Botswana Medicines Regulatory Authority

Approved By:

Dr P. Gurumurthy
Director
Pharmacovigilance and Control of Clinical Trials

Date of Approval (DD/MM//YY)

Table of Contents

Revision status sheet

Page	Changes made	Issue No	Process owner's name	Date

1 Purpose

The purpose of this document is to provide guidance to healthcare professionals and other stakeholders on Adverse Events Following Immunisation (AEFIs) recognition, reporting and investigation.

2 Scope

This guideline is applicable to AEFIs reported for human vaccines which occurred in Botswana.

3 Definitions and abbreviations

3.1 Definitions

The following definitions shall apply;

3.1.1 Adverse Event Following Immunisation (AEFI) - Any untoward medical occurrence which follows immunization, and which does not necessarily have a causal relationship with the usage of the vaccine. The adverse event may be any unfavourable or unintended sign, abnormal laboratory finding, symptom, or disease (WHO, 2020).

3.1.2 Adverse event of special interest (AESI)- AESI refers to adverse events of significant scientific, medical, and public interest among pandemic vaccines.

3.1.3 Causality assessment a systematic review of data about AEFI case(s) to determine the likelihood of a causal association between the event and the vaccine(s) received.

3.1.4 Serious adverse drug reactions - adverse drug reactions that are; life-threatening or fatal; cause or prolong hospital admission; cause congenital abnormality, persistent incapacity, or disability.

3.1.5 Adverse Event or Experience - any untoward medical occurrence that may present/occur during treatment with a medicine, but which may not be causally related to the medicine.

3.1.6 Cluster Two or more cases of the same or similar events related in time, geography (place), and/or vaccine administered. AEFI clusters are usually associated with a particular supplier/provider, health facility, and/or a vial of vaccine or a batch of vaccines.

3.1.7 Serious Adverse Events (SAE) - adverse events that are life-threatening or fatal; cause or prolong hospital admission; cause congenital abnormality, persistent incapacity, or disability.

3.1.8 Individual Case Safety Report (ICSR) - an adverse event report for an individual patient.

3.1.9 Lack of Efficacy – failure of the medicine to produce the expected therapeutic effect.

3.1.10 National Pharmacovigilance Centre - WHO-approved pharmacovigilance centre in countries participating in the WHO Programme for International Drug Monitoring and is usually a part of or closely linked to the national medicine's regulatory agency i.e. BoMRA for Botswana

3.1.11 Pharmacovigilance (PV) - the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem.

3.1.12 Clinical Trial - a clinical trial is any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes.

3.1.13 Side Effects - any unintended effect of a pharmaceutical product occurring at doses normally used in humans, which is related to its pharmacological properties.

3.1.14 Signal - reported information on a possible causal relationship between an adverse event and a drug, the relationship being unknown or incompletely documented previously.

Note: Usually more than one report is required to generate a signal depending on the seriousness of the event and the quality of the information.

3.1.15 Unexpected Adverse Reaction - an adverse reaction, the nature or severity of which is not consistent with domestic labelling or market authorization or expected from characteristics of the drug. Here the predominant element is that the phenomenon is unknown.

3.1.16 WHO-UMC - WHO Collaborating Centre for International Drug Monitoring

3.2 Abbreviations

The following abbreviations shall apply;

3.2.1 ADR – Adverse Drug Reaction

3.2.2 HCP- Health Care Professional

3.2.3 ICSR – Individual Case Safety Report

3.2.4 MAH – Marketing Authorisation Holder

3.2.5 MHRA - Medicines and Healthcare products Regulatory Agency

3.2.6 PV – Pharmacovigilance

3.2.7 SAE – Serious Adverse Events

3.2.8 WHO-UMC –World Health Organisation - Uppsala Monitoring Centre

3.2.9 VPDs- Vaccine preventable diseases

4 Introduction

4.1 General

Immunization is one of the most effective public health interventions for protecting the individual and the public from vaccine-preventable diseases (VPDs). Immunization has saved millions of lives. Modern vaccines are safe and effective. However, like other medicinal products, vaccines are not free from adverse reactions.

Vaccines rarely cause serious adverse reactions, and common reactions are minor and self-limited. We monitor the safety of vaccines by looking for adverse events following immunizations (AEFIs). An AEFI may be caused by a vaccine reaction but often, particularly if the event is serious, the event is coincidental to vaccination. Other events may be caused by an error in administration or handling of the vaccine.

Irrespective of the specific cause, an AEFI may lead to public suspicions of vaccines and parents may refuse further immunization for their children, making them susceptible to VPDs which are disabling and life-threatening. Vaccine pharmacovigilance, which includes the surveillance of AEFI (i.e. systematic collection of data on medically important events following immunization, which provides information on investigation leading to necessary follow-up action), should be part of all immunization programmes as this helps sustain public confidence in the programme.

The goal of immunization is to protect the individuals and the public from vaccine preventable diseases (VPDs). Vaccines used in this country are safe and effective. However, like drugs and other pharmaceutical products, vaccines are not entirely without risk and adverse reactions may occur. AEFI surveillance program demonstrates the country's intent of delivering quality immunization services with safe vaccines and ensure vaccine confidence. The AEFI surveillance system has been in place since 1988. The function has been transferred from Expanded programme on immunisation (EPI) within the Ministry of Health and Wellness (MoHW) to BOMRA in March 2021. The guidelines provide information to health care providers and programme managers at national, district, block and primary health care levels for establishing a sensitive AEFI surveillance system. The national AEFI guidelines provide complete guidance and other details for reporting, investigating and conducting the causality assessment of cases reported as AEFIs.

