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Guideline

National Agency for Food and Drug Administration and Control (NAFDAC)

Nigerian Guidelines for Detecting & Reporting of Adverse Reactions For Pharmaceutical products and Medical Devices

Contents

1 Introduction

This Guideline for the Nigerian Pharmaceutical Vigilance System has been developed to support the orientation of all healthcare professionals on the important concepts of Pharmacovigilance, vaccine vigilance, and medical device safety. It gives an overview of what pharmaceutical vigilance is, and how to detect and classify adverse reactions. It also describes the reporting system to the National Pharmacovigilance Center.

The reporting requirements stated in this guideline are based mainly on international guidelines including the International Conference for Harmonization (ICH) and the European Medicine Agency (EMA).

2 Scope

Its ultimate goal is to enhance efforts in ensuring that safe, efficacious, and quality pharmaceutical products and medical devices are made available for all Nigerians. All healthcare professionals are encouraged to actively participate in pharmaceutical vigilance and to report all suspected adverse reactions to help safeguard the population's health.

3 Definitions

Adverse Event/ Adverse Experience: Any untoward medical occurrence that may present during treatment with a pharmaceutical product / Medical device but which does not necessarily have a causal relationship with this treatment.

- *Adverse Drug Reaction (ADR):* A noxious and unintended response to a pharmaceutical product which occurs at doses normally used in humans for the prophylaxis (prevention), diagnosis, or

therapy (treatment) of diseases, or for the modification of physiological function. Contrary to an adverse reaction, an ADR is characterized by the suspicion of a causal relationship between the medicine and the occurrence, i.e. judged as being at least possibly related to treatment by the reporting or a reviewing health professional.

AEFI: An Adverse event following immunization is any untoward medical occurrence that follows immunization and which does not necessarily have a causal relationship with the usage of the vaccine. The adverse event may be any unfavorable or unintended sign, abnormal laboratory finding, symptom, or disease.

Causality assessment: The evaluation of the likelihood that a medicine was the causative agent of an observed adverse reaction. Causality assessment is usually made according to established algorithms.

Clusters: Two or more instances of an event related in time, place, population subgroup, or common exposure (e.g., vaccine). AEFI clusters are usually associated with a particular provider, health facility, and/or a vial of vaccine that has been inappropriately prepared or contaminated.

Drug/ Medicine: Any substance in a pharmaceutical product that is used to modify or explore physiological systems or pathological states for the benefit of the recipient. The term drug/medicinal product is used in a wider sense to include the whole formulated and registered product, including the presentation and packaging, and the accompanying information.

Dechallenge: The withdrawal of medicine from a patient; the point at which the continuity, reduction, or disappearance of adverse effects may be observed.

EPI: Expanded program for immunization

NAFDAC: National Agency for Food Drug Administration and Control

Expected of the adverse drug reaction: The expectedness of the reaction is assessed in accordance with the approved product information; the reaction is defined as expected if it is included in the package insert or the summary of product characteristics (SPC).

Field safety corrective action (FSCA): It is an action taken by a MANUFACTURER to reduce a risk of death or serious deterioration in the state of health associated with the use of a medical device that is already placed on the market.

Lack of Efficacy: Unexpected failure of a medicine to produce the intended effect as determined by previous scientific investigation.

Medical device: Any instrument, apparatus, appliance, software, implant, reagent, material, or

other article intended by the manufacturer to be used, alone or in combination, for human beings for one or more specific medical purposes.

Minor AEFI: an AEFI that usually contains all of the following criteria

- An event that is not "serious" and that has no potential risk to the health of the recipient of the vaccine.
- Usually occurs within a few hours of injection.
- Resolve after a short period and pose little danger.

National Pharmacovigilance Center: A single, governmentally recognized center (or integrated system) within a country with the clinical and scientific expertise to collect, collate, analyze, and give advice on all information related to medicine safety.

Rechallenge: The point at which a medicine is again given to a patient after its previous withdrawal. (see Dechallenge)

Serious Adverse Event or Reaction: A serious adverse event or reaction is any untoward medical occurrence that at any dose results in:

* Death
* Is life-threatening
* Requires inpatient hospitalization or prolongation of existing hospitalization
* Persistent or significant disability/incapacity
* Congenital Anomaly
* Medically important event or reaction

To ensure no confusion or misunderstanding of the difference between the terms 'serious' and 'severe', the following note of clarification is provided:

The term 'severe' is not synonymous with serious. In the English language, 'severe' is used to describe the intensity (severity) of a specific reaction (as in mild, moderate, or severe). However; the reaction itself may be of relatively minor medical significance (such as severe headache).

Serious AEFI:

Like other ADRs from medications, An AEFI will be considered serious, if it meets any of the following

- Results in death,
- Is life-threatening,
- Requires in-patient hospitalization or prolongation of existing hospitalization,
- Results in persistent or significant disability/incapacity,

- Is a congenital anomaly/birth defect?

Requires intervention to prevent permanent impairment or damage
Seriousness (not severity) based on patient/reaction outcome or action criteria serves as a guide for defining regulatory reporting obligations.

Severe event:

Severe reaction is a term including serious reactions but also other severe reactions

- Usually do not result in long-term problems.
- Could be disabling.
- Rarely life-threatening.

Side Effect: Any unintended effect of a pharmaceutical product occurring at doses normally used in humans, which is related to the pharmacological properties of the medicine.

Signal: Reported information on a possible causal relationship between an adverse reaction and a drug, the relationship being unknown or incompletely documented previously. Usually, more than a single report is required to generate a signal, depending upon the seriousness of the reaction, the quality of the reaction, and the quality of the information.

Spontaneous Reporting: A system whereby case reports of adverse drug reactions are voluntarily submitted from health professionals and pharmaceutical manufacturers to the national regulatory authority.

Unexpected Adverse Reaction: An adverse reaction, the nature or severity of which is not consistent with domestic labeling or market authorization, or expected from characteristics of the medicine.

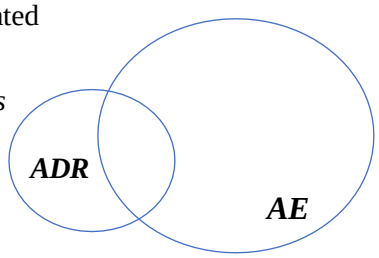
4 Content

4.1 What is Pharmacovigilance?

According to the WHO, Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problem.

This term is expanded to include other pharmaceutical products and Medical devices as well.

Adverse drug reaction (ADR) Vs. Adverse Events (AE)



Adverse drug reaction is any response that is noxious and unintended, and which occurs at doses normally used in humans for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function.
Adverse Event is any untoward medical occurrence that may present during treatment with a pharmaceutical product but which does not necessarily have a causal relationship with this medicinal product.
An adverse drug reaction is distinguished from an adverse event by; the former has a suspicion of a causal relationship between the medicinal product and the reaction, i.e. judged as being at least possibly related to the reaction by the reporting or the reviewing health professional, while the adverse event does not necessarily have such causal relationship.

Importance of Pharmacovigilance

The information about pharmaceutical products collected during the pre-marketing phase is incomplete about adverse drug reactions and this is mainly because:

- Patients enrolled in clinical trials are limited in number and are not representative of the public at large.
- In addition, the conditions of use of medicines differ from those in clinical practice and the duration is limited.
- Information about rare but serious adverse reactions, chronic toxicity, use in special groups (such as children, the elderly, or pregnant women), or drug interactions is often incomplete.

  - ❖ Therefore, monitoring the pharmaceutical products in the post-marketing settings is important to permit detection of less common but sometimes very serious ADRs. Therefore, healthcare professionals worldwide should report on Adverse Reactions as they can save the lives of their patients and others.

