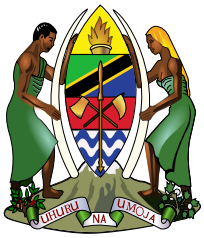

THE UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH AND SOCIAL WELFARE

GUIDELINES FOR SURVEILLANCE OF ADVERSE EVENTS FOLLOWING IMMUNIZATION

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TFDA
Tanzania Food & Drugs Authority

IVD

World Health Organization

Contents

Foreword

Vaccines are largely used to protect individuals particularly children from acquiring deadly infectious diseases which are preventable. Such products are relatively safe and can rarely cause adverse events following immunization (AEFI). AEFI may occur during immunization campaigns when vaccinating large populations in a short period or when new vaccines are introduced. Because serious adverse events are very rare and occur primarily in children who were apparently healthy, monitoring vaccine safety is of paramount importance in a healthcare system.

Additionally, AEFI surveillance system focuses on vaccine safety and it utilizes tools, guidelines and procedures geared to assure public health protection through the use of vaccines with proven safety profile.

The most common AEFIs in Tanzania are immunization error related, which occur as a result of inappropriate storage, handling, preparation and administration of vaccines. It is important that these AEFIs are reported, investigated and corrective measures taken to prevent additional incidents.

In Tanzania, the Expanded Programme on Immunization (EPI) which was established in 1975 has been involved in increasing immunization coverage to all age groups in the country through the Immunization and Vaccine Development Programme (IVD). In line with the Global Vaccine Safety Blueprint (2012) endorsed by the World Health Assembly, Tanzania envisions a vaccine safety system with national dedicated vaccine pharmacovigilance capacity, with designated staff, with clear mandates and well-defined structures and roles.

The current system for monitoring medicines safety (pharmacovigilance) is being coordinated by the National Medicines Regulatory Authorities (NMRAs), the Tanzania Food and Drugs Authority (TFDA). The TFDA has been able to improve patient care and safety in relation to the use of medicines and other medical interventions. Monitoring of vaccine safety has been challenging as IVD, which has actively been engaged in enhancing immunization coverage is also primarily collecting vaccine safety data from the districts. AEFI reports which reach IVD may not find their way to TFDA for further regulatory actions. Furthermore, since the establishment of the pharmacovigilance system, the TFDA has not been able to send any AEFI reports to the global safety Vigiflow database managed by World Health Organization (WHO). Currently IVD and TFDA have established coordinating mechanisms for sharing vaccine safety data.

By bringing these important stakeholders together, as well as engaging healthcare providers at all levels, the AEFI surveillance system will be well coordinated and vaccines will also be monitored to improve public health through detection of AEFI and communicate the findings in a timely manner. This will contribute to assessing risks, benefits and effectiveness of vaccines which will help minimize harm and risks while maximizing known benefits.

An effective and well-functioning AEFI surveillance system will eventually boost trust, public confidence and will also help improve the quality of the immunization programme in the long run. It is therefore essential that all stakeholders like IVD, TFDA, vaccine manufacturers, laboratories and healthcare providers make concerted efforts to provide documented evidence through an effective AEFI surveillance system. This will ensure that the best immunization services are being provided to the community including effective monitoring and response to AEFIs.

These guidelines were developed in line with the strategic objective 4 of the Global vaccine Action Plan (GVAP) 2011 - 2020 (Strong immunization systems that are an integral part of a well -functioning health system) to ensure capacity for vaccine safety activities, including capacity to collect and interpret safety data, with enhanced capacity in countries that introduce newly developed vaccines.

It is envisaged that this document will guide stakeholders at all levels to be involved in and take part in the strengthening of the AEFI surveillance system in Tanzania.

Readers are also requested to provide inputs and suggestions that will be used when reviewing the guidelines in the future.

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Glossary

Causal association	A cause-and-effect relationship between a causative (risk) factor and an outcome. Causally associated events are also temporally associated (i.e. they occur after vaccine administration), but events which are temporally associated may not necessarily be causally associated.
Causality assessment	In the context of AEFI surveillance, it is 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.
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.
Coincidental events*	An AEFI that is caused by something other than the vaccine product, immunization error or immunization anxiety.
Contraindication	A situation where a particular treatment or procedure, such as vaccination with a particular vaccine, must not be administered for safety reasons. Contraindications can be permanent (absolute), such as known severe allergies to a vaccine component, or temporary (relative), such as an acute/ severe febrile illness.
Injection safety	The public health practices and policies dealing with various aspects of the use of injections (including adequate supply, administration and waste disposal) so that the provider and recipient are not exposed to avoidable risks of adverse events (e.g. transmission of infective pathogens) and creation of dangerous waste is prevented. All injections, irrespective of their purpose, are covered by this term (see definition of safe injection practices).
Immunity	The ability of the human body to tolerate the presence of material 'indigenous' to the human "body" (self) and to eliminate "foreign" (non-self) material. This discriminatory ability provides protection from infectious diseases, since most microbes are identified as foreign by the immune system.
Immunization safety	The process of ensuring the safety of all aspects of immunization, including vaccine quality, adverse events surveillance, vaccine storage and handling, vaccine administration, disposal of sharps and management of waste.
Immunization safety Surveillance	A system for ensuring immunization safety through detecting, reporting, investigating, and responding to AEFI.
Non-serious AEFI	An event that is not 'serious' and does not pose a potential risk to the health of the recipient. Non-serious AEFIs also should be carefully monitored because they may signal a potentially larger problem with the vaccine or immunization, or have an impact on the acceptability of immunization in general.

Safe injection practice	Practices which ensure that the process of injection carries the minimum of risk, regardless of the reason for the injection or the product injected.
Serious AEFI	An event that results in death, is life-threatening, requires in-patient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect. Any medical event that requires intervention to prevent one of the outcomes above may also be considered as serious.
Severe vaccine reaction	It refers to the intensity of vaccine reactions. A severe reaction refers to the high grade intensity of its grading such as mild moderate and severe. Severe reactions may include both serious and non-serious reactions.
Signal * (safety signal)	Information (from one or multiple sources) which suggests a new and potentially causal association, or a new aspect of an own association, between an intervention and an adverse event or set of related adverse events, that is judged to be of sufficient likelihood to justify verificatory action.
Surveillance	The continuing, systematic collection of data those are analysed and disseminated to enable decision-making and action to protect the health of populations.
Trigger event	A medical incident following immunization that stimulates a response, usually a case investigation.
Vaccine	A biological preparation that improves immunity to a particular disease. In addition to the antigen, it contains multiple components (excipients) and each component may have unique safety implications.
Vaccine pharmacovigilance*	The science and activities relating to the detection, assessment, understanding and communication of AEFI and other vaccine- or immunization-related issues, and to the prevention of untoward effects of the vaccine or immunization.
Vaccine product-related reaction *	An AEFI that is caused or precipitated by a vaccine due to one or more of the inherent properties of the vaccine product, whether the active component or one of the other components of the vaccine (e.g. adjuvant, preservative or stabilizer).
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.

Vaccination failure*	Vaccination failure may be defined on the basis of clinical endpoints or immunological criteria where correlates or surrogate markers for disease protection exist. Primary failure (e.g. lack of sero-conversion or sero-protection) needs to be distinguished from secondary failure (waning immunity). Vaccination failure can be due to (i) failure to vaccinate, i.e. an indicated vaccine was not administered appropriately for any reason or (ii) because the vaccine did not produce its intended effect
Vaccine reaction	An event caused or precipitated by the active component or one of the other components of the vaccine. It may also relate to a vaccine quality defect.
Vaccine safety	The process, which maintains the highest efficacy of and lowest adverse reaction to a vaccine by addressing its production, storage and handling. Vaccine safety is a part of immunization safety.
Cluster of AEFI	A cluster is defined as two or more cases of the same or similar event, which is related in time and has occurred within the same district or geographical unit or associated with the same vaccine, same batch number administered or same vaccinator.
Signal	Information that arises from one or multiple sources which suggests a new potentially causal association or a new aspect of a known association, between an intervention and an event or set of related events, either adverse or beneficial, that is judged to be of sufficient likelihood to justify verificatory action.

Abbreviations

ADRs	-	Adverse Drug Reactions
AEFI	-	Adverse Events Following Immunization
BCG	-	Bacillus Calmette-Guerin
CHMTs	-	Council Health Management Teams
DT	-	Diphtheria Tetanus
DTaP	-	Diphtheria Tetanus Acellular Pertussis vaccine
DTwP	-	Diphtheria Tetanus Whole Cell Pertussis vaccine
DTPa-HepB-Hib	-	Diphtheria Tetanus Acellular Pertussis, Hepatitis B and Haemophilus influenza vaccine
EPI	-	Expanded Programme on Immunization
FEFO	-	First Expired First Out
FIFO	-	First In First Out
GIVS	-	Global Immunization Vision and Strategy
IPV	-	Inactivated Polio Vaccine
IVD	-	Immunization and Vaccine Development Programme
MDVP	-	Multi-Dose Vial Policy
MMR	-	Measles Mumps Rubella
MNH	-	Muhimbili National Hospital
MoHSW	-	Ministry of Health and Social Welfare
NHLQAC	-	National Health Laboratory Quality Assurance Training Centre
NITAG	-	National Immunization Technical Advisory Group
NRA	-	National Regulatory Authority
OPV	-	Oral Polio Vaccine
PSURs	-	Periodic Safety Update Reports
RHMTs	-	Regional Health Management Teams
TFDA	-	Tanzania Food and Drugs Authority
TTCIH	-	Tanzania Training Center for International Health
UDOM	-	University of Dodoma
VAPP	-	Vaccine Associated Paralytic Poliomyelitis
VVM	-	Vaccine Vial Monitor
WHO	-	World Health Organization
ZFDB	-	Zanzibar Food and Drugs Board

1. Introduction

Vaccines are biological substances that are administered to individuals to elicit immunity (protection) against specific diseases. Such products are formulated together with adjuvants and/or excipients, and like all medical products, may cause adverse events following their administration to some individuals. Despite the fact that such adverse events following immunization (AEFIs) are infrequent, measures still need to be put in place to monitor and prevent their occurrence and take appropriate regulatory action(s) on the products themselves if needed.

AEFIs can arise for different reasons: these include inherent vaccine product related, quality defect related, immunization error related, immunization anxiety related, coincidental or events undetected during pre-licensure clinical trials. A robust AEFI surveillance system in a country will help authorities detect, manage and prevent AEFIs.

In Tanzania, the Ministry of Health and Social Welfare (MoHSW) operates the Expanded Programme on Immunization (EPI) through the IVD department. IVD is responsible for setting up policy guidelines and standards for selection, supply and utilization of vaccines in the country. IVD has done a tremendous job and some of the notable achievements of the programme include achieving immunization coverage of over 90 % for all primary immunization, establishing a cold chain system, engaging regional and district authorities in monitoring vaccine use, training and developing healthcare providers as well as establishing linkages and networking with international stakeholders.

Likewise, the National Medicines Regulatory Authorities - NMRAs (Tanzania Food and Drugs Authority –TFDA and Zanzibar Food and Drugs Board – ZFDB) monitor the safety of medical products to include vaccines. The TFDA uses spontaneous pharmacovigilance system to collect any suspected adverse drug reactions experienced by patients. The TFDA is also responsible for authorization of marketing all medicines including vaccines. All vaccine manufacturers are required by law to register their products before supplying and distributing them in the country.

Reporting of AEFI and subsequent investigation may trigger regulatory action including withdrawing the marketing authorization of a vaccine, instructing vaccine manufacturers to change their product labels, restricting the use of vaccines to specific patient groups or recalling defective vaccine batches from the market.

These guidelines outline processes and procedures to be followed by healthcare providers in reporting, documenting and preventing AEFIs, as well as the roles and responsibilities of stakeholders responsible for the planning and delivery of immunization programs in Tanzania in close partnership. The guidelines also outline the surveillance system and provide tools and procedures needed to report AEFIs. An understanding of the types of AEFIs, investigation techniques, specimen collection managing AEFIs and communication including communicating with the media, are also delineated in this document.

It is anticipated that healthcare providers will read and use these guidelines and thus appropriately manage, report, and prevent AEFIs in the country. The overall goal is the protection of the health and well-being of infants, children and pregnant women who depend on vaccines to protect them from serious vaccine preventable diseases (VPD). The guidelines will also bring together stakeholders and allow for networking and improved collaboration in the process of detecting, analysing and preventing AEFIs. A brief introduction to causality assessment has been provided in these guidelines. Advanced readers are encouraged to access the WHO website http://www.who.int/vaccine_safety/publications/gvs_aefi/en/ for more information.

2. Basic concepts of vaccines and Adverse Events Following Immunization

2.1 Vaccines

A vaccine is a biological product that produces and enhances immunity to the particular VPD for which it is targeted. A vaccine contains the disease-causing microorganism or virus, or a portion of it, in a form that is incapable of causing the actual disease. It is usually made from either live attenuated or inactivated (killed) forms of the microbe, or from its toxin or one of its surface proteins.

