NATIONAL AGENCY FOR FOOD AND DRUG ADMINISTRATION AND CONTROL (NAFDAC)

REPORT OF RISK-BASED POST-MARKET SURVEILLANCE OF SELECTED MEDICAL PRODUCTS IN NIGERIA CARRIED OUT IN 2021, 2022 & 2023.

POST MARKETING SURVEILLANCE DIRECTORATE, NAFDAC

EXECUTIVE SUMMARY

The National Agency for Food and Drug Administration and Control (NAFDAC), established by Decree No. 15 of 1993 as amended by Decree No. 19 of 1999 and now cited as NAFDAC Act Cap N1 Laws of the Federation of Nigeria (LFN) 2004, NAFDAC is a parastatal of the Federal Ministry of Health, with the mandate to regulate and control the manufacture, importation, exportation, distribution, advertisement, sale and use of Food, Drugs, Cosmetics, Medical devices, Packaged Water, Chemicals and Detergents (collectively known as regulated products). In line with the mandate, NAFDAC seeks to reduce significantly poor quality (substandard or falsified) medicines from the Nigerian market by conducting post-market surveillance activities and taking appropriate regulatory actions when poor quality medicines/drugs are found.

2021 Surveillance

Post-Marketing Surveillance (PMS) Directorate formerly Pharmacovigilance and Post Marketing Surveillance Directorate of NAFDAC in collaboration with other relevant Directorates such as Drug Registration and Regulation (DR& R), Laboratory Services (LS), Drug Evaluation and Research (DER), Ports Inspection Directorate (PID), Investigation and Enforcement (E& I), that formed the NAFDAC PMS Technical Working Group (TWG) in the year 2021, took necessary steps to identify and categorize the drugs available in Nigeria based on intrinsic and extrinsic risks, with eleven (11) high-risk medical products incorporated into the work plan for the year 2021 post-market quality monitoring.

The TWG developed a risk-based post-market surveillance protocol for 2021 priority medical products. These medical products were Misoprostol 200mcg, Oxytocin 10iu, Normal Saline, Dextrose Saline, Artemether/ Lumefantrine (AL), Artesunate/ Amodiaquine (AA), Sulphadoxine/ Pyrimethamine (SP), Dihydroartemisin/ Piperaquine Phosphate (DP), Quinine Sulphate tablet (QS), Artemether injection (ART) & Artesunate Injection (AST) circulating in Nigeria.

The survey was conducted between July to December 2021. In line with the approved survey protocol, the medical products were sampled in 21 States in the six geopolitical zones of the country and from different levels in both the public and private sectors of the medicine distribution chain. The samples were tested for quality against established standards. NAFDAC inspectors were trained and collected a total of **1,097 samples** for quality monitoring and conducted initial visual inspections and screenings. After an initial triage, 31 samples were excluded from laboratory testing for not meeting approved sample collection criteria hence 1,061 samples were sent to NAFDAC laboratories for testing.

On aggregate, out of the 1,061 medicine samples tested, 96.3% (1,022) passed while 3.7% (39) failed. The infusion products (normal saline - 146) and dextrose saline - 135) recorded no failure (100% pass). Similarly, no laboratory-tested samples of ART (28), AST (34), DP (31), and QS (70) failed. Meanwhile, SP has the highest failure rate of 10.1% (7 out of 69) laboratory-tested samples and 89.9% pass (62). AL followed this with 9.2% (10 out of 109) samples and 90.8% pass (99 of 109). AA results showed 8.4% (9 out of 107) failure and 91.6% (98) pass. For MNCH

samples tested, 10 (7.3 %) of 137 Oxytocin tested samples failed while 127 samples (92.7%) passed. Misoprostol recorded a lower rate of 1.5% failed (3 out of 195) with 192 (98.5%) passes.

2022 Surveillance

NAFDAC in collaboration with PQM+ also conducted Risk-Based Post Market Surveillance (RB-PMS) of seven selected high-risk medical products that were identified using the Medicine Risk Assessment (MedRS) tool and incorporated into the work plan for the year 2022 for quality monitoring and safety. These medical products include Amoxicillin Capsules, Amoxicillin dispersible tablets, Artesunate injections, Artemether injections, Ciprofloxacin tablets, Amoxicillin/Clavulanic acid Capsule, Artemether/Lumefantrine tablets circulating in seven states of Nigeria.

These medical products were sampled in 7 States (Abia, Akwa Ibom, Anambra, Borno, Imo, Kano, and Niger) and tested for quality against established standards outlined in reference/official books between July to December 2022. The samples were subjected to virtual screening to verify the label claims (level 1), simple disintegration testing (level 2), and high-performance chromatography (level 3) were deployed for identification and quantification of drug content.

Sample collectors were trained and collected 387 samples during the exercise. 14 samples (3.62%) deviated from the protocol requirements and were not included in the assessment. Such deviations are products less than 6 months to the expiry date and products with strengths not stated in the sampling protocol. 8 samples were also not assessed due to the insufficient quantity of the molecule (Amoxicillin Dispersible Tablet) found in the market, thereby making 22 (5.68%) samples not considered for assessment. Out of 365 samples assessed, 6 (1.64%) failed level 1 screening, and 359 (98.36%) samples were sent to the laboratories for compendial analyses. The tested samples in the laboratories showed that 321 (89.42 %) were satisfactory and 38 (10.58%) were unsatisfactory. See Table 3 for a summary of medical products and the results.

2023 Surveillance

Following internal procedures, the molecules considered for the 2023 survey consisted of medical products pre-selected inputs/information from the following NAFDAC formations (Ports Inspectorate, Drug Research & Evaluation, Drug Laboratory Services, Pharmacovigilance, Post Marketing Surveillance, and Investigation & Enforcement) based on internal risk considerations. These selected medical products were subjected to MedRS tool for risk categorization. The following medical products were selected: Metformin 500mg, Glimepiride 4mg, Nifedipine 20mg, Amlodipine 10mg, Telmisartan 80mg, Oxytocin 10IU, Artemether/Lumefantrine Suspension 20/120mg & Tablet 80/480mg, Amoxicillin 250mg & 500mg, Cefuroxime 250mg and Rifampicin 200mg. However, due to time constraints, four of the products - Amoxicillin 250mg & 500mg, Cefuroxime 250mg, and Rifampicin 200mg could not be sampled. These products may be sampled

in the next phase of this survey. Sample collectors were trained for sample collection methods and handling before sampling commenced.

A total number of 825 samples were collected. 167 (20.2%) samples did not meet visual screening and were deemed to have failed at Level 1. Hence, only 658 (79.8%) were sent to the laboratory for analysis. A total of 553 (84%) samples were tested. The Nifedipine 20mg samples 105 (16%) were not tested due to unavailability of reference standards. The laboratory reports show that out of 553 samples tested, 94.2% passed, while 5.8% of samples failed quality testing.

The agency undertook different regulatory actions on the failed samples. Such actions included evaluation of the results/risk assessment, engagement with market authorization holders, directive for the recall of batches and products from circulation, directive to correct labeling lapses, mop of the batches from circulation, administration of regulatory charges, current good manufacturing practice (cGMP) reassessment for local manufacturers, and good distribution practice (GDP) inspection of storage facilities.

Also, efforts should be geared towards further strengthening the quality control capacity of the Agency, improving surveillance methods, and establishing a framework for compulsory and transparent reporting of poor-quality medicines.

ACKNOWLEDGMENT

We acknowledged the valuable support of Prof. Mojisola Christiana Adeyeye, Director General of NAFDAC, during the 2021, 2022 & 2023 PMS Risk-Based Post Market Surveillance of Selected Medicines in Nigeria.

NAFDAC wishes to acknowledge the technical and financial support of the Promoting the Quality of Medicines Plus (PQM+) program, funded by the United States Agency for International Development (USAID) and implemented by United States Pharmacopeia (USP), during the development and implementation of this risk-based post-market surveillance (RB-PMS). The Agency also appreciates and acknowledges the continuous technical and financial support of the BMGF for the development of the National Action Plan and Strategies to mitigate SFs in Nigeria

All Directors and staff in the Directorates of NAFDAC involved in this survey are appreciated.

ACRONYMS

AA	Artesunate/ Amodiaquine
AL	Artemether-Lumefantrine
ART	Artemether injection
AST	Artesunate
DP	Dihdroartemisin/ Piperaquine Phosphate
FCT	Federal Capital Territory
FMOH	Federal Ministry of Health
FY	Fiscal Year
HPLC	High Performance Liquid Chromatography
ISO	International Organization for Standardization
IEC	International Electrotechnical Commission
NCZ	North Central Zone
NEZ	North-East Zone
NGO	Nongovernmental Organization
NWZ	North-West Zone
PMI	President's Malaria Initiative
PMS	Post-marketing Surveillance
PQM	Promoting the Quality of Medicines
QA	Quality Assurance
QC	Quality Control
QS	Quinine Sulphate
SP	Sulfadoxine-Pyrimethamine
SEZ	South- East Zone
SSZ	South-South Zone
SWZ	South-West Zone
TWG	Technical Working Group
USP	U. S. Pharmacopeial Convention
WHO	World Health Organization
DER	Drug Evaluation and Research
DGO	Director General Office
DR&R	Drug Registration & Regulatory Affairs
I & E	Investigation and Enforcement
IMCI	Integrated Management of Childhood Illnesses
LMIC	Low and middle-income countries
LS	Laboratory Services
MedRS	Medicine Risk Surveillance

MNCH	Maternity, Neonatal and Child Health
MRA	Medicine Regulatory Authority
PID	Post Inspection Directorate
PQM+	Promoting the Quality of Medicines Plus
PRS	Planning, Research & Statistics
PY	Programme Year
SF	Substandard/Falsified
TWG	Technical Working Group
USAID	United States Agency for International Development
BMGF	Bill and Melinda Gates Foundation
LMIC	Low- and Middle- Income Countries
NMRA	National Medical Products Regulatory Authority
NQCL	National Quality Control Laboratory

INTRODUCTION

BACKGROUND

Post-market surveillance of pharmaceutical products is crucial for ensuring their safety, efficacy, and quality after they have been approved and made available to the public. In Nigeria, the quality, safety, and efficacy of medical products in circulation are the focus of NAFDAC and other regulatory agencies and healthcare providers. These surveys aim to assess the quality of selected medical products in Nigeria through a risk-based approach using the MedRS tool.