Objectives of Pharmacovigilance

- ✓ To improve patient care and safety about the use of pharmaceutical products
- ✓ To improve public health and safety concerning the use of pharmaceutical products.
- ✓ To detect problems related to the use of pharmaceutical products and communicate the findings promptly.
- ✓ To contribute to the assessment of the benefit, harm, effectiveness, and risk of medicines, leading to the prevention of harm and maximization of benefit
- ✓ To encourage the safe, rational, and more effective (including cost-effective) use of medicines; and
- ✓ To promote understanding, education, and clinical training in pharmacovigilance and its effective communication to health professionals and the public.

4.2 WHO Program for International Drug Monitoring (PIDM)

As a means of pooling existing data on ADRs, WHO's Program for International Drug Monitoring (PIDM) was started in 1968. Initially, with a pilot project in 10 countries with established national reporting systems for ADRs, the network has since expanded significantly

as more countries worldwide developed national Pharmacovigilance centers for the recording of ADRs. Currently, many countries participate in the program, which is coordinated by WHO together with its collaborating center in Uppsala, Sweden (UMC). The collaborating center is responsible for maintaining the global ADR database, Vigibase.

The WHO Collaborating Center analyses the reports in the database to:

1. Identify early warning signals of serious adverse reactions to medicines.

2. Evaluate the hazard

3. Undertake research into the mechanisms of action to aid the development of safer and more effective medicines.

Through an advisory committee, WHO plays an important role in the provision of expert advice on all matters relating to the safety of pharmaceutical products. The Committee also exists to facilitate consistent policies and action among member countries and to advise those who may be concerned about action taken in another country.

Nigeria has been a full member of the Program for International Drug Monitoring since 2004, allowing communication with vigilance centers globally and access to safety information gathered globally, and sharing the collected Nigerian data with the Global database.

Introduction to the Nigerian National Pharmacovigilance System

The Nigerian National Pharmacovigilance Centre (NPC) was established within the National Agency for Food and Drug Administration and Control (NAFDAC) in response to the global need for monitoring the safety of medicines. Launched in 2004, it operates under the Pharmacovigilance Directorate, playing a crucial role in safeguarding public health by ensuring pharmaceutical products' safety, efficacy, and quality throughout their life cycle. NPC acts as the regulatory body overseeing pharmaceutical companies in matters relating to drug safety, in line with national and international standards. To extend its reach and effectiveness, NPC has established regional pharmacovigilance centres across the country, allowing for better collection and dissemination of safety information from all states in Nigeria. This decentralized approach promotes awareness and enhances reporting practices at grassroots levels. The centre actively gathers safety data including adverse drug reactions (ADRs), lack of efficacy, drug interactions, overdoses, misuse, medication errors, off-label use, issues related to substandard and falsified medicines, as well as incidents involving medical devices. By addressing these concerns, NPC ensures the continued safety of the Nigerian population.

4.3 Types of Adverse Drug Reactions:

Type A effects

- Augmented pharmacologic effects - dose dependent and predictable (medicine actions) are those which are due to (exaggerated) pharmacological effects. Type A effects tend to be fairly common, dose related (i.e. more frequent or severe with higher doses) and may often be avoided by using doses which are appropriate to the individual patient. Such effects can usually be reproduced and studied experimentally and are often already identified before marketing.

Type B effects

- Bizarre effects (or idiosyncratic) - dose independent and unpredictable (Patient reactions) characteristically occur in only a minority of patients and display little or no dose relationship. They are generally rare and unpredictable, and may be serious and are notoriously difficult to study. Type B effects are either immunological or non-immunological and occur only in patients, with - often unknown - predisposing conditions. Immunological reactions may range from rashes, anaphylaxis, vasculitis, inflammatory organ injury, to highly specific autoimmune syndromes. Also, non-immunological Type B effects occur in a minority of predisposed, intolerant, patients, e.g. because of an inborn error of metabolism or acquired deficiency in a certain enzyme, resulting in an abnormal metabolic pathway or accumulation of a toxic metabolite. **Examples** are chloramphenicol aplastic anemia and isoniazid hepatitis.

Type C effects

- Chronic effects refer to situations where- often for unknown reasons- the use of a medicine increases the frequency of a "spontaneous" disease. Type C effects may be both serious and common (and include malignant tumors) and may have pronounced effects on public health. *Type C effects may be coincidental and often concern long term effects; there is often no suggestive time relationship and the connection may be very difficult to prove.*

Type D effects

- Delayed effects, example is tardive dyskinesia after decades of using typical antipsychotics.

Type E effects

- End-of-treatment effects refer to the undesired effects of ceasing the drug (withdrawal reactions). Example: opiate withdrawal.

Type F effects

- Failure of therapy.

Seriousness of Adverse drug reactions

A serious adverse event or reaction is any untoward medical occurrence associated with the use of a medical product in a patient that at any dose, the patient outcome is one of the following:

1. *Death:* Report if the patient's death is suspected as being a direct outcome of the adverse reaction.

2. *Life-Threatening*: Report if the patient was at substantial risk of dying at the time of the adverse reaction or if it is suspected that the use or continued use of the product would result in the patients death.

> ***NOTE***
> *The term "life-threatening" in the definition of "serious The term "life-threatening" in the definition of "serious" refers to an event/reaction in which the patient was at risk of death at the time of the event/reaction; it does not refer to an event/ reaction which hypothetically might have caused death if it were more severe.*

3. *Hospitalization (initial or prolonged): Report if admission to the hospital or prolongation of a hospital stay results because of the suspected adverse reaction*

> ***NOTE***
> *"Hospitalization" refers to inpatient hospitalization that includes initial admission to the hospital on inpatient basis.*
> *An emergency room visit, examination or treatment delivered as an outpatient -which does not result in admission to the hospital- does not qualify for this outcome but it should be evaluated for one of the other serious outcomes (e.g., life-threatening; required intervention to prevent permanent impairment or damage; other serious medically important event).*

4. *Disability:* Report if the adverse reaction resulted in a significant, persistent, or permanent disability/ incapacity; (change, impairment, damage, or disruption in the patient's body function/structure, physical activities, or quality of life).

5. *Congenital Anomaly*: Report if there are suspicions that exposure to a medical product in one of the parents before conception or during pregnancy resulted in an adverse outcome in the child (birth defect).

6. *Medically important event or reaction*: Medical and scientific judgment should be exercised in deciding whether other situations should be considered serious such as important

medical events that might NOT be immediately life-threatening or result in death or hospitalization but might cause danger to the patient or might require intervention to prevent one of the other outcomes listed in the definition above. Examples:

- Acetaminophen overdose that could induce hepatotoxicity and require treatment with acetylcysteine to prevent permanent damage;
- Burns from radiation equipment requiring medicine therapy;
- Breakage of a screw requiring replacement of hardware to prevent malunion of a fractured long bone.
- Any suspected transmission via a medicinal product of an infectious agent is also considered a serious adverse reaction.
- Intensive treatment in an emergency room or at home for allergic bronchospasm,
- Convulsions that do not result in hospitalization,
- Development of medicine dependency or medicine abuse

NOTE

- *It is important to note that 'serious' and 'severe' are often used as interchangeable terms but they are not synonyms*
- *Severe is used to describe the intensity of a specific event (as in mild, moderate, or severe); the event itself, however, may be of relatively minor medical significance (such as severe headache).*
- *Seriousness (not severity) is based on patient/reaction outcome.*

The Spontaneous reporting structure is the voluntary and the most common way the regulatory bodies collect safety information for pharmaceutical products and medical devices once they are on the market.