2.1.1 Primary components of vaccines

Vaccines may be monovalent or multivalent (polyvalent). A monovalent vaccine contains a single strain of a single antigen/immunogen (e.g. measles vaccine), whereas a polyvalent vaccine contains two or more strains/serotypes of the same antigen/immunogen (e.g. t OPV and IPV each of which contain three attenuated polio virus types).

Combination (or combined) vaccines contain two or more different antigens (e.g. DTwP, DTPa-HepB-Hib). The potential advantages of combination vaccines include reduction in the cost and difficulty of shipping and storing and administering multiple vaccines, avoiding multiple injections, reducing the cost of extra health-care visits, improving timeliness of vaccination, and facilitating the addition of new vaccines into immunization programmes.

There is no evidence that the administration of several antigens in combined vaccines increases the burden on the immune system, which is capable of responding to millions of antigens at a time. Combining antigens usually does not increase the risk of adverse reactions and can lead to an overall reduction in adverse reactions. For instance, it can decrease the number of anxiety-related reactions and the chances of immunization error-related reactions.

2.1.2 Other components of vaccines

In addition to the primary antigen(s), vaccines contain small quantities of other substances. Sometimes AEFI can result from one of the other substances. They include,

Adjuvants: Substances added to a vaccine to enhance the immune response, thus making it possible, in some cases, to reduce the amount of antigen (immunogen) per dose or the total number of doses needed to achieve immunity.

Antibiotics: Antibiotics are used during the manufacturing phase to prevent bacterial contamination of the tissue culture cells in which the viruses are grown.

Preservatives: These are chemicals (e.g. thiomersal, phenol derivatives) that are added to killed or subunit vaccines in order to inactivate viruses, detoxify bacterial toxins, and remain in the vial to prevent serious secondary infections in multidose vials as a result of bacterial or fungal contamination after they are opened.

Stabilizers: Stabilizers are used to help the vaccine maintain its effectiveness during storage.

2.1.3 Classification of vaccines

As alluded to above, there are four types of vaccines: live attenuated, inactivated (killed antigen), subunit (purified antigen) and toxoids (inactivated toxic compounds). The characteristics of these vaccines differ, and the characteristics determine how the vaccine works.

Table 2.1. Classification of vaccines

Live attenuated vaccines (LAV)	**Bacteria**: BCG vaccine
	Virus: Live Japanese encephalitis vaccine, oral poliovirus vaccine, measles vaccine, mumps vaccine, rotavirus vaccine, rubella vaccine, yellow fever vaccine
Inactivated (killed antigen) vaccines	**Bacteria**: Whole -cell pertussis (wP)
	Virus: Inactivated Japanese encephalitis vaccine, inactivated poliovirus vaccine (IPV)
Subunit vaccines (purified antigens)	**Protein-based:** Hepatitis B vaccine Acellular pertussis vaccine(aP)
	Polysaccharide: Meningococcal polysaccharide vaccine Pneumococcal polysaccharide vaccine Typhoid Vi polysaccharide vaccine
	Conjugate vaccine: *Haemophilus influenzae* type b (Hib) conjugate vaccine, meningitis A and B conjugate vaccine Pneumococcal conjugate vaccines (PCV-7, PCV-10, PCV-13) Vi conjugate vaccine
Toxoids	Tetanus toxoid Diphtheria toxoid

2.1.4 Contraindications and precautions to vaccination

A contraindication to vaccination is a rare characteristic in a recipient that increases the risk of a serious adverse reaction if the vaccine is given. Ignoring contraindications can lead to avoidable vaccine reactions. One of the most serious reactions following vaccination is anaphylaxis which is the only contraindication applicable to subsequent doses of the same vaccine. Most contraindications such as severe acute illnesses (e.g. acute respiratory tract infection) or treatment with steroids are temporary and the vaccination can be administered later. These are called temporary or relative contraindications.

Precautions, in contrast, are events or conditions that should be considered in determining if the benefits of the vaccine outweigh the risks (especially if the would-be recipient is immune compromised or pregnant). Precautions stated in the product labelling may sometimes be inappropriately interpreted as contraindications, resulting in missed opportunities to vaccinate.

2.2 Adverse Events Following Immunization (AEFI)

An adverse event following immunization is any untoward medical occurrence (unfavourable or unintended sign, abnormal laboratory finding, symptom or disease) which follows immunization and which does not necessarily have a causal relationship with the usage of the vaccine. Reported adverse events can either be true adverse events - i.e. resulting from the vaccine or immunization process - or coincidental events that are not due to the vaccine or immunization process but are temporally associated with immunization. The five categories of AEFI as defined by CIOMS and WHO are described in table 2.1

Table 2.1 Cause-specific categorization of AEFI (CIOMS/WHO 2012)

Cause-specific type of AEFI	Definition
Vaccine product-related reaction	An AEFI that is caused or precipitated by a vaccine due to one or more of the inherent properties of the vaccine product.
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 (formerly "programme error")	An AEFI that is caused by inappropriate vaccine handling, prescribing or administration and thus by its nature is preventable.
Immunization anxiety-related reaction	An AEFI arising from anxiety about the immunization.
Coincidental event	An AEFI that is caused by something other than the vaccine product, immunization error or immunization anxiety, but a temporal association with immunization exists.

2.2.1 Vaccine reactions

Based specifically on cause, seriousness and frequency, vaccine reactions may be grouped into two broad categories:

i. Cause-specific vaccine reactions:
   - vaccine product-related reaction and
   - vaccine quality defect-related reaction

ii. Vaccine reactions by seriousness and frequency:
   - common or minor reactions;
   - rare or serious reactions.

2.2.1.1 Cause-specific vaccine reactions

i) ***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 replication of the vaccine-associated microbial agent (e.g. vaccine-associated poliomyelitis following OPV which contains attenuated live virus).

ii) ***Vaccine quality defect-related reaction:*** This is a 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 agent (e.g. wild polio virus) during the manufacturing process or contamination introduced during the manufacturing process could cause the vaccine quality defect-related reactions.

2.2.1.2 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 2.2 describes the frequency of occurrence of reported adverse events.

Table 2.2 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%

i) ***Common, minor vaccine reactions:*** They are caused when 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 injection site. Systemic reactions include fever irritability and malaise. A successful vaccine reduces these reactions to a minimum while producing the best possible immunity. Table 2.3 describes the common minor vaccine reactions by antigen and the treatment for the same.

Table 2.3 Common minor vaccine reactions by antigen and treatment

Vaccine	Local adverse events (pain, swelling, redness)	Fever (> 38^{0}C)	Irritability, malaise and systemic symptoms
BCG[1]	90%-95%	-	-
Hepatitis B	Adults up to 15% Children up to 5%	1 – 6%	-
Hib	5-15%	2%-10%	
Measles/MR/MMR	~10%	5%-15%	5% (Rash)
OPV	None	Less than 1%	Less than 1%[2]
Pertussis (DTwP)[3]	up to 50%	up to 50%	up to 55%
†Pneumococcal conjugate	~20%	~20%	~20%
Tetanus/DT/aTd	~ 10%[4]	~ 10%	~ 25%
Treatment	Cold cloth at injection site and Paracetamol*	Give extra oral fluids, wear cool clothing, tepid sponge or bath and Paracetamol*	Supportive treatment

[1] Local reactogenicity varies from one vaccine brand to another, depending on the strain and the number of viable antigen in the vaccine.
[2] Diarrhoea, Headache and/or muscle pains
[3] When compared with whole cell pertussis (DTwP) vaccine, acellular pertussis (DTaP) vaccine rates are lower.
[4] Rate of local reactions are likely to increase with booster doses, up to 50 -85%.
* Paracetamol dose: up to 15mg/kg every 6-8 hours, maximum of 4 doses in 24 hours
† Source: http://www.cdc.gov/vaccines/pubs/ACIP-list.htm

ii) Rare, more severe (and serious) 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 Hyporesponsive Episodes (HHE), prolonged crying etc.

Severe AEFI are considered serious by definition if they:

- Result in death
- are life-threatening
- require in-patient hospitalization or prolongation of existing hospitalization
- result in persistent or significant disability/incapacity
- area congenital anomaly/ birth defect

ALL serious AEFI should be reported, investigated and the causality assessed.

The rate of occurrence of the rare and more serious reactions has been summarized in table 2.4. Note that children less than six months or over six years of age are unlikely to have febrile seizures. If this happens, a thorough investigation should be conducted to determine the underlying cause(s).

Table 2.4 Severe vaccine reactions, onset interval and frequency

Vaccine	Reaction	Onset Interval	Rate per million (1,000,000) doses
BCG	Suppurative lymphadenitis	2-6 months	100-1000
	BCG osteitis	1-12 months	1 -700
	Disseminated BCG infection	1-12 months	~ 1-2
Hib	None		
Hepatitis B	Anaphylaxis	0 – 1 hour	1 – 2
Measles/MMR/MR	Febrile seizures	6-12 days	330
	Thrombocytopenia	15-35 days	30
	Anaphylaxis	0-1 hour	~1
	Encephalopathy	6-12 days	< 1
Oral poliomyelitis	VAPP	4-30 days	0.4 - 3 million[2]
Tetanus Toxoid, DT	Brachial neuritis	2-28 days	5-10
	Anaphylaxis	0-1 hour	1 – 6
Pertussis (DTwP)	Persistent (>3 hours) inconsolable screaming	0-24 hours	1000-6000
	Seizures	0-3 days	80-570[3]
	Hypotonic, hypo responsive episode(HHE)	0-48 hours	30-990
	Anaphylaxis	0-1 hour	20
	Encephalopathy	0-2 days	0-1

Notes

1. Reactions (except anaphylaxis) do not occur if already immune (~90% of those receiving a second dose are immune): children over six years unlikely to have febrile seizures
2. VAPP Risk is higher following the first dose (1 in 750,000 compared to 1 in 5.1 million for subsequent doses) and for adults and immunocompromised.
3. Seizures are mostly febrile and the risk depends on age, with much lower risk in infants under the age of 4 months.

2.2.2 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 2.5. The identification and correction of these errors in a timely manner are, therefore, of great importance.

Table 2.5 Immunization error-related reactions

Immunization error		Related reaction
Error in vaccine handling:	Exposure to excess heat or cold as a result 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 as a result of 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 multidose 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 vaccine that have been contaminated or inappropriately prepared. For instance, freezing vaccine during transport may lead to an increase in local reactions. The details of an approach to investigating AEFI clusters are described later.

2.2.2.1 Immunization anxiety-related reactions

Individuals and groups can become stressed and may react in anticipation to, and as a result 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 as a result 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. Young children may also scream or run away to avoid the injection.

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 is necessary to differentiate.

2.2.2.2 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 vaccine through a chance association.

For example, 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.

A calculation is shown in Table 2.6 relating to the incidence of infant (under one year) deaths in selected countries to the number of deaths temporally associated with routine DTP or pentavalent vaccine (PVV) immunization. As shown, infant mortality rates result in coincidental deaths in the day, week and month after immunization which are only temporally related to immunization. The actual number of coincidental deaths depends on the population size and infant mortality rate.

Table 2.6 Estimated numbers of coincidental infant deaths that could be temporally linked to immunization (for example with DPT/PVV) in the month, week and day after immunization in Tanzania and selected countries

Country	Infant mortality rate per 1000 live births (IMR)	Number of births per year (N)	Estimated number of infant deaths in			Estimated number of PVV/DTP immunizations* in		
			a month	a week	a day	a month	a week	a day
Tanzania	***45***	***1913 000***	***7173***	***1655***	***235***	TBC	TBC	TBC
Bhutan	42	15 000	53	12	2	3233	746	106
Canada	5	388 000	162	37	5	86 864	20 045	2856
China	13	16 364 000	17 728	4091	583	3 634 035	838 624	119 475
Indonesia	25	4 331 000	9023	2082	297	950 113	219 257	31 237
Iran	21	1 255 000	2196	507	72	276 445	63 795	9089
Mexico	13	2 195 000	2378	549	78	487 455	112 490	16 026
Sudan	57	1 477 000	7016	1619	231	313 382	72 319	10 303
United Kingdom	4	761 000	254	59	8	170 540	39 355	5607

3. Prevention and management of AEFI

3.1 General principles of prevention and management of AEFI

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. Vaccine anaphylaxis is very rare. However, it is recommended that preparedness to provide emergency treatment for anaphylaxis is necessary in 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 6–8 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 advice 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.

3.2 Prevention and management immunization error-related reactions

As mentioned in the previous chapter, immunization error-related reactions are preventable and identification and correction of these errors in a timely manner are important. Prior to the introduction of auto-disable (AD) syringes, the most common immunization error was an infection as a result of a non-sterile injection because of contamination of the vaccine or diluent vial or the injecting device (syringe and/or needle). The infection could manifest as a local reaction (e.g. suppuration, abscess) or a severe systemic reaction (e.g. sepsis, toxic shock syndrome). In addition, there was the perception of a risk linking immunization with blood borne infections. Nevertheless, one needs to consider infection that can occur in cases of mass vaccination or in disaster situations, particularly if there is a shortage of supplies or problems with logistics. This can be avoided by proper planning and preparedness of programme managers.