The incidence of Substandard and Falsified (SF) medical products has been recognized as a universal threat to humanity and such a burden cannot be over-emphasized in Nigeria. NAFDAC is tasked with the vital responsibility of monitoring the quality, effectiveness, and safety of medical products in the market. Product quality monitoring is achieved through different approaches such as random or scheduled sampling and testing, investigation of consumer complaints & incidences of suspected therapeutic failure and Post Market Surveillance (PMS) exercises to determine the regulatory status of products on the market.

The conduct of traditional PMS posed certain challenges such as:

- **Finance**: Limited financial resources allocated for marketing surveillance.
- **Human Resources**: Limited number of qualified personnel to manage post-marketing surveillance programs and limited NQCL capacity to properly test medical product samples.
- **Management and Planning**: Medical product safety activities are often limited to adverse drug reaction monitoring and reporting. Post-marketing surveillance of medical products is usually restricted to scattered medical product quality surveys funded mostly by donors, or a few medical product samples collected randomly as part of inspections by NRAs. Lack of international model guidelines to support the agency in building integrated, effective, and sustainable post-marketing programs.
- **Sampling and Testing Methodology**: Traditional surveillance is conducted without predefined objectives or unclear objectives, sampling methodology is not well defined, justified, or planned, sampling methodology does not properly account for biases, etc.
- **Coordination and Communication**: Inadequate coordination and information sharing among involved stakeholders, Data are not shared or disseminated appropriately and are not used to inform decision making.

Therefore, NAFDAC's risk-based approach is based on a quality management system and international best practices which is a move away from the sporadic/traditional medical product quality monitoring activities to a robust risk-based post-marketing surveillance program that NAFDAC began in 2021. This could have started earlier in 2020, but the COVID-19 pandemic caused a shift in the implementation timeline.

For the year 2021, NAFDAC following a risk-based approach, considered maternal healthcare products (oxytocin and misoprostol), infusion products (dextrose and normal saline), and seen antimalarial products (artemether/ lumefantrine (AL), artesunate/ amodiaquine (AA), sulphadoxine/ pyrimethamine (SP), dihydroartemisin/ piperaquine phosphate (DP), quinine sulphate tablet (QS), artemether injection (ART) & artesunate injection (AST) in her risk-based surveillance activities.

For the year 2022, the medical products surveyed and sampled are selected Antimalarial (Artemether/Lumefantrine tablet, Artesunate injection, Artemether injection), and antibiotic products (Amoxicillin Capsule, Amoxicillin dispersible tablet, Ciprofloxacin tablet, Amoxicillin/Clavulanic acid Caplet/Tablet).

For the year 2023, The selected medical products for this survey include Metformin 500mg, Glimepiride 4mg, Nifedipine 20mg, Amlodipine 10mg, Telmisartan 80mg, Oxytocin 10IU, Artemether/Lumefantrine Suspension 20/120mg & Tablet 80/480mg, Amoxicillin 250mg & 500mg, Cefuroxime 250mg, and Rifampicin 200mg. However, due to time constraints, four products - Amoxicillin 250mg & 500mg, Cefuroxime 250mg, and Rifampicin 200mg could not be sampled; these products will be sampled later.

Objectives of the Study:

Overall Objective:
To assess the quality of specific medical products available within the country's designated distribution and supply chain levels in 2021, 2022 & 2023 respectively.

Specific Objectives:

- To document the presence and the extent of the spread of substandard and falsified ***Antimalarial products, Maternal health, infusion products, Antibiotics, Anti-Infectives, Anti-diabetics, and Anti-hypertensives*** in the Nigerian market.
- To verify/confirm the registration status of the medical products sampled.
- To generate evidence-based data for regulatory actions in the country.
- To take informed regulatory actions based on validated data.
- To determine the trend in quality status of the selected medical products.
- To estimate the severity of deviation from pharmacopeia standards.
- To study the practices in the supply chain at the sampling site.

METHODOLOGY

Survey scope and period (2021-2023)

The surveys were nationwide, covering all selected sites identified by the MedRS Tool. The sampling plan covered the public, private, and informal sector in urban, semi-urban, and rural areas according to an algorithm using random stratified combined with convenience sampling methods. PMS officers who were trained on the MedRS Tool developed the study protocol for each year.

Selection of medical products for sampling and testing

The medicine selection for this quality survey was based on the survey objectives, and potential public health impact using a series of risk factors using the Medicine Risk Assessment Tool. The list was finalized by the Top Management of NAFDAC and validated based on final considerations related to budget and other technical matters related to quality control testing capacities in the NAFDAC Laboratories. Following these reviews, in the year 2021, eleven (11) medicines were selected for inclusion in this survey.

In the year 2022, The medicines surveyed and sampled are selected Antimalarial (Artemether/Lumefantrine tablet, Artesunate injection, Artemether injection), and antibiotic products (Amoxicillin Capsule, Amoxicillin dispersible tablet, Ciprofloxacin tablet, Amoxicillin/Clavulanic acid Caplet/Tablet). The specific class of medicines collected from each state was identified by the MedRS tool. Solid (tablets and capsules) formulations and injectables formulations were collected based on the agreed strength and the availability of products in the selected facilities at the time of sample collection.

For 2023, the medical products surveyed and sampled were MNCH, Anti-diabetics, and Anti-hypertensives. The specific class of drugs to be collected from each state was identified using the MedRS tool. Solid dosage forms (tablets, except for the maternal health product) were collected based on the agreed strength available in the selected facilities at the time of sample collection.

The following are some risk factors that were considered during the selection of the medical products:

- Stability of the medical products
- Therapeutic risks
- Extent of harm due to poor quality
- Availability of the medicine during the survey period
- Safety and quality history of the product (PV or medicine quality information from prior studies)
- Extent of distribution and use of the medicine in the country
- Widely prescribed and used products.
- Products with frequently reported cases of suspected therapeutic ineffectiveness
- Products used in critical public health interventions.
- GMP compliance.

Selection of areas, regions, or countries

The risk-based selection approach was used to identify the sampling outlets from the selected sampling cities under the geographical area/site. The total number of outlets was determined using the MedRS tool based on the input from the PMS state officers to determine a statistically significant number of outlets to target at each level. Using the Medical Products Risk Assessment tool (MedRS), risks were assigned to facilities at the sites based on the facility level. Risk numbers were assigned to the different levels with the highest risk at the levels where the medical products are dispensed to the patients with no regulatory oversight.

The facilities were then stratified and randomly selected to ensure representative outlets were for the survey. Looking at the pre-selected medical products, geographical area, cities, and the following levels of the actual facilities from which the sample collection was conducted were targeted for sampling.

Level II: Regulated outlets: Wholesaler and distributor pharmacies.

Level III: Regulated dispensaries: Retail pharmacies, hospitals, health centers, and patent and proprietary medicine vendors licenses.

Level IV: Illegal outlets selling medical products outside the approved distribution system otherwise called the informal sector. The informal sector includes Informal or unauthorized open markets, stalls, and mobile drug peddlers.

Level V: Virtual or online marketing.

Note: Using the Medicine Risk Assessment tool (MedRS), risk levels were attributed to each level with the highest risk at level V and lowest at level II. Level 1(The manufacturers' warehouse was not identified by the tool).

The following proportion was used as a baseline good practice to estimate the sample size for each medicine at different levels of the supply chain in these studies.

Table 1: Proportion of Samples at Various Screening Levels in the 2021 PMS

COLLECTION SITE	% TOTAL SAMPLES
LEVEL II	10%
LEVEL III	65%
LEVEL IV	20%
LEVEL V	5%

Table 2: Proportion of Samples at Various Screening Levels in the 2022 PMS

COLLECTION SITE	% TOTAL SAMPLES
LEVEL II	10%
LEVEL III	70%
LEVEL IV	20%

Table 3: Proportion of Samples at Various Levels in the 2023 PMS

COLLECTION SITE	% TOTAL SAMPLES
LEVEL II	10%
LEVEL III	65%
LEVEL IV	20%
LEVEL V	5%

Note: A higher percentage of products was sampled from level III since most patients rely on medical products from this level.

Sampling design and selection of sample collection sites

The Medical Products Risk-based Surveillance (MedRS) tool is designed to identify the most vulnerable medical products objectively, determine the necessary sample size for statistical significance, prioritize sampling at high-risk locations, and facilitate the consistent implementation of risk-based approaches while maximizing available resources.

MedRS integrates and automates the science and practice of risk-based post-marketing surveillance into a single platform. The tool is also designed to perform stratified randomized sampling of facilities based on their risk profile. The tool can also accommodate less rigorous sampling methods such as convenience sampling.

MedRS combines statistical methods and risk evaluation techniques to determine the number and location of outlets for sampling that will provide statistically representative coverage for outlets that pose the greatest risk to patients.

The risk factors used for evaluating the risks in the tool are derived in part from the WHO guideline on the conduct of surveys of the quality of medical products and the European Directorate for the Quality of Medical Products.

To document the presence and level of spread of substandard/falsified medical products in the country, some selected medical products based on the quality history of products, previous analysis of survey reports, and laboratory results have been included in this survey (Table 1).

These medical products were also chosen because of storage issues which impacted stability and therapeutic tendencies by using the MedRS tool.