4.2 Cause Specific Classification

Adverse events following immunizations are classified into five main categories. The figure bellow illustrates the categories.

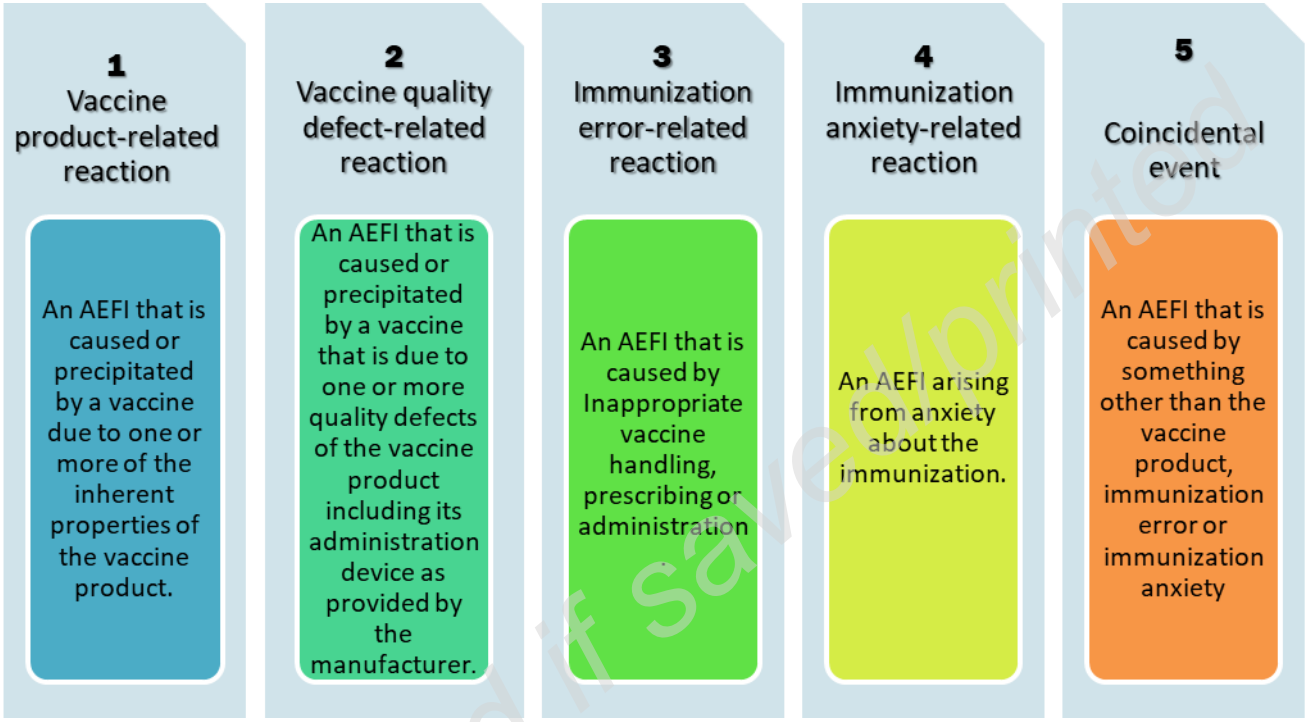


Figure 4.2: *CIOMS/ WHO cause-specific definition of AEFIs*

4.2.1 Vaccine product-related reaction

This is an individual's reaction to the ***inherent properties*** of the vaccine, even when the vaccine has been prepared, handled, and administered correctly. Most often the exact mechanism of a vaccine product-related reaction is poorly understood. The reaction may be due to an idiosyncratic immune mediate reaction (e.g. anaphylaxis) or to the replication of the vaccine-associated microbial agent (e.g. vaccine-associated poliomyelitis following OPV which contains attenuated live virus).

4.2.2 Vaccine quality defect-related reaction

This is due to a defect in a vaccine (or its administration device) that occurred during the ***manufacturing process***. Such a defect may have an impact on an individual's response and thus increase the risk of adverse vaccine reactions. Insufficient inactivation of wild-type vaccine agents (e.g. wild poliovirus) during the manufacturing process or contamination introduced during the manufacturing process could cause the vaccine quality defect-related reactions.

4.2.3 Immunization error-related reactions

The term "Immunization" as used here means the "use" of a vaccine for the purpose of immunizing individuals. "Use" includes all processes that occur after a vaccine product has left the manufacturing/packaging site – i.e. handling, prescribing, and administration of the vaccine.

Immunization error-related reactions are usually preventable, and they divert attention from the benefit of the immunization programme. Some of them are described in Table 4.1 The

identification and correction of these errors in a timely manner are, therefore, of great importance.

Table 4.1: Immunization error-related reactions

Immunization error		Related reaction
Error in vaccine handling:	Exposure to excess heat or cold because of inappropriate transport, storage, or handling of the vaccine (and its diluents where applicable)	Systemic or local reactions due to changes in the physical nature of the vaccine, such as agglutination of aluminium-based excipients in freeze-sensitive vaccines
	Use of a product after the expiry date	Failure to protect because of the loss of potency or no viability of an attenuated product
Error in vaccine prescribing or non-adherence to recommendations for use	Failure to adhere to a contraindication	Anaphylaxis, disseminated infection with a LAV e.g. Disseminated BCG
	Failure to adhere to vaccine indications or prescription (dose or schedule)	Systemic and/or local reactions, neurological, muscular, vascular, or bony injury due to incorrect injection site, equipment, or technique
Error in administration	Use of an incorrect diluent or injection of a product other than the intended vaccine	Failure to vaccinate due to incorrect diluent, reaction due to inherent properties of whatever was administered other than the intended vaccine or diluent
	Incorrect sterile technique or inappropriate procedure with a multi-dose vial	Infection at/beyond the site of injection

An immunization error-related reaction may sometimes lead to a cluster of events associated with immunization. These clusters are usually linked to a particular provider or health facility, or even to single or multiple vials of vaccines that have been contaminated or inappropriately prepared. For instance, freezing the vaccine during transport may lead to an increase in local reactions.