The symptoms arising from an immunization error may help to identify the likely cause. For instance, children immunized with contaminated vaccine (usually the bacterium *Staphylococcus aureus*) become sick within a few hours with an injection site reaction (local tenderness, redness and swelling) and then develop systemic symptoms (vomiting, diarrhoea, high temperature, rigors and circulatory collapse). Bacteriological examination of the vial, if still available, can confirm the source and type of infection.

Sterile abscesses, while rare (~1 per 100 000 doses) are local reactions from aluminium-containing vaccines, especially DTP. They, along with other local reactions, are more likely to occur if there is inadequate shaking of the vaccine before use, superficial injection and use of vaccine that had been frozen. Contamination of vaccine or injection equipment can lead to a bacterial abscess. For BCG vaccine, injection abscess can result from improper technique of injection (subcutaneous rather than intradermal injection).

Ignoring contraindications may lead to serious vaccine reactions and is considered as an immunization error. The immunization team should be clearly aware of such contraindications and any precautions. Any uncertainty should be referred to a higher level – a programme manager, paediatrician or physician. However, it is equally important not to overreact to concerns of false contraindications as this may lead to missed opportunities for vaccination, reducing coverage and thereby increasing the risk of disease in both individuals and the community.

Health-care workers also need a clear understanding of contraindications and precautions. As mentioned in the previous chapter, precautions are not contraindications, but a decision on whether to vaccinate requires a case-based assessment where the risk of the vaccine is balanced against the potential benefits. The use of live vaccines in pregnancy is a good example of this. To avoid/minimize immunization error, the following should be observed.

i. It is both important and necessary to maintain the cold chain at all levels.
ii. Vaccines must be reconstituted only with the diluents supplied by the manufacturer.
iii. Reconstituted vaccine should be maintained in the recommended cold chain and used within six hours after reconstitution; it must be discarded at the end of each immunization session and should never be retained.
iv. Other than vaccines, no other drugs or substances should be stored in the refrigerator of the immunization centre.
v. Immunization workers must be adequately trained and closely supervised to ensure that proper procedures are followed.
vi. Careful epidemiological investigation of an AEFI is needed to pinpoint the cause and to correct immunization practices.
vii. Prior to immunization, adequate attention must be given to contraindications.

Follow-up and corrective actions following immunization error-related reactions should be based on the findings of the investigation. Depending on the nature of the immunization error, these actions can be both general (e.g. training and awareness) and specific (e.g. strengthening cold chain maintenance if the problem found to be related to cold chain issues). Continued monitoring and supportive supervision can help to minimize these adverse events.

3.3 Prevention and management of immunization anxiety-related reactions

Training and awareness to enable health staff to identify and manage medical emergencies appropriately is important. Fainting does not require any clinical management beyond placing the patient in a recumbent position. Syncopal hypoxic convulsions are short-lived generalized tonic-clonic seizures which can be managed by keeping the child lying down and securing the airway by placing the child on one side to prevent aspiration should the child vomit. The seizure will end spontaneously but, if prolonged or focal, further investigations may be required.

The likelihood of fainting should be anticipated when immunizing older children. It can be reduced by minimizing stress among those awaiting injection, through short waiting times, comfortable room temperatures, preparation of the vaccine outside the recipient's line of vision, and privacy during the procedure. Sometimes, cases with hysteria may even require hospitalization and can cause public concern. Clear explanations about the immunization and a calm, confident delivery will decrease the level of anxiety about the injections and thus reduce the likelihood of an occurrence.

Careful observation and clinical judgement to differentiate between anaphylaxis and syncope is necessary.

3.4 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 1–2 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 vaccinating centre 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 three or four times a year. It is important to note that health-care workers may misdiagnose syncope attack as anaphylaxis and administer adrenaline as a part of the 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 intracardiac adrenaline or by repeated administration, may cause harm.

For all cases of suspected anaphylaxis it is important that all symptoms and signs are 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. Table 2.7 lists conditions which may be mistaken for anaphylaxis.

Table 2.7 Conditions that may be mistaken for anaphylaxis post-immunization

Diagnosis	Onset: symptoms and signs
Vasovagal event	Symptoms are usually immediate (< 5minutes) and commence during the injection process. No skin rash, bradycardia not tachycardia, no respiratory involvement, spontaneous resolution when prone.
Hypotonic hyporesponsive episode	Onset 2–6 hours post-immunization, sudden pallor, hypotonia and unresponsiveness, usually in an infant. No skin rash, respiratory or cardiovascular compromise.
Seizure	Onset usually at least 6–8 hours post-vaccination with a killed vaccine. Sudden unresponsiveness usually with tonic-clonic movement, usually febrile, no cardiovascular compromise, no respiratory compromise unless apnea or aspiration.
Aspiration of oral vaccine (e.g. OPV or rotaviral vaccine)	Immediate respiratory symptoms (cough, gagging, stridor or wheeze) during administration, usually in infant. No skin rash or cardiovascular compromise.
Somatic conversion symptoms	Immediate or delayed respiratory symptoms, syncope, neurological symptoms without objective respiratory or neurological signs.
Severe coincidental diseases	Usually due to coincidental – unrecognized congenital heart disease or occult infections. May have respiratory or cardiovascular compromise but there are usually symptoms, signs or investigations to indicate alternate cause.
Immunization- error related	Immediate toxic drug reaction with symptoms and signs due to drug toxicity. Reported with immunization related errors which have resulted from inadvertent administration of a muscle relaxant or insulin.

4. AEFI surveillance in Tanzania

Surveillance for adverse events following immunization (AEFI) is an integral part of the Tanzanian National Immunization and Vaccine Development (IVD) Program, and reinforces the safe use of all vaccines in the country while also helping maintain public confidence in its immunization program. As shown in fig 4.1, this is done systematically.

The objectives of AEFI surveillance are to:

- Rapidly detect and respond on time to the occurrence of an AEFI
- Identify, correct and prevent immunization error related reactions.
- Facilitate AEFI causality assessment.
- Recognize clustering or unusually high rates of AEFI, including those that are mild and/or “expected”.
- Identify potential safety signals (including previously unknown vaccine reactions), and generate hypotheses that may require further investigation.
- Generate information with which to effectively communicate with parents, the community, media and other stake holders, regarding the safety of vaccines used in Tanzania.

Vaccine recipients themselves and/ or parents of immunized infants/children, health care providers at immunization facilities and staff in immunization facilities are most likely to recognize or detect AEFIs when they first occur. Any AEFI case that is therefore notified to any health care provider working within the health care system, should be reported to the District Immunization and Vaccine Officer (DIVO) using the standard reporting form (Annex 1) through the fastest means possible. The DIVO should in fact be informed of any Serious AEFI cases by telephone and this should be followed up by completion and submission of the reporting form.

The reportable AEFI include serious AEFI, AEFI as a result of potential immunization errors, clusters, AEFI causing parental or community concern, those that are unexpected, and any that are known but occur with unexpected frequency. Table 4.1 below provides case definitions of commonly reportable AEFI. However it needs to be stressed that health workers should report all cases that are notified to them.

Table 4.1 Case definitions of the reportable adverse events.

AEFI	Case definition	Vaccine
Anaphylaxis	A clinical syndrome characterized by sudden onset (within one hour), rapid progression of signs and symptoms involving multiple (more than two) organ systems - Skin – urticaria (Hives), angioedema (swelling of face/body), Respiratory – persistent cough, wheeze, stridor, Cardiovascular – low blood pressure (hypotension) or reduced circulation (fast weak pulses), Gastrointestinal – vomiting, abdominal pain.	All
BCG Osteitis/ Osteomyelitis	Inflammation of the bone with isolation of Mycobacterium bovis BCG strain.	BCG
Disseminated BCG infections	Widespread infection occurring within 1 to 12 months after BCG vaccination and confirmed by isolation of Mycobacterium bovis BCG strain. Usually in immuno-compromised individuals.	BCG
Encephalopathy	Acute onset of major illness characterized by □ Depressed or altered level of consciousness and/or distinct change in behaviour lasting for one day or more	Measles, Pertussis
Fever	The fever can be classified (based on rectal temperature) such as □ Mild fever: 100.4 ^{0}F to 102 ^{0}F (38 to 38.9oC), □ Moderate fever: 102 ^{0}F to 104.7^{0}F (39 to 40.4^{0}C) and □ Severe fever: 104.7^{0}F or higher (>40.5^{0}C).	All
Hypotonic, Hyporesponsive Episode (HHE or shock-collapse)	Event of sudden onset occurring within 48 [usually less than 12] hours of vaccination and lasting from one minute to several hours, in children younger than 10 years of age. All of the following must be present: □ limpness (hypotonic) □ reduced responsiveness (hypo responsive) □ pallor or cyanosis – or failure to observe/ recall	Mainly DPT, rarely others

AEFI	Case definition	Vaccine
Injection site abscess	Fluctuant or draining fluidfilled lesion at the site of injection. Bacterial if evidence of infection (e.g. purulent, inflammatory signs, fever, positive bacterial culture), Sterile abscess if no evidence of bacterial infection on culture. Sterile abscesses are usually due to the inherent properties of the vaccine.	All injectable vaccines
Lymphadenitis (includes suppurative lymphadenitis)	Either at least one lymph nodes enlarged to >1.5 cm in size (one adult finger width) or a draining sinus over a lymph node. Almost exclusively caused by BCG and then occurring within 2 to 6 months after receipt of BCG vaccine, on the same side as inoculation (mostly axillary).	BCG
Persistent inconsolable screaming	Inconsolable and continuous crying lasting 3 hours or longer accompanied by highpitched screaming.	DPT, Pertussis
Seizures	Occurrence of generalized convulsions that are not accompanied by focal neurological signs or symptoms. Febrile seizures: if temperature elevated >100.4 ^{0}F or 38 ^{0}C (rectal) Afebrile seizures: if temperature is normal	All, especially Pertussis, Measles
Sepsis	Acute onset of severe generalized illness due to bacterial infection and confirmed (if possible) by positive blood culture.	All injectable vaccines
Severe local reaction	Redness and/or swelling centered at the site of injection and one or more of the following: □ Swelling beyond the nearest joint □ Pain, redness and swelling of more than 3 days and interfering with daily activities □ Requires hospitalization. Local reactions of lesser intensity occur commonly and are trivial and do not need to be reported.	All injectable vaccines
Toxic shock syndrome (TSS)	Abrupt onset of fever, vomiting and watery diarrhoea within a few hours of immunization. Often leading to death within 24 to 48 hours.	All injectable vaccines
Vaccine Associated Paralytic Poliomyelitis (presenting as AFP)	Acute onset of flaccid paralysis and neurological deficits, compatible with diagnosis of poliomyelitis, with isolation of vaccine virus and absence of wild virus in stool.	OPV
Serious AEFI: Any AEFI causing • Death • Hospitalization • Disability, congenital anomaly • Other severe and unusual events	No time limit, if they are thought by health workers or the public to be related to immunization	

All vaccination staff must be able to recognize AEFIs and report them. However, accurate diagnosis of AEFIs requires staff training and education. Health care providers also have the additional responsibility to manage AEFI and, if necessary, refer such patients for any required treatment.

4.1 Stakeholders in AEFI reporting and investigation; their roles and responsibilities

4.1.1 Subnational Stakeholders

The subnational stakeholders in AEFI reporting and investigation are;

i. Health workers
ii. The District Immunization and Vaccine Officer (DIVO)
iii. The Regional Immunization and Vaccine Officer (RIVO)

4.1.2 National stakeholders in AEFI investigation

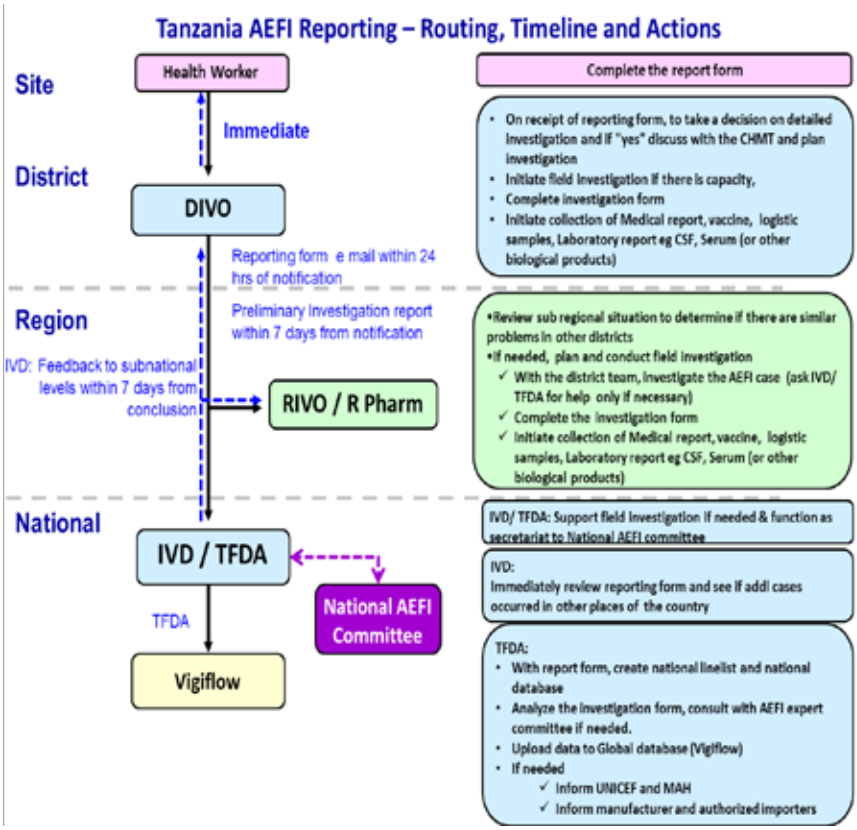
The national stakeholders are

i. Tanzania IVD and Tanzania Food and Drugs Authority (TFDA)
ii. National AEFI committee

4.1.3 Field investigation of AEFI

The purpose of investigating AEFI cases are:

i. To confirm the reported diagnosis and/or propose other possible diagnoses as well as clarify the outcome of the medical incident comprising the AEFI.
ii. To ascertain the particulars, circumstances and procedures around the vaccine used to immunize the affected recipient. Most importantly, identify any potential vaccine related link to the given AEFI.
iii. To examine the operational aspects of the programme. Even if an event seems to be vaccine product induced or coincidental.
iv. To determine whether a reported event was a single incident or one of a cluster and if it is a cluster, confirm that the suspected immunizations were indeed given and the individual vaccines that were used.
v. To determine whether unimmunized people are experiencing the same medical incidents.