The selected survey sites within the country were finalized by MedRS Tool based on other public health, supply chain systems, and availability in all sectors in each state before the final validation of the study protocol. The risk-based approach is applied to guide informed decisions by the Top management of NAFDAC. The following are some of the selection criteria that were considered:

- Degree of urbanization
- Income
- Population density
- Prevalence of disease
- Medicine quality
- Distribution complexity
- Illegal or unauthorized outlets
- Other risk (user defined)
- Epidemiological data
- High probability of the presence of SF medicine for selected medical products
- Ease of accessibility of the site of sampling
- Potential presence of unauthorized medicine outlets (could include smuggled/illegally imported products)
- Major transport corridor for goods and people/ Port of entry by land
- Selected priority cross-border (inter-country) site
- Health system: known to be weak/strong sites to be strengthened.

Sample collection and transportation

To ensure uniformity in the collection of medical products, it is essential to define the attributes of a sample. For this survey, a sample is a given medicinal product with a product name, active ingredient, manufacturer, dosage form, unit dose (strength), batch/lot number, collection outlet, and packaging material.

The sample size was determined based on the availability of resources, evaluation of the information obtained from the PMS state officers using the MedRS tool, and statistical evaluation of information. The MedRS tool was crucial in determining the appropriate sample size while balancing the study budget, associated risks, and selected medications. Based on the RBPMS tool (MedRS), the total number of each medicine's samples was calculated for each state, according to the budget. The main goal of this exercise was to collect data and use it to address public health challenges and inform decision-making by the Agency to address any medicine quality issue identified by this survey.

The study protocol guided sample collectors to substitute samples in one of the following scenarios:

a. If the medicine is not available or the dispenser/seller is not willing to offer
b. If the available medicine in the outlet has less than six months shelf life
c. When the stock available is limited and the medicine is essential for the life of the patient

d. When there is the possibility of not getting the minimum quantity of medical products in the collection outlet.

Number of units per sample:

This survey is for the public health interest and the principle of good practices for pharmaceutical quality control laboratory will be followed. The number of dosage units per sample collected using the Cochran tool should allow sufficient samples for:

- Conducting the planned tests.
- Investigation and confirmatory testing for out-of-specification samples.
- Retention samples to be used in the case of dispute.

Determination of sample size

Using the Cochran formula for calculating sample size, (Cochran, W.G. (1977) we have

$$n_0 = \frac{z^2 pq}{e^2}$$

where $z = 1.96$ (from normal distribution table)

p = Probability of success = 0.5

q = Probability of failure $= (1-q) = 0.5$

and e = margin of error or desired level of precision = 0.05 at 95% Confidence interval (CI).

$$n_0 = \frac{(1.96)^2 (0.5)(0.5)}{(0.05)^2} = 384$$

For 2021, this MedRS tool assisted in identifying the facilities in different states from which samples were collected. A breakdown of the samples by states revealed that FCT accounted for the majority (11.7%), followed by Oyo state (9.6%), while Bauchi, Benue, and Kaduna states accounted for 9.1%, 8.9%, and 6.7% respectively. Following the sample size determination from the MedRS tool, samples were further allocated to urban and rural & semi-urban sites at 30% and 70% respectively.

For 2022, the MedRS tool alongside the Cochran formula gave a sample size of 379 from the total of 46, 319 facilities hence the sample size was considered statistically significant and adequate.

For 2023, the MedRS tool assisted in adjusting the sample size for Oxytocin from ***143 to 104***, Metformin 500mg from ***462 to 210***, Glimepiride 4mg from ***118 to 90***, Nifedipine 20mg from ***208 to 135***, Amlodipine 10mg from ***340 to 180***, Telmisartan 80mg from ***175 to 120***, Artemether/Lumefantrine Suspension 20/120mg from ***230 to 144*** & Tablet 80/480mg from ***640 to 240***.

Where it is not possible to buy a large quantity in one attempt, the team was encouraged to make repeated purchases from the same site or outlet using different mystery shoppers, until they had bought the desired quantity with the same batch number.

Sample Collectors:

Regulatory officers from the NAFDAC state offices were responsible for sample collection. Samples were collected in each site by a team from the state office supervised by a representative from the PMS Directorate/Zonal office using a letter of introduction for overt sampling at level II outlets and posing as mystery shoppers (covert sampling) at level II-IV outlets where applicable. Training was provided before the commencement of sampling and all sampling activities were conducted strictly according to the written and validated protocol.

The sample collection team in each site had the following functions:

- Buy samples from selected private outlets.
- Buy samples from public health institutions using the letter of introduction.
- Replace, as needed, samples collected from public facilities to ensure there are no stockouts of selected products because of the sampling.
- Pack and label samples collected properly using appropriate containers.
- Properly complete the Sample Information Collection Form for each sample collected.
- Submit samples to the relevant collection site for shipment to the testing laboratory with the completed hard copy of the sample information collection sheet and the Excel data sheet.
- Submit a copy of the completed sample information collection sheet and the Excel data sheet to the PMS Directorate.

Sample Collection Method:

Two kinds of sampling techniques were used: **OVERT** and **COVERT**.

Overt sampling techniques were used in public/private level II health establishments while Covert sampling (mystery shoppers) was used in private/public level II-IV establishments as applicable.

Sample collection logistics:

Two staff from each NAFDAC state office collected samples from each site.

- The sample collectors used land transport or any other means depending on the transportation system and accessibility of the sites in the state.
- The number of days needed was determined by state situation since the distance from the state office to the sites may vary from state to state.
- Collected samples were shipped to the triaging center or directly to the Laboratory for testing and any relevant transportation system was used for shipping the samples to the Laboratory.

Sample Collection Instructions and Precautions:
Every effort was made to collect samples in their original packaging. The team filled and signed the sample information collection form immediately for each sample collected. This was done after leaving the sampling site, to avoid triggering unnecessary suspicion and questions.

To avoid confusion, each sample was identified by a unique code number (A/B/C/D as indicated below) consisting of the State code, sample code, sample serial number, and date of collection e.g. FCT/AHT/001/050423

A: Name of the state (The first three letters of the state e.g., KAD for Kaduna);
B: Sample code (OXY for Oxytocin, MET for Metformin, ALM Artemether/Lumefantrine, etc.)
C: The sample serial number.
D: Date sample was collected.

Testing laboratories
NAFDAC has Seven (7) laboratories; however, for this survey samples were sent to three of the ISO/IEC 17025 certified laboratories – Central Drug Control Laboratory (CDCL) Yaba, Kaduna Area Laboratory, and Agulu Laboratory Services. The CDCL is also a WHO-prequalified laboratory. These three laboratories have an accreditation scope that covers basic quality control test methods for medical products.

Quality tests performed, and test methods and specifications used

- Laboratory analysis of all samples collected was conducted at NAFDAC's ISO-17025 accredited laboratories.
- The sample testing was performed using a risk-based testing approach and guidance for implementing risk-based post-market surveillance on the quality of medical products in Low- and Middle-Income Countries. Please see the details in the Table below.

Table 4: Types of sample testing per the three testing stages used in the 2021,2022 & 2023 RBPMS

Test	Testing scope	Specification
Stage 1: Visual &Physical Inspection	All samples collected must go through visual inspection to determine registration and package integrity, among others, at the field, at the time of collection	Pharmacopoeia or registration file (manufacturer's requirement)
Stage1: Labelling		Pharmacopoeia or registration file (manufacturer's requirement)
Stage 2: Identification (TLC)		

Stage 2: Disintegration test	Samples complying with stage 1 go for further screening at stage 2, at regional or sentinel sites.	Relevant Pharmacopeial Monograph
Stage 3: Compendial	20% of samples that complied at stage 2 and all failed at stages 1 and 2 and doubtful samples	Relevant Pharmacopeial Monograph

- The final confirmatory testing was done applying a risk-based testing approach, critical test attributes of confirmatory testing were considered in assessing the quality of collected samples.
- Any sample that fails a test was investigated per the testing laboratories' Out of Specification (OOS) procedures. Once the result was confirmed, the sample analysis did not continue to the next test. The determination of the path forward for a contested result was based on the procedures of the Agency.
- Tests were conducted on only unexpired medical products.

Definition of compliance of samples with standards

All samples collected were checked to confirm if registered by NAFDAC. The registered products were assessed for compliance with the requirement for marketing authorization where possible. The proportion of unregistered medical products was determined. Both registered products and unregistered products were sent to the laboratory for testing.

RESULTS

2021 SURVEY REPORT:

Overview of samples collected

In total, **1,097** medicine samples were collected from 21 states (including FCT) in six geopolitical zones of the Federation in accordance with the MedRS protocol and outcome. Out of the 1,097 samples, 281 (25.6%) were infusion products (refer to Table 5- Infusion products collected from States and FCT), 461 (42.0%) were Anti-Malarial (refer to Table 6 – Antimalarial products collected from States and FCT) and 355 (32.4%) were Maternal Health Product (refer to Table 7- Maternal Health products collected from states and FCT). The dosage forms of the medicines sampled were also noted; 602 (54.9%) samples were tablets, 281 (25.6%) were infusions and 214 (19.5%) were injectables.

Table 5. Infusion product samples collected during RB-PMS from selected states in 2021.