4.2.4 Immunisation-anxiety related reactions

Individuals and groups can become stressed and may react in anticipation to, and because of, any kind of injection. This reaction is unrelated to the constituents of the vaccine product. Fainting (vasovagal syncope or syncope) is relatively common, particularly in children over five years of age and among adolescents. Some children who faint may have a syncopal hypoxic convulsion. Hyperventilation because of anxiety about the immunization leads to specific symptoms such as light-headedness, dizziness, tingling around the mouth and in the hands. This is also common in mass vaccination campaigns.

Younger children may have breath-holding and vomiting as a common symptom of anxiety. Some individuals may have needle-phobia. In group immunization, mass hysteria is possible, especially if one or more of the vaccinees is observed by others to faint or have some other reaction such as itching, weakness of limbs, and so on.

Sometimes a fainting episode can be misdiagnosed as anaphylaxis. Careful observation and clinical judgement are necessary to differentiate the two.

4.2.5 Coincidental events

An event may occur coincidentally with immunization and sometimes be falsely attributed to the vaccine i.e. a chance temporal association is falsely attributed to immunization. Such temporal associations are inevitable especially in a mass immunization campaign.

Vaccines are normally administered early in life when infections and other illnesses are common, including manifestations of underlying congenital or neurological conditions. It is, therefore, possible to encounter many events, including deaths that can be falsely attributed to the vaccine through a chance association.

For example, the incidence of sudden infant death syndrome (SIDS or "cot death") peaks around the age of early childhood immunization. Consequently, many SIDS cases will occur in children who have recently been immunized. However, several well-designed studies have shown that the association of SIDS and immunization is coincidental and not causal.

Coincidental adverse events may be predictable. The number of events to be expected depends upon the size of the population and the incidence of disease or death in the community. Knowledge of these background rates of disease and deaths, particularly age-specific disease incidence rates, allows estimation of the expected numbers of coincidental events.

4.3 Types of AEFIs

Vaccine reactions may be further classified by seriousness and frequency. These can be grouped into two broad categories:

Vaccine reactions by seriousness and frequency:

- Common or minor reactions.
- Rare or serious reactions

4.3.1 Vaccine reactions by seriousness and frequency

Most vaccine reactions are minor and subside on their own. Serious reactions are very rare and, in general, do not result in death or long-term disability. **Table 4.3.1** describes the frequency of occurrence of reported adverse events.

Table 4.3.1: Frequency of occurrence of reported adverse reactions

Frequency category	Frequency in rate	Frequency in %
Very common	≥ 1/10	≥ 10%
Common (frequent)	≥ 1/100 and < 1/10	≥ 1% and < 10%
Uncommon (infrequent)	≥ 1/1000 and < 1/100	≥ 0.1% and < 1%
Rare	≥ 1/10 000 and <1/1000	≥ 0.01% and < 0.1%
Very rare	< 1/10 000	< 0.01%

4.3.2 Common, minor vaccine reactions

They are caused when the recipient's immune system reacts to antigens or the vaccine's components (e.g. aluminium adjuvant, stabilizers or preservatives) contained in the vaccine. Most AEFI are minor and settle on their own. Minor AEFI could be local or systemic. Local reactions include pain, swelling and redness at the injection site. Systemic reactions include fever, irritability, and malaise. A good quality vaccine reduces these reactions to a minimum while producing the best possible immunity. **Table 4.3.2** describes the common minor vaccine reaction associated with COVID-19 vaccines.

Table 4.3.2: Common minor covid-19 vaccine reactions and treatment

Top Reported Preferred Terms (MedDRA)	`Percentage
PT: Headache	29,0%
PT: Pyrexia	24,9%
PT: Fatigue	16,1%
PT: Myalgia	16,1%
PT: Chills	14,0%
PT: Nausea	13,0%
PT: Injection site pain	9,5%
PT: Arthralgia	9,3%
PT: Dizziness	7,2%
PT: Pain in extremity	7,1%