The ultimate goal of an AEFI field investigation is to find the cause of the reported AEFI(s) and prevent recurrence. Remedial action needs to be taken promptly for immunization error related AEFI. Even if the cause cannot be identified or the cause of the event was due to some other reason, the fact that staff had investigated the incident itself will increase public confidence in the immunization program.

4.2.1 Role of the Sub national stakeholders

4.2.1.1 Role of the health worker

As outlined earlier in this chapter, the main role of the health worker is to provide primary medical care and report the basic details about the patient and the adverse event to the district by completing the AEFI reporting form (preceded if appropriate with a preliminary report by telephone if a serious event).

4.2.1.2 Role of stakeholders at the district and the regional level

When an AEFI report is received by the DIVO, they should review the report and determine if the reported AEFI case meets the criteria required for a detailed investigation. If necessary they should contact the primary reporter and visit the locality of the event and interview relevant stakeholders for additional information. If the DIVO considers the case as;

1. A minor AEFI or a severe but not serious AEFI warranting detailed investigation, they should indicate this on the reporting form and email the same to the regional and national levels to the following;

    i. the concerned regional immunization and vaccine officer (RIVO)

    ii. the TFDA at the info@tfda.or.tz

2. In case of a Serious AEFI (death, hospitalization, significant disability, life threatening, or congenital anomaly/ birth defect or a part of a group of events above expected rate/ severity, or a suspected signal, they should discuss the same with the CHMT and plan a detailed field investigation. Prior to initiating an investigation, they should e-mail the report to the regional and national levels as described above.

    If the DIVO and the CHMT feel that the investigation can be done locally, they can visit the patient and locality and initiate the detailed investigation along with appropriate members of the local health care team. If however assistance is required for investigation from the regional or national level, the RIVO and the IVD/ TFDA should be contacted and assistance for an investigation solicited. National investigations should be led by a team from the national AEFI committee, supported by the IVD and the TFDA.

    During field investigations, the investigators should seek to document any deficiencies found in a generic way and suggest corrective measures, and not single out any individuals to blame. While an individual may have been at fault, it is more effective to focus on identifying the problems in the system and procedures leading to the event. This is more effective in avoiding similar errors in the future, than blaming or punishing individuals. Such an approach is essential to ensure that AEFI reporting is encouraged for the ultimate benefit of all patients and the immunization program as a whole. It is also much more likely to improve system performance. Errors provide opportunity for learning and creating a system that encourages continued improvement. Hiding errors will only serve to form the basis for more errors.

    The specific activities conducted at this point will include the following.

    i. Confirm the AEFI, assign a unique report identifying number, complete ALL details in the AEFI reporting form (in case any of them were missing when reporting) and initiate AEFI investigation.

    ii. Convene a Council Health Management Teams (CHMT) planning meeting prior to the investigation.

    iii. With the CHMT, the DIVO should visit as required the patient, the care provider(s) and the hospital; interview relevant stakeholders (parents, health worker, treating doctor, vaccine supply focal person); and conduct the investigation of the AEFI case.

    iv. Complete the AEFI investigation form.

    v. Initiate collection of medical reports, a post-mortem report (if available), vaccine vials (if necessary, and kept under cold chain conditions), logistic samples, and laboratory reports e.g. CSF, Serum (or other biological products).

Generally before the AEFI is attributed to any vaccine product related problems, the investigator should rule out any potential immunization errors and obvious coincidental events, as these are more common. Therefore, the investigation should first try to rule out immunization errors related to the storage, handling, reconstitution or administration of vaccines.

Attention can then focus on other events. Details of coincidental events can be determined by reviewing hospital admissions for similar conditions during the same period and verifying their vaccination status. A quick review of the morbidity pattern of similar conditions in the previous years can also indicate if the event is a part of a similar pattern observed in the previous years. The medical literature can also help, as the estimated background incidence of various conditions may be available in the published domain.

Once the investigation is initiated, the District / Regional investigator should inform the IVD Tanzania and the TFDA on the status and progress of the investigation. This is necessary, as a national level officer should be the spokesperson of the government to the media and the public about the investigation. The completed case investigation form along with the supporting documents such as the medical report, vaccine, logistic samples, laboratory reports e.g. CSF, Serum (or other biological products) should be sent to the IVD/ TFDA within 7 days of initial case notification. If this is not possible, at least a progress report should be made with details on when the completed report can be expected.

It is important to remember that in case regional or national assistance for an investigation is requested, more accurate information can be obtained by a joint investigation rather than a piecemeal investigation. Table 4.2 summarises the key steps in an AEFI investigation.

Investigator(s) may use the "WHO Aide Memoire on AEFI Investigation" as a guide. This is available at www.who.int. immunization_safety/en

Table 4.2 Steps in an AEFI investigation

	Step	**Actions**
1	Confirm information in report	Obtain patient's medical file (or other clinical record) Check details about patient and event from medical file and document the information. Obtain any details missing from AEFI Report Form.
2	Investigate and collect data: About the patient:	Immunization history Previous medical history, including prior history of similar reaction or other allergies Family history of similar events.
	About the event:	History, clinical description, any relevant laboratory results about the AEFI and diagnosis of the event Treatment, whether hospitalized and outcome.
	About the suspected vaccine(s):	Conditions under which the vaccine was shipped, its present storage condition, state of vaccine vial monitor and temperature record of refrigerator Storage condition of vaccine at all levels before it arrived at health facility, Vaccine Vial Monitor. The date of manufacture, lot and batch numbers of vaccine and diluent
	About other people:	Whether others received the same vaccine and developed illness and whether they need to be included in the investigation. Whether others had similar illness (may need working case definition); if so exposure of cases to suspect vaccine(s) Discuss with other immunization service providers to obtain an idea of the local standard practices

3	Assess the service provided by asking about:	Vaccine storage (including open vials), distribution and disposal Diluents storage and distribution Reconstitution(process and time kept) Use and sterilization of syringes and needles Number of immunizations (greater than normal?) Details of training in immunization practice, supervision and vaccinator(s)
	Observing the service in action:	Refrigerator – what else is stored (note if similar containers stored next to vaccine vials which could be confused); which vaccines/diluents stored with other drugs; whether any vials have lost their label Immunization procedures (reconstitution, drawing up vaccine into the syringe, injection technique, safety of needles and syringes; disposal of opened vials) If any open vials look contaminated
4	Formulate a working hypothesis:	On the likely/possible cause(s) of the event.
5	Test working hypothesis	Does case distribution match working hypothesis? Laboratory tests may help (see text).
6	Conclude investigation	Reach a conclusion on the cause. Complete AEFI Investigation Form Take corrective action and recommend further action.

4.2.1.3 Role of the National stakeholders

When the IVD Tanzania receives the AEFI reporting form, it is essential to review it in the context of other reported AEFI received from all parts of the country, particularly in the same period of time, to see if this report may constitute a signal. This can be done by appending data into a national AEFI linelist with information from the reporting form and reviewing the data or running analyses as needed. If similar cases were reported earlier, it is essential to determine if an epidemiological linkage or other pattern can be identified if there is one. The need for technical or operational assistance for the investigation has to be assessed. Expert advice can be sought from the National AEFI Committee at this point.

The TFDA and the National AEFI Committee play a key role in supporting the immunization program for AEFI investigation and causality assessment. They also provide recommendations to the Tanzania National Immunization Technical Advisory Group (NITAG), the MoHSW and EPI on vaccines based on their causality assessment findings. The TFDA and the IVD Tanzania together constitute the National AEFI secretariat and together they coordinate and provide technical/logistical support to conduct the meetings of the National AEFI Committee (Fig 4.2).

IVD is responsible for providing all feedback to the relevant stakeholders at the regional and district level within 7 days of causality assessment or potential signals determined by data review/analysis at the national level. They are also responsible on following up on the actions recommended at the national level and regional level (e.g. change in logistics, cold chain, training after program errors etc.) and ensuring that they are implemented.

The TFDA as the national pharmacovigilance centre is responsible to upload the information into the Global pharmacovigilance database – Vigiflow®, maintained by the Uppsala Monitoring Centre under the WHO International Drug Monitoring Program – using information available in the completed case investigation form. A copy of the uploaded case details in Vigiflow® should be provided to IVD Tanzania on a monthly basis. The TFDA can also provide information on the vaccines and lots distributed in the country when requested by the AEFI committee, IVD Tanzania and the Tanzania National Immunization Technical Advisory Group (NITAG). The TFDA can also provide additional information on AEFI from other sources.

4.2.2 Investigation of AEFI with fatal outcome

In the event of an identified death following immunization, the field investigation has to be initiated immediately. Within 24 hours the death should be notified to all administrative levels concerned, including the District and Regional IVOs, the IVD Tanzania and the TFDA. Investigation of the case should be carried out by a team of experts from relevant areas, including clinicians. As a death causally linked immunization is extremely rare (anaphylactic reactions being one of the only 2-3 known events), major programmatic errors may be involved and thus an investigation to rule those out has to be conducted without any delay to prevent further cases. As any fatality temporally linked to a vaccination can cause panic, the public will also demand an immediate explanation.

A post mortem is preferred and recommended following all deaths suspected to be caused by a vaccine / immunization. However, the decision to conduct a post mortem should be within the religious, cultural acceptance and legal framework of the local population.

4.2.2.1 Investigating AEFI clusters

A cluster of AEFI is defined as two or more cases of the same adverse event related in time, place or vaccine administration. Apart from checking on these three factors, the investigator should look for AEFI occurring in similar age groups and populations with genetic predisposition or disease.

Cluster investigation begins by establishing a case definition for the AEFI and related circumstances and by identifying all cases that meet the case definition. The investigator should demarcate the cluster and identify common exposure factors within the cluster

Cluster identification (i.e. cases with common characteristics) is done by gathering details (when and where) of vaccines administered. This can be achieved by collecting and recording

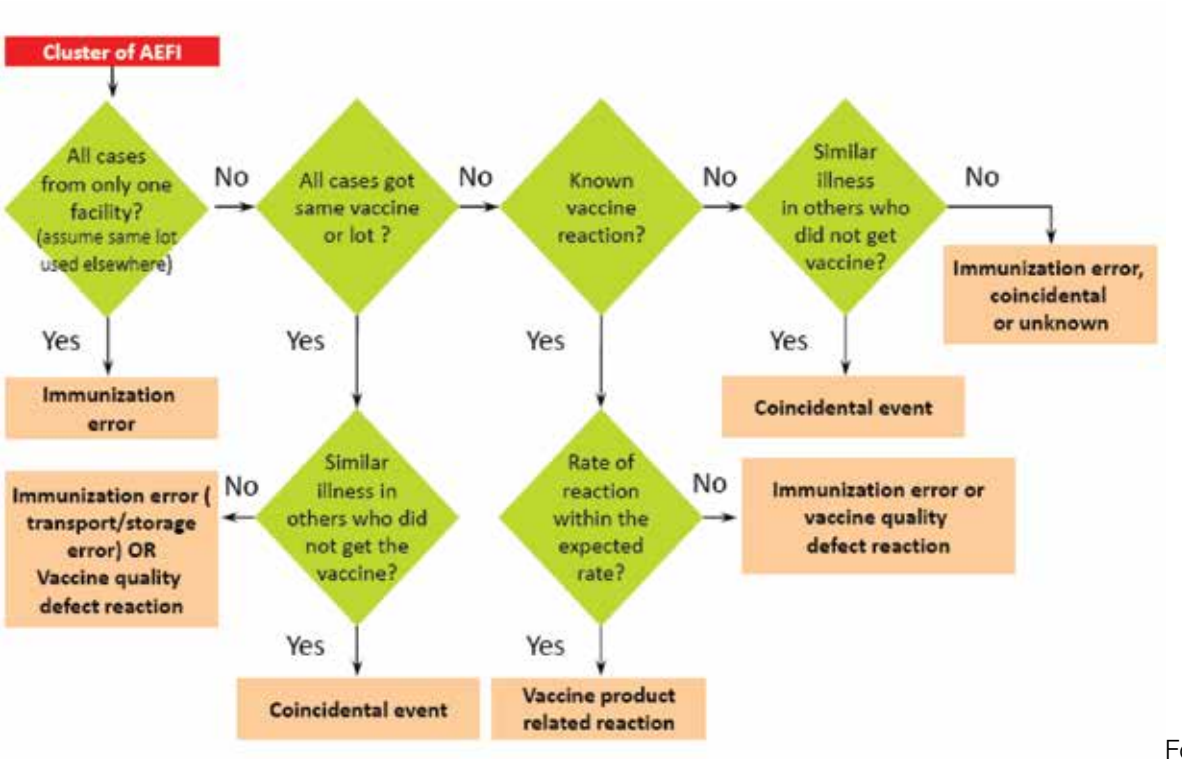
i. detailed data on each patient;
ii. programme-related data (storage and handling, etc.); and
iii. immunization practices and the relevant health workers' practices.