	STATE/SAMPLING LOCATION	INFUSION PRODUCT		
		NORMAL SALINE	DEXTROSE SALINE	TOTAL
1	ABIA	20	20	40
2	BAUCHI	20	20	40
3	BENUE	20	20	40
4	EDO	24	20	44
5	FCT	22	17	39
6	KANO	20	18	38
7	OYO	20	20	40
	Total	146	135	281

Table 6. Antimalarial samples collected during RB-PMS from selected states in 2021

	State/Sampling Location	Antimalarial							
		AA	AL	AST	ART	DP	SP	QS	TOTAL
1	Akwa Ibom	9	9	3	3	3	6	6	39
2	Bauchi	9	9	3	3	3	6	6	39
3	Benue	9	10	3	3	3	5	6	39
4	Cross River	9	9	3	3	3	6	6	39
5	Ebonyi	9	9	3	2	3	6	6	38
6	Fct	8	10	3	3	3	5	6	38
7	Kebbi	9	9	3	3	3	6	6	39
8	Nasarawa	9	9	3	3	3	6	6	39
9	Oyo	9	9	2	3	2	6	4	35
10	Plateau	9	9	3	3	3	6	6	39
11	Sokoto	9	9	3	2	3	6	6	38
12	Zamfara	9	9	3	3	3	6	6	39
	Total	107	110	35	34	35	70	70	461

Table 7. Maternal Health samples collected during RB-PMS from selected states in 2021

	State/Sampling Location	Maternal Health		
		Misoprostol	**Oxytocin**	**Total**
1	Abia	30	-	30
2	Edo	30	-	30
3	Fct	30	21	51
4	Gombe	30	-	30
5	Kaduna	30	-	30
6	Kwara	30	-	30
7	Oyo	30	-	30
8	Bauchi	-	21	21
9	Benue	-	19	19
10	Enugu	-	21	21
11	Kano	-	21	21
12	Lagos	-	21	21
13	Rivers	-	21	21
	Total	210	145	355
	Remarks Following Lab Decisions	15 Samples were dropped by the laboratory for not meeting requirements. Only 195 samples were subjected to testing out of the 210	8 Samples were dropped by the lab for not meeting requirements. Only 137 samples were subjected to testing out of the 145	A total of 332 samples of MNCH were Analysed in the Lab

Furthermore, 552 (60.9%) of the samples collected were imported, 354 (39.1%) were manufactured locally. The imported products from India and China ranked first and second, accounting for 42.3% and 14.2%, respectively.

Finally, out of the 1,097 samples collected, 1,061 (96.7% of 1,097) samples were analyzed in the lab of which 1,022 (96.3% of 1,061 samples) of the samples were satisfactory or passed lab tests, while 39 samples (3.7% of 1,061 samples) were unsatisfactory or failed lab test. 36 (3.3%) of 1,097 originally collected samples) were not analyzed due to laboratory criteria of being less than six (6) months to their expiry date. See Tables 8-10 for the summary of results of medical products collected and analyzed for this survey.

Laboratory results by type of medical products

Table 8. Infusion products

S/NO	Products	Number of samples submitted	Number of Samples Analysed	Passed (%)	Failed (%)
1	Normal Saline	146	146	100	0
2	Dextrose Saline	135	135	100	0
	Total		281	100	0

Table 9. Maternal health product

S/NO	Products	Number Samples Submitted	Number of the Samples Analyzed	Number Passed	%Passed	Number Failed	% Failed
1	Misoprostol	210	195	192	98.5	3	1.5
2	Oxytocin	145	137	127	92.7	10	7.3
	Total		332	319	96.1	13	3.9

Table 10. Antimalarials

S/NO	Products	Number of Samples Submitted	Number of the Samples Analyzed	Number Passed	% Passed	Number Failed	% Failed
1	Artemether/Lumefantrine	110	109	99	90.8	10	9.2
2	Artesunate/ Amodiaquine	107	107	98	91.6	9	8.4
3	Sulphadoxine/ Pyrimethamine	70	69	62	89.9	7	10.1
4	Dihydroartemisinin/ Piperaquine Phosphate	35	31	31	100	0	0
5	Quinine tablet	70	70	70	100	0	0
6	Artemether injection	34	28	28	100	0	0
7	Artesunate Injection	35	34	34	100	0	0
	Total	461	448	422	94.2	26	5.8

Results of specific quality tests for individual products

Classification of medicine samples based on Therapeutic Indication

Figure 1 depicts the proportion of samples analyzed based on Therapeutic Indication. Out of the 1,061 samples, 42.24% (448) of the samples were Antimalarial; 31.29% (332) of the samples were MNCH products and 26.48% (281) samples were Infusion products.

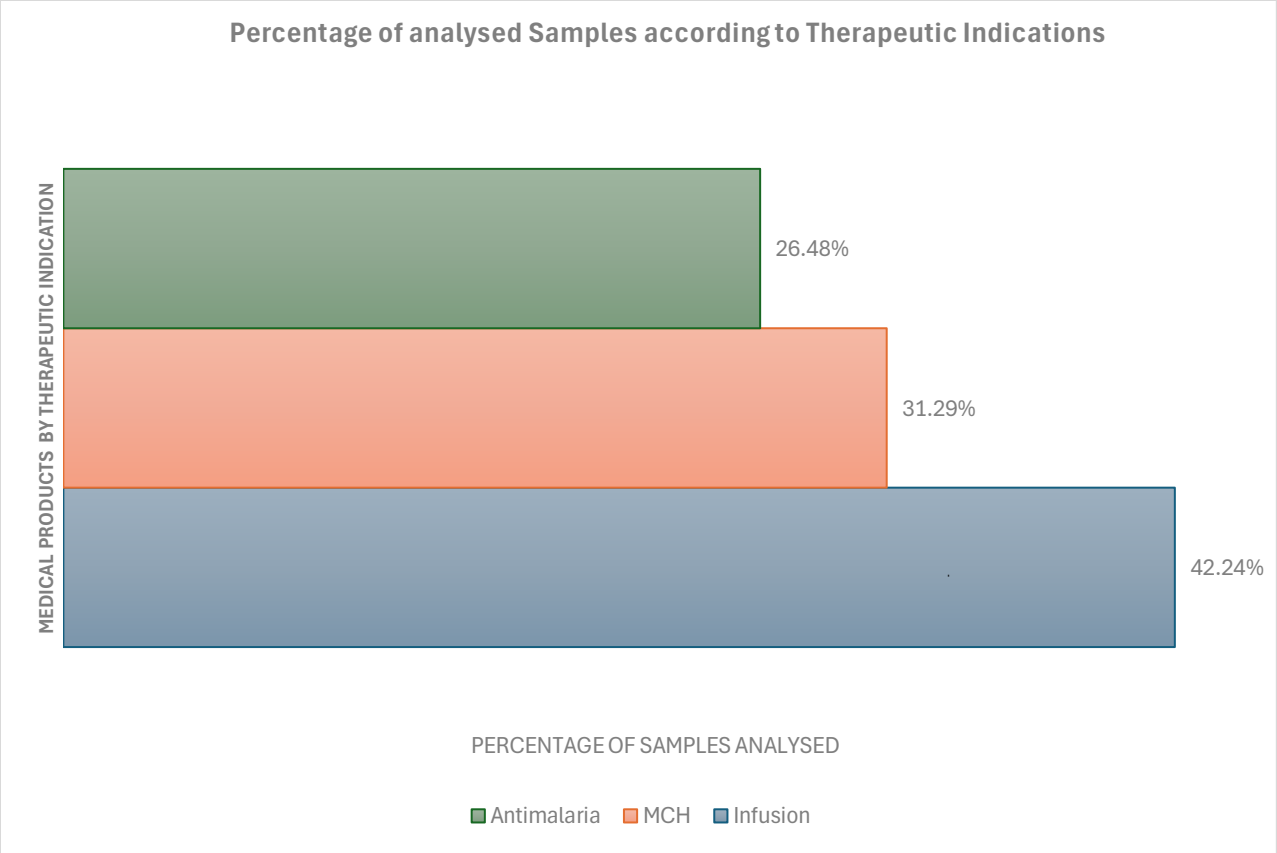


Figure 1: Proportion of medicine samples in 2021 according to therapeutic indication

Medicine samples as classified according to Active Pharmaceutical Ingredients (API)

Figure 2 below shows the distribution of samples analyzed according to the APIs. Misoprostol shows the highest number of samples 195 (18.9%) while the least was artemether injection-28 (2.6%)

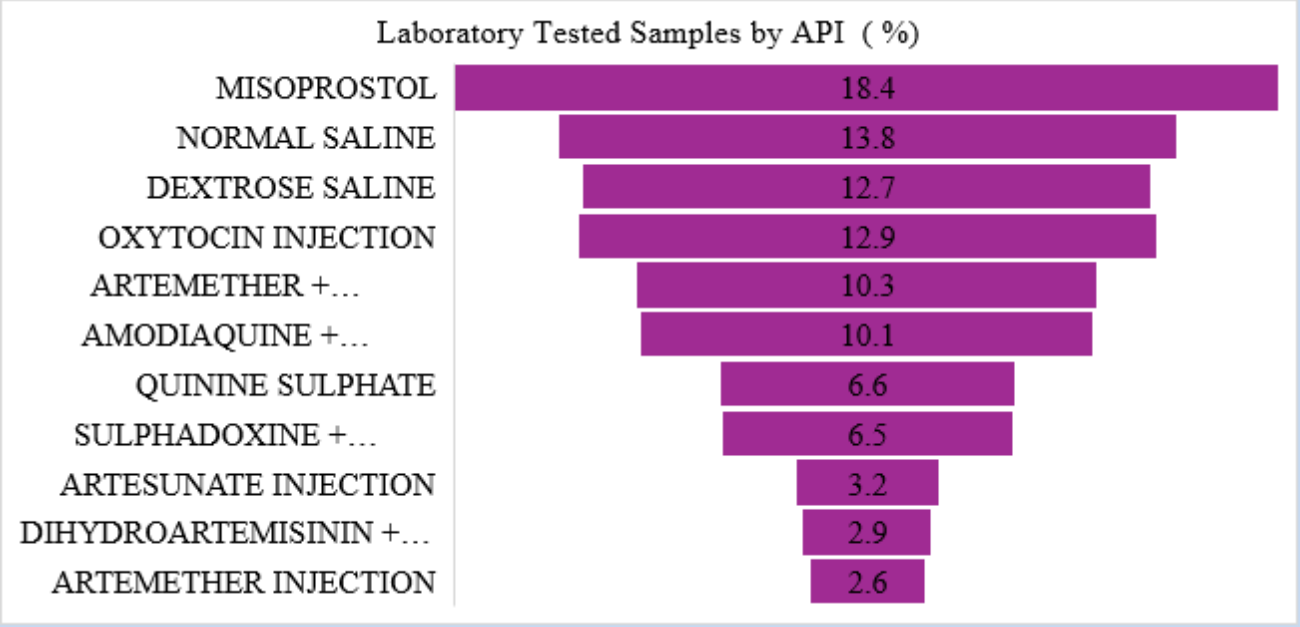


Figure 2: Percentage of laboratory-tested samples in 2021 according to API

Medicine samples as classified according to dosage form

Figure 3 depicts, in decreasing order of frequency, the number and percentage of processed samples based on dosage forms. The graph shows that most of the samples were in tablet form, accounting for 64% of the total samples, followed by infusion (29%), and powder for oral suspension was the least (0.8%).