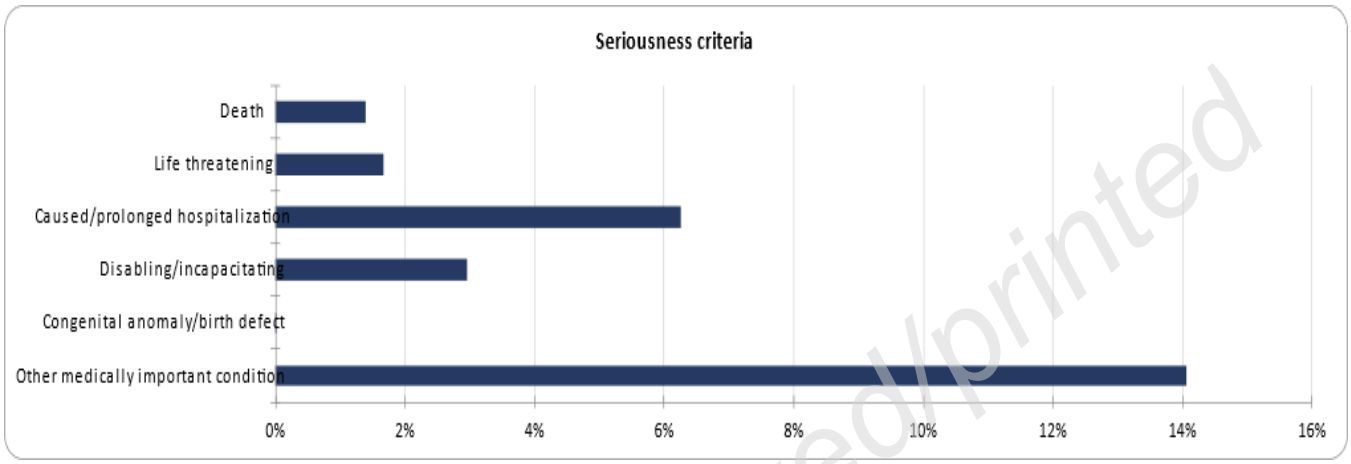
4.3.3 Rare and more severe vaccine reactions

They are caused by the body's reaction to a particular component in a vaccine. The term "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. Severe AEFI can be disabling but are rarely life-threatening. Some examples are seizures, thrombocytopenia, Hypotonic Hypo-responsive Episodes (HHE), prolonged crying etc.

4.3.4 Serious AEFIs

A serious AEFI is an event that results in death, hospitalization, or prolongation of an existing hospitalization, persistent or significant disability or incapacity, congenital anomaly/birth defect or is life-threatening or is a medically important event or reaction.

ALL AEFIs should be reported. Serious AEFIs must be investigated, and causality assessed. The rate of occurrence of the rare and more serious reactions associated with the COVID-19 vaccines has been summarized in Figure 4.3.4



Source; VigiLyze 2021

Figure 4.3.4: Severe vaccine reactions, onset interval, and frequency

4.4 Prevention and Management of AEFI

4.4.1 Prevention of Minor AEFIs

The figure below shows ways which AEFIs can be prevented. This is very much relevant to immunization -error related reactions.

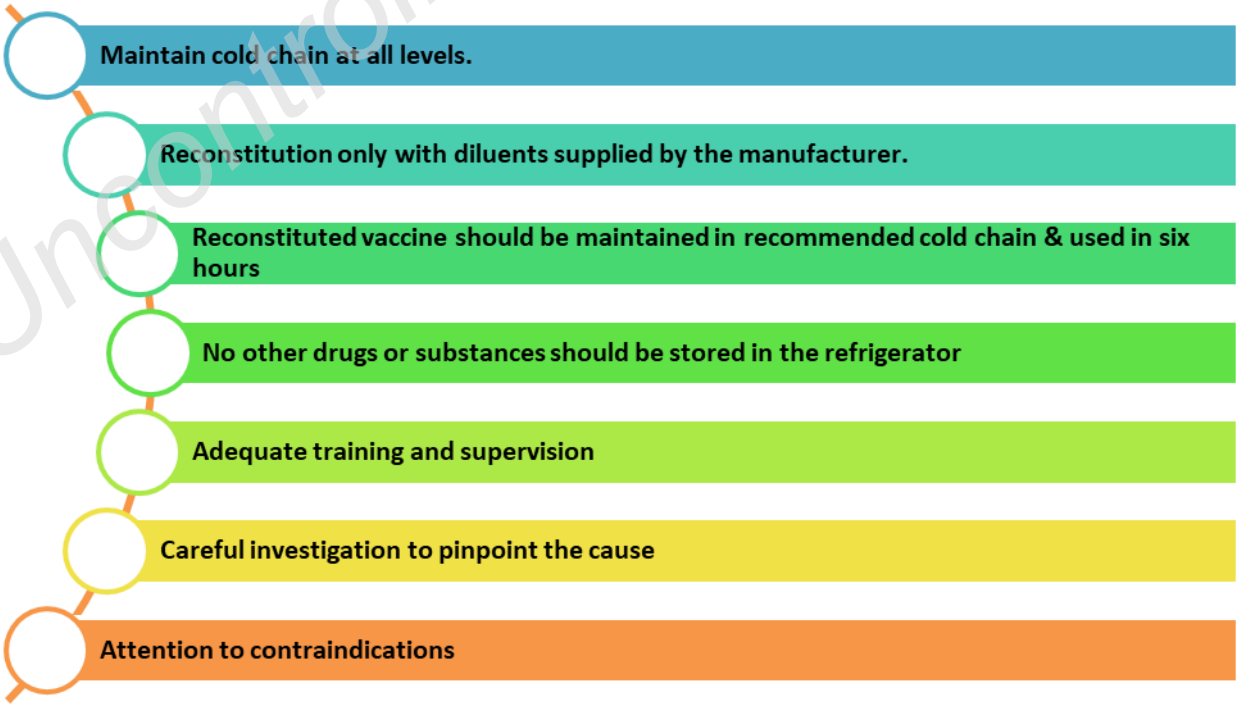


Figure 4.4.1: Prevention of immunization error-related reaction

4.4.2 Management of Minor AEFIs

Vaccines are very rarely contraindicated. However, it is important to check for contraindications to avoid serious reactions. For example, a vaccine is contraindicated if there is a history of anaphylaxis to a given vaccine or its components in previous vaccinations.

