RWANDA FDA
Rwanda Food and Drugs Authority

GUIDELINES FOR ADVERSE EVENTS FOLLOWING IMMUNIZATION (AEFI) SURVEILLANCE

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FOREWORD

Rwanda Food and Drugs Authority is a regulatory body established by the law N°003/2018 of 09/02/2018 with mandate of to protect public health, especially in its article 3 paragraph 2 and article 9 paragraph 8 whereby the Authority is mandated to conduct pharmacovigilance and post marketing surveillance for safety and quality of regulated products, including vaccines, among other regulatory functions. The Regulations No: CBD/TRG/016 Rev_0 governing pharmacovigilance of pharmaceutical products and medical devices especially in its article 29, the Authority has the mandate to issue guidelines and SOPs to implement the regulations.

Vaccines are largely used to protect individuals from acquiring deadly infectious diseases which are preventable. Such products are relatively safe and rarely cause adverse events following immunization (AEFI). A proportion of these 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 recipients who were apparently healthy, monitoring vaccine safety is of paramount importance in a healthcare system of any country.

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.
In Rwanda, the Expanded Programme on Immunization (EPI) since it was established in 1978 has been involved in increasing immunization coverage to all targeted beneficiaries. EPI offers now 12 antigens in routine immunization with vaccination coverage of 95% in 2017 (IMCS 2017).
Rwanda FDA is committed in strengthening AEFI surveillance system with national dedicated pharmacovigilance and safety monitoring division, with designated trained staff, with clear mandates and well-defined structures and roles and responsibilities.

Monitoring vaccine safety has been challenging as the Expanded Programme on Immunization (EPI), which has actively been engaged in enhancing immunization coverage is also primarily collecting vaccine safety data from the districts. AEFI reports which reach EPI may not find their way to different stakeholders and the country has not been able to share AEFI reports with the Global community through the WHO Programme for International Drug Monitoring. Currently EPI and Rwanda FDA are in the process of establishing 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 the safety of vaccines will be effectively monitored. This will contribute to assessing risks, benefits and effectiveness of vaccines thus minimizing 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 RBC/EPI, AEFI committee of experts' members, 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.

This document will serve as guide to stakeholders at all levels involved in and take part in the strengthening of the AEFI surveillance system in Rwanda.

We are thankful to RBC / EPI program for their substantial contributions in drafting and revising these guidelines. We also acknowledge the contributions of World Health Organization as well as national and local stakeholders for the guidance and technical support offered in developing these guidelines.

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Director General

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		Editorial and formatting changes were made as needed in accordance with the current document control SOP.

CONTENTS

ACRONYMS AND ABBREVIATIONS

ADRs	Adverse Drug Reactions
AEFI	Adverse Events Following Immunization
AESI	Adverse Event of Special Interest
BCG	Bacillus Calmette-Guerin
CIOMS	Council of the International Organization of Medical Sciences
COVID-19	Coronavirus disease 2019
CSF	Cerebrospinal fluid
DIO	District Immunization Officer
DHMT	District Health Management Team
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
DPT3	Diphtheria Tetanus Pertussis 3
EPI	Expanded Programme on Immunization
GVAP	Global Vaccine Action Plan
Hep B	Hepatitis B Vaccine
Hib	Haemophilus influenza type b vaccine
IPV	Inactivated Polio Vaccine
EPI	Expanded Programme on Immunization
OPV	Oral Polio Vaccine
MAH	Marketing Authorization Holder
MMR	Measles Mumps Rubella
MoH	Ministry of Health
NITAG	National Immunization Technical Advisory Group
OPV	Oral Polio Vaccine
PVV	Pentavalent Vaccine
Rwanda FDA	Rwanda Food and Drugs Authority
SIDS	Sudden Infant Death Syndrome
VAPP	Vaccine Associated Paralytic Poliomyelitis
VPD	Vaccine Preventable Disease
WHO	World Health Organization

GLOSSARY OF TERMS

In the context of these guidelines, the following words/phrases are defined as follows.