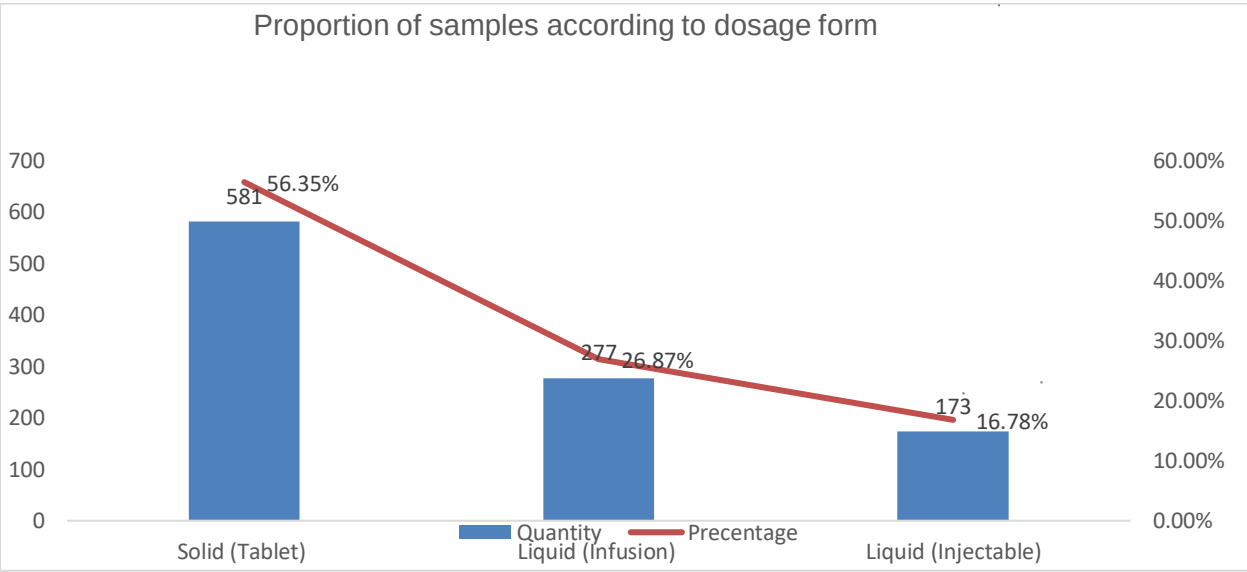


Figure 3: Proportion of samples tested in 2021 according to Dosage Form

Medicine samples according to sampling location (state)

A state-by-state distribution of the samples revealed that the Federal Capital Territory (FCT) has 12% of the total number of samples collected, followed by Oyo State (9.6%), and Lagos and Rivers had the fewest (1.9 % each), as can be seen in Figure 5 below.

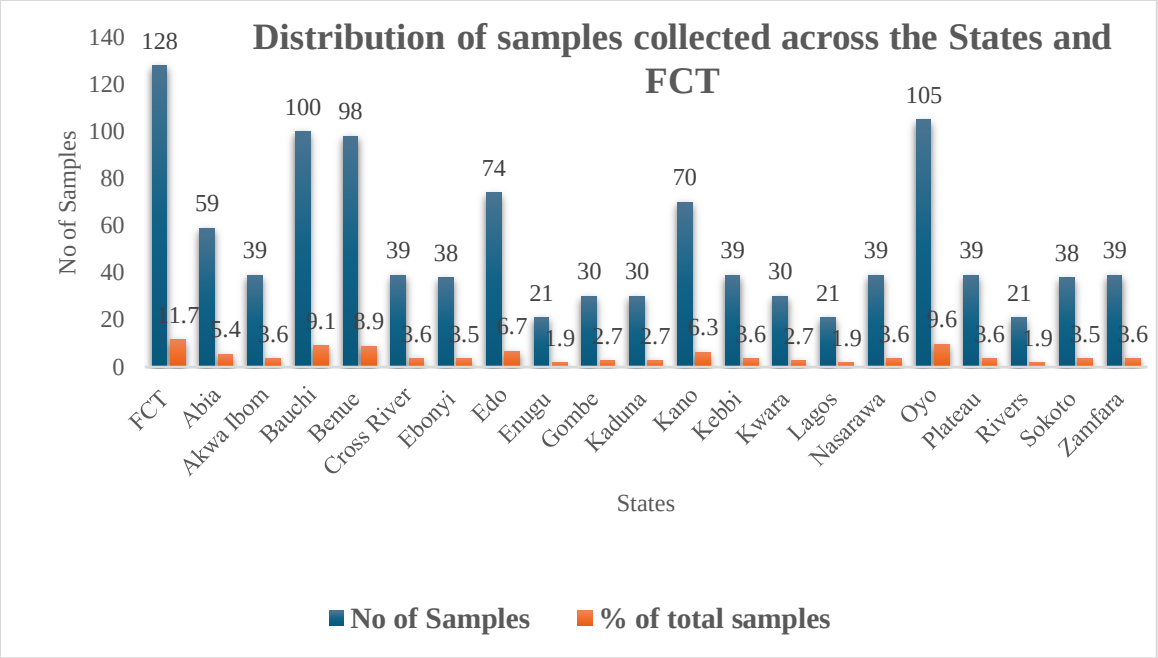


Figure 4: **Distribution of samples collected across the States and FCT in 2021**

Medicine samples as classified according to geopolitical sampling zone.

Figure 6 depicts the sample proportions by geopolitical zone. According to the graph, NCZ (30.4%), NWZ (18.7%), SSZ (15.8%), NEZ (11.9%), SEZ (11.8%) and the SWZ had the fewest samples (11.5%).

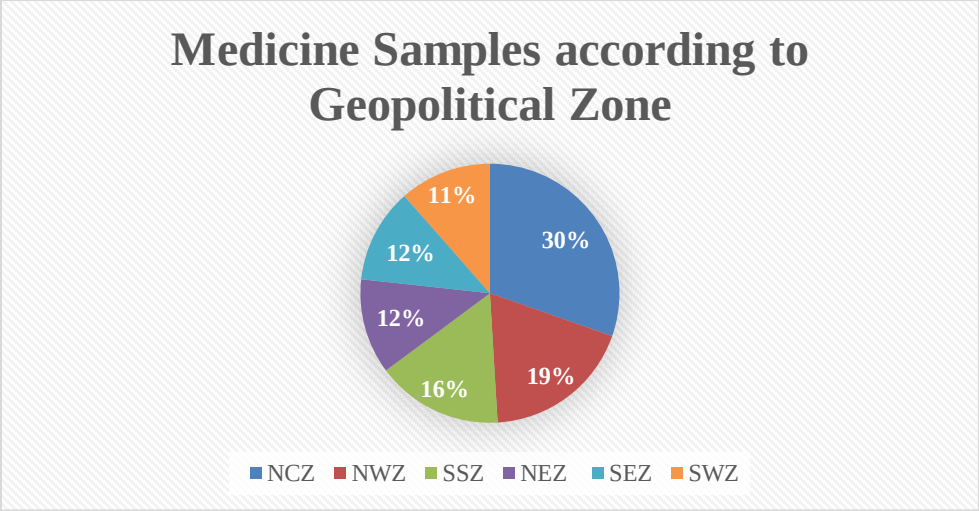


Figure 5: 2021 Medicine samples classified according to geopolitical sampling zone.

Table 11: Cross-tabulation of medicine samples in 2021 by zone and laboratory test results

Zone	Total	Satisfactory	%	Unsatisfactory	%
NCZ	331	323	97.6	8	2.4
NEZ	123	118	96.0	5	4.0
NWZ	196	187	95.4	9	4.6
SEZ	117	108	92.3	9	7.7
SSZ	170	165	97.1	5	2.9
SWZ	124	121	98.0	3	2.0
Total	**1061**	**1022**	**97.3**	**39**	**3.7**

Table 12: Number and percentage of satisfactory/unsatisfactory samples in 2021 based on country of origin.

Country of Origin	Total	Satisfactory	%	Unsatisfactory	%
India	418	393	94.8	25	5.2
Nigeria	384	370	97.8	14	2.3
China	221	221	100	0	0
Vietnam	20	20	100	0	0
England	12	12	100	0	0
Turkey	4	4	100	0	0
France	1	1	100	0	0
USA	1	1	100	0	0
Total	**1061**	**1022**	**97.3**	**39**	**3.7**

Table 13: Number and percentage of satisfactory/unsatisfactory samples in 2021 based on origin

Origin	Satisfactory	%	Unsatisfactory	%
Imported	652	96.3	25	3.7
Local	370	96.4	14	3.6
Total	**1022**	**97.3**	**39**	**3.7**

2022 SURVEY RESULTS:

Summary of key findings:

Amoxicillin Dispersible tablet was collected in just 3 or 4 states; thus, it was excluded from the survey. 14 samples representing 3.69% of collected samples were rejected due to deviations from the sampling protocol. These deviations ranged from expiry dates of less than 6 months and products whose dosage strength was not stated in the sampling protocol.

Only 6 samples (1.64%) of 365 accepted samples failed level 1 screening; 2 samples of artemether injections have no NAFDAC market authorization (unregistered) and 4 amoxicillin capsules failed because of labeling lapses. Out of the 359 samples sent to the ISO/IEC 17025 accredited laboratories- (CDCL- 136, Kaduna Area Lab- 114, Agulu Area Lab-109) for compendia analysis, 321 (89.42%) passed, while 38 samples (10.58%) failed.

