PHARMACOVIGILANCE NEWSLETTER

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Ensuring Vaccine Safety, Statistical summary of AEFIs

Content

Health professionals and patients are encouraged to **report adverse events** or **quality problems** experienced with the use of **vaccines and medicines** to the nearest NAFDAC office or via pharmacovigilance@nafdac.gov.ng or via eReporting platform available on the NAFDAC website www.nafdac.gov.ng or via Med Safety Application available for download on Android and IOS stores.

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EDITOR'S NOTE...

We wish to thank our numerous stakeholders who have been working tirelessly with the National Pharmacovigilance Centre (NPC) to ensure the safe use of medicines in Nigeria. The NPC is committed to sending out the quarterly newsletter to its stakeholders. The objectives of the Newsletter are to disseminate information on Pharmacovigilance activities nationally and globally, to educate stakeholders on medicine safety issues, to promote rational use of drugs and to promote reporting of Adverse Drugs Reactions (ADRs) and AEFIs. This edition of the newsletter focuses on: **Ensuring Vaccine Safety, Statistical summary of AEFIs**

We encourage Health care Professionals and other stakeholders to continue to report all adverse drug reactions and AEFIs. Your valued comments and acknowledgement of receipt of this issue through our email addresses (pharmacovigilance@nafdac.gov.ng, fdic@nafdac.gov.ng) would be most appreciated.

Thank you for your relentless efforts in strengthening Pharmacovigilance System in Nigeria.

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Introduction

Vaccines and other essential health technologies are among the main therapeutic tools used by health professionals for the prevention of diseases. Like other medical products, the administration and use of vaccines may produce adverse effects, requiring continuous vigilance to ensure that the benefits outweigh the risks. Safety monitoring (pharmacovigilance) should therefore be more explicit in efforts to strengthen health systems and prepare for pandemics (Wang et al, 2023). As new vaccines become available to prevent new diseases globally, the demand for effective pharmacovigilance systems in low- and middle-income countries (LMIC) is increasing. Each year, vaccines prevent more than 2.5 million child deaths world-wide. Usually, by the time vaccines are introduced in low- and middle-income countries (LMIC), experience had been gained over decades helping to understand the safety profile of those vaccines from countries with developed pharmacovigilance systems (Amarasinghe et al, 2013).

Adverse events following immunization (AEFI) may occur because of a vaccination, or purely by chance following a vaccination in a coincidental temporal association; differentiating between these is increasingly complex. Like medicines, no vaccine is 100% safe. However, unlike medicines, vaccines are primarily used in otherwise healthy recipients for prevention at a population level. This places an even greater responsibility upon the principle of primum non nocere (first do no harm), as no symptoms or underlying pathology are being treated at the time of receipt, with potential future benefit being the rationale. Even sizeable clinical trials, with tens of thousands of participants, are unlikely to detect rare or even uncommon adverse events following immunization (AEFI). Post-licensure implementation is a source of information about uncommon and rare adverse events, as well as the safety of vaccines in varied populations, as well as those who may have been excluded from clinical trials. Some examples of proven signals include Vaccine Induced Thrombosis and Thrombocytopenia (VITT) following some adenoviral vectored vaccines, and myocarditis following mRNA vaccines. Vaccine safety concerns may arise due to an apparent increase in the rate of a known AEFI or apparent increased reporting of a presentation not previously described as an AEFI. Even a solitary case of sufficient severity may represent a potential signal. A safety signal in pharmacovigilance has been defined by the WHO in 2002 as "Reported information on a possible causal relationship between an adverse event and a drug, the relationship being previously unknown or incompletely documented." However, it may also occur with an unexpected change in observed rate of an adverse event already established as having a causal relationship (Buttery & Clothier, 2022).

Unfounded vaccine safety concerns have the potential of seriously derailing effective immunization activities and vaccine pharmacovigilance systems have the responsibility to address these issues. Careful monitoring of immunization programs is essential to minimize serious vaccine-associated adverse events although these events are rare (Amarasinghe et al, 2013).