The pharmaceutical product reporting form NAFDAC Yellow form- (Annex I,) is used by the National Pharmacovigilance Center to collect information on medicinal products' ADRs from healthcare professionals and members of the public. Each NAFDAC yellow form concerns an individual case experienced ADRs. There is a special consideration concerning the reporting for vaccines clarified in Appendix I

The Medical Devices Incident User Report Form (Pink Card) (Annex IV, V) is used by NPC to collect information on Medical Devices' incidents from healthcare professionals and members of the public. The Medical Devices Vigilance System is clarified in (Appendix II).

Who should report?

1. Healthcare Professionals are the preferred source of information in pharmaceutical vigilance. This includes:
   - Physicians who prescribe pharmaceutical products and follow up with the patients.
   - Family practitioners, medical specialists, and dentists.
   - Nurses and other health workers who may administer medicines should report relevant adverse drug reactions experienced by their patients.

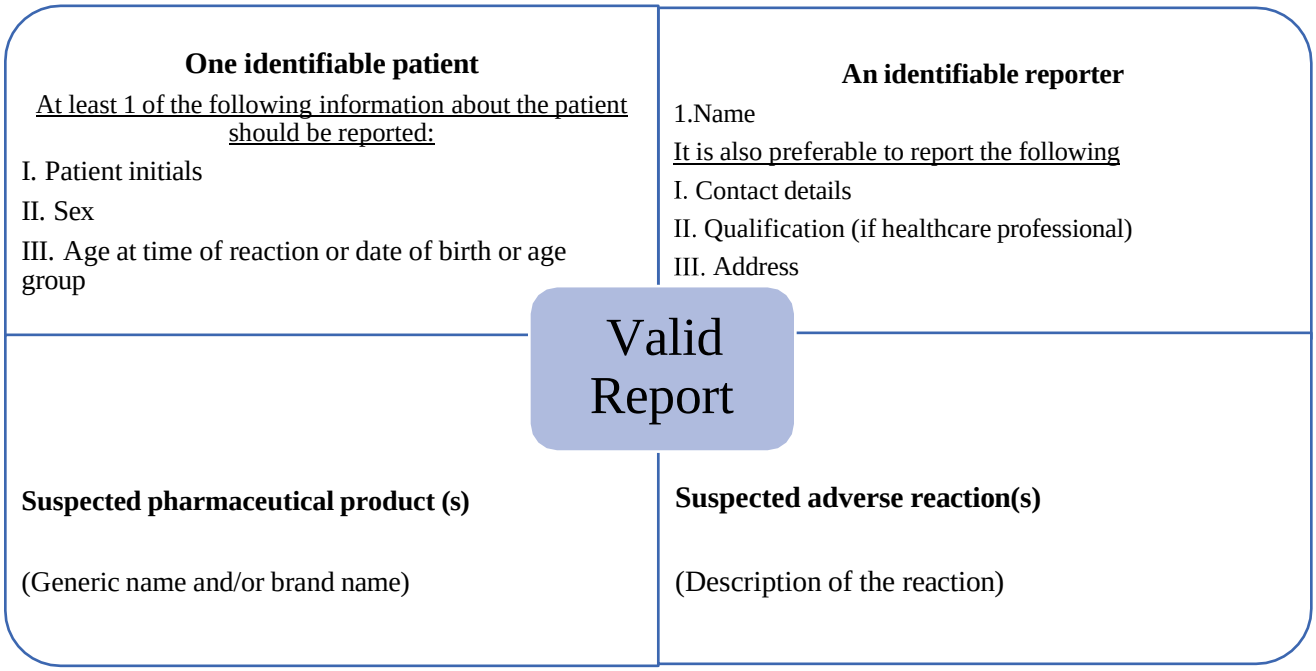
   - Pharmacists who play an important role in the stimulation of reporting and the provision of additional information (for example, on co-medication and previous medicine use).
2. Patients or users and their relatives: They can also report their experienced adverse drug reactions directly to NPC, or through their healthcare professionals. In this case, the patient's permission is sought to contact their healthcare professionals for additional information and data verification.

3. Marketing authorization holder (MAH): As being responsible for the safety of their products, are obligated to report serious adverse drug reactions they receive about their products to NPC.
   - Importers, exporters, and distributors should report directly to the MAHs within the timelines specified in the safety exchange agreement (under the good pharmacovigilance practices guidelines for MAHs).

4.4 Minimum Criteria for a valid report

At least four basic pieces of information should be present for a report to be valid. It should be subsequently entered into the national ADR database and made available for signal generation. When one or more of this information is missing, a follow-up should be done to validate the report and complete its processing as described above.

As follows*:*


One identifiable patient
At least 1 of the following information about the patient should be reported:
I. Patient initials
II. Sex
III. Age at time of reaction or date of birth or age group
An identifiable reporter
1.Name
It is also preferable to report the following
I. Contact details
II. Qualification (if healthcare professional)
III. Address
Valid Report
Suspected pharmaceutical product (s)
(Generic name and/or brand name)
Suspected adverse reaction(s)
(Description of the reaction)

Characteristics of the good case report

The quality of the reports is critical for the appropriate evaluation of the relationship between the product and adverse reaction; thus, a good case report includes the following elements:

1. Description of the adverse reaction, including time to onset of signs or symptoms and the seriousness of the reaction/s; date the reaction stopped, the clinical course of the reaction, and patient outcome with relevant investigation results (if available)
2. Suspected and concomitant medicines details (i.e., Name, strength, dose, frequency, dosage form, route of administration, indication for use, duration of use, and batch number especially for vaccines and other biological products), including over-the-counter medications, dietary supplements, and recently discontinued medications;
3. Patient characteristics, including the initials, age, sex, weight, and baseline medical condition before product therapy, co-morbid conditions, relevant family history of disease, and presence of other risk factors;
4. Documentation of the diagnosis of the reactions, including methods used to make the diagnosis;
5. Clinical course of the reaction and patient outcomes (e.g., hospitalization or death);
6. Relevant therapeutic measures and laboratory data at baseline, during therapy, and after treatment, including blood levels, as appropriate;
7. Information on dechallenge and rechallenge.
8. Any other relevant information (e.g., other details relating to the reaction or information on benefits received by the patient, if important to the assessment of the reaction).

What should be reported?

<u>Any suspected adverse reaction</u> that a patient has experienced should be reported, especially the following:

Medicines under additional monitoring*:* When new drugs and vaccines are first marketed, they are intensively monitored to confirm the product's risk/benefit profile.

- For established medicines or well-known medicines report all serious or unusual, unexpected suspected adverse reactions.
- Report if an increased frequency of a given reaction is suspected.
- Report all suspected ADRs associated with drug-drug, drug-food, or drug-food supplements (including herbal and complementary products) interactions.

- Report ADRs in special fields of interest such as:
  - ADRs occurring from overdose or medication error.
  - Medicine abuse and misuse.
  - Medicine use in pregnancy (including teratogenicity) and during lactation.
  - In children under the age of 18, all suspected ADRs occurring, should be reported regardless of whether the medicine is licensed for use in children. Children are often not exposed to medicines during clinical trials and many medicines are used in children even if they are not licensed for this purpose. This means that monitoring of medicine safety is particularly important for this age group.

  - ADRs in Geriatrics: since they are more likely to experience them as a result of age-related increases in the frequency of drug use, sensitivity to drug effects, and prevalence of predisposing conditions.
  - ADRs in patients with impaired kidney or liver function, ADRs are more frequent among them because of alterations in their pharmacokinetics and pharmacodynamics parameters and multiple comorbidities

How to recognize ADRs in patients?