Looking at the failed samples, Amoxicillin Clavulanic Acid Tablets recorded the highest failure rate of 27.27% (9 out of 33 samples), followed by 13.11 % of Amoxicillin capsules (8 out of 61 samples). Similarly, 12.16% of Ciprofloxacin tablets (9 out of 74 samples) failed and 10.53 % (12 out of 114) Artemether Lumefantrine samples also failed. Comparatively, 100% (20 of 20) of Artesunate injections and 100% of artemether injections (57 out of 57) passed laboratory testing per the objectives of the survey. See Table 15 – Summary of samples collected and overall percentage results and Table 16 - Summary for the overview of the results of medical products surveyed in RB-PMS of 2022.

Table 14. Summary of samples collected and overall results.

	Total Sampled	**Total rejected**	**Total Assessed**	**Level 1 Assessment**	**Levels 2 & 3 (Lab testing)**
No of samples	379	14	365	365	359
No. Passed	-	-	321	359	321
% Passed	-	-	87.95	98.36	89.42
No. Failed	-	-	44	6	38
% Failed	-	-	12.05	1.64	10.58

Table 15. Overview of Results in the 2022 RBPMS.

S/N	Product category	Medicine name	No. sampled	No. of valid samples for the lab. Analysis	No and % of tested Samples Passed	No of tested samples failed.	% Passed	% Failed
1	Anti-Malarial	Artemether/ Lumefantrine Tablet	114	114	102	12	89.47	10.53
2		Artesunate Injection	20	20	20	0	100	0
3		Artemether Injection	59	57	57	0	100	0
4	Anti-Biotics	Ciprofloxacin Tablet	74	74	65	9	87.84	12.16
5		Amoxicilin/ Clavunanic Acid Tablet	33	33	24	9	72.72	27.27
6		Amoxicillin Capsule	65	61	53	8	86.89	13.11
		Total	365	359	321	38	89.42	10.58

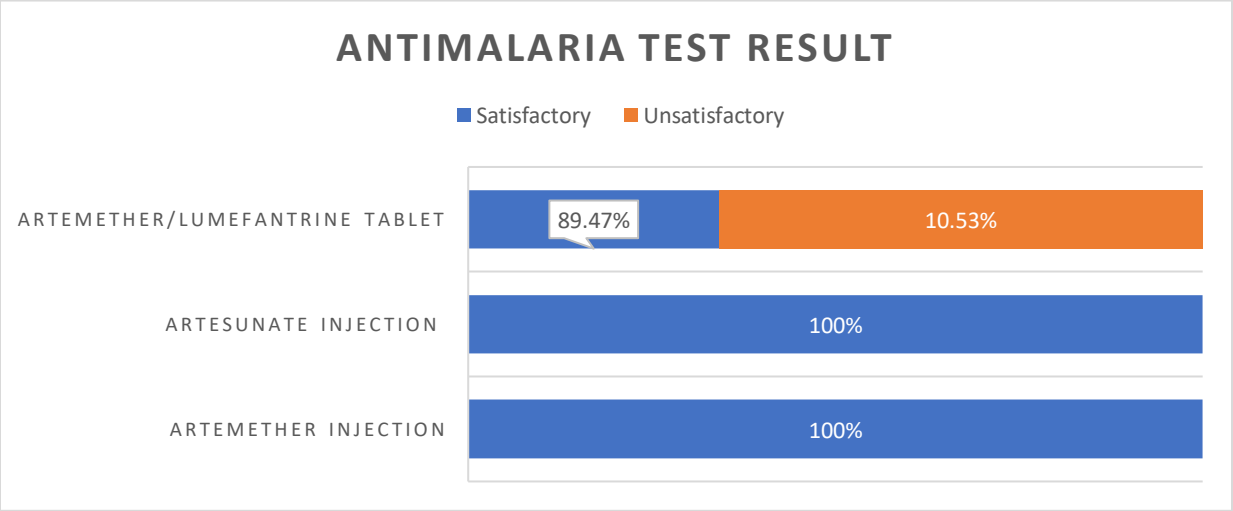
Laboratory test results of medicine samples in RBPMS 2022

Antimalarials

Out of the 321 samples that were tested satisfactory, it is worth knowing that artesunate (20) and artemether (57) injections were all satisfactory and recorded no failure. On the other hand, Artemether Lumefantrine recorded 89.47% passes (102 of 114), while 12 (10.53%) failed laboratory testing. The low composition of lumefantrine (below specification) was attributed to the failures.

Table 16. Anti-malarial Laboratory Test Results

S/N	Product category	Product name	No. sampled	No. of valid samples for the lab. Analysis (N)	The total no of samples failed. (n)	The total no of samples that passed	% Passed (n/N)	% Failure (n/N)
1	Anti-Malarial	Artemether/ Lumefantrine Tablet	114	114	12	102	89.47%	10.53%
2		Artesunate Injection	20	20	0	20	100%	0.00%
3		Artemether Injection	59	57	0	57	100%	0.00%



6: Graphical representation of antimalarials test results

Antibiotics

Out of the 359 samples tested in the laboratories, Amoxicillin Clavulanic Acid Tablets recorded the highest failure rate of 27.27% (9 out of 33 samples), followed by 13.11 % of Amoxicillin capsules (8 out of 61 samples). Similarly, 12.16% of Ciprofloxacin tablets (9 out of 74 samples) failed, as shown in Table 17. The major reason for the failure was attributed to low assay results for the active pharmaceutical ingredients (APIs).

Table 17: Antibiotics Lab Test Results

S/N	Product category	Product name	No. sampled	No. of valid samples for the lab. Analysis	The total no. of failed samples.	% Failure	% Passed
1	Anti-Biotics	Ciprofloxacin Tablet	74	74	9	12.16	87.84
2		Amoxicilin/ Clavunanic Acid Tablet	33	33	9	27.27	72.72
3		Amoxicillin Capsule	65	61	8	13.11	86.89

Distribution of samples collected across the 7 States of Nigeria

Table 18 and Figure 7– show the distribution of samples collected from the seven states for the survey. The highest number of samples was collected from Anambra State with 25.21% (92 of 365) samples, while the lowest percentage of samples 4.66% (17 of 365) was collected from Akwa Ibom State.

Table 18: Showing samples collected in the States.

S/N	STATE	ABIA	AKWA IBOM	ANAMBRA	BORNO	IMO	KANO	NIGER	TOTAL
1	Artemether/ Lumefantrine Tablet	31	3	29	22	10	9	10	114
2	Artesunate Injection	-	3	3	6	2	5	1	20
3	Artemether Injection	5	3	15	12	8	8	8	59
4	Ciprofloxacin Tablet	14	3	21	15	7	9	5	74
5	Amoxicillin Capsule	8	3	17	11	5	9	12	65
6	Amoxicilin/ Clavunanic Acid Tablet	3	2	7	7	5	4	5	33
	TOTAL	**61**	**17**	**92**	**73**	**37**	**44**	**41**	**365**

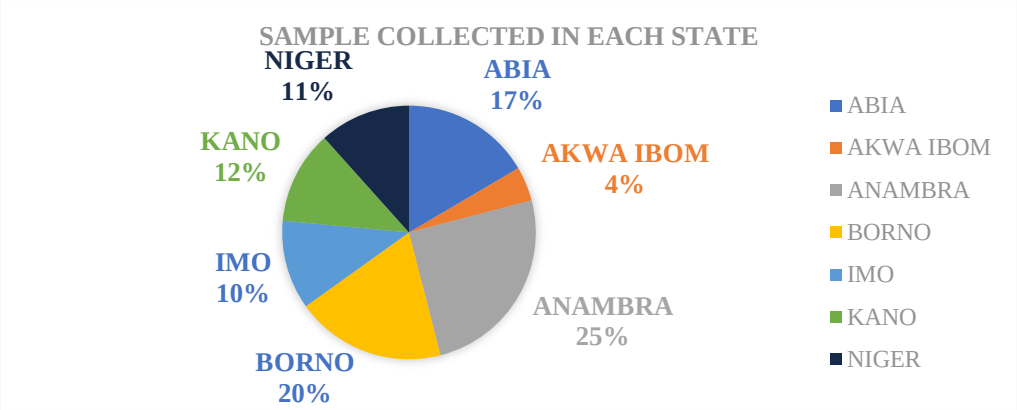


Figure 7: Percentage distribution of samples collected across the 7 States of Nigeria

Medicine samples classified by Country of Origin

According to a breakdown of medicine samples by country of origin, India ranked first, accounting for 55.34% (202) of total samples collected, followed by China which accounted for 28.22% (103), and Nigeria came third with 14.79% (54) samples.

Table 19: Medicine samples classified by country of origin.