The World Health Organization (WHO) Global Advisory Committee for Vaccine Safety recommended a new case-based indicator of national capacity to monitor immunization safety: at least one serious AEFI reported per 1 million total population per year. To achieve this indicator, WHO countries rely upon data

generated from functional AEFI surveillance systems. Among WHO countries, 51 (24%) of 214 implemented the new indicator in 2020, 111 (52%) of 214 implemented it in 2021, and 92 (43%) of 215 in 2022. In 2020, 19% of the WHO countries reported AEFI data jointly from EPIs and NRAs; this increased to 55 (26%) in 2021 and 57 (27%) in 2022. These findings, resulting in part from the intensified support for COVID-19 vaccination, demonstrate that national AEFI surveillance systems increasingly support the timely use and sharing of case-based immunization safety data, but work is still needed to strengthen global vaccine safety monitoring (Blau, 2023).

The WHO Vaccine Safety Blueprint 2.0 highlighted the need for more comprehensive indicators for national, regional, and global safety surveillance systems. Subsequently, in December 2020, WHO's Global Advisory Committee for Vaccine Safety recommended the adoption of a new case-based indicator for monitoring progress in AEFI surveillance for all age groups: the number of serious AEFIs reported per 1 million total national or subnational population in a year. This case-based reporting indicator was proposed to facilitate accurate AEFI reporting and increase national system sensitivity in detecting vaccine safety signals (Blau, 2023).

In Nigeria, like in many WHO countries, effective AEFI surveillance relies on the collaboration of the national regulatory authorities (NRAs), which are national organizations responsible for ensuring that pharmaceuticals and biologics are properly evaluated and that they meet international standards of quality, safety, and efficiency, as well as the National Primary Health Care Development Agency (NPHCDA). NPHCDA is the the national expanded program on immunization (EPI), the EPIs typically oversee national procurement, storage, and delivery of vaccines, including the staffing and training of health care workers responsible for administering vaccines and caring for patients reporting AEFIs. As a result, NPHCDA plays an important role in identifying and reporting AEFIs. NRAs are mandated to perform post authorization and post licensure AEFI surveillance and must work in tandem with EPIs to support health care–worker training and management of AEFI reports and investigations, including support for independent assessments of causality for serious AEFIs. Coordination of AEFI reporting among EPIs and NRAs improves data quality, completeness, and usability, so that safety signals can be detected and identified quickly (Blau, 2023).

The COVID-19 pandemic response and subsequent national immunization activities likely contributed substantially to the progress in global immunization safety monitoring, especially due to increased funding and provision of intensified technical support from global partners. With nationally focused activities to increase COVID-19 vaccine distribution and vaccination coverage paired with new vaccine safety monitoring approaches (e.g., smartphone applications), the highest proportion of WHO countries meeting the new indicator was observed in 2021. Most AEFI cases reported in 2021 were associated with COVID-19 vaccines, reinforcing that case-based data from national AEFI surveillance systems can be shared globally (to VigiBase). Despite these gains, a slight decrease was observed in the proportion of WHO countries meeting the new reporting indicator in many WHO regions during 2022, likely because of a decline in national COVID-19 vaccination campaigns and less intensive AEFI surveillance. The current findings show that more measures are required to strengthen global vaccine safety monitoring though technical support, standardized tools,

and guidelines, and that more effective approaches to promote nationally coordinated AEFI reporting among EPIs and NRAs are needed (Blau, 2023).

Information systems for monitoring vaccine Safety

Immunization activities in the community relies upon post-licensure vaccine safety surveillance to maintain safe vaccination programs and to detect rare AEFI that were not observed in clinical trials. Various forms of health information related to adverse event following immunization (AEFI) are potentially suitable for vaccine safety surveillance. Each surveillance type has advantages and disadvantages and are often complementary to each other. Most of them are "hypothesis generating," detecting potential safety signals. The Information systems for monitoring vaccine Safety include Spontaneous (passive) surveillance, Active surveillance methodologies, Solicited surveillance, Syndromic surveillance and Data-Linkage (Buttery & Clothier, 2022).

❖ Spontaneous (passive) surveillance and background rates

Spontaneous (passive) surveillance is the mainstay of most national and international pharmacovigilance systems. It relies on health-care workers (and sometimes community members) to report AEFI. Spontaneous systems have the advantage of drawing from the entire population, with the primary disadvantage of under- reporting, even for severe AEFI. The advent of online reporting has facilitated spontaneous surveillance, with some systems. Spontaneous surveillance is the primary mechanism for detecting unexpected and rare AEFI worldwide and is primarily "hypothesis generating" in its nature, with more active surveillance often used to confirm and investigate potential safety signals (Buttery & Clothier, 2022).