Common exposures among the cases can be identified by reviewing:

i. all data on vaccine(s) used (name, lot number, etc.);
ii. data on other people in the area (also non-exposed); and
iii. any potentially coincident factors in the community.

When an AEFI cluster has been identified, the cause-specific definitions provide a framework for investigation and causality assessment. Usually the key considerations will be to investigate the possibility of an immunization error vaccine or a quality defect. The possibility of immunization error must be considered when events cluster in one setting without a similar change in frequency in other settings using the same vaccine. On the other hand, if an increased frequency of events is reported from multiple settings the possibility of a quality defect must be considered more strongly. Clusters of fainting after immunization are well-recognized immunization anxiety-related reactions during immunization programmes targeting adolescent girls.

Fig 4.3 Identifying cause of AEFI cluster



For relatively new vaccines or established vaccines used in new target populations, a cluster may represent a previously unrecognized vaccine product-related reaction. Knowledge of the background incidence of events which may occur in causal relationship with a vaccine is therefore essential for assessing a cluster in terms of the strength of the signal it may provide.

4.2.2.2 Interpretation of results from AEFI clusters

If all cases received vaccines from the same health worker/facility and there are no other cases, an immunization error is likely. If all cases received the same vaccine or lot, and there are no similar cases in the community, a problem with the vaccine or the respective lot is likely. If the event is a known vaccine reaction but is found to occur at an increased rate, an immunization error or a vaccine problem are likely causes. Finally, if cases in the unvaccinated population are occurring at about the same rate/proportion as among the vaccinated from the same area in the same age group, the adverse event was probably coincidental (Fig 4.3).

5. Laboratory testing of specimens

Laboratory testing of samples is rarely necessary. It is not mandatory following an AEFI, particularly if the cause is evident such as a coincidental event or a program error. However, laboratory testing is at times required to confirm or rule out the suspected cause. The testing of specimens includes:

5.1 Human specimens

i. Histopathology, body fluids etc. can be done at laboratories identified and approved by the MoHSW.

ii. Autopsy specimens at approved and accredited government forensic laboratories as identified by MoHSW

Vaccines and logistics

i. Vaccines and diluents for sterility and chemical composition.

ii. Syringes and needles for sterility.

Only the appropriate specimen in the correct quantity required for the investigation should be collected. Laboratory specimens should be stored and transported as recommended and accompanied by clear supporting documents, reasons for specimen collection and any additional information required by the investigators. In case laboratory investigation is required, AEFI laboratory request form (Annex 3) should be completed and sent with any specimen collected.

- **Laboratory testing is not a routine requirement but may be a part of an investigation.**
- **Laboratory testing is costly and is recommended only when it is necessary.**
- **However, securing samples (vaccine vials, syringes, blood etc.) and storing them correctly is important because later investigation may require them. Therefore, proper storage and transport of suspected samples is recommended.**

v.1 Human Specimens

It is difficult to generalize what specimens will be required in a given situation as it will depend on the symptoms and signs of the patient and the clinical decisions made by the doctor in charge of the case. Table 5.1 gives a general outline of some of the specimens that could be collected. The list is not exhaustive. It is necessary to record the type date and time of collection of each and every sample collected. Documents of clinical investigations and medical records related to the incident will support correct lab investigations. It is advised to consult the treating clinician(s) to make a decision on samples to be tested.

For biochemical, histo-pathological and microbiological examination, specimens should be handled at the district hospital and forwarded to the nearest laboratory, where facilities are available to carry out requested laboratory testing. If facilities for essential laboratory testing are not available at intermediate level (Region/District) institutions, sending samples to national laboratory or an accredited laboratory abroad need to be considered after discussing with IVD.

In case of death suspected to be due to an AEFI, an autopsy needs to be performed as soon as possible (within 72 hours) to avoid tissue lysis (for e.g. in the adrenal glands), which can alter diagnosis. Samples for both toxicology and pathological examination should be sent to the reference laboratories identified by IVD as early as possible to avoid loss of biological samples due to decomposition. It is essential to ensure that a detailed patient's history is included in the autopsy form and submitted to the autopsy team to help them look for any underlying pathologies.

v.2 Guide to human specimen sample collection

The details of the type of AEFI, the tests to be performed, the specimens to be collected, the process of storage and shipment and the labs are outlined in Table 5.1

Table 5.1 Type of AEFI, the tests to be performed, the specimens to be collected, storage and shipment procedures and the labs conducting tests

Suspected AEFI	Diagnostic Method	Specimen	When to collect	Preparation, Storage and shipment	Referral of Specimens
Injection site abscesses	Microscopy and Culture/ sensitivity	Pus Swab	At contact	Use Transport media to transport Pus swabs to the next level	**Next Level with Culture and Sensitivity Facilities**
BCG lymphadenitis	Microscopy, Culture and serology	Blood, LN Aspirate or Biopsy and Suspected Vial Batch	At Contact	Wrap in leak proof and water proof container transport. Vaccine sample should be transported in reverse cold chain	**National Health Laboratory, Quality Assurance Training Center**
Collapse or shock-like state	Microscopy, Culture and serology	Blood and Suspected Vial Batch	At Contact	□ Blood smear □ Blood sugar tests at site □ Ensure asepsis for blood collection for culture	**District or Regional Hospital Lab or NHLQATC**

Convulsions or Seizures	Microscopy, Culture and antigen detection	Collect CSF from affected cases	At Contact	□ Ensure aseptic techniques of lumbar puncture □ Never use vials that contained antibiotics □ Sugar and cell counts should be done at site □ Transport to referral laboratory immediately	**District or Regional Hospital Lab or NHLQATC**
Encephalitis	Microscopy, Culture and antigen detection	Collect CSF from affected cases	At Contact	□ Ensure aseptic techniques of LP □ Never use vials that contained antibiotics □ Sugar and cell counts should be done at site Transport to referral laboratory immediately	**District or Regional Hospital Lab or NHLQATC**
Death	Serology	(1) Venous Blood (2) Vial Batch	Immediate	□ Never use vials that contained antibiotics □ Transport to referral laboratory immediately □ Transport sampled vial batch in reverse cold chain	**NHLQATC/ TFDA lab**

v.3 Vaccines and logistics

Vaccines and logistics samples from the site and the distribution point(s) should be collected as soon as possible and kept in cold chain. They should be sent to the laboratory for testing only on the recommendation of the CHMTs.

Testing of vaccines and logistics should be requested on a clear suspicion and not as routine and never before the working hypothesis has been formulated (Table 5.2). Determining which samples to send for testing (if any) depends on the working hypothesis for the cause of the event(s). If the used vial of suspect vaccine is available, it should be sent along with unused vials of the same lot.

The DIVO will be responsible for the packaging, cold chain maintenance and shipment of samples in the correct temperature to the national laboratory at TFDA laboratory. ALL specimens sent to the lab should be accompanied by a laboratory request form (Annex 3).

The laboratory will process the specimens and send the laboratory results to National IVD Manager and TFDA Director General. Laboratories will also send a copy of the laboratory results to all persons with contact details (complete address with postal code, phone and fax numbers and email address) mentioned in the lab request form

Table 5.2 Laboratory testing to investigate AEFI by working hypothesis

Working hypothesis	Specimens to send	Laboratory test
Vaccine transportation or storage	Vaccine vial	Visual test for clarity, presence of foreign matter, turbulence, discoloration or flocculation (examine under magnification)
Reconstitution error	Vaccine vial and/or diluents	Chemical composition analysis for abnormal components (e.g. suspect drug used instead of vaccine or diluent), or microbiological culture for bacterial contamination

Non-sterile injection	Needle, syringe, vaccine vial and diluents	Sterility, if an infectious cause is suspected
Vaccine problem	Vaccine vial	Chemical composition analysis: preservatives, adjuvant level, etc. (e.g. aluminium content) or biological tests for foreign substances or toxins if abnormal toxicity is suspected

6. Data and performance analysis

6.1 Sources of AEFI data

Information on vaccine safety and the possible occurrence of AEFIs can be obtained from clinical examinations, interviews of health workers, parents and community leaders, review of registers (ANC, OPD and Immunization), Vaccine and Injection logbooks, observation of immunization administration, vaccine handling and storage and laboratory reports. Analysis of data on AEFIs consists of reviewing data from the following sources;

i. Data collated into a line list
ii. Case investigation forms for each reported AEFI case,
iii. Laboratory information (Human and vaccine related)
iv. Records about similar events in the community
v. Records of the implicated vaccine

6.2 Analysis of AEFI reports

It is essential that all notified cases are reported (serious and serious AEFI) using the AEFI reporting form (Annex 1). All reported AEFI cases should be line-listed at all levels using the AEFI line-list (Annex 4). This is the first step of data management. Before the analysis, verify and reassure the data for accuracy. In addition to basic time, place and person analysis that should be done by the district and regional program managers, other key analysis, some of which also relate to the performance of the surveillance system, include;

i. Timeliness and completeness of receiving AEFI forms.
ii. Identifying health institutions where AEFIs are not reported by checking on “zero reporting” or “nil reporting”. Determine whether it is due to failure of reporting or whether there are no AEFIs to be reported.
iii. Assessing AEFI case reports received during stipulated time period.
iv. Assessing number of events and reporting rate per 1,000 or 10,000 or 100,000 doses of vaccine used.
v. Analyses by the type of AEFI
vi. Analysing programme errors by number and rates per 100 or 1,000 doses of relevant vaccines used.
vii. Compare the rates with available or known background rates.

6.3 Data analysis at different levels

Data analysis could be carried out by the responsible focal persons at different levels in the immunization safety surveillance system:

i. at the district level by DIVO and relevant staff
ii. at Regional level by RIVO
iii. at national level by the IVD and TFDA.

Analysis of data at district level is important to identify the programme errors. This helps to carry out corrective action in a timely manner. Table 6.1 describes the type of analysis and the purpose.

Table 6.1 Types and purpose of data analysis at different levels

Programme implementation level	Suggested Analysis	Purpose of analysis at this level
Local level **E.g. district**	• Number of reports by clinics, hospitals, villages by a given time • Reported AEFIs by Place (clinics, hospitals), Persons and time • Reported AEFIs by antigen	• These are programme operation indicators such as timeliness and completeness • Identify immunization errors and thereby will lead to corrective action • Will identify vaccine reactions and coincidence.
Intermediate level **(Regional/ town etc.,)**	• Number of reports by local level • Reported AEFIs by Place (clinics, hospitals), Person and Time • Cluster analysis • Reported AEFIs by antigen	• These are programme operation indicators (timeliness, completeness) at local level • Identify immunization (programme) errors and thereby will lead to corrective action. • Cluster analysis too lead to identify immunization errors, but also coincidence and vaccine reactions too. • Will identify vaccine reactions and coincidence.
National level	• Number of reports by intermediate levels • Reported AEFIs by Place (clinics, hospitals), Persons and time • Cluster analysis • Reported AEFIs by antigen	• These are programme operation indicators (timeliness, completeness) at intermediate level • Identify immunization (programme) errors and thereby will lead to corrective action. • Cluster analysis too lead to identify immunization errors, but also coincidental events and vaccine reactions. • Will identify vaccine reactions including signal detection • Lead to take operational and policy decisions in the country.

6.4 Process of data analysis

Before analysis of the line list at the national level, it is important to re-check the case definitions adopted by the reporting sources. The case should fit into a case definition such as the Brighton collaboration case definitions (www.brightoncollaboration.org) or any definition selected by the National AEFI Committee.

Line lists should be used to sort data by place, person and time. Analysis should be done by antigens by type of reported adverse events (e.g. high fever, abscess) after stratifying data. Number of doses administered for each antigen is the best denominator for calculating reported AEFI rates for each antigen in a given time period (by month, quarter or year). Various denominators and their limitations are described in table 6.2. Analysis can be expanded to AEFI rates by first or second or third dose, when the antigen is administered more than once. For this, the number of doses administered of the given antigen by first, second or third need to be used as the denominator.