S/N	Country of origin	Number	Percentage
1	India	202	55.34 %
2	China	103	28.22%
3	Cyprus	1	0.27%
4	Malaysia	1	0.27%
5	Nigeria	54	14.79%
6	Turkey	2	0.55%
7	UK	2	0.55%
	Total	365	100%

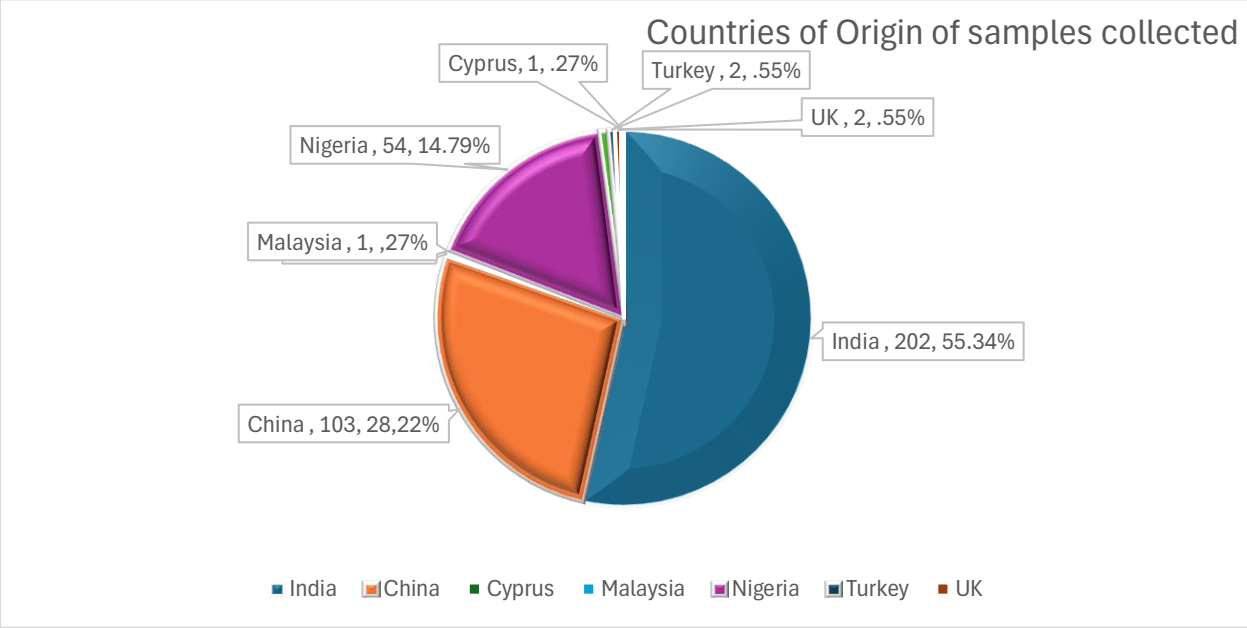


Figure 8: Medicine samples classified by country of origin.

2023 SURVEY RESULT:

Overview of samples collected

For this survey, we considered the following distinct product types: maternal health, antidiabetic, anti-hypertensives, antimalarials, and anti-infectives. A total of 825 medical products were sampled. 179 samples did not pass level 1 screening and 12 failed the laboratory test. Based on the total number of samples tested, the aggregate result indicated that 19% of the sampled products fail

Table 20. The Results of the Various Tests Conducted in the 2023 PMS Survey

S/No.	Product category	Medicine name	No. Sampled	Total No. of samples tested in the Lab	Total no of samples that failed lab Test	% Failure Level 1	% Failure Lab Test
1	MCH	Oxytocin	87	33***	6	62.1	18.1
2	ADB	Metformin	209	175	1	16.3	0.6
3	ADB	Glimepiride	87	72	1	17.2	1.4
4	AHT	Amlodipine	182	156	0	14.3	0.0
5	AHT	Telmisartan	121	105	4	13.2	3.8
6	AHT	Nifedipine	139	105	R	-	-
TOTAL			825	646	12	22.0	1.9

***Note:**

- ***After the level I screen, 41 Oxytocin samples were stepped down for multiple reasons including closeness to the expiry date, labelling laps, etc.**
- ****The total of 54 samples of Oxytocin that failed at level 1 i.e. (1+12+41=54)**
- *****Only 33 Samples of Oxytocin were tested in the lab with a 6 (18.1%) failure rate.**

Maternal Health

Table 21: Results of Oxytocin Samples

S/N	Products	Number of products Sampled	No of Sample Tested in the Lab	Number passed	Number failed	%Passed	%Failed
1	Oxytocin	87	33	27	6	81.18	18.18

Antidiabetic And Antihypertensive

Table 22: Results of Metformin Samples

S/NO	Product Category	Products	No of Sample	Percentage Passed	Percentage Failed	Remark
1	Anti-Diabetics	Metformin	175	174 (99.4%)	1 (0.6%)	1 sample failed lab test
2		Glimepiride	72	71 (98.61%)	1(1.39%)	1 sample failed lab test
3	Anti-Hypertensives	Amlodipine	156	156(100%)	0 (0%)	Zero samples failed the lab test
4		Telmisartan	105	101 (96.2%)	4 (3.8%)	4 samples failed the lab test

Selected Drug Classes

Table 23: The medical products selected by MedRS tool for the 2023 RBPMS

PHASE	PHARMACEUTICAL CLASS	DRUGS
1	Anti-Diabetics	Metformin 500mg & Glimepiride 4mg
2	Anti-Hypertensives	Nifedipine 20mg, Amlodipine 10mg & Telmisartan 80mg
3	Maternal & Child Health Product	Oxytocin 10IU
4	Anti-Malarials	Artemether/Lumefantrine Suspension 20/120mg & Tablet 80/480mg
5	Anti-Infectives	Amoxicillin 250mg & 500mg, Cefuroxime 250mg, Rifampicin 200mg
q		

Manufacturers and batches

Please, refer to the comprehensive list of medical products sampled.

Sampling Location (States)

Table 24: Showing Allocation of Oxytocin Samples to States

S/N	Zone	State	Number of Sample (Unit) Per Zone	Level 1 (30%) Urban	Level 2 (70%) Rural & Semi-Urban
1	NCZ	FCT, Kogi	16(50)	3 samples	5 samples
2	NEZ	Adamawa, Jigawa Taraba	24(50)	3 samples	5 samples
3	NWZ	Kebbi, Sokoto	16(50)	3 samples	5 samples
4	SEZ	Enugu, Anambra	16(50)	3 samples	5 samples
5	SSZ	Cross River	8(50)	3 samples	5 samples
6	SWZ	Lagos, Oyo, Ogun	24(50)	3 samples	5 samples

Table 25: Showing Allocation of Antidiabetics Samples to States

S/N	Zone	State	Number of Samples (Unit) Per Zone	Level 1 (30%) Urban	Level 2 (70%) Rural & Semi-Urban
Metformin					
1	NCZ	Kwara, Niger Plateau	42(100)	12 samples	30 samples
2	NEZ	Borno, Taraba	28(100)	8 samples	10 samples
3	NWZ	Kaduna, Kano Katsina, Zamfara	56(100)	16 samples	40 samples
4	SEZ	Abia, Imo	28(100)	8 samples	10 samples
5	SSZ	Edo	14(100)	4 samples	10 samples
6	SWZ	Lagos, Ondo Osun, Oyo	56(100)	16 samples	40 samples
Glimepiride					
1	NCZ	Kwara, Niger Plateau	18(100)	6 samples	12 samples
2	NEZ	Borno, Taraba	12(100)	4 samples	8 samples
3	NWZ	Kaduna, Kano Katsina, Zamfara	24(100)	8 samples	16 samples
4	SEZ	Abia, Imo	12(100)	4 samples	8 samples
5	SSZ	Edo	6(100)	2 samples	4 samples
6	SWZ	Lagos, Ondo Osun, Oyo	24(100)	8 samples	16 samples

Table 26: Showing Allocation of Antihypertensives - nifedipine, Amlodipine and Temisartan Samples to States

S/N	Zone	State	Number of Sample (Units) Per Zone	30% Urban	70% Rural & Semi-Urban
Nifedipine					
1	NCZ	Benue, FCT, Kwara	27(100)	9 sample	18 samples
2	NEZ	Borno, Jigawa Gombe	27(100)	9 sample	18 samples
3	NWZ	Kano, Sokoto	18(100)	6 sample	12 samples
4	SEZ	Abia, Ebonyi, Enugu	27(100)	9 sample	18 samples
5	SSZ	Rivers	9(100)	3 sample	6 samples
6	SWZ	Ekiti, Lagos, Ogun	27(100)	9 sample	18 samples
Amlodipine					
1	NCZ	Benue, FCT, Kwara	36(100)	12 sampl	24 samples
2	NEZ	Borno, Jigawa, Gombe	24(100)	9 sample	15 samples
3	NWZ	Kano, Sokoto	24(100)	9 sample	15 samples
4	SEZ	Abia, Ebonyi, Enugu	36(100)	12 sampl	24 samples
5	SSZ	Rivers	12(100)	4 sample	8 samples
6	SWZ	Ekiti, Lagos, Ogun	36(100)	12 sampl	24 samples
Telmisartan					
1	NCZ	Benue, FCT, Kwara	24(100)	9 sample	15 samples
2	NEZ	Borno, Jigawa, Gombe	24(100)	9 sample	15 samples
3	NWZ	Kano, Sokoto	16(100)	6 sample	10 samples
4	SEZ	Abia, Ebonyi, Enugu	24(100)	9 sample	15 samples
5	SSZ	Rivers	8(100)	3 sample	5 samples
6	SWZ	Ekiti, Lagos, Ogun	24(100)	9 sample	15 samples

Table 27: Showing Allocation of Anti-Malarial Samples to Zones

S/N	Zone	State	Number of Sample (Units - l or tablets) Per Zone	Level 1 (30%) Urban	Level 2 (70%) Rural & Semi-Urban
Artemether/ Lumefantrine Suspension 20/120mg					
1	NCZ	Kwara, Niger Nasarawa	27 (6 bottles)	9 samples	18 samples
2	NEZ	Borno, Taraba Jigawa	27(6 bottles)	9 samples	18 samples
3	NWZ	Kano, Sokoto Kebbi	27(6 bottles)	9 samples	18 samples
4	SEZ	Enugu, Anambra	18(6 bottles)	6 samples	12 samples
5	SSZ	Edo, Rivers	18(6 bottles)	6 samples	12 samples
6	SWZ	Lagos, Oyo, Osun	27(6 bottles)	9 samples	18 samples
Artemether/ Lumefantrine Tablet 80/480mg					
1	NCZ	Kwara, Niger Nasarawa	45(100)	15 samples	30 samples
2	NEZ	Borno, Taraba Jigawa	45(100)	15 samples	30 samples
3	NWZ	Kano, Sokoto Kebbi	45(100)	15 samples	30 samples
4	SEZ	Abia, Imo	30(100)	10 samples	20 samples
5	SSZ	Edo, Rivers	30(100)	10 samples	20 samples
6	SWZ	Lagos, Osun Oyo	45(100)	15 samples	30 samples

Storage and transportation conditions

- Samples collected were packed, transported, and stored in such a way as to prevent any deterioration, contamination, or adulteration. Samples collected should be stored and transported in their original containers and in accordance with storage instructions for the respective product.
- Adequate care and measures were taken to ensure that samples reached the laboratory where

the tests were performed without any physical or chemical damage.

