The TB case notification and treatment are reported on quarterly and annually basis to NTP	Annual and quarterly of NTP, please break down for TB (not including leprosy)
		How many ADR reports were received, referring to the exposed population?	1,210	The PV and aDSM forms are collated on quarterly basis	PV and aDSM forms
P4.3	Percentage of patients in public health programs for whom drug-related, serious unexpected/unknown adverse events were reported in the previous calendar year	What is the total number of patients receiving medicines under the PHP?	45,528	The TB case notification medicines management are quarterly reported NTP	The National quarterly report on TB
		What is the total number of patients receiving medicines in the PHP who experienced drug-related, serious, unexpected adverse events?	1,210	The PV and aDSM forms are transmitted PHP (NTP)	the PV and aDSM reports
		How many of those were reported to the national PV centre?	156	The data are reported directly from the facilities to PV centre.	Facilities copies of the report
P4.4	Number of suspected product quality issues detected through public health programs	What is the number of suspected product quality issues detected through the PHP in the previous calendar year?	nil		
P4.5	Number of reports on therapeutic ineffectiveness in the previous year	What is the number of reports on therapeutic ineffectiveness received by the PHP in the previous calendar year?	nil		

P4.6	Number of medicine-related hospital admissions per 1000 individuals exposed to medicines in the PHP in the previous year	What is the number of medicine-related hospital admissions of individuals exposed to medicines in the PHP in the previous year?	number unknown	they know of cases that have led to hospital admission and death	can be extracted through the e-TB Manager
P4.7	Number of active surveillance activities initiated, ongoing or completed during the past three years	How many active surveillance studies have been conducted in the last three years (36 months)?	Nil		
		Indicate what type (e.g. cohort event monitoring, targeted spontaneous reporting, etc.) and stage of completion (e.g. initiated, on-going or completed) for each study *Request research protocols*	n/a		
P4.8	Functional collaboration/involvement in risk management plans with the PV centre	Do the PHP and PV centre communicate on risk management plans?	No		
		How often have the PHP and PV centre met to discuss risk management in the previous calendar year?	None		
Component 5. Risk Management and Communication					
P5.1	Average time lag between identification of safety signal of a serious ADR or significant medicine safety issue generated nationally and communication to health care workers and the public	How long does it take from when a safety signal or significant safety issue is identified to when it is communicated to health workers and the public? *Please enter your answer in days for each signal.*	1 day	The use of electronic information system	Report from National Electronic TB information Management system (NETIMS)
P5.2	Existence of a program-related newsletter that routinely features ADR or medicine safety information	Is there a program-related newsletter, bulletin or other publication that routinely features ADR or medicine safety information?	No		
P5.3	Number and percentage of medicine safety information requests addressed in the previous calendar year	How many requests for information about medicine safety were received in the previous calendar year?	0		
		How many requests for medicine safety information were addressed in the previous calendar year?	None	Prevalence of hearing loss with kanamycin, switch to other injectables, subcommittee was set up to look at the effects of kanamycin and capreomycin. Committee did not have access to the right data.	National Drug Resistance TB committee
P5.4	Number of medicine safety issues of local relevance identified from outside sources (e.g., from another country or international sources) and acted on locally in the previous calendar year	How many medicine safety issues identified from outside sources were acted on locally in the previous calendar year?	1		
P5.5	Number of public or community education activities relating to	How many public or community education activities relating to medicine safety were carried out by the PHP in the previous calendar year?	0		