It is recommended that preparedness to provide emergency treatment for anaphylaxis is necessary for all clinic settings. All immunization providers need to be trained and develop competence in recognizing and managing anaphylaxis and have epinephrine (adrenaline) available. For parents, advice should be given on managing the common minor reactions, in addition to instructions on seeking proper medical care if there are more severe symptoms. Such action will help to reassure parents about immunization and prepare them for common reactions.

Antipyretic drugs, in a recommended dosage and schedule, can be given as recommended by the prescriber (or manufacturer). For example, paracetamol, at a dose of up to 15 mg per kg every 6 to 8 hours with a maximum of four doses in 24 hours, is useful for common minor reactions; it eases pain and reduces fever. However, it is important to advise against overuse of paracetamol or any other antipyretic drug as overdosing may harm the vaccinee. A febrile child can be cooled with a tepid sponging or bath, and by wearing light cool clothing. Extra fluids need to be given to children with fever. For a local reaction, a cold cloth applied to the site may ease the pain.

Using local remedies for any serious vaccine reaction can risk the health and life of the vaccinee and is strongly discouraged. Early medical care by a qualified clinician will minimize any unwanted outcome and ensure early recovery and may also save lives.

4.4.3 Management of Suspected Anaphylaxis or Collapse after Vaccination

Sudden and severe events occurring post-vaccination, especially syncope, are frequently reported as anaphylaxis. However, anaphylaxis following vaccination is very rare and the risk (in general) is 1 or 2 cases per million vaccine doses.

The onset of anaphylaxis can occur after several minutes (> 5 minutes) but rarely up to two hours following vaccination. The progression of symptoms is rapid and usually involves multiple body systems, almost always with skin involvement (generalized erythema and/or urticaria), as well as signs of upper and/or lower respiratory tract obstruction and/or circulatory collapse. In young children (though anaphylaxis occurs at any age) limpness, pallor, or loss of consciousness may reflect hypotension. In general, the more rapid the onset, the more severe is the reaction.

Events happen without warning. Emergency equipment must be immediately at hand whenever immunizations are given. All vaccinators must be familiar with the practical steps necessary to save life following anaphylaxis. Each health facility must have an emergency kit with adrenaline. The expiry date of the adrenaline should be written on the outside of the emergency kit and the whole kit should be checked daily. It is important to note that health-care workers may

misdiagnose syncope attacks as anaphylaxis and administer adrenaline as a part of emergency care. If the correct dose of adrenaline according to age and weight is administered via the intramuscular route, no harm is likely to occur. However, an overdose, by administering intravenous or intra-cardiac adrenaline or by repeated administration, may cause harm.

For all cases of suspected anaphylaxis all symptoms and signs must be well documented by health-care providers. Because anaphylaxis is very rare, other causes of sudden and severe symptoms post-immunization that is more common than anaphylaxis need to be considered.

4.4.4 Contents of an AEFI Management Kit)

- **Adrenalin (1:1000) solution:** 2 ampoules
- **Disposable syringe** (insulin type) having 0.1 ml graduations and 26 G IM needle: 2 sets
- Scalp vein set: 2 sets with medium bore needles
- **IV cannula**
- **Paracetamol (500 mg)**: 10 tabs
- **IV fluids (Ringer lactate or normal saline) and drip set**: 1 unit in plastic bottle
- Cotton wool + adhesive tape
- AEFI notification and reporting forms
- **Drug dosage tables** for injecting adrenaline
- At hospital, **oxygen** support and airway intubation facility

4.4.5 Management of Anaphylaxis

- Stop administering any further vaccines.
- Place the vaccine recipient in the **lying down position**, or if the vaccine recipient has difficulty breathing, place him/her in a semi-supine (sitting) position.
- Assess **Airway, Breathing and Circulation** (ABC). If appropriate, begin **cardiopulmonary resuscitation** (CPR).
- Give **adrenaline** (1:1000) by deep IM injection (0.5 mls for all over 14 years of age or a weight greater than 50kg)
- Give **oxygen** by face mask, if available.

- **Repeat** the same dose of adrenaline IM every 5-10 minutes if symptoms are ongoing, up to a maximum of three doses.
- Call for emergency help after the first injection of adrenaline, or sooner.
- Record, vital signs (pulse rate, respiratory rate and blood pressure), other symptoms and signs, as well as time and exact dose of any medication given. Make sure the details accompany the vaccine recipient when s/he is transferred to an expert care centre.

4.5 AEFI surveillance in Botswana

Surveillance for adverse events following immunization (AEFI) is an integral part of the Expanded Program on Immunization (EPI) and reinforces the safe use of all vaccines in the country while also helping to maintain public confidence in its immunization program. As shown in Figure 4.5.1 this is done systematically.