❖ Active Surveillance

Active surveillance involves actively looking for AEFI, these could be events known to occur following vaccination, or adverse events of special interest (AESI). Traditional active surveillance includes hospital-based surveillance for AESI, using manual or electronic searching within the hospital. Active surveillance can be both hypothesis generating and allow hypothesis testing (Buttery & Clothier, 2022).

❖ Solicited surveillance

Solicited surveillance was widely deployed as part of COVID-19 vaccine implementation in multiple countries and settings, such as V-SAFE in the United States, the Yellow Card Vaccine Monitor in the United Kingdom and AusVaxSafety in Australia. categorical responses such as specific local and systemic reactogenicity questions allow rapid automated calculation of rates in respondents to assess whether these are similar to those observed in clinical trials or exceed the expected thresholds. (Buttery & Clothier, 2022)

- **Syndromic surveillance**

Syndromic surveillance systems use diagnoses or diagnosis surrogate terms from de-identified near real-time data systems to detect changes in rates of events of interest. Potentially capable of operating at massive scale, the best-known example is the use of Google search terms to detect influenza outbreaks. Syndromic systems carry the potential advantages of broad coverage, high sensitivity, and cost-effectiveness but due to potential lack of specificity are likely to have an adjunctive role in AEFI signal detection and characterization (Buttery & Clothier, 2022).

- **Data-Linkage**

The emergence of large-linked dataset-based surveillance enables rapid investigation of emergent potential AEFI signals, for both uncommon and rare AEFI. Vaccine safety data linkage systems balance the public benefit with potential privacy implications for community members whose data are contained within the system (Buttery & Clothier, 2022)

Analysis of reports associated with vaccines (AEFIs) from 2020 to 2025

An analysis of ICSRs received from 1st January 2020 to 9th May 2025 revealed that 35,102 cases of AEFI were reported. The AEFIs reported have been analysed with regards to year received, patient age, suspect vaccines, reported terms (reactions) and seriousness; this is summarily presented below:

Table 1: Reports received on AEFIs from 2020 to 2025

S/N	VigiBase initial date	Count	Percentage
1	2020	4	0.0%
2	2021	7,845	22.3%
3	2022	15,068	42.9%
4	2023	8,894	25.3%
5	2024	3,250	9.3%
6	2025	41	0.1%

Table 2 - Vigilyze analysis for patient age

S/N	Patient age	Count	Percentage
1	0 - 27 days	171	0.5%
2	28 days to 23 months	1,101	3.1%
3	2 - 11 years	1,733	4.9%
4	12 - 17 years	310	0.9%
5	18 - 44 years	18,539	52.8%
6	45 - 64 years	6,063	17.3%
7	65 - 74 years	771	2.2%
8	≥ 75 years	258	0.7%
9	Unknown	6,156	31.0%

Table 3- Top 30 Reported Preferred Terms (MedDra)

S/N	Reported preferred terms (MedDRA)	Count	Percentage
1.	PT: Pyrexia	16,071	45.8%
2.	PT: Injection site pain	10,432	29.7%
3.	PT: Headache	8,069	23.0%
4.	PT: Local reaction	3,465	9.9%
5.	PT: Malaise	3,055	8.7%
6.	PT: Fatigue	2,227	6.3%
7.	PT: Myalgia	1,878	5.4%
8.	PT: Chills	1,806	5.1%
9.	PT: Pain	1,634	4.7%
10.	PT: Asthenia	1,633	4.7%
11.	PT: Arthralgia	1,363	3.9%
12.	PT: Injection site swelling	1,162	3.3%
13.	PT: Dizziness	914	2.6%
14.	PT: Injection site nodule	735	2.1%
15.	PT: Adverse drug reaction	647	1.8%
16.	PT: Injection site induration	642	1.8%
17.	PT: Nausea	537	1.5%
18.	PT: Limb discomfort	512	1.5%
19.	PT: Pain in extremity	481	1.4%
20.	PT: Injection site warmth	416	1.2%
21.	PT: Diarrhoea	387	1.1%
22.	PT: Nasopharyngitis	372	1.1%
23.	PT: Vomiting	367	1.0%
24.	PT: Cough	307	0.9%