	medicine safety carried out in the previous calendar year				

Annex 3. PMDT sites assessment tool

TB treatment facility name, person interviewed, and date of interview		**Facility name: Zaria; Dr. Abdullahi (clinician)** Date: 25/09/2018	**Facility name: Ibadan; Mr. Ganiyu (Pharmacist)** Date: 25/09/2018
Nr	**Question**	**Answer**	**Answer**
1	Has staff been trained on PV / aDSM?	Yes, 1 of 2/3 pharmacists + nurses (but part of them have been transferred) + 1 clinician (but clinician left)	yes, pharmacist did conduct step-down training for nurses; reporting frequency has increased indeed
	- By whom?	NTBLP, with facilitators from Zaria (but staff transferred to other PHPs)	NAFDAC/IHVN SPARTY project
2	Is equipment (e.g. audiometry, ECG machine) in place to monitor for possible AE?	yes	
	If yes, is the equipment functioning?	yes	
	Have any problems with the equipment occurred?	No, but not all lab tests available in-house - e.g. liver function tests, hypokalemia; tests are done elsewhere but this results sometimes in delays	
	If yes, how did you solve these?	portable ECG machine - QTc not readily available (Bazet instead of Fridericia) use computer software to calculate intervals	
3	Is treatment monitoring (lab tests, audiometry etc.) provided free of charge to patients?	yes	
4	Are ancillary drugs available free of charge to patients who need it?	in principle yes, but budget cut-down forces hospital to prioritize	yes
5	Are AE/ADR reporting forms easily accessible for staff?	since last week: aDSM forms to be used for SAE and AE of special interest; and yellow form	Both forms are used; Yellow forms used for all AE (incl. SAE), and aDSM form only for SAE; as till recently only yellow forms were forwarded to NAFDAC. In future, for reporting of SAE and AE of special interest, aDSM form will be used for patients on new drugs and regimens
6	Are AE/ADR reporting forms electronically or paper-based?	paper-based	
7	Do you receive feedback on AE reports?	yes	
	If yes: what type of feedback? (*If available: ask for the documentation.)*	Acknowledgement of receipt only	
8	Are AEs that require treatment change being discussed amongst MDR-TB experts/consilium before treatment change is made?	Discussed in facility consilium (meets 1x/months, so sometimes informal mtgs); can consult specialists if needed (optomologist, psychiatrist)	Clinicians and nurses sometimes take the decision on their own; can consult specialists if needed (optomologist, psychiatrist)
9	How many patients were started on TB treatment in the previous calendar year?	approx. 35 (needed admission)	last calendar year: n=31 in total, but admission was stopped to prepare for new drugs and regimens; this year: 14 ITR, 12 on STR
10	a. Who supervises patient treatment at home? b. Are they trained on pharmacovigilance?	a. DOT providers (HCW); also provide hearing aids; b. some are trained, but even low-cadre trainings are in English monitoring becomes less after intensive phase not all patients report their AE to the DOT provider	a. DOT providers (HCW); also provide hearing aids; b. some are trained
11	How often did you think of AE in the past week?	nurses often report AE to clinicians	nurses are reporting Aes using pictures and send in follow-up pictures
12	How often did you report an AE in the past week?	nurses report themselves	Nurses expect pharmacist to report

13	If you did not report all suspected AE, what were the reasons?	AE not reported if not considered serious enough - only SAE are to be reported	AE extracted from patient files by the pharmacist; pharmacist also picks up oral signals from nurses, not written in patient file. Workload is considered high; personal resources are needed to scan the report and send it by email.
14	Do you report all AEs requiring medical intervention that are recorded in the patient file? If not: why not?	Yes	Not always; only 1 doctor instead of 4 in clinic; and clinician is not always on duty.
15	When would you report an AE? (e.g. all AE or only specific ones? Only when sure it is caused by a certain drug?)	Non-serious, non-severe AEs are not reported	any suspected ADRs are reported (as per national requirement)
16	How do you experience aDSM? (What are advantages and disadvantages to your opinion?)	More emphasis on active monitoring needed; aDSM form fits needs of the DR-TB patients better	in the yellow form there is no specific field for laboratory test results; the aDSM form is more guiding but does not capture all AEs that is why yellow forms are still needed
	Does it help to improve patient care?	Yes	
	Is it feasible regarding workload?	Yes; there is enough manpower in the facility	Yes
17	What are barriers for reporting AE?		electronic reporting is preferred (adding aDSM form to eTB manager); low staffing (only 1 medical officer, only 1 pharmacist)
18	What would facilitate reporting of AE?	Receive feedback on the reports; continuous training on PV, supportive supervision, M&E. Sustainability (no transfers of trained and motivated staff; or has trained other staff in the facility before leaving); government should be supportive; buy-in from management boards of all health facilities; budgeting and funding provisions need to be made in PV policy.	