As soon as possible
*Reports on **all suspected** adverse reactions*
- known or not, serious or not –are welcome and useful
*If there is any doubt about whether or not, it is an ADR; it is always **the best practice to submit***

ADRs are difficult and sometimes impossible to distinguish from the disease being treated since they may act through the same physiological and pathological pathways. However, the following approach helps assess possible drug-related ADRs:

1. Ensure that the medicine ordered is the medicine received and taken by the patient at the dose advised.
2. Take a proper history and do a proper examination of the patient
   - ✓ A full medicine and medical history should be taken
   - ✓ An ADR should be your first differential diagnosis at all times
   - ✓ Ask if the adverse reaction can be explained by any other cause e.g. Patient's underlying disease, other medicines including over-the-counter medicines or traditional medicines, toxins or foods
   - ✓ It is essential that the patient is thoroughly investigated to decide what the actual cause of any new medical problem is.

- ✓ A medicine-related cause must be considered, especially when other causes do not explain the patient's condition

3. Establish time relationships by answering the following question: Did the ADR occur immediately following the medicine administration?
   Some reactions occur immediately after the medicine has been given while others take time to develop. The time from the start of therapy to the time of onset of the suspected reaction must be logical.
4. Carry out a thorough physical examination with appropriate laboratory investigations if necessary. Try to describe the reaction as clearly as possible- Where possible, provide an accurate diagnosis.
5. The effect of Dechallenge and Rechallenge should be determined
6. Check the known pharmacology of the medicine
7. Check if the reaction is known to occur with the particular suspected medicine as stated in the package insert or other reference
   - ✓ Remember: if the reaction is not documented in the package insert, it does not mean that the reaction cannot occur with that particular suspected *medicine.*

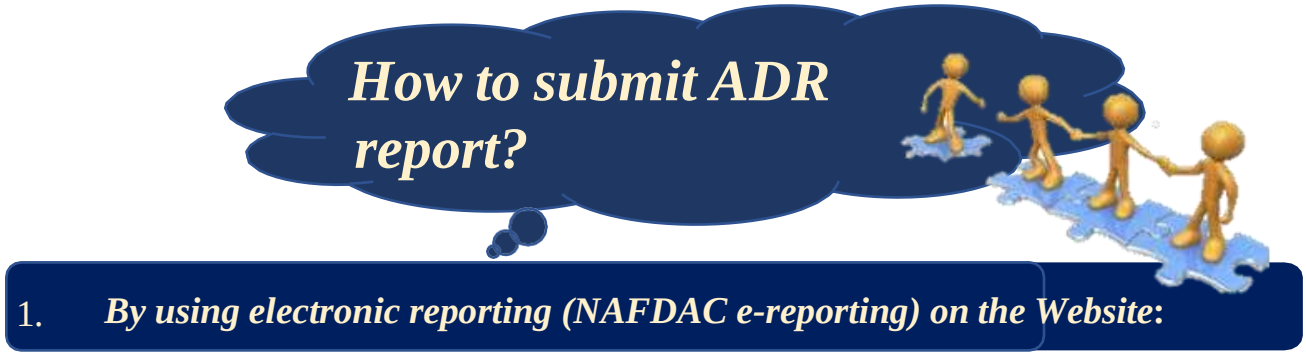
What are the benefits of these reports for the patients and the health care providers?

The reporting by the healthcare provider and patient is completely voluntary, they will stand to benefit

- Improvement in the quality of care offered to patients
- Reduction of medicine-related problems leading to better treatment outcome
- Improved patient confidence in professional practice, hence professional growth
- Improved knowledge
- Access to feedback information on medicine-related problems reported within the country and internationally

Will reporting have any negative consequences on the reporter?

- The adverse drug reaction report does not constitute an admission that the reporter or any other health professional or the medicine contributed to or caused the reaction in any way.
- The names of the reporters / any other health professionals named on the report and the patient will be removed before any details about a specific adverse drug reaction are used or communicated to others.
- The information obtained from the report will not be used for commercial purposes. It is only meant to improve our understanding and safe use of medicines in Nigeria.



1. ***By using electronic reporting (NAFDAC e-reporting) on the Website:***

https://vigiflow-eforms.who-umc.org/ng/adr

(If the link does not take you to the form, copy the link on your browser and that takes you to the form).

Alternatively, the form may also be accessed through the NAFDAC website: https://www.nafdac.gov.ng/

2. By using the Med Safety mobile APP:

- Open Play Store (Android) or App Store (iOS)
- Search **"Web Radr"** or a keyword e.g **"Med Safety App"**
- Tap the **"Med Safety"** icon
- Tap **'Install**' to download the app to your smartphone
- Tap **"Open"**–
- Select **"Nigeria"** as your country of choice which takes you to the log-in page with the **"NAFDAC logo"**
- Key in a functional e-mail address and a password which must have a minimum of 8 alphanumeric characters and a symbol

Click **"Create an account"** as a new user

3. *In case of using the printed NAFDAC yellow.form:*

After filling out the form; it can be sent to the NPC by:

Website: www.nafdac.gov.ng (NA)

Address: Any NAFDAC Office nearest to you

E-mail: pharmacovigilance@nafdac.gov.ng

Hotline:

Adverse reaction resulting from vaccines, can be reported through the above-mentioned ways. However, for mandatory vaccines; it is better to report to the Health facility where the vaccine was given.

4.5 Remember: The Basic principles of efficient reporting

- **In-time reporting**
  - ✓ Report the suspected adverse drug reaction as soon as it occurs.
  - ✓ Send the report quickly to the National Pharmacovigilance Centre.

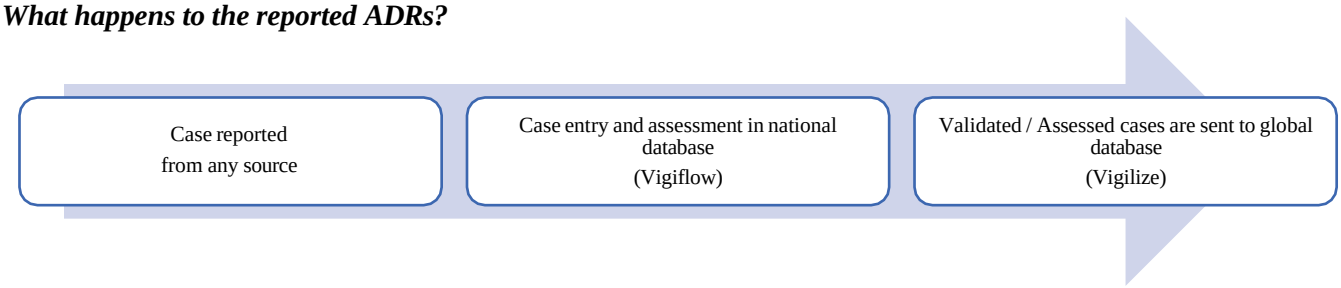
- **Suspicion:**
  - ✓ Continue your suspicion of the medicine-induced illness in the same patient and in other patients. You don't have to be sure to report.
  - ✓ Be Vigilant for signs and symptoms that indicate Adverse Reactions

- **Follow-up**
  - ✓ Follow – up with the patient (if possible) to know the reaction(s) outcome and document it with any new available supplementary information to submit to the National Pharmacovigilance Centre as a "Follow–up" report
  - ✓ When submitting a "Follow–up" report, clearly state that it is "a follow-up report" and include enough details to allow accurate linking to the originally submitted report (especially patient's identifiers such as initials, age, weight, and patient's file number)

- **Accuracy and completeness**
  - ✓ Ensure that each reported suspected adverse reaction is accurate with all the necessary information, as much as is available to you. This is very important for accurate causality assessment of the medicine to have caused that reaction.