Table 6.2 Selection of denominators and their limitations

Denominator	Limitations
Administered doses of vaccines	Most reliable, but not often available
Distributed doses	Greater than administered doses, thus may reduce rate (underestimate)
Coverage x Population	May be less accurate because of variability in coverage estimates
Target population	Proxy measure for vaccine population (may also under-estimate)

Use of proper multiplier in data analysis is important and also varied by purpose and level of analysis. At local level, percentage (x100= %) is the best choice, whereas at regional and national levels, one may use 1000, 100,000 or million as multiplier. For common, minor vaccine reactions, percentage is recommended and for rare serious reactions, 10,000, 100,000 or 1,000,000 (million) can be used.

6.5 Interpretation of data

Available expected rates for each type of AEFI for a given antigen is provided at http://www.who.int/vaccine_safety/initiative/tools/vaccinfosheets/en/index.html. This can help to make decision on corrective action to be taken on reported AEFIs. It is also important to know about background rates of reported medical events in the country. Comparison of background rates with reported rates of AEFI will guide to a possible hypothesis of a coincidental event. For example, febrile seizures with bacterial or viral infection aetiologies are common among young children and may also occur following some vaccines such as DTwP. Therefore it is important to know the rate of febrile seizures due to other reasons and expected rates following a given antigen.

If the values exceed the expected background rates, then one should consider true increase or coincidence due to ongoing other diseases.

6.6 Evaluating the performance of the AEFI surveillance system

The AEFI surveillance system performance needs to be regularly reviewed at all levels to ensure that the system is sensitive enough to identify and respond to AEFI rapidly. The "standard overall" indicator to determine the quality of AEFI surveillance is *"Serious AEFI reporting rate per 10,000 births per year"*

This is calculated as;

Serious AEFI reporting rate per 10,000 births per year → Total number of live births in the same area/ locality per year / Number of serious* AEFI cases reported from an area/ locality per year

Death, Hospitalization or prolongation of existing hospitalization, persistent or significant disability or incapacity, congenital anomaly/birth defect or life-threatening

Districts and provinces are encouraged to achieve a target of at least 1 serious case per 10,000 live births per year.

Some of the other key indicators that help to monitor the system include;

i. Timeliness and completeness of AEFI reporting

ii. Percentage of AEFI cases reported on time (< 24 hours of notification) to the national level

iii. Percentage of serious AEFI cases investigated on time (< 48 hours of onset) using standard formats.

iv. Number (%) of AEFI investigation conclusions supported by findings of special tests (clinical specimens, Post-mortem findings (among AEFI deaths), lab findings for vaccine samples).

v. Number (%) AEFI cases where final classification including causality assessment by AEFI committee is completed within 30 days of receipt of all documentation from districts.

vi. Number (%) AEFI cases reviewed by National AEFI committee following receipt of reported AEFI cases from region at National level.

vii. Number (%) AEFI cases reviewed by National AEFI committee and not assessable due to lack of information.

viii. Response to AEFI by the program particularly those related to programme error.

7. Brief overview of AEFI causality assessment

This section is a short introduction and practical overview of the purpose, process and classification of AEFI cases after causality assessment A comprehensive guide and background to causality assessment has been published by WHO and can be accessed online at;

http://www.who.int/vaccine_safety/publications/gvs_aefi/en/.

Causality assessment is the systematic evaluation of the information obtained about an AEFI to determine the likelihood that the event might have been caused by the vaccine/s received. Causality assessment does not necessarily establish whether or not a definite relationship exists, but generally ascertains a degree of association between the reported adverse events and the vaccine/vaccination. Nevertheless, causality assessment is a critical part of AEFI monitoring and enhances confidence in the national immunization programme. Causality assessment is important for:

i. identification of vaccine-related problems;

ii. identification of immunization error-related problems;

iii. excluding coincidental events;

iv. detection of signals for potential follow-up, testing of hypothesis and research; and

v. validation of pre-licensure safety data with comparison of post-marketing surveillance safety data.

7.1 Case selection for causality assessment

The cases for which causality is ascertained include;

i. Serious AEFI

ii. Clusters & events above expected rate/ severity

iii. Evaluation of suspected Signals

iv. Other AEFI (if required)as decided by reviewing team / committee including

v. If immunization error is suspected

vi. Significant events of unexplained cause within 30 days of vaccination

vii. Events causing significant parental or community concern (e.g. Hypotonic Hyporesponsive Episode (HHE), febrile seizures etc.)

7.2 Preparation for causality assessment

Prior to causality assessment,

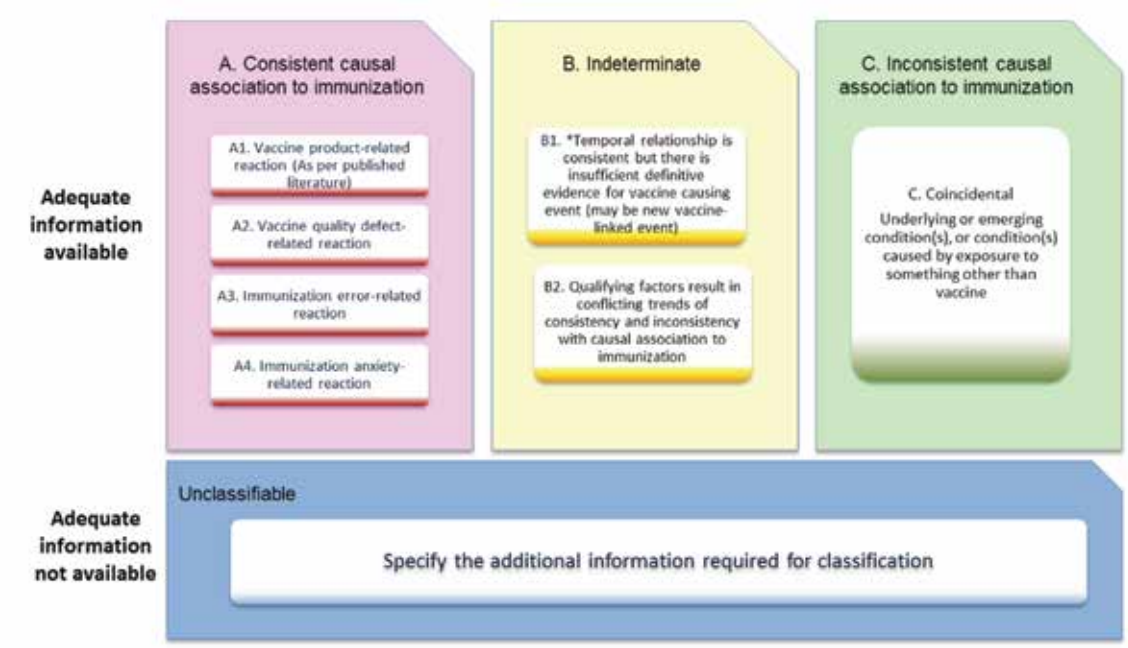
i. The AEFI case investigation should have been completed

ii. All details of the case such as case report form, case investigation form, completed clinical case record, lab reports, autopsy report, details of field investigations etc. should be available at the time of assessment

iii. There must be a "valid diagnosis" which is which the extent to which the unfavourable or unintended sign, abnormal laboratory finding, symptom or disease is defined.

With inadequate or incomplete case information, an adequate causality assessment cannot be performed or if attempted, the AEFI may be deemed unclassifiable or not assessable due to lack of information. On the other hand, even with complete information the AEFI may be categorized indeterminate due to the lack of clear evidence of a causal link, or conflicting external evidence or other inconsistencies. Nevertheless, these assessments should be recorded because the reporting of more cases may lead to a stronger signal and a plausible hypothesis, or stronger refutation of any link.

Figure 7.1 Final classification of cases after determining causality



*B1 : Potential signal and maybe considered for investigation

7.3 Causality assessment team

Causality assessment in Tanzania is done by a reviewing team/ committee at the national level that is

i. Independent
ii. free of real or perceived government, industry conflicts of interest
iii. Has broad range of expertise in the areas of 'infectious diseases, epidemiology, microbiology, pathology, immunology, neurology, vaccine program.

The committee has written terms of reference (ToR). In summary, causality assessment of serious cases needs high levels of expertise and will be done by an expert committee only at the national level. An assessment usually will not prove or disprove an association between an adverse event and the immunization. It is meant to assist in determining the level of certainty of such an association. A definite causal association or absence of association often cannot be established for an individual event.

8. Action and response to AEFI

Responding to AEFI may involve immediate short-term activities or/and long-term follow-up activities. Follow-up activities should be based on findings of investigations, causality assessments and recommendations by the investigation/expert committees.

Proper and early treatment should be provided to patients regardless of the diagnosis. Case management and referral will vary depending on the seriousness. Mild symptoms such as mild fever and pain are likely to be of short duration and can be managed by assuring and educating parents during immunization. If parents return to seek medical attention, these cases should be documented and reported in the standard form. In case patients need hospitalization, a clear system for referral should be in place.

Table 8.1 Actions to be taken upon completion of the investigation/causality assessment

Type of AEFI	Follow-up action
Vaccine-related reaction	If there is a higher reaction rate than expected from a specific vaccine or lot, obtain information from the manufacturer and consult with the WHO regional office to consider: □ withdrawing that lot; □ investigating with the manufacturer; □ obtaining vaccine from a different manufacturer.
Immunization error related	Correct the cause of the error. This may mean one or more of the following: □ changing logistics for supplying the vaccine; □ changing procedures at the health facility; □ training of health workers; □ intensifying supervision. Whatever action is taken, it is important to review at a later date to check that the immunization error related events have been corrected.
Coincidental	The main objective is to present the evidence showing that there is no indication that the AEFI is a vaccine-related reaction or immunization-related error and, that the most likely explanation is a temporal association between the event and vaccine/vaccination. This communication can be challenging when there is widespread belief that the event was caused by immunization. Sometimes, it may be useful to enlist further expert investigation to ensure that the event was truly coincidental. The potential for coincidental events to harm the immunization programme through false attribution is immense.

Depending on the nature of the event(s), the number of people affected, and community perceptions, an investigation may be conducted. In general, it is not advisable to discontinue the immunization programme while awaiting the completion of the investigation. If AEFI causality is not established – depending on the nature of the event, its extent and whether it is ongoing – a further investigation or epidemiological study may be warranted. However, it must be accepted that in some cases the relationship to vaccine will never be clear.
Communication and training are two important follow-up actions that have long term implications.

9. Communication and media management

9.1 Risk communication

Communication makes stakeholders aware of the process at each stage of the Investigation. The identification of particular interest groups and their representatives should comprise a part of an overall communication strategy. Decisions including what, whom and how, should be part of an overall communication strategy.

9.1.1 Need for improved communication

Concerns are frequently raised about vaccines and immunization programs by members of the general public and in the media. These concerns can be serious and are often misplaced. The graphic below (Fig 9.1) illustrates some of factors that may trigger public concerns; hence the need for improved quantity, quality and targeted communication about vaccine safety.

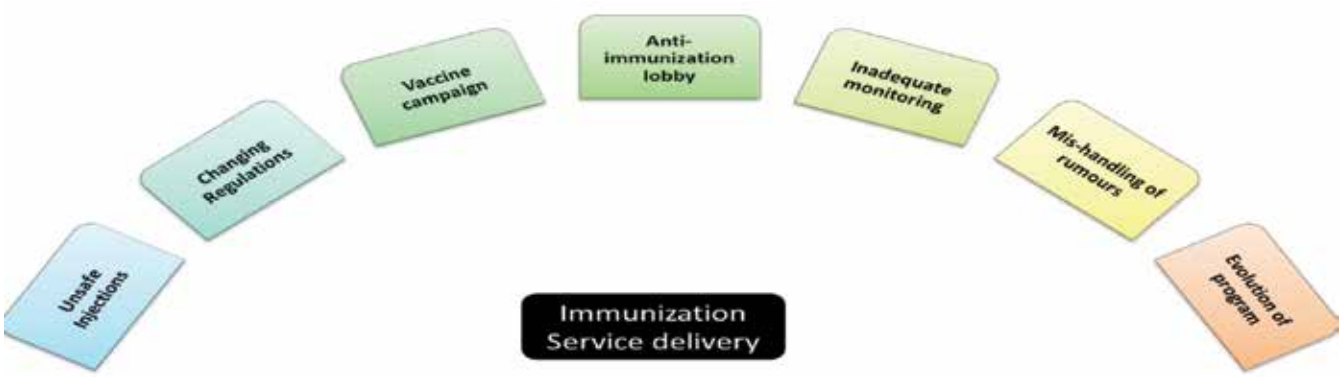


Fig 9.1 Factors triggering public concerns to immunization

9.1.2 Challenges to effective communication

Challenges that need to be overcome with effective communication include among others:

i. Decline of childhood infections and deaths from VPD
ii. Parents view that infectious disease is a thing of the past
iii. Introduction of new vaccines and related information gaps
iv. Mass campaigns or Supplemental Immunization Activities (SIAs)
v. need for transparency and accountability

9.2 Communication with clients, parents or guardian and community

Communication with parents, other members of the community, health staff and media need to be carried out under all circumstances. They should be kept informed about the investigation, results and action taken already or going to be taken regarding the AEFI. It is crucial to highlight the benefits of immunization while communicating on AEFI with the public and stakeholders.