Adverse event following immunization (AEFI)	Any untoward medical occurrence which follows immunization and which does not necessarily have a causal relationship with the usage of the vaccine. The adverse event may be any unfavourable or unintended sign, abnormal laboratory finding, symptom or disease.
Adverse Event of Special Interest	A pre-identified and predefined medically-significant event that has the potential to be causally associated with a vaccine product that needs to be carefully monitored and confirmed by further specific studies.
Adverse Drug Reactions (ADRs)	A response to a medicine which is noxious and unintended, and which occurs at a dose normally used in human for prophylaxis, diagnosis or therapy of disease or for the modification of physiological function. The term adverse drug reaction should be considered for harmful or seriously unpleasant effects occurring at doses intended for therapeutic, prophylactic or diagnostic effect and which calls for reduction of dose or withdrawal of the medicine and/or forecast hazard from future administration.
Adverse Event	(AE): Any untoward medical occurrence that may present during treatment with a pharmaceutical product but which does not necessarily have a causal relationship with the treatment. An adverse event can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporarily associated with the use of the product whether or not related to the product. For the purposes of this compendium, adverse events will cover adverse drug reactions, adverse events following immunizations and incidences following the use of a medical device
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.
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 anxiety-related reaction	An AEFI arising from anxiety about the immunization.
Immunization error-related reaction	An AEFI that is caused by inappropriate vaccine handling, prescribing or administration and thus by its nature is preventable.
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.
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).
Medical product	Any substance or combination of substances presented as having properties for treating or preventing disease in human beings; or which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or making a medical diagnosis.
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)	Reported information on a possible causal relationship between an adverse event and a medical product. The relationship being unknown or incompletely documented previously. Usually more than a single report is required to generate a signal, depending upon the seriousness of the event and the quality of the information.

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.

CHAPTER 1. INTRODUCTION

1.1 Background

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 mostly mild and very rarely severe, 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.

A good vaccine is one that provides the best protection and gives rise to minimum adverse events. AEFIs can arise through a variety of reasons: these include events that could be inherent to the vaccine product, or related to the quality, or immunization error or immunization anxiety or could be coincidental. A robust AEFI surveillance system in a country will help authorities to detect, manage and prevent AEFIs.

In Rwanda, the Ministry of Health (MoH) operates the Expanded Programme on Immunization (EPI) through the Rwanda Biomedical Centre/Maternal, Child and Community Division. The Expanded Programme on Immunization (EPI) 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 and all the Districts reporting DPT3 Coverage above 80%, establishing a cold chain system, engaging national and district authorities in monitoring vaccine use, training and developing capacity of healthcare providers as well as establishing linkages and networking with international stakeholders.

Rwanda Food and Drugs Authority (Rwanda FDA) is established and mandated by the Law Nº 003/2018 of 09/02/2018 to regulate and protect public health by assuring Safety, Efficacy and Quality of Human and Veterinary medicines, vaccines and other biological products, processed foods, poisons, medicated cosmetics, medical devices, household chemical substances, tobacco & tobacco products and conduct of clinical trials.

In its article 9 paragraphs 8 of law N° 003/2018 of 09/02/2018 establishing Rwanda FDA, the authority is mandated to conduct pharmacovigilance and post-marketing surveillance of all regulated products including vaccines. The Authority sets out modalities for reporting, analysis and feedback of the safety data reported from all key stakeholders in the medical products entire supply chain.

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.

The overall goal is the protection of public health and wellbeing of the entire population particularly infants, children, pregnant women and the general population who depend on vaccines to protect them from serious vaccine preventable diseases (VPD). These guidelines outline the 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 Rwanda in close partnership. These guidelines also outline the surveillance system and provide tools and procedures needed to report and manage AEFIs. An understanding of the types of AEFIs, investigation techniques, specimen collection, managing AEFIs and communication including communicating with the media, are also described 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 guidelines will also bring together stakeholders and allow for networking and improved collaboration in the process of detecting, analysing and preventing AEFIs.