  - ✓ Remember the 4 basic components that make a report valid are:
    i. One identifiable patient
    ii. Identifiable reporter
    iii. One or more adverse reactions or product problem
    iv. One or more pharmaceutical products (suspected)
    If the above information is missing, the report will not be valid
  - ✓ Remember to fill in all information accurately and in clear legible writing

What happens to the reported ADRs?



- A healthcare professional or a marketing authorization holder reports a suspected adverse drug reaction related to one or more pharmaceutical products, to NPC. Reports are made in writing (e.g. using reporting forms) or electronically via the e-reporting link or through the Med Safety App.
- Reports are collected, collated, validated, and assessed (causality assessment clarified below) by the NPC and then entered into the national database. Serious reactions are handled with the highest priority. The details of the report are stored in the national database and submitted to the global database (monitored by the Uppsala Monitoring Center (UMC) for more analysis.
- The information compiled in the national database is used to identify potential signals,

clarify risk factors and apparent changes in reporting profiles, and promote safe use of medicines at the local, national, and international levels.

- A suitable action may be recommended accordingly, such as:
  - Requesting Additional investigations into the use of a pharmaceutical product
  - Appropriate changes in the package insert
  - Enhancing educational initiatives to improve the safe use of pharmaceutical products
  - Other regulatory and health promotion interventions as the situation may warrant including withdrawal/recall.

Thus, the ultimate purpose of ADR reporting and monitoring is to reduce risks associated with drug prescribing and administration and improve patient care, safety

4.6 Causality assessment

Causality is the relationship between two events (the cause and the effect), where the second event is a consequence of the first.

Causality assessment is the method by which the extent of the relationship between a medicine and a suspected reaction is established i.e. to attribute clinical events to medicines in individual patients or in case reports.

NPC Adopts the WHO probability scale

Term	***Description***
Certain	▪ A clinical reaction, including laboratory test abnormality, occurring in a plausible time relationship to medicine administration, and which ▪ Cannot be explained by concurrent disease or other medicines or chemicals. ▪ The response to withdrawal of the medicine (dechallenge) should be clinically plausible. ▪ The reaction must be definitive pharmacologically or phenomenologically, (i.e. an objective and specific medical disorder or a recognized pharmacological phenomenon) ▪ Using a satisfactory rechallenge procedure if necessary.

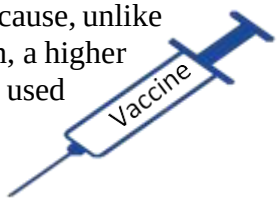
Probable / Likely	▪ A clinical reaction, including laboratory test abnormality, with ▪ A reasonable time sequence for administration of the medicine, ▪ Unlikely to be attributed to concurrent disease or other medicines or chemicals, and which ▪ Follows a clinically reasonable response on withdrawal (dechallenge). ▪ Rechallenge information is not required to fulfill this definition.
Possible	▪ A clinical reaction, including laboratory test abnormality, with ▪ A reasonable time sequence to the administration of the medicine, but which could also be explained by concurrent disease or other medicines or chemicals. ▪ Information on medicine withdrawal may be lacking or unclear.
Unlikely	▪ A clinical reaction, including laboratory test abnormality, with ▪ a temporal relationship to medicine administration which makes a causal relationship improbable, and ▪ Other medicines, chemicals, or underlying diseases provide plausible explanations.
Conditional/ Unclassified	Event or laboratory test abnormality ▪ More data for proper assessment needed, or ▪ Additional data under examination

Unassessable/ Unclassified	A report suggesting an adverse reaction ▪ Cannot be judged because the information is insufficient or contradictory ▪ Data cannot be supplemented or verified

*The terms "Conditional/unclassified" and "Unassessable/unclassifiable" are not causality terms, they describe the status of adverse reaction reports and therefore allow for practical communication about ADR issues.

4.7 Appendix I

Adverse Event Following Immunizations (AEFI)



The general public has a low tolerance to any adverse events following vaccination because, unlike medications, vaccines are given to healthy persons to prevent disease. For this reason, a higher standard of safety is expected of immunizations compared with medications that are used to treat people who are sick. This lower tolerance for risks from vaccines translates into a greater need to detect and investigate any adverse event following immunization (AEFI) than is generally expected for other pharmaceutical products. Vaccine pharmacovigilance aims to detect adverse events early to trigger accurate risk assessment and appropriate response to the problem and to lessen the potential negative impact on

users and immunization programs

AEFI categories:

AEFIs are divided into 5 categories as follows

Vaccine product-related reaction:	• An AEFI that is caused by a vaccine due to one or more of the inherent properties of the vaccine product. • Example: Extensive limb swelling following DTP vaccination.
Vaccine quality defect-related reaction:	• An AEFI that is caused or precipitated by a vaccine that is due to one or more quality defects of the vaccine product including its administration device as provided by the manufacturer
Immunization error-related reaction:	• An AEFI that is caused by inappropriate vaccine handling, prescribing or administration and thus by its nature is preventable. such as: o Reconstitution of vaccines with an incorrect diluent. o Inadequate shaking of vaccine. • Injection at incorrect site
Immunization Anxiety-related reaction:	• An AEFI arising from anxiety about the immunization. • Example: Vasovagal syncope that leads to fainting in an adolescent during/following vaccination.
Coincidental event:	• Event occurs after a vaccination has been given but is not caused by the vaccine or its administration.
	• i.e. AEFI that is caused by something other than the vaccine, immunization error or immunization anxiety. • Example: A fever occurs at the time of the vaccination (temporal association: Two or more events that occur around the same time.

Who should report an AEFI?

- As mentioned before, all HCPs should report adverse reactions. Health workers (workers at immunization facilities and staff of accident and emergency rooms in hospitals) have the responsibility to detect AEFIs and report AEFIs when appropriate.
  They also have the responsibility to treat or refer patients for treatment.
- Parents of vaccinated children and any vaccine user who experienced adverse events believed to be because of the vaccine should report

Which AEFIs should be reported?

Any AEFI that is of concern to the parents or to the healthcare worker should be reported.

Especially:

1. Serious AEFIs
2. Any adverse events associated with a newly introduced vaccine.
3. AEFIs that may have been caused by an immunization error.
4. Significant events of unexplained cause occurring within 30 days after vaccination. (Recommended by WHO to be investigated)
5. Events causing significant parental or community concern.
   Example: HHE (Hypotonic-Hyporesponsive Episodes, Seizures)
6. Swelling, redness, soreness at injection site if it last for more than 3 days or swelling extended to the nearest joint.
7. Any clusters of minor AEFIs.