Key points to consider when communicating with the vaccine recipient (patient or client) or parents and guardians of the patient, community and health staff are;

i. Listen to the client, parents or guardian and their concerns empathetically.
ii. Reassure and support the client, parent or guardian but do not make false promises.
iii. Assist the client, parents and guardian for hospitalization if necessary.

iv. Frequent communication with the client, parents or guardian regarding the progress of the patient.

v. Prepare a fact sheet on adverse event for the client, parents or guardian, community, health staff and media.

vi. Build up and maintain relationship among health staff, community and media.

vii. Inform the individual client, parent or guardian about possible common adverse events and how to handle them.

viii. Continuously communicate with the client, parent or guardian and community during the investigation period to assure understanding the risk-benefit of vaccination.

9.3 Role of health Care worker in community communication on AEFI

AEFI can have repercussions on the entire routine immunization programme as well as campaigns. Where medical interventions are necessary, they should be carried out as rapidly as possible. Suppressing reports of AEFI or slow reaction can cause considerable damage to the immunization programme in the long-term. Messages relating to adverse events must be disseminated rapidly to prevent rumours spreading.

Once an AEFI has occurred, responses should include the following communication elements:

i. Communicate immediately with the MoHSW, the ICC and other high officials.

ii. Provide the parents with factual information. Remember that some parents may seek information elsewhere and you may lose credibility if you do not provide a trustworthy and technically sound response. The public and the other stakeholders have a right to know exactly what happened.

iii. Reassure parents, caregivers and adults that necessary measures are being taken so that the members of the community and caregivers are informed of what is happening.

iv. Communicate the results of the investigation to the programme managers and to the EPI officers at all levels.

v. If the AEFI was caused by immunization error, tell the public what steps are being taken to prevent similar events in the future.

vi. Broadcast an official statement about the event on radio and television and publish a statement in newspapers.

vii. Repeat the message to dispel all fears.

viii. Constantly reassure the public of the safety of vaccines.

9.4 Communication with health care staff

i. Communicate among all level of health authorities involved.

ii. Reinforce their knowledge, ability, skills and performances.

iii. Update them on investigation process, progress and findings.

iv. Reassure the staff of ongoing confidence in the immunization programme; quality of the vaccine and their services provided

v. Do not blame health care worker, instead focus on the correction and quality of the IVD program.

9.5 Communicating with stakeholders

Vaccine safety information needs to be shared with other stakeholders in order to ensure dissemination of correct information and thereby ensuring the smooth functioning of national immunization programme. Depending on the need stakeholders mentioned below will be given preliminary information at initial stage and final report after completion of investigation and causality assessment at a later stage.

i. Tanzania Food and Drug Authority (TFDA)

ii. ICC (Inter-agency Coordinating Committee)

iii. RHMT and CHMT

iv. AEFI Committees at all levels

v. Politicians

vi. Professional associations

vii. Universities and hospitals

viii. International agencies and development partners

ix. Manufacturers

9.6 Communicating with media

The media is an important gateway to inform the public and shapes their view and attitudes towards vaccines and immunization, especially including the occasional mass campaign. In the long-term, building partnerships with the media is key to keep the public regularly informed about immunization, its benefits and to motivate families and communities to make use of immunization services.

9.6.1 Advance preparedness

Effective communication with the media includes efficient coordination with the field staff, a plan, trained personnel, budget and practiced responses to potential issues around AEFI. Effective communication should be in place before an immunization campaign starts and as part of the on-going communication to support routine immunization programmes.

9.6.2 A database of journalists

It is essential to maintain a database of print and electronic media journalists covering health (local, national, international) with contact information. They need to be contacted and informed about the circumstances of the AEFI.

9.6.3 Information packages:

Keep media informed through email or hardcopy by sending regular updates on any plans, programs and decisions. Sensitize media about health benefits of immunization and its impact globally and nationally. Prepare monthly or quarterly updates. Provide an updated information package with documents including Frequently Asked Questions (FAQs) on immunization in general, for specific disease and AEFI (Factsheet or a technical brief on a specific vaccine preventable disease etc.).

9.6.4 Draft media release:

The draft media release must specifically answer the 6 W's for journalists:

i. Who is affected/is responsible?

ii. What has happened?

iii. What is being done?

iv. Where has it happened?

v. When did it happen?

vi. Why did it happen?

vii. Will it happen again?

In the media release, mention the name and contact details of the AEFI focal person(s) and the name and contact details of the official spokesperson for further details should journalists have additional questions (at the end).

9.6.5 A spokesperson system:

The district level shall be the first authority in releasing the information to the media. For this purpose the District Medical Officer shall be responsible for communicating the AEFI to media, public and stakeholders. This limits the possibility of conflicting messages coming from different sources. Ensure spokesperson has the important information.

9.6.6 Orientation workshops and field visits for media:

Regular orientation workshops and field visits for journalists will help them achieve a better understanding of immunization advantages as well as the complexities of an immunization programme. This will also help to identify in advance the kind of questions or concerns that journalists specifically have.

9.6.7 Media Management during an AEFI crisis

While every single AEFI must be investigated in detail, all AEFI cases may not be a crisis situation. A crisis often occurs from inaction rather than from taking appropriate action on AEFI.

9.6.8 Monitoring of media:

When an AEFI occurs, media should be monitored for authenticity of their reporting. The AEFI Committee should move very quickly to correct any inaccuracies. The AEFI Committee could take the following immediate actions:

i. Analyze rumor, its level and potential to cause damage.

ii. Anticipate how situations might evolve following response; prepare before responding.

iii. Deal with a simple mistake in reporting with a simple solution. If it is an isolated error, make a polite call to the reporter and offer to help the reporter with correct data and facts then and in the future.

iv. If the rumor is confined to a small audience, correct it within that group only. If the error is widely reported, it may be necessary to call a media conference to present the correct facts before it leads to further damage.

v. Plan how to prevent future rumours.

9.6.9 Prepare a media release:

An effective media release should include a complete account of the event, framed in its context (e.g. an isolated event or a cluster of AEFI or coincidental event). The media release should have;

i. An outline of actions taken or planned (such as the AEFI investigation).

ii. A description of the cause of the event (but only when this is known with certainty).

iii. An assurance that corrective action has been taken or will be taken.

i. Reference to any relevant publication, video material or web site.

ii. Sender's name and spokesperson's details.

iii. Limited to one page of matter (400-500 words max).

iv. Short sentences (not exceeding two lines).

Quotes from key officials may be used after seeking their permission. The quotes must be positive and carry the key messages.

9.6.10 Call a media conference:

Media conferences may need to be conducted if AEFI is being reported extensively and widely and there is a need to provide accurate facts and de-sensationalize the story. A media conference enables all journalists to have the same information, thus there is then less likely of event being 'sensationalized'. Consider the following steps when preparing for the media conference:

i. AEFI Committee takes the lead but identifies who facilitates the press conference.

ii. If there are several members on the panel, agree beforehand on the key message(s) in response to the AEFI.

iii. Agree on roles of each panel member beforehand, including the type of questions (media, political etc.) each panel member may best handle.

iv. Panel members must avoid contradicting each other in the press conference unless it is critical to clarify something incorrect that has been said.

v. Have a media kit ready and share it with journalists. The media kit may consist of a media release with all the essential information, supplementary background information, benefits and a set of frequently asked questions about immunization.

9.7 Media Management post AEFI

9.7.1 Keeping promises to the media:

If it has been promised that media will be kept updated about the investigation findings, make sure the media is updated by the promised date. If the findings have been delayed, ensure the media is informed because they would be expecting answers.

9.7.2 Providing answers to unanswered questions

During media conferences, if a question could not be answered for any reason – for example due to absence of data or if you were unprepared to answer the questions – get back to the media with the answers as soon as possible.

9.7.3 Keeping media informed about subsequent developments

If any decision or action is taken at the highest levels following AEFI investigations or during the investigations and the public must know about it, keep the media informed though a press release or hard copy document. The website of the Ministry of Health can also be used to update the media.

9.8 Dealing with rumours and misinformation

In the context of immunization, rumour is defined as an unverifiable assertion that is circulating, or a statement without facts to confirm its truth. Rumours and misinformation about immunization are amongst the most serious threats to the success of any immunization programme. Once rumours start they can be very hard to stop.

Some examples of rumours:

i. "Vaccines are a contraceptive to control population or to limit the size of a certain ethnic group."

ii. "Vaccines are contaminated by the AIDS virus or mad cow disease."

iii. "Children are dying after receiving vaccines."

Unless the rumour can very easily be contained and addressed you must refer the matter to your supervisors **as quickly as possible**. You will need to work under their direction - action may even need to be taken at the national level. The consequences of rumours can be serious and, if unchecked, they can travel quickly beyond your local area.

9.8.1 Common causes of Rumours

i. Inadequate information sharing by health care providers or

ii. Failure to communicate correct information about vaccine effects and schedules,

iii. Failure to check whether caregivers know and understand information,

iv. Failure to give clients opportunities to ask questions

v. Parents/caregivers' negative attitudes about immunization services

9.8.1.1 What you can do at the health facility

Under the direction of your supervisor:

i. Meet with key opinion leaders (politicians, traditional and religious leaders, community leaders, other health workers).

ii. Organize meetings at sites where the individuals/groups are comfortable and feel at ease to ask questions.

iii. If there is a national mass media response, encourage your community members to watch and talk about it.

9.8.1.2 Words of advice

i. React swiftly and adapt your ongoing activities to give a quick response.

ii. Develop strong relationships and trust with your community in advance (religious, social and media groups).

iii. Give clear and consistent messages.

Annex 1

TANZANIA FOOD AND DRUGS AUTHORITY REPORT OF SUSPECTED ADVERSE REACTION

TO MEDICINES OR VACCINES

Note: Identities of reporter, patient and institution will remain confidential

I. PARTICULARS OF PATIENT	
Patient Initials or Record No.: - _____ Date of Birth (dd-mm-yyyy) or age:- _____	Sex: - Male ☐ Female ☐ Weight in kg:- _____

II. DETAILS OF ADVERSE REACTION	
Description of reaction: …… …… …… …… ……	Date Reaction Started /→ / ____ _____ Date Reaction Stopped (if known) →/ + ____ ____ _____ Onset latency……

Health related information: Medical history (e.g. hepatic, renal, HIV), allergies, pregnancy, smoking, alcohol use, etc. ***Please write any relevant medical and laboratory results including dates (if done)***.....
....
.....

III. DETAILS OF SUSPECTED MEDICINE/VACCINE USED							
Name of suspected medicine(s)/ vaccine(s) (Specify brand name or manufacturer if known).	**Dosage**	**Frequency**	**Route**	**Therapy Date**		**Batch. No & Expiry date (If known)**	**Reason for use**
				Start	**Stop**		
1.							
2.							
3.							
Other medicines used at the same time and or one month before (including herbal medicines)							
1.							
2.							
3.							

IV. MANAGEMENT OF ADVERSE REACTION

Reaction subsided after stopping the suspected drug/reducing the dose: ☐ Yes ☐ No ☐ Unknown

Reaction reappeared after reintroducing drug: ☐ Yes ☐ No ☐ Not applicable

Seriousness of the Reaction **(please tick all that apply):**

☐ Discomfort but able to work
☐ Discomfort could not work
☐ Required or prolonged hospitalization
☐ Life threatening
☐ Caused persistent disability or incapacity
☐ Caused a congenital anomaly
☐ Patient Died
☐ Others, please give details……..

Treatment of adverse reaction ☐ No ☐ Yes **(if yes please specify)**:……

……
……..

Outcome of the reaction Not yet recovered ☐ Recovered (Date):___ ____ ____

Cause of death……..……..

V. THERAPEUTIC FAILURE

PLEASE WRITE IF THE MEDICINE(S)/VACCINE(S) SHOWED LACK OF EFFICACY BELOW: (Continue at the back)

VI. MEDICATION ERRORS AND OVERDOSAGE

PLEASE WRITE DETAILS OF MEDICATION ERRORS AND OVERDOSAGE BELOW:

PLEASE WRITE ANY OTHER RELEVANT ADDITIONAL INFORMATION BELOW :

VII. PARTICULARS OF REPORTER /HEALTH CARE PROVIDER		
Name: _____Profession: _____ Contact phone No: _____ E-mail: _____ Signature: _____ Date of this report:		Name and Address of the health facility: _____ _____
☐ *Please tick if you wish to receive information about other local reports associated with the suspected drug(s)*		
Thank you for your cooperation	***Submission of an ADR case report does not discredit the competence of the reporter.***	***Ref No. (for official use)***

First Fold

Guide to filling the form

How to report?