4.5.1 The objectives of AEFI surveillance are to:

a) Rapidly detect and respond on time to the occurrence of an AEFI

b) To determine the observed vaccine reaction rate and relate this to the expected vaccine reaction rates in the population by country, by region and globally.

c) Identify, correct, and prevent immunization error-related reactions.

d) to ensure that coincidental events are not mistaken for vaccine reactions and thus negatively affect the immunization programme.

e) To ensure and facilitate causality assessment of individual AEFI reports (cases).

f) To identify clustering or unusually high rates of AEFI, even if they are considered mild.

g) Identify potential safety signals (including previously unknown vaccine reactions) and generate hypotheses that may require further investigation.

h) Generate information with which to effectively communicate with parents, the community, media, and other stake holders, regarding the safety of vaccines used in Botswana.

i) To maintain the confidence of the community and health staff in the immunization programme by appropriate and timely responses to their concerns about immunization safety;

j) To collaborate and share information with the other regulatory authorities in order to ensure vaccine safety;

k) To ensure that channels of communication on AEFI between BOMRA and the EPI are clear, and that information is provided regularly by the unit responsible for immunization safety surveillance;

l) To collaborate and share information with the WHO regional offices and globally to generate additional information on vaccine safety.

m) To train key stakeholders on their roles in vaccine safety surveillance

Figure 4.5.1 AEFI Surveillance Cycle

4.5.2 Types of immunization safety surveillance

4.5.2.1 Passive surveillance:

This encompasses all spontaneous AEFI reporting from immunization service providers/ hospitals /patients to the first administrative level (e.g. health post, clinics, district hospitals) in the surveillance system. From there, reports are sent to the next reporting subnational/district level(s), ending at the national-level unit and global institutions responsible for AEFI surveillance.

Passive surveillance systems theoretically allow anyone in a country to report, and due to their broad coverage, they can provide the first indication of an unexpected AEFI. Therefore, the main strength of passive surveillance is to detect early the unknown serious AEFI (signals). However, passive surveillance has many limitations, including underreporting. Thus, passive surveillance is often not useful for determining whether the rate of an adverse event has increased. Thus, newly introduced vaccines and/or special immunization campaigns should have added layers of active surveillance and/or epidemiological studies to maximize the effectiveness of passive AEFI surveillance (e.g. enhanced spontaneous surveillance introduced during special immunization campaigns to encourage reporting by service providers or receivers).

4.5.2.2 Active surveillance:

This is primarily used for characterization of the AEFI profile, rates, and risk factors, but logistical and resource constraints limit its wide application. Countries may carry out active AEFI surveillance only for selected AEFI at selected institutions (sentinel sites). Active surveillance can also be carried out in the community setting (e.g. cohort event monitoring).

4.5.2.3 Ad hoc studies:

Epidemiological studies (e.g. cohort study, case-control study, case series studies) may be conducted in order to further expand immunization safety surveillance activities. These studies are focused on selected vaccine safety concerns (e.g. testing causality hypotheses).

In this guideline, the focus is on routine Immunization safety i.e. passive surveillance systems at district, national and international levels to ensure effective monitoring and prompt action in response to AEFI. However, within or parallel to the spontaneous reporting of a passive system, an active surveillance system can be established with specific objectives for a specified period. Immunization safety surveillance needs to be a collaborative venture between the immunization programme and the NRA, as both parties are responsible for the safety of vaccines.

Immunization safety reporting systems should build on and mutually strengthen any existing system of reporting information (e.g. immunization coverage reports, disease incidence reports, and adverse drug reaction reports). The best AEFI reporting system is the one which encourages a high level of appropriate reporting and takes timely action in response to reports.

4.5.3 Roles and responsibilities at the level of the immunization service provider

In these guidelines, the immunization service-provider level refers to the lowest administrative level at which immunization services are provided to the public. Among the tasks of immunization service providers are the following:

a) Detection of AEFI

Reporting of AEFI by the vaccine recipient, or by the parent or guardian of the recipient, should be encouraged by clinics and hospitals. It is the responsibility of the clinic and hospital staff to detect and report cases of AEFI. If treatment is necessary for a particular condition, the child or recipient with an AEFI should be referred to the nearest hospital or health facility.

b) Recording of AEFI

All reported AEFI must be recorded on AEFI Reporting Forms ***BOMRA-PCT-PV-P07-F01***. The forms will be availed at all healthcare facilities and can also be downloaded from BOMRA website. All necessary data should be entered into the forms/records/registers.

c) Reporting of AEFI

The next higher administrative/operational level (district level) should be immediately informed of all serious events (including death) and/or unusual AEFI. Other cases should be reported routinely, as instructed by the higher administrative/operational level.

d) Public education/communication

Public should be educated on expected AEFIs during vaccination session. Whenever an opportunity is available, the public should be informed of what is being done pertaining to investigations. People should be educated regarding AEFI.

4.5.4 Roles and responsibilities at the subnational/district AEFI C level

The District AEFI committee is a sub-committee of the district health management team, (DHMT) which is tasked with the surveillance of AEFIs at district level. Below are the roles of the committee:

a) Reporting of AEFI

The district AEFI committee should report all AEFIs from lower levels to the national level. Serious AEFIs (including deaths) and/or unusual AEFIs should be reported immediately. Other cases should be reported routinely, as stipulated by the national authority. All records on AEFI surveillance should be maintained on the line list.

b) Investigation of AEFI

All investigations required for reported AEFI i.e., Serious AEFIs, cluster cases and AESIs need to be carried out as early as possible. In most settings, the capacity to conduct a comprehensive investigation is not available at the level of the immunization service provider; therefore, collection of preliminary information on detailed investigations is often the responsibility of the district AEFI committee. The findings of the investigation should be shared with the national AEFI secretariat to enable National AEFI Committee to conduct causality assessment.

c) Corrective and preventive actions

Both corrective and preventive actions should be taken as early as possible. However, such actions should be based on the findings of the investigation. In practice, the subnational level has the greatest responsibility for implementing corrective actions in terms of both logistics and administration. For example, if any immunization error-related reactions are observed, preventive actions such as strengthening supportive supervision, training and even logistic replacements should be implemented by authorities at this level.

d) Analysis of AEFI

Analysis of data relevant to this level is necessary. AEFI Line list must be maintained and constantly updated. Reports need to be produced based on the findings of data analyses and investigations.

e) Monitoring, supervision and training

Monitoring, supervision, and training are key functions at this level. The authorities at this level need to develop the capacity to carry out these functions efficiently and effectively. Whenever necessary, the national level can assist subnational level with these activities, including providing standard formats for supportive supervision, guidelines, and training materials.

f) Public education/communication

Whenever an opportunity arises, the public should be informed of what is being done and should be educated regarding AEFI.