1.2 Scope

These guidelines cover different AEFI surveillance activities including prevention and management of AEFI, structure of AEFI surveillance in Rwanda, Laboratory testing of specimens, data and performance analysis, brief overview of AEFI causality assessment, action and response to AEFI, signal detection, management of vaccine safety crises, and AEFI related communication and media management.

CHAPTER 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. A vaccine can also be made from a messenger RNA (mRNA) coding for an antigenic protein that is generated in vitro and encased with suitable material (e.g. lipid-based nanoparticle emulsion) that assures the delivery into the cell.

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 five types of vaccines: live attenuated, inactivated (killed antigen), subunit (purified antigen), toxoids (inactivated toxic compounds) and nucleic acid. 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

Nucleic Acid Vaccines	**Messenger RNA (mRNA):** COVID-19 vaccines (Pfizer-BioNTech and Moderna) **DNA vaccines (viral vector vaccines):** COVID-19 vaccines (AstraZeneca and Jansen/Johnson and Johnson)

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 immunocompromised 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 2.2

Table 2.2 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:

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

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

A. Cause-specific vaccine reactions

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).

Vaccine quality defect-related reaction: This is due to a defect in a vaccine (or its administration device) that occurred during the manufacturing process. Such a defect may have an impact on an individual's response and thus increase the risk of adverse vaccine reactions. Insufficient inactivation of wild-type vaccine 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.

B. 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 2.3 describes the frequency of occurrence of reported adverse events.

Table 2.3 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%

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 2.4** describes the common minor vaccine reactions by antigen and the treatment for the same.

Table 2.4 Common minor vaccine reactions by antigen and treatment

Vaccine	Local adverse events (pain, swelling, redness)	Fever (> 38^0C)	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%
COVID-19 Vaccines (Pfizer-BioNTech)	80-89%	10-16%	70-83%
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

https://www.cdc.gov/vaccines/covid-19/info-by-product/pfizer/reactogenicity.html

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 is rarely life threatening. Some examples are seizures, thrombocytopenia, Hypotonic Hyporesponsive Episodes (HHE), prolonged crying, thrombosis (AstraZeneca COVID-19 vaccine), 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;
- are congenital anomaly/birth defect.

All serious AEFI should be reported, investigated and the causality assessment conducted.

The rate of occurrence of the rare and more serious reactions has been summarized in **table 2.5.** 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 2.5 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
COVID-19 Vaccine	Anaphylaxis	0-2.5 hours*	~11

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.
4. *This information is for only Pfizer-BioNTech COVID-19 vaccine https://www.cdc.gov/mmwr/volumes/70/wr/mm7002e1.htm. More than 70% of anaphylaxis cases occurred with 15 min of vaccination.

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

Table 2.6 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.

2.2.3 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 are 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.

2.2.4 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 2.7 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 2.7 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 Rwanda 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**
Rwanda	***32***	***354734***	***946***	***236***	***34***	***84249***	***210626***	***3009***
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

2.3 Adverse event of special interest (AESI)

2.3.1 Introduction

AESI is a relatively new AEFI classification that stared with pandemic vaccine development. AESI refers to adverse events of significant scientific, medical, and public interest among pandemic vaccines.

AESIs are usually identified through active vaccine safety surveillance (AVSS) systems. Conditions commonly considered as AESIs include serious events that have followed other immunizations, for example:

- Guillain-Barré syndrome (GBS);
- acute disseminated encephalomyelitis (ADEM);
- anaphylaxis;
- serious events potentially related to novel platforms;
- serious events potentially related to adjuvants;
- serious events related to vaccine failure/immunogenicity (vaccine-associated enhanced disease (VAED)); or
- events that are potentially important for specific populations.