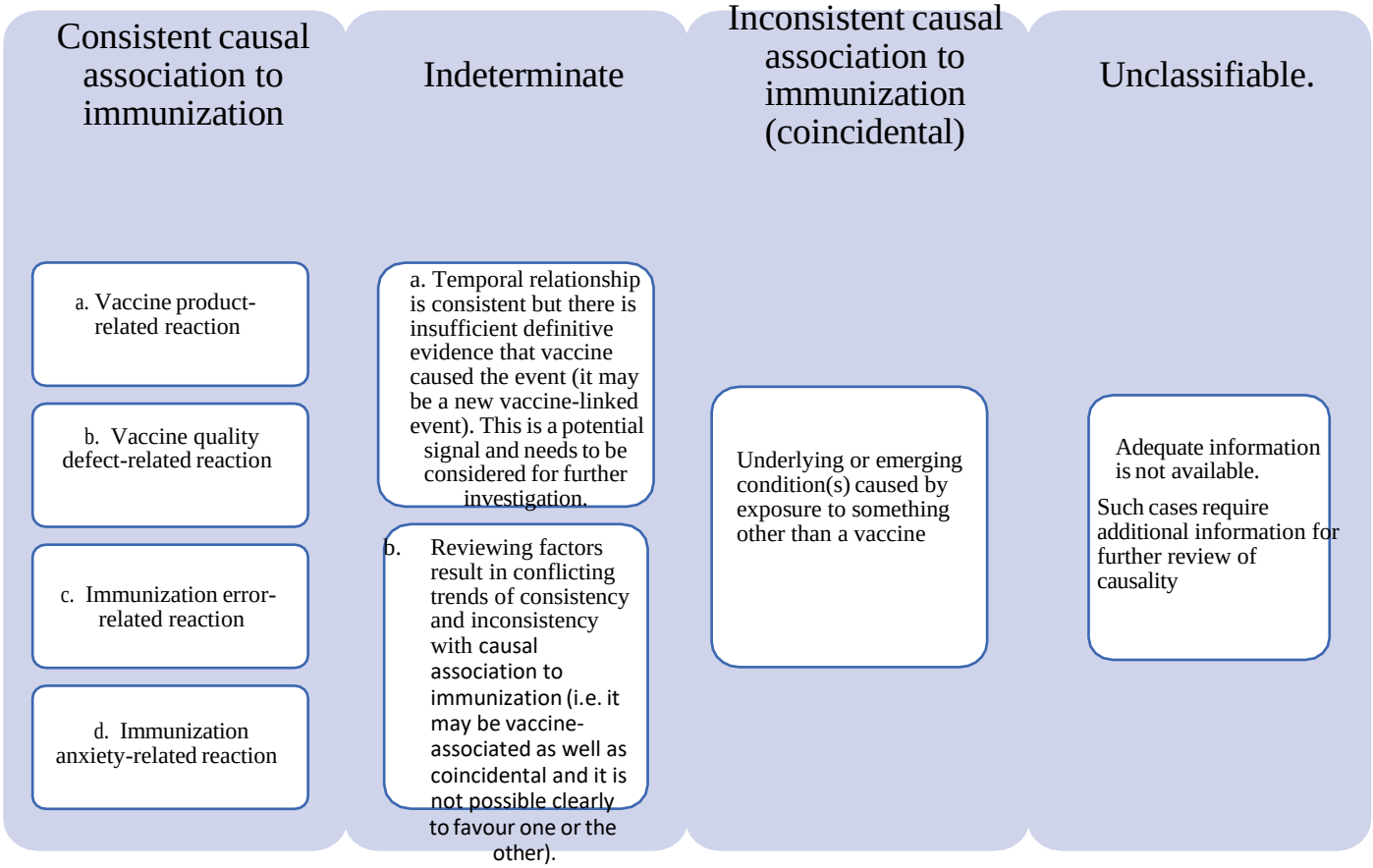
AEFI reporting form:

AEFI can be reported on vaccines specific reporting form (annex II), those forms should be filled and submitted through the previously mention routes.

Causality Assessment of AEFIs:

Causality assessment is the systematic review of data about an AEFI case. It determines the likelihood of a causal association between the event and the vaccine(s) received.

An AEFI with adequate information for a causality conclusion can be classified as follows:



4.8 Appendix II

MEDICAL DEVICES VIGILANCE SYSTEM

It is critically important that the safety and performance of medical devices are continually assessed when they are in use i.e. post-marketing, as the information collected during the pre-marketing phase is incomplete with regard to adverse incidents and this is mainly because:

- Data available in the pre-marketing review process cannot predict all possible device failures or incidents arising from device misuse in the post-marketing phase.
- It is through actual use that unforeseen problems related to safety and performance can occur.

Medical device means any instrument, apparatus, appliance, software, implant, reagent, material or other article intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the following specific medical purposes:

- diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease,
- diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury or disability.
- investigation, replacement or modification of the anatomy or of a physiological or pathological process or state.
- providing information by means of in vitro examination of specimens derived from the human body, including organ, blood and tissue donations, and which does not achieve its principal intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its function by such means.

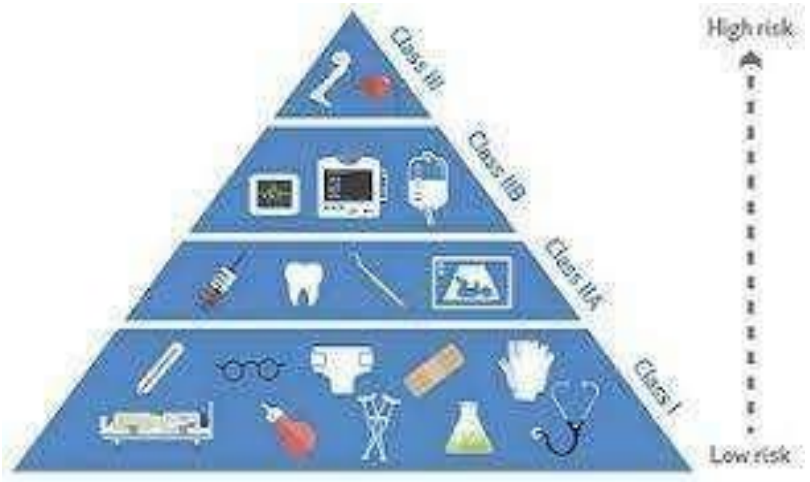
The following products shall also be deemed to be medical devices:

- Devices for the control or support of conception;
- Products specifically intended for the cleaning, disinfection or sterilization of devices.

Classification of Medical Devices:

Devices shall be divided into classes I, IIa, IIb and III, taking into account the intended purpose of the devices, their inherent risks, the duration of contact with the patient, the degree of invasiveness and the part of the body affected by the use of the device

The Medical Device Vigilance System was set up under the medical device directives to minimize risks to the safety of patients, users and others.



Medical device safety issues can be identified through manufacturer or health professional (user) reporting, through identification and reporting of issues by members of the public, or through information sharing with other competent authorities.

Objectives of the Vigilance System are:

1. To improve the protection of the health and safety of patients, users, and others by reducing the repetition of the same type of adverse incident.
2. To enable the competent authorities to monitor the effectiveness of the Manufacturers' follow-up on reported incidents.
3. To facilitate direct and early implementation of Field Safety Corrective Actions (FSCAs).
4. To enable the healthcare professionals and users who are responsible for the maintenance and the safety of medical devices to take the necessary steps once the corrective (or other) action is identified.
5. Competent authorities may also monitor experience with devices of the same kind (for instance, all defibrillators or all syringes), but made by different manufacturers.

The Medical device vigilance system achieves its objectives in several ways:

- Through manufacturers and users submitting vigilance reports to the relevant competent authorities (The National Agency for Food Drug Administration and Control - NAFDAC).
- Through the evaluation of reported incidents by the competent authorities.
- Through the dissemination of information, which may be used to prevent recurrence of the

incident, or to alleviate the consequences of such incidents, in cases when it's necessary to do so.

- By the device being updated, modified or taken off the market in cases when it's necessary to do so.

Vigilance issues can be related to an adverse incident or field safety corrective actions.

4.9 Responsibilities of the Users

USERs are encouraged to have an active role in the Vigilance System. Furthermore, for the successful operation of the vigilance system to be established, their involvement is vital. It is through the users that:

- Suspected incidents are made known to the manufacturers, and
- With their close involvement and cooperation, the implementation of FSCAs is made possible.

The involvement of users is promoted and encouraged through the relationship the manufacturer develops with his customer (the user). This user involvement may also be reinforced by separate advice from the National Pharmacovigilance Centre NAFDAC.