25.	PT: Injection site pruritus	298	0.8%
26.	PT: Malaria	271	0.8%
27.	PT: Catarrh	245	0.7%
28.	PT: Anaphylactic reaction	237	0.7%
29.	PT: Muscular weakness	213	0.6%
30.	PT: Abscess	208	0.6%

Table 4 - Vigilyze Analysis for Vaccines

S/N	Drug (WHODrug)	Count	Percentage
1	AI variant: COVID-19 vaccine NRVV Ad (ChAdOx1 nCoV-19)	12,881	36.7%
2	AI variant: Elasomeran	8,337	23.8%
3	AI variant: COVID-19 vaccine NRVV Ad26 (JNJ 78436735)	7,242	20.6%
4	AI variant: Tozinameran	2,929	8.3%
5	AI variant: Polio vaccine live oral type 2	1,215	3.5%
6	AI variant: Meningococcal vaccine A/C/W/Y/X conj	803	2.3%
7	AI variant: Measles vaccine	640	1.8%
8	AI variant: Smallpox and mpox vaccine live (MVA-BN)	270	0.8%
9	AI variant: Diphtheria vaccine toxoid; Hepatitis b vaccine; HIB	148	0.4%

	vaccine; Pertussis vaccine; Tetanus vaccine toxoid		
10	AI variant: Meningococcal vaccine A conj (tet tox)	89	0.3%
11	AI variant: Diphtheria vaccine toxoid; Hepatitis b vaccine rHBsAg; HIB vaccine conj (tet tox); Pertussis vaccine whole cell; Tetanus vaccine toxoid	87	0.2%
12	AI variant: Yellow fever vaccine	85	0.2%
13	AI variant: Polio vaccine inact	58	0.2%
14	AI variant: Bcg vaccine	40	0.1%
15	AI variant: Diphtheria vaccine toxoid; Tetanus vaccine toxoid	32	0.1%
16	AI variant: Hepatitis b vaccine r	31	0.1%
17	AI variant: Measles vaccine live; Mumps vaccine live; Rubella vaccine live	22	0.1%
18	AI variant: Covid-19 vaccine	20	0.1%
19	AI variant: Pneumococcal vaccine conj	17	0.0%
20	AI variant: Pneumococcal vaccine	16	0.0%

21	AI variant: Polio vaccine live oral	15	0.0%
22	AI variant: Meningococcal vaccine A/C/Y/W conj (dip tox)	14	0.0%
23	AI variant: Rotavirus vaccine live reassort oral 5v	13	0.0%
24	AI variant: Diphtheria vaccine toxoid; HIB vaccine conj (tet tox);Pertussis vaccine acellular 2-component; Polio vaccine inact 3v (Vero); Tetanus vaccine toxoid	13	0.0%
25	AI variant: Diphtheria vaccine toxoid; Hepatitis b vaccine r;HIB vaccine conj; Pertussis vaccine; Tetanus vaccine toxoid	12	0.0%
26	AI variant: Rotavirus vaccine	9	0.0%
27	AI variant: HPV vaccine	9	0.0%
28	AI variant: HPV vaccine VLP rL1 4v (yeast)	8	0.0%
29	AI variant: Tetanus vaccine toxoid	7	0.0%
30	AI variant: Yellow fever vaccine live (17D-204)	6	0.0%
31	AI variant: Polio vaccine	6	0.0%
32	AI variant: Meningococcal vaccine	6	0.0%

33	AI variant: Meningococcal vaccine A	6	0.0%
34	AI variant: Meningococcal vaccine conj	6	0.0%
35	AI variant: Vaccines	6	0.0%
36	AI variant: Hepatitis b vaccine	5	0.0%
37	AI variant: Polio vaccine live oral type 1/3	4	0.0%
38	AI variant: Hepatitis b vaccine rHBsAg (yeast)	3	0.0%
39	AI variant: Rotavirus vaccine live oral 1v	3	0.0%
40	AI variant: Tetanus vaccine	3	0.0%
41	AI variant: Famtozinameran; Tozinameran	3	0.0%
42	AI variant: Measles vaccines	2	0.0%
43	AI variant: Bcg vaccine live intradermal (Tice)	2	0.0%
44	AI variant: Cholera vaccine	2	0.0%
45	AI variant: Pneumococcal vaccine conj 10v	2	0.0%
46	AI variant: Varicella zoster vaccine	2	0.0%