4.5.5 Roles and responsibilities at the national level BOMRA, EPI and National AEFI Committee

a) Investigation and causality assessment of AEFI

Investigations that require the services of national-level experts need to be prioritized (e.g. serious cases, deaths, AEFI with public concerns). Causality assessment by the national AEFI committee should be facilitated by all levels of the immunization programme, the BOMRA as secretariat to the committee and the EPI as Ex-officio member. If necessary, further research should be conducted to test a hypothesis generated by the surveillance system/investigation.

b) Corrective and preventive actions

Both corrective and preventive actions should be taken as early as possible. However, such actions should be based on the findings of the investigation and causality assessment. Vaccines should be withdrawn or suspended only if available data are strongly supported by a causative link to the vaccines. Preventive actions can lead to policy or/and programme strategy changes

c) Analysis and sharing of AEFI data

Reports should be produced on the findings of data analyses and investigations. AEFI data must be shared periodically among all stakeholders responsible for the country's immunization programme, including EPI managers, BOMRA and National AEFI committee, academia and, when necessary, manufacturers and the public. Countries are encouraged to share data regionally and globally through the WHO Programme for International Drug Monitoring to generate additional and new information on vaccine safety.

d) Feedback

Feedback is one of the most important elements of any surveillance system. Feedback ensures and encourages reporting, which is the basis of AEFI surveillance, through the continued interest of the staff at the subnational and service-delivery levels. In addition, feedback is a learning process for the service-provider level and helps staff to improve the immunization services. Weekly, monthly, quarterly, and annual reports with statistics, updates, new developments, findings of investigations and lessons learned are effective means of feedback in AEFI surveillance. National AEFI Committee must give feedback to all stakeholders.

e) Public education/communication

Whenever there is a need, informing the public and media through special awareness programmes is necessary. Developing a communication plan is also essential.

f) Monitoring, supervision and training

Staff awareness on AEFI should be assessed when monitoring and supervising immunization services. Guidance and adequate training on AEFI surveillance and good quality immunization practices should be provided to the staff. Whenever necessary, the staff must be re-trained. Training materials should be developed, with WHO support if necessary.

g) Resource allocation

Sustainability depends on the availability of adequate resources at each level of the surveillance system. Therefore, it is important that the national level (and possibly subnational level) identify and allocate resources.

4.5.6 National AEFI Committee

The National AEFI Committee is a committee of independent medical experts. The Committee plays a critical role in conducting the causality assessments of serious AEFIs, cluster cases and selected investigations. The committee roles, selection and composition is contained in the ***Terms of Reference for National AEFI Committee ToR No. 2***

Medical experts should be invited for the review of specific events. The committee needs to be independent and have support from, and work in close communication with, both the immunization programme and the NRA.

4.5.6.1 The following are the roles of the national AEFI Committee:

a) assessing potential causal links between AEFI and a vaccine;
b) monitoring reported AEFI data for potential signals of previously unrecognized vaccine-related adverse events;
c) reviewing all reported serious AEFI presented for expert opinion, making arrangements to investigate further to establish causality, and making the necessary recommendations to rectify problems (the expert committee may use the WHO Aide-mémoire on causality assessment as resource material18 and is encouraged to use in its investigations the comprehensive case definitions developed by the Brighton Collaboration19);
d) making final decisions on causality assessment following inconclusive investigations and ensuring quality control of the immunization surveillance system;
e) communicating with other national and international experts, when required, to establish causality and to resolve vaccine quality issues;
f) advising the EPI programme (manager) and NRA on AEFI-related issues when requested by these institutions; and
g) advising the Ministry of Health and Wellness on vaccine and immunization safety-related matters when requested by the ministry.

No industry participation: It is important to emphasize that employees of vaccine manufacturing companies cannot be members of the expert committee. This is because they will have conflicts of interest which could undermine the credibility and acceptance of the committee's conclusions. However, the committee may choose to question company representatives if the industry is potentially the best source for certain information. For example, the committee might invite the industry to describe a specific production process in one of their meetings.

4.6 Reporting of AEFIs

Case detection is the first important step in AEFI surveillance. The primary reporter (i.e. the one who first reports an AEFI) may be a vaccinee, a volunteer, parent or any other person who detects the AEFI.

4.6.1 What to report?

For reporting of AEFI's the responsible officer(s) should report **All AEFIs** that are brought to for notice, this includes non-serious AEFIs as well.

4.6.2 When to report

Serious AEFIs report must be made as quickly as possible so that an immediate decision can be made on the need for action and investigation. For incidents with many cases or a high level of community concern, an urgent telephone call/fax/email to the decision making administrative/operational level is appropriate. The district AEFI committee must notify national level within 24 hrs of knowledge of AEFI.

In the case of serious AEFI, inform your supervisor and/or AEFI focal person immediately (Over telephone) and complete the reporting form within 24hrs. All serious AEFIs should be investigated, and the investigation form should be filled and sent to the BoMRA. Non- serious AEFIs must be reported to BoMRA within 5 days of knowledge of AEFI.