1. Reporting Guidance

An adverse incident is an event during the use of the device which might lead to or might have led to the death of a patient, user or other persons or to a serious deterioration in their state of health. This should be reported to the NPC/NAFDAC.

1.1. What to Report

USERs or those given specific responsibility for reporting incidents that have occurred with medical devices should report incidents that meet the criteria within this guideline to the manufacturer and/or to NPCNAFDAC.

1.2. Who Should Report

The NPC/NAFDAC strongly encourages those who have experienced a safety issue with a medical device to report that issue to us. A voluntary reporting system is currently operated for users of medical devices, healthcare professionals or any other person who identifies a medical device safety issue.

1.3. When to Report

USERs are encouraged to report all adverse incidents as soon as possible. Serious cases ought to be reported by the fastest means possible. Initial incident reports should contain as much relevant detail (e.g. Medical Device name, type, model … etc.) as is immediately available, but reporting ought not to be delayed for the sake of gathering additional information.

1.4. How to Report

The USERs are encouraged to use the "USER Reporting Form - in accordance with this guidance and to provide contact details when reporting to the manufacturer or NPC/NAFDAC. (Annex 111)

1.5. What to Do with the Device

- All items and relevant packaging materials should be quarantined, not repaired or discarded.
- The device should be returned to the manufacturer in accordance with their instructions unless otherwise required by NPC/NAFDAC or other legal requirements.
- USERS ought to contact the manufacturer to obtain information about the procedure for returning the suspect device. The device should be appropriately decontaminated, securely packaged, and clearly labeled, including the CA (Registration No.) or manufacturer reference number if needed.

- Medical devices ought not to be sent to NPC/NAFDAC unless it has been specifically requested.

1.6. Further Local Information

Reporters are encouraged to cooperate with the manufacturer and NPC/NAFDAC by providing further information

- Concerning incidents which should become available e.g. relevant outcomes of internal investigations.
- Concerning the device or patient outcomes e.g. subsequent death.

2. Field Safety Corrective Actions Guidance

A field safety corrective action (FSCA) is an action taken by a MANUFACTURER to reduce a risk of death or serious deterioration in the state of health associated with the use of a medical device that is already placed on the market. Such actions, whether associated with direct or indirect harm, should be reported and should be notified via a Field Safety Notice (FSN). The Field Safety Corrective Actions (FSCA) may include, for example:

- The repair/replace/return of a medical device to the supplier;
- Device modification/adjustment/relabelling;
- Advice given by manufacturer regarding the use of the device and/or the follow-up (monitoring) of patients, users or others.

2.1. Importance of Field Safety Notices (FSNs)

Field Safety Notices are an important means of communicating safety information to medical device users in all healthcare areas. Field Safety Notices may also be used to provide updated information and request feedback.

It is therefore important that users are encouraged to develop effective closed loop systems that ensure the dissemination of the Field Safety Notices and the timely completion of the actions outlined.

2.2. Distribution

Healthcare organizations should be encouraged to help ensure that the FSN reaches all in the organization that needs to be aware and/or take the recommended action.

2.3. Action

USERs responsible for the maintenance and the safety of medical devices are encouraged to take actions advised in the manufacturer's Field Safety Notice. These actions ought to be taken in co-operation with the manufacturer where required. They may also include associated actions recommended by NPC/NAFDAC and/or inspection department in connection with the FSCA, including providing any requested feedback.

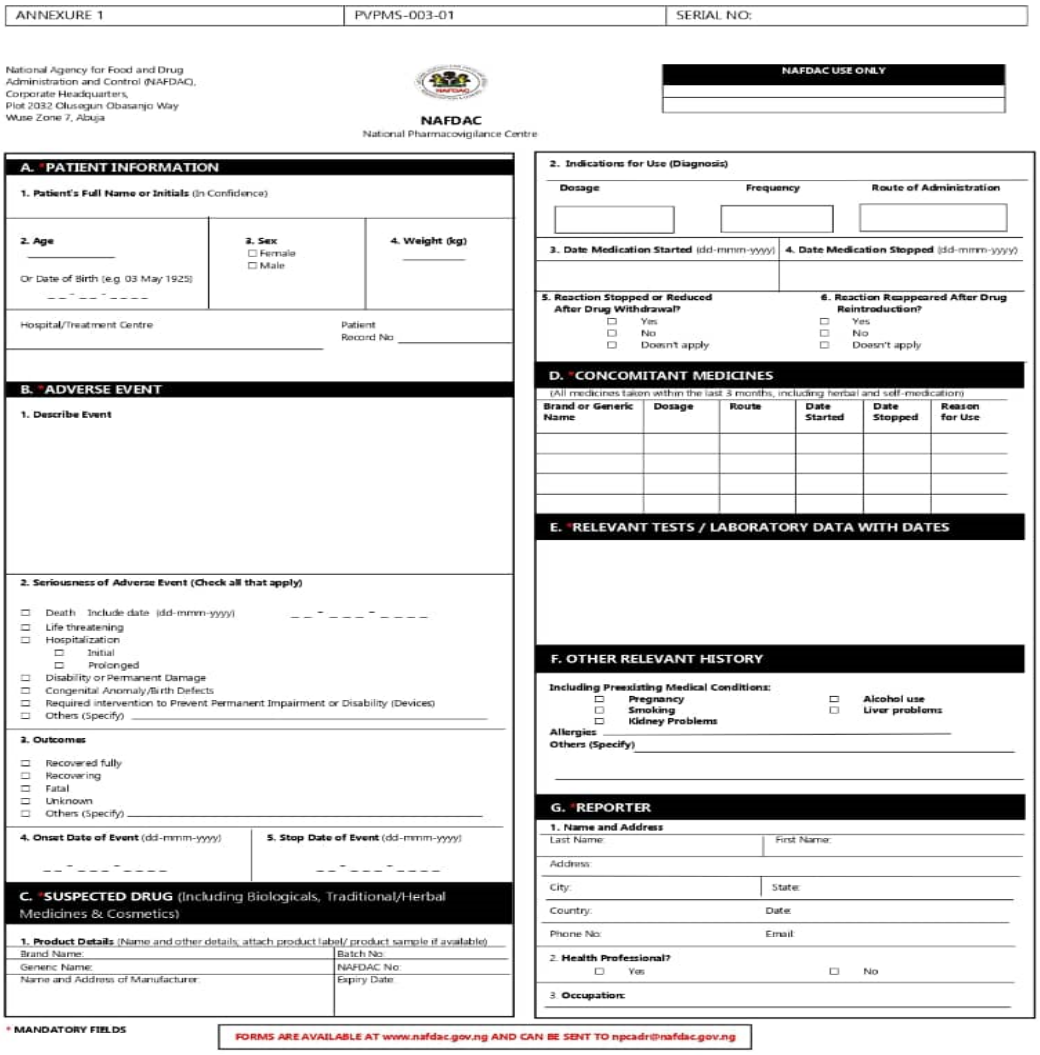
2.4. Access to Devices

USERs are responsible for the maintenance and the safety of medical devices and are encouraged to:

a. Facilitate manufacturer access to the device if this is required, and
b. Work with the manufacturer when needing to balance the individual risks and benefits for any dependent patients using affected devices.