- Appropriate care was taken to provide adequate packaging to protect samples during transportation. All containers were sealed and appropriately labeled.
- After the completion of the sample collection, the sample collection team wrote a summarized sample collection report using the format prepared.

Registration status of sampled products

Please, refer to the comprehensive list of medical products sampled and their registration status.

Compliance with Specifications

Confirmatory tests (level 3) were conducted using pharmacopeia methods from USP, BP, and international pharmacopeia as relevant. (Refer to laboratory reports

DISCUSSION

The study carried out in 2021, generally recorded a significant decline in the percentage of failed samples of medicines particularly Oxytocin when compared with the previous survey on the product[1].

The southern part of Nigeria had a lower number of failed samples compared to the northern part of the country; this is consistent with the last survey report in 2019[2].

There was less number/percentage of unregistered drug products sampled during the quality monitoring exercise compared to the last report 2019[4]. This is an encouraging finding since the Nigerian medicine market is believed to have a higher number of unregistered medicines due to the porous nature of our borders. The registration of medicines is one of the core functions of NAFDAC. Product registration helps to screen out substandard and falsified medicinal products.

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[1] Chimezie Anyakora, Yetunde Oni, Uchenna Ezedinachi, Adekoya Adekola, Ali Ibrahim, Charles Nwachuku, Charles Esimore, Victor Abiola & Jude Nwokike. Quality Medicines in maternal Health: The results of Oxytocin, Misoprostol, Magnesium Sulphate and Calcium Gluconate Audit. BMC Pregnancy and Childbirth. 30th January 2018.
https://bmcpregnancychildbirth.biomedcentral.com/articles/10.1186/s12884-018-1671-y

[2] NAFDAC Report on Monitoring of Quality of Medicines (antimalarial) round 6 in collaboration with USP 2019 (unpublished).

The study carried out in both 2021 & 2022 provides comprehensive information on the quality of the selected medicines circulating in Nigeria. Other similar research in the past have recorded similar outcomes like the findings of this study indicating that the quality of medicines in Nigeria seems to have improved over the years.

Some limitations in this study could have minimally affected the generalization of the findings. Sampling from some importers and distributors especially in the southeast was slightly more difficult because comprehensive lists and location addresses were difficult to access. Also, some states like Borno, Katsina, etc have unique security challenges, they may have higher figures of SF since the activities of regulators may not cover them. Furthermore, the medicines selected in this survey may not be the target of counterfeiters at this time.

From the survey carried out in 2023, the Laboratory results of Oxytocin indicate that from the 33 samples submitted and analyzed, 81.9% passed the quality standards, while 18.1% failed.

For Visual screening, 54 samples of Oxytocin did not meet the criteria **(with 1 unregistered, 12 falsified, and 41 oxytocin samples near the expiry date**). This outcome raises great concerns about the quality and consistency of Oxytocin products (in 2021 %failure was 7.3 and in 2023 18.18) in circulation in Nigeria. The relatively high percentage of failures indicates a significant portion of the samples did not meet the necessary standards, posing potential risks to patients who rely on this medication for critical medical interventions.

The implications of this result are serious, as it suggests potential issues with storage conditions, or product handling that may compromise the efficacy and safety of Oxytocin. For patients, receiving substandard medication could lead to ineffective treatment outcomes ultimately leading to high maternal mortality rates in Nigeria.

This result underscores the importance of stringent quality control measures and regulatory oversight in the pharmaceutical industry. Also, it highlights the need for manufacturers to consistently adhere to Good Manufacturing Practices (GMP) and for continued efforts by NAFDAC to ensure that only standard medical products are distributed and sold in Nigeria.

Out of 209 samples of Metformin submitted and analyzed, an impressive 99.4% passed the quality standards, while only one (1) sample (0.6% failed to meet the required criteria in the lab. However,

34 of the 209 samples (16.3%) failed visual screening. Overall, 35 (16.7%) of Metformin samples failed. Similarly, out of the 87 samples of Glimepiride tablets collected 15 failed visual screening while 1 failed laboratory analysis. The total failure for the Glimepiride tablet is 16(18.4%) while the total pass is 71 (81.6%).

The samples of Amlodipine tablets collected is 182 out of which 156 (85.7%) passed visual and compendial testing and 26(14.3%) failed the visual test. Similarly, Telmisartan showed an overall passing rate of 83.5% (101 samples) with only 20 (16.5%) failing to meet the standards (see details in Table 9). It should be noted that only 105 (86.8%) samples of Telmisartan were tested in the lab, and only 4 (3.8%) of 105 samples failed the quality test. These outcomes suggest a high level of quality control in the production and distribution of Metformin and Telmisartan, as most of the samples met the expected standards.

The implication of this result is twofold. Firstly, it reflects positively on the manufacturing processes and quality assurance measures put in place by the companies producing these medical products. A high percentage of samples passing the analysis indicates that these processes are effective in ensuring the consistency and reliability of the medication, which is crucial for patient safety and therapeutic effectiveness.

Secondly, the low percentage of samples failing the analysis suggests that product quality issues are relatively rare. Though the failure rate is low, it underscores the importance of continued vigilance in monitoring product quality and promptly addressing the issues to maintain the high standards observed in most samples.

The limitations in our survey could have minimally affected the generalization of the findings. The laboratory confirmatory tests were on risk-based quality priorities. Hence, full compendial tests were not conducted for all products sent to the laboratory.

REGULATORY ACTIONS

Following this survey carried out in each respective year (2021. 2022 & 2023), the Agency carried out the following regulatory actions based on available data and evidence.

Year 2021.

1. The two (2) samples identified as unregistered were mopped up from the collection site, and other state offices were directed to carry out surveillance on the product/batches and mop out of circulation.
2. After the release of the laboratory reports, the PMS Directorate evaluated the reports, products of the same batch that failed in one site but passed in other sites were attributed to issues of poor storage and handling. Officers were directed to mop up from the site of collection.
3. Products that failed in several sites were attributed to the manufacturing process. Based on this result, decisive steps were taken by the NAFDAC SF Focus group (R&R, DER, CDCL, PV/PMS, I&E, and PID), such steps included:
    a. DER conducted GMP reassessments of local facilities that produced failed products.
    b. The SF Focus group had consultative meetings with the marketing authorization holders (MAH) of failed products and were sanctioned accordingly.
    c. The PMS Directorate conducted a good storage and distribution practice (GSDP) audit at MAH warehouses to ensure compliance with a good storage and distribution practices requirement.

Year 2022.

1. The PMS Directorate evaluated the failed samples and liaised with the R&R Directorate to verify the registration status of the failed medicines sampled for possible regulatory decisions.
2. Consultative meetings were held with the MAHs whose products were unsatisfactory to address why the products failed.
3. The Agency took informed regulatory actions based on the laboratory evidence by instituting product recalls.
4. DER was mandated to carry out cGMP on the local manufacturer's facilities to address the root cause and institute CAPA where practicable. The outcome revealed that the cGMPs were not satisfactory.

Year 2023.

1. Engagements with Market Authorization Holders of the failed samples and directives to recall all affected batches immediately were issued.
2. A public alert notice was immediately placed on the Agency's website to sensitize the public.
3. NAFDAC officers across the country were directed to conduct surveillance and mop up all violating batches of products.
4. The registration package submitted for the Oxytocin registration was confirmed and compared with those found during the sampling.
5. Other product registration applications and requests by the affected MAHs were put on hold until they were all cleared of outstanding issues.
6. Good storage and distribution practice inspections were conducted at the storage facilities of the affected MAHs (importers).

CONCLUSIONS

The surveys have indicated that the prevalence of substandard and falsified (SF) medical products varies, and the type or product category influences the rate. The prevalence rate of SF for infusions and injectable antimalaria products is 0%. In 2021, the sampled maternal health products had a pass rate of 98.5% for Misoprostol and 92.7% for Oxytocin. However, the pass rate for Oxytocin injection decreased in 2023, with 81.9% meeting quality standards and 18.1% failing. This Agency will step up the cold-chain monitoring and the manufacturers/importers especially considering the increase in failure rate from 7.3% in 2021 to 18.1% in 2023.

The prevalence rates for the three commonly used antimalarial products (Artemether/Lumefantrine, Artesunate/Amodiaquine, and Sulphadoxine/Pyrimethamine tablets) in Nigeria in 2021 were 9.2%, 8.4%, and 10.1% respectively. In 2022, the prevalence rate for Artemether/Lumefantrine slightly increased to 10.5%. Additionally, the prevalence rate for antibiotics is higher than for other products or classes of products: ciprofloxacin- 12.16%, Amoxicillin/clavulanic acid- 27.27%, and Amoxicillin- 13.11%. More focus is being placed on amoxicillin products as part of the high focus on pre-and post-marketing monitoring of MNCH medical products. The prevalence rates for antidiabetic and antihypertensive products are lower

than those for antibiotics and oxytocin injections. Specifically, Metformin has a prevalence rate of 0.6%, Glimepiride has a prevalence rate of 1.39%, Amlodipine has a prevalence rate of 0%, and Telmisartan has a prevalence rate of 3.8%.

Stakeholders have been advised to take appropriate action to prevent, detect, and respond to society's substandard and falsified medical products. It is recommended that a follow-up survey be conducted to assess the effectiveness of these actions.

The agency will improve collaboration with all stakeholders to align with the implementation strategies of the National Action Plan on the prevention, detection, and response to substandard and falsified medical products. This is necessary to prevent unauthorized medical products from entering the supply chain. In addition, more training of regulatory personnel and the industry on good manufacturing practices, storage and distribution practices, and the implementation of quality management systems will continue

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