4.6.3 Where to report

The AEFI Reporting Forms ***BOMRA-PCT-PV-P07-F01*** must be fully completed and submitted to district AEFI committee. Forms are available from all healthcare facility and alternatively can be downloaded from BoMRA website; www.bomra.co.bw .Once completed the District AEFI committee should submit forms to BOMRA. The following platforms can be used;

a) Email: aefi@bomra.co.bw
b) Fax: +267 318 6254
c) Telephone: 3731754/66
d) Watts app: 75846041/ 75846037
e) Postal Address: Private Bag 002
   Gaborone Station
   Botswana

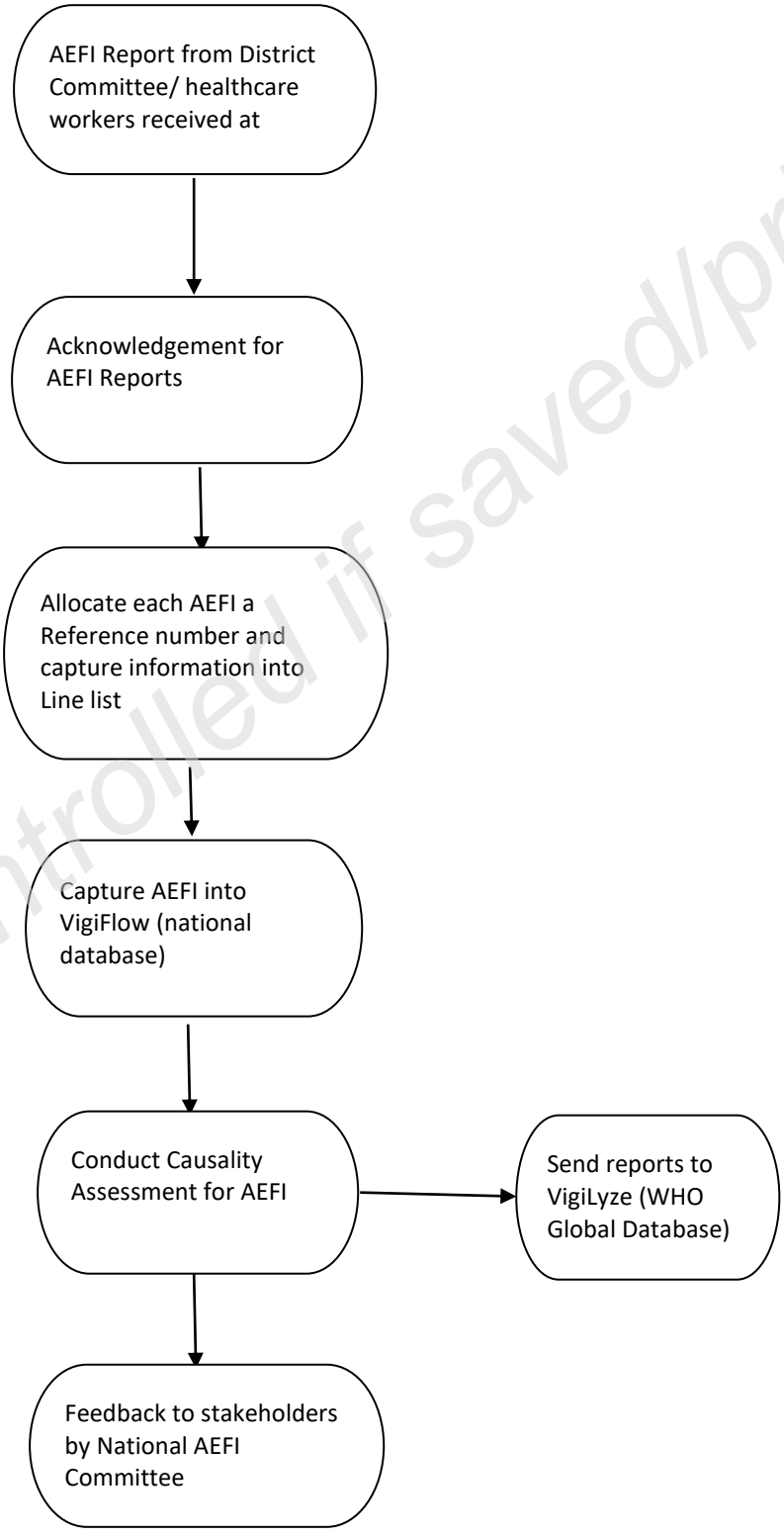
4.7 Investigation of AEFIs

The reported AEFI must be investigated if it:

a) appears to be a serious event (as defined by WHO) of known or unknown cause.
b) belongs to a cluster of AEFI.
c) is a previously unrecognized event associated with an old or newly introduced vaccine.
d) Involves an increased number or rates of known cause.
e) appears on the list of events defined for AEFI surveillance; and
f) causes significant parental or public concern.

Improved reporting can lead to more AEFI reports without a real increase in true adverse reaction rates or concerns about the vaccine product or its quality. The investigator should determine if there is a real increase in these reaction rates, as well as identifying the cause of the increase. For example, a change in vaccine manufacturer or in vaccine lot can lead to a change in the reaction rate. Investigation is conducted based on the AEFI Investigation form which is also acting as a guide for the investigation.

4.8 What happens to the AEFI reports at BOMRA



5.0 Records

5.1 AEFI Report form ***BOMRA-PCT-PV-P07-F01***

5.2 AEFI Investigation form

5.3 Line List ***BOMRA-PCT-PV-P07-F02***