5 Annexes:

5.1 ANNEX I: NAFDAC ADR Reporting Form



ANNEXURE 1	PVPMS-003-01	SERIAL NO:

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

NAFDAC
National Pharmacovigilance Centre

NAFDAC USE ONLY

A. *PATIENT INFORMATION

1. **Patient's Full Name or Initials** (In Confidence)

2. **Age** _____
Or Date of Birth (e.g. 03 May 1925)
__ - __ - ____

3. **Sex**
☐ Female
☐ Male

4. **Weight (kg)** _____

Hospital/Treatment Centre

Patient Record No

B. *ADVERSE EVENT

1. **Describe Event**

2. **Seriousness of Adverse Event (Check all that apply)**

☐ Death Include date (dd-mmm-yyyy) __ - ___ - ____
☐ Life threatening
☐ Hospitalization
  ☐ Initial
  ☐ Prolonged
☐ Disability or Permanent Damage
☐ Congenital Anomaly/Birth Defects
☐ Required intervention to Prevent Permanent Impairment or Disability (Devices)
☐ Others (Specify) _____

3. **Outcomes**

☐ Recovered fully
☐ Recovering
☐ Fatal
☐ Unknown
☐ Others (Specify) _____

4. **Onset Date of Event** (dd-mmm-yyyy)
__ - ___ - ____

5. **Stop Date of Event** (dd-mmm-yyyy)
__ - ___ - ____

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

1. **Product Details:** (Name and other details, attach product label/ product sample if available)

Brand Name:	Batch No:
Generic Name:	NAFDAC No:
Name and Address of Manufacturer:	Expiry Date:

2. **Indications for Use (Diagnosis)**

Dosage	Frequency	Route of Administration

3. **Date Medication Started** (dd-mmm-yyyy)

4. **Date Medication Stopped** (dd-mmm-yyyy)

5. **Reaction Stopped or Reduced After Drug Withdrawal?**
☐ Yes
☐ No
☐ Doesn't apply

6. **Reaction Reappeared After Drug Reintroduction?**
☐ Yes
☐ No
☐ Doesn't apply

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

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

E. *RELEVANT TESTS / LABORATORY DATA WITH DATES

F. OTHER RELEVANT HISTORY

Including Preexisting Medical Conditions:
☐ **Pregnancy**
☐ **Smoking**
☐ **Kidney Problems**
☐ **Alcohol use**
☐ **Liver problems**

Allergies _____
Others (Specify) _____

G. *REPORTER

1. **Name and Address**

Last Name:	First Name:
Address:	
City:	State:
Country:	Date:
Phone No:	Email:

2. **Health Professional?**
☐ Yes ☐ No

3. **Occupation:**

* **MANDATORY FIELDS**

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

ANNEX II: AEFI Reporting Form

FEDERAL REPUBLIC OF NIGERIA
FEDERAL MINISTRY OF HEALTH

Identification number /_____ - _____ - _____ - _____ - _____/ to be assigned by the LGA DSNO
Country code – State code – LGA code — Year – Case number

REPORTING FORM

ADVERSE EVENTS FOLLOWING IMMUNIZATION (AEFI)

This form should be filled by the health worker in charge of the patient and sent to the LGA DSNO
Fill this form ***for ALL (serious and non serious*** *AEFI)*

1. REPORTING **Date of report :** ____/____/_____

Date of reporting ___/___/___	Full Names of the person reporting	Designation of person reporting ☐Physician ☐Pharmacist ☐Nurse ☐Other (specify)	Telephone number/email	Signature of the person reporting
State :	LGA	Ward	Health Facility/Vaccination Center	

2. PATIENT's IDENTIFICATION

First / Last name	Full Address (with landmarks)	Birth-date dd/mm/yyyy ___/___/___	Age _____years _____months	Sex (tick) ☐M ☐F

Past medical history (including history of similar reaction or other allergies), concomitant medication and other relevant information (e.g. other cases). *Use additional sheet if needed:*

3. VACCINES ADMINISTERED

Name of Vaccines Received within last 30 days	*Date of vaccination*	*Time of vaccination*	*Dose (e.g. 1st, 2nd...)*	*Administration*		*Batch/ Lot number*
				Route	*Site*	
						Vaccine
						Diluent
						Vaccine
						Diluent
						Vaccine
						Diluent
						Vaccine
						Diluent

Intervention: ☐Routine immunization ☐SIA ☐Other prescription (specify)_____
Strategy: ☐Fixed ☐Outreach ☐Mobile

4. ADVERSE EVENTS

Describe the AEFI (signs and symptoms)	Date & Time AEFI started (DD/MM/YYYY): ☐☐ /☐☐ /☐☐☐☐ . ☐☐ Hr ☐☐Min Was the patient hospitalized? ☐Yes ☐No Date patient notified event to health facility (DD/MM/YYYY): ☐☐ /☐☐ /☐☐☐☐
Treatment(s) received	Was this a serious AEFI? (tick) ☐Yes ☐No - ☐Hospitalised - ☐Incapacitated - ☐Life Threatening - ☐Death
Outcome: ☐ Recovering ☐ Recovered Completely ☐ Recovered with sequelae ☐ Not Recovered ☐ Unknown ☐ Died Date of latest information on the outcome (DD/MM/YYYY): _____ /_____ /_____	

Toll free numbers 08031230415 / 0803120416 ⋆ Send free sms to 20543 (PRASCO)

DOCUMENTATION AT STATE LEVEL :

Date AEFI report received from the LGA

Quality score of the report: ☐ Q0 ☐Q1 ☐ Q2 ☐ Q3 ☐ Q4 If data is incomplete, state the areas of gap:

State actions taken :

5.2 ANNEX III: Medical Device Reporting Form

MEDICAL DEVICE INCIDENT USER REPORT FORM

I. Patient Information:			
Name/Initials:	Sex: ☐ Male ☐ Female	Weight:	Age:
II. Medical Device Information:			
Name Of Medical Device:		Type Of Medical Device:	
Manufacturing Date:		Expiry Date:	
Reference/Registration Number:		Code/Mode No:	
Catalogue No:	Lot/Batch No:	Serial No:	
Manufacturer Name: Address: Phone:		Supplier Name: Address: Phone:	
Quantity Defective (Number):		Current Location:	
Has the manufacturer/supplier been contacted? ☐ Yes ☐ No (Keep the device till the supplier requests it. Please Do not discard the device or related consumables & packing. Do not send medical devices to NPC/NAFDAC unless you have been specifically asked to do so)			
III. Incident Information:			
Incident Description/Nature of Device Defect (includes any action by patient, career or healthcare professional, or by the manufacturer or supplier):			
Action Taken:			
Type of injury: ☐ Death ☐ Serious ☐ Non-Serious ☐ None		Date of Incident:	
IV. Reporter Information (Will Be Kept Confidential)			
Reporter's Name:		Position/Occupation:	
Organisation:		Address:	
Phone/Mobile No:		Email:	
V. Other Comments:			

Headquarters:
National Pharmacovigilance Center
National Agency for Food and Drug Administration and Control

Address:
NAFDAC Corporate Headquarters
Plot 2032, Olusegun Obasanjo Way
Zone 7, Wuse, Abuja, Nigeria.

For Enquires: 0700-1-NAFDAC (0700-1-623322)
+234(0)-1-4609750

Email: pharmacovigilance@nafdac.gov.ng
Website: www.nafdac.gov.ng

North Central Zonal Pharmacovigilance Centre Office:
University of Ilorin Teaching Hospital, Ilorin Kwara State.
North West Zonal Pharmacovigilance Centre Office:
Ahmadu Bello University Teaching Hospital Zaria, Kaduna State.
North East Zonal Pharmacovigilance Centre Office:
University of Maiduguri Teaching Hospital, Borno State.
South-South Zonal Pharmacovigilance Centre Office:
University of Benin Teaching Hospital, Edo State.
South West Zonal Pharmacovigilance Centre Office:
Lagos University Teaching Hospital Lagos State.
South East Zonal Pharmacovigilance Centre Office:
Federal University Teaching Hospital Owerri, Imo State.

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