2.3.2 Difference between an AESI and an AEFI

Though AESIs may be considered as a class of AEFIs these 2 categories of adverse events present a number of differences. The table below summarizes the comparison between AESIs and AEFIs in the context of COVID-19.

Table 2.8 Differences between AESIs and AEFIs and their implications in real practice

	AESI	**AEFI**
What	A pre-specified event that has the potential to be causally associated with a vaccine product that needs to be carefully monitored and confirmed by further special studies.	Any untoward medical occurrence that follows immunization, and that does not necessarily have a causal relationship with the usage of the vaccine. The adverse event may be any unfavourable or unintended

		sign, abnormal laboratory finding, symptom or disease.
Purpose of collecting information	To identify pre-specified specific events by a set criterion and determine if the event is associated with COVID-19 vaccination	To identify all events after vaccination – determine if serious, investigate (serious) and do causality assessment.
Identification method	Identified via an active surveillance system in sentinel sites or electronic health record by a health care worker or other staff in the system.	Identified via spontaneous reporting by vaccine recipients or their parents, or health care workers or other persons who first notice the event.
Case definitions	Critical	Important
Type of reporting	All events identified through active surveillance that fit the case definition, irrespective of immunization status.	All events that follow immunization and are notified to the health care system.
Training	Immunization staff and other health care workers in sentinel sites and predefined active surveillance systems, EPI mangers, NRA, research staff, national AEFI committee.	All frontline immunization staff in health care facilities (public and private); and other relevant staff for reporting, investigation, data analysis, and causality assessment.
Users	Sentinel site staff, EPI managers, NRA, epidemiologists, national AEFI committees, study teams.	Health care workers, NIP/EPI managers, NRA, surveillance and information managers, epidemiologists, surveillance and information managers, vaccine safety partners including the community

Source: https://www.who.int/docs/default-source/covid-19-vaccines-safety-surveillance-manual/covid19vaccines_manual_aesi.pdf

2.3.3 Data to be collected for AESIs in active vaccine safety surveillance (AVSS) systems

Individual data, linked by a unique identifier, should be collected in the defined population for vaccination events, health events or outcomes and demographic characteristics. This identifier

could be a national identification number, such as a social security number, a trial or study participant number, and if not, available linkage could be done using demographic identifiers, such as initials, date of birth or address. Core and complete data to be collected for AVSS are compiled in the table below.

Table 2.9 Data to be collected for AESI in AVSS systems

Vaccination data	**Health events or outcomes**	**Demographic data**
*Vaccine brand name	Adverse event(s)	Age at onset
*Lot number	Date of onset of symptoms	Gender
*Date of vaccination	Serious	Medical conditions
*Dose number	Outcome	Medication
*Site of vaccination	-	-
Place of vaccination	Place of care	-
Vaccine antigens	-	-
Concomitant vaccines	-	-
Route of administration	-	-

***** *Part of the core data set for AESI AVSS systems*

CHAPTER 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 an 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 of 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 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:

- It is both important and necessary to maintain the cold chain at all levels.
- Vaccines must be reconstituted only with the diluents supplied by the manufacturer.
- 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.
- Other than vaccines, no other drugs or substances should be stored in the refrigerator of the immunization centre.
- Immunization workers must be adequately trained and closely supervised to ensure that proper procedures are followed.
- Careful epidemiological investigation of an AEFI is needed to pinpoint the cause and to correct immunization practices.
- 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.

Sometime, 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. However, an accidental administration of a single dose of adrenaline (intramuscularly) to a vaccine with only syncope does not harm the vaccine.

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 3.1 lists conditions which may be mistaken for anaphylaxis.

Table 3.1 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 rotavirus 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.