47	AI variant: HPV vaccine VLP rL1 2v (baculovirus)	2	0.0%
48	AI variant: Diphtheria vaccine toxoid;Hepatitis b vaccine rHBsAg;HIB vaccine conj (tet tox);Pertussis vaccine acellular 2-component;Polio vaccine inact 3v (Vero)	1	0.0%
49	AI variant: Bcg vaccine live intradermal	1	0.0%
50	AI variant: Smallpox and mpox vaccine	1	0.0%
51	AI variant: Smallpox and mpox vaccine live (LC16m8)	1	0.0%
52	AI variant: Typhoid vaccine conj Vi (tet tox)	1	0.0%
53	AI variant: Pneumococcal vaccine conj 13v (CRM197)	1	0.0%
54	AI variant: Pneumococcal vaccine conj 7v (CRM197)	1	0.0%
55	AI variant: Hepatitis b vaccine rHBsAg	1	0.0%
56	AI variant: Malaria vaccine	1	0.0%
57	AI variant: Measles vaccine live	1	0.0%
58	AI variant: Polio vaccine inact 3v (Vero)	1	0.0%

59	AI variant: Polio vaccine live oral type 1	1	0.0%
60	AI variant: Meningococcal vaccine A/C/Y/W conj (tet tox)	1	0.0%
61	AI variant: Varicella zoster vaccine live (Oka/Merck)	1	0.0%
62	AI variant: Diphtheria vaccine toxoid; Paratyphoid vaccine A/B; Tetanus vaccine toxoid; Typhoid vaccine inact	1	0.0%
63	AI variant: Hepatitis a vaccine inact; Hepatitis b vaccine rHBsAg (yeast)	1	0.0%
64	AI variant: Diphtheria vaccine toxoid; Pertussis vaccine acellular; Tetanus vaccine toxoid	1	0.0%
65	AI variant: Diphtheria vaccine; Hepatitis b vaccine; Pertussis vaccine acellular; Polio vaccine inact; Tetanus vaccine	1	0.0%
66	AI variant: Diphtheria vaccine; HIB vaccine conj (tet tox); Pertussis vaccine; Polio vaccine inact; Tetanus vaccine	1	0.0%
67	AI variant: Measles vaccine; Mumps vaccine; Rubella vaccine	1	0.0%
68	AI variant: Measles vaccine live (Schwartz); Mumps vaccine live (RIT 4385); Rubella vaccine live (Wistar RA 27/3)	1	0.0%
69	AI variant: Diphtheria vaccine toxoid; Hepatitis b vaccine HBsAg; HIB vaccine conj (tet tox); Pertussis vaccine whole cell; Tetanus vaccine toxoid	1	0.0%

70	AI variant: Tetanus vaccines	1	0.0%

Table 5 - Vigilyze Analysis of Seriousness

S/N	Seriousness criteria	Count	Percentage
1	Death	34	0.1%
2	Life threatening	250	0.7%
3	Caused/prolonged hospitalization	541	1.5%
4	Disabling/incapacitating	321	0.9%
5	Congenital anomaly/birth defect	5	0.0%
6	Other medically important condition	1,923	5.5%

validation and investigation at national and international levels, with multisite data linking networks offering the ability to confirm or reject vaccine associations (Buttery & Clothier, 2022).

Conclusion

Spontaneous reporting of suspected AEFIs and ADRs remains a critical aspect of safety monitoring of vaccines and all adverse events that occur in association with the use of vaccines or other medical products should be reported to the National Pharmacovigilance Centre. Health professionals and patients are encouraged to report adverse events or quality problems experienced with the use of vaccines and medicines to the nearest NAFDAC office or via pharmacovigilance@nafdac.gov.ng or via eReporting platform available on the NAFDAC website www.nafdac.gov.ng or via Med Safety Application available for download on Android and IOS stores.

Vaccine safety surveillance is a source of timely information to policymakers, health-care providers and the community. Spontaneous surveillance is the mainstay of surveillance in most settings and is essential for the detection of rare and unexpected "unknown unknowns." Active surveillance systems can augment signal detection, especially for common and uncommon AEFI, and contribute to vaccine confidence with reactogenicity and safety profiles using real-world data. They also allow responsive signal

LINK TO ELECTRONIC REPORTING:

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

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