Dully fill in the form as required

Use a separate form for each patient

Report direct to TFDA through the following addresses:-

Mail : Tanzania Food and Drugs Authority,

P. O. Box 77150, Dar es Salaam

Fax:: 22- 2450793

Phone: 22-2450512 / 2450751

Internet; http://www.tfda.or.tz

E-mail: adr@tfda.or.tz

The ADR reporting form and the guidelines are also available for downloading at http://www.tfda.or.tz

An Adverse Drug Reaction (ADR) is defined as a reaction which is noxious and unintended, and which occurs at doses normally used in human for prophylaxis, diagnosis, or therapy of a disease, or for the modification of physiological function.

What to report?

Please report all undesirable patient effect suspected to be associated with drugs, cosmetics or medical devices use.

Report even if:

- You're not sure that the product caused the event
- You don't have all the details

When to report?

As soon as possible

Submission of follow-up reports:

Any follow-up information for an ADR that has already been reported can be sent on another ADR form or it can be communicated directly to TFDA by telephone, fax or e-mail. Please indicate that it is a follow-up report.. It is very important that follow-up reports are identified and linked to the original report.

Moisten gum and fold. For maximum adhesion, press down for few seconds

►Second Fold ◄

POSTAGE WILL BE PAID BY LICENCEE

No postage stamp required If posted in Tanzania

BUSINESS REPLY SERVICE LICENCE No. BRS 01

TO: THE DIRECTOR GENERAL

TANZANIA FOOD AND DRUGS AUTHORITY

P. O. BOX 77150

DAR ES SALAAM

Annex 2

AEFI INVESTIGATION FORM

(Only for Serious Adverse Events Following Immunization - Death / Disability / Hospitalization / Cluster

Section A — **Basic Details**

Province/State | District | Case ID

Place of vaccination (√): ☐ Govt Health Facility ☐ Private Health Facility ☐ Other (specify)_____

Vaccination in (√): ☐ Campaign ☐ Routine ☐ Other (specify)_____

Address of vaccination site:

Name of Reporting Officer

Date of investigation:_____/_____/_____

Date of filing this form_____/_____/_____

Designation / position:

This report is: ☐ First ☐ Interim ☐ Final

Telephone# Landline (with code): Mobile: Email:

Patient Name

(Use a separate form for each case in a cluster)

Date of birth (DD/MM/YYYY):_____/_____/_____

OR Age at onset_____years_____Months_____Days OR Age group: ☐ < 1 year ☐ 1-5 years ☐ > 5 years

Patient's full address with landmarks (Street name, house number, locality, phone number etc):

Name of vaccines/diluent received by patient	Date of vaccination	Time of vaccination	Dose eg 1st 2nd etc	Batch/ Lot number	Expiry date
				Vaccine	Vaccine
				Diluent	Diluent
				Vaccine	Vaccine
				Diluent	Diluent
				Vaccine	Vaccine
				Diluent	Diluent
				Vaccine	Vaccine
				Diluent	Diluent
				Vaccine	Vaccine
				Diluent	Diluent

Type of site (√) ☐ Fixed ☐ Mobile ☐ Outreach ☐ Other_____

Date of first/key symptom (DD/MM/YYYY):_____/_____/_____ Time of first symptoms (hh/mm_____/_____

Date of hospitalization (DD/MM/YYYY): _____/_____/_____

Status on the date of investigation (√): ☐ Died ☐ Disabled ☐ Recovering ☐ Recovered completely ☐ unknown

If died, date and time of death (DD/MM/YYYY):_____/_____/_____ (hh/mm_____/_____

Autopsy done? (√) ☐ Yes (date_____ ☐ No ☐ Planned on (date) _____Time_____

Attach report (if available)

Section B Relevant patient information prior to immunization

Criteria	Finding	Remarks
Past history of similar event	Yes / No /unkn	
Adverse event after previous vaccination(s)	Yes / No /unkn	
History of allergy to vaccine, drug or food	Yes / No /unkn	
Pre - existing illness (30 days) / congenital disorder	Yes / No /unkn	
History of hospitalization in last 30 days, with cause	Yes / No /unkn	
Patient currently on concomitant medication? (If yes, name the drug, indication, doses & treatment dates)	Yes / No /unkn	
Family history of any disease (relevant to AEFI) or allergy	Yes / No /unkn	

For adult women

- Currently pregnant_____/ No / Unknown
- Currently breastfeeding? ☐ Yes ☐ No

For infants

- The birth was ☐ full-term ☐ pre-term ☐ post-term Birth weight:_____
- Delivery procedure was ☐ Normal ☐ Cesarean ☐ Assisted (forceps, vacuum etc) ☐ with complication (specify)

Section C Details of first examination of serios AEFI case**

Source of information (√ all that apply): ☐ Examination by investigator ☐ Documents ☐ Verbal autopsy

☐ Other _____ if from verbal autopsy, please mention source_____

Name of the person who first examined /treated the patient: _____

Name of other persons treating the patient: _____

Other sources who provided information (specify): _____

Signs and symptoms in chronological order from the time of vaccination:

Name and contact information of person completing these clinical details	Designation:	Date/time

** Instructions -Attach copies of ALL available documents (including case sheet, discharge summary, case notes, laboratory reports and autopsy reports) and then complete additional information NOT AVAILABLE in existing documents, i.e

- *If patient has received medical care* -attach copies of all available documents (including case sheet, discharge summary laboratory report and autopsy reports) if available and write only the information that is not available in the attached document
- *If patient has not received medical care*-obtain history, examine the patient and write down your findings below (add additional sheets if necessary)

Provisional / Final diagnosis

Section D	**Details of vaccines provided at the site linked to AEFI on the corresponding day**									
Number immunized for each antigen at session site. Attach record if available	Vaccine name									
	Number of doses									

a) When was the patient immunized? (√ the ☐ below and respond to ALL questions)	
☐ Within the first vaccinations of the session ☐ within the last vaccinations of the session ☐ Unknown	
In case of multidose vials, was the vaccine given ☐ within the first few doses of the vial administered? ☐ within the last doses of the vial administered? ☐ unknown?	
b) Was there an error in prescribing or non-adherence to recommendation for use of this vaccine?	Yes* / No
c) Based on your investigation, do you feel that the vaccine (ingredients) administered could have been unsterile?	Yes* / No / Unable to assess
d) Based on your investigation, do you feel that the vaccine's physical condition (e.g. colour, turbidity, foreign substances etc) was abnormal at the time of administration?	Yes*/ No / Unable to assess
e) Based on your investigation, do you feel that there was an error in vaccine reconstitution /preparation by the vaccine vaccinator (e.g wrong product, wrong diluent, improper mixing, improper syringe filling etc)	Yes* / No / Unable to assess
f) Based on your investigation, do you feel that there was an error in vaccine handling (e.g. break in cold chain during transport, storage and / or immunization session etc)	Yes* / No / Unable to assess
g) Based on your investigation, do you feel that the vaccine was administered incorrectly (e.g. wrong dose, site or route of administration, wrong needle size, not following good injection practice e.tc.)	Yes* / No / Unable to assess
h) Number immunized from the concerned vaccine vial /ampoule	
i) Number immunized with the concerned vaccine in the same session	
j) Number immunized with the concerned vaccine having the same batch number in other locations. Specify location:_____	
k) Is this case a part of a cluster?	Yes* / No / Unkn
l) If yes, how many other cases have been deleted in the cluster?	
a. Did all the cases in the cluster receive a vaccine from the same vial?	Yes* / No / Unkn
b. If no,number of vials used in the cluster (enter details separately)	

**** it is compulsory for you to provide explanations for these answers separately***

Section E	**Immunization practices <u>at the place(s) where concerned vaccine was used</u>** ***(Complete this section by asking and / or observing practice)***
Syringes and needles used:	
• Are AD syringes used for immunization?	Yes* / No / Unkn
If no, specify the type of syringes used: ☐ Glass ☐ Disposable ☐ Recycled disposable ☐	
Specific key findings/additional observations and comments	

Reconstitution: (Complete only if applicable, (√) NA if not applicable			
• Reconstitution procedure (√)	Status		
Same reconstitution syringe used for multiple vials of same vaccine?	Yes	No	NA
Same reconstitution syringe used for reconstituting diferent vaccine?	Yes	No	NA
Seperate reconstitution syringe for each vaccine vial?	Yes	No	NA
Seperate reconstitution syringe for each vaccination?	Yes	No	NA
• Are the vaccines and diluents used the same as those recommended by the manufacturer?	Yes	No	NA
Specific key findings/additional observations and comments			

Section F	**Cold Chain and transport** ***Complete this section by asking and / or observing practice***
Last vaccine storage point:	
• Is the temperature of the vaccine storage refrigerator monitored?	Yes / No
If "yes", was there any deviation outside of 2-8 ^{0}C after the vaccine was placed inside?	Yes / No
If "yes", provide details of monitoring seperately	
• Was the correct procedure for storing vaccines, diluents and syringes followed?	Yes / No / Unkn
• Was any other item (other than EPI vaccines and diluents) in the refrigerator or freezer?	Yes / No / Unkn
• Were any partially used reconstituted vaccines in the refrigerator?	Yes / No / Unkn
• Were any unusable vaccines (expired, no label, VVM at stages 3 or 4 frozen) in the refridgerator?	Yes / No / Unkn
• Were any unusable diluents (expired, manufacturer not matched, cracked dirty ampoule) in the store	Yes / No / Unkn
Specific key findings/additional observations and comments:	

Vaccine transportation	
• Type of vaccine carrier used	
• Was the vaccine carrier sent tothe site on the same day as vaccination	Yes / No / Unkn
• Was the vaccine carrier returned from the site on same day as vacinnation?	Yes / No / Unkn
• was a conditioned ice-pack used?	Yes / No / Unkn
Specific key findings/additional observations and comments	

Section G	**Community investigation (please visit locality and interview parents/others**
Were any similar events reported within a time period similar to when the adverse event occured and in the same locality? Yes / No Unknown If "yes" describe:	
If "yes" how many events/episodes?	
Of those effected, how many events/episodes • Vaccinated: _____ • Not vaccinated:_____ • Unknown:_____	
Other comments:	

Section H	**Other findings/observations/commentss**

Annex 3

AEFI LABORATORY REQU SITION FORM (LRF) **(To be completed by XXX. LRF should be accompanied with specimens)**
(For Serious Adverse Events Following Immunization)
AEFI category (Encircle): **Death / Hospitalized / Cluster / Disability**

Province		**Case ID**	
District			
Sub District			
Name of person sending the specimen: Designation: Phone Number :		Date of filling LRF :	
Case Name			
Date of Birth	D D M M Y Y Y Y	Age (in months)	Sex: Male / Female
Complete Address of the patient with landmarks (Street name, house number, village, block, Tehsil, PIN No., Telephone No. etc.)			
P H O N E			

Date of vaccination	D	D	M	M	Y	Y	Y	Y	Date of Onset	D	D	M	M	Y	Y	Y	Y

Date of collection of specimen	D	D	M	M	Y	Y	Y	Y	Time of collection of specimen	H	H	M	M	(	AM	PM	)

. Precise description of samples:

a) For vaccine/diluents specimens: (to be transported in reverse cold chain)

Mention vaccine/ diluent	Quantity Sent	Name of Manufacturer (in BLOCK Letters)	Batch No.	Manufacturing Date	Expiry Date

b) For logistics specimens: (AD, Reconstitution, Disposable syringes)

Mention Logistics	Quanti-ty Sent	Name of Manufacturer (in BLOCK Letters)	Batch No.	Manufa-cturing Date	Expiry Date

c) For Biological product specimen: (CSF, Blood, Urine, etc)

2. Test requested:
3. Preliminary clinical diagnosis (working hypotheses):

4. Name & complete address of officials to whom laboratory results should be sent:

Send to	Complete address	Phone/ Fax	Mobile	Email -ID
National Level				
Province/ State level				
District level				
Others (specify)				

To be completed by lab officials after receiving the specimen

Date of receipt of specimen at laboratory	D	D	M	M	Y	Y	Y	Y

Name of person receiving specimen(s) at laboratory	

Condition of specimen upon receipt at lab (*encircle*)	Good	Poor	Unknown

Comments by pathologist, virologist or bacteriologist:

Date specimen results sent from this lab	D	D	M	M	Y	Y	Y	Y

Name of laboratory professional	

Signature

Phone number:	Email Id:

Annex 4

AEFI Line listing

													Name/ID
													Village/Town / District
													Date of birth (dd/mm / yyyy) and age
													Date of immunization(dd/mm/ yyyy)
													Reaction type (code) [1] Minor [2] Severe/ Serious
													Outcome (Recovered disability / Died)
													Suspect vaccine (name and dose, e.g. Penta-2)
													Vaccine batch/Lot number
													Diluent batch number
													Onset time interval (hours, days, weeks)
													Date reporting (dd/mm/ yyyy)
													Investigated? (If yes, date)
													Cause (code)

Establishing codes for area, reaction type, cause of AEFI, and certainty of cause will facilitate recording, data entry and analysis. Because of the potential for coding errors, the code should be double-checked.

Coding for cause of AEFI:

[A1] Vaccine-related	[A2] Immunization error-	[A3] Immunization anxiety-	[B] Indeterminate	[C] Coincidental	[D] Inadequate information

TFDA
Tanzania Food & Drugs Authority

IVD

World Health Organization