Table 3.2 Management of some serious AEFI in health facilities

SERIOUS AEFI	MANAGEMENT	DIFFERENTIAL DIAGNOSIS	TESTS
Syncope, malaise	Have the patient sit or lie down and observed until or he/she regain consciousness	Orthostatic hypotension induced by drug or in case of diabetic neuropathy	Cervical rachis Xray Interview, BP
Anaphylactic shock	**Evacuation / Hospitalization according to the technical capacity** - Adrenaline / Corticoids/ IV fluids **LabTest:** Ionogram, serum creatinine, azotemia, blood-sugar, complete blood count **Sample collection (blood and urine)** **NB** : other tests eventually and following the alert	Cardiogenic shock (infarctus) Septic shock Hypovolemic shock (hemorrhage, diarrhea) Vaso-vagal syncope Hypoglycemic coma	ECG Blood culture, blood-sugar CBC, ionogram, History of the present complaint, heart beat(bradycardia)
Bronchospasm	**Evacuation / Hospitalization according to the technical capacity** - Adrenaline/Corticoids / Salbutamol / IV fluids CBC, Chest X Ray **Sample collection (Blood and urine)** **NB** : other tests eventually and following the alert	Asthma crisis, inhalation or foreign objects Laryngitis	Chest Xray, Interview++ CBC, ENT consultation, Breath functional exploration
Quincke Edema, Angioedema			
Stevens-Johnson/Lyell Syndrome, **Erythema multiforme**	**Evacuation / Hospitalization according to the technical capacity** - Local wound care (permanganate, aqueous eosine), / IV fluids + ions. Avoid	Dermal staphylococcus infection, herpetic infection, pemphigus, herpetiform dermatitis	CBC, blood culture, pyoculture, hystology

	corticoids Ionogram, serum creatinine, azotemia, blood-sugar **Sample collection (Blood and urine)** **NB** : other tests eventually and following the alert		
Purpura	**Evacuation / Hospitalization according to the technical capacity** CBC, PT, TCA, TS Treatment after hematologist's advice **Sample collection (Blood and urine)** **NB:** other tests eventually and following the alert	Purpura secondary to an infection: Meningococcus, Streptococcus, Staphylococcus, hepatitis B	CBC, blood culture, HBs Ag markers,

Table 3.3 Management of some serious AEFI in referral hospital

SERIOUS AEFI	MANAGEMENT	DIFFERENTIAL DIAGNOSIS	TEST
Meningitis-like syndrome	**Evacuation / Hospitalization according to the technical capacity** Thick smear, CBC, CSF CBE + chemistry and/or solubles Ab, PCR Malaria Treatment depending on the results **Sample collection (blood, CSF and urine)** **NB**: other tests eventually and following the alert		

Guillain-Barré Syndrome	**Evacuation / Hospitalization according to the technical capacity** CBC, CSF CBE + solubles Ab, chemistry, blood ionogram, blood-sugar, HIV serology, CD4 count Treatment after neurologist's advice **Sample collection (blood, CSF and urine)** **NB**: radio rachis, scanne eventually and following the al	Polymyositis, PAA Hypokaliemic periodic paralysis	Transaminases, CBC, CPK, LDH, EMG, stools Ionogram
Transverse myelitis		Infectious myelitis/encephalomyélitis (CMV, VZV, Poliovirus, HIV measles) Medullar compression Hypermagnesemia, hypophosphatemia	CBC, ionogram, HIV serology, CD4 count, other serologies, EEG, Rachis X ray, city scan /CSF, PCR
Acute disseminated Encephalomyélitis			
Encephalopathy	**Evacuation / Hospitalization according to the technical capacity** Thick smear, CBC, blood ionogram Treatment: IV, neurologist's advice **Sample collection (blood, CSF and urine)** **NB**: city scan, EEG and o eventually and following the al		
Hypotonic hyporesponsive episode			
Facial palsy	HIV serology, CD4 lymphocyt **Sample collection (blood and**	Central facial palsy	History, neurological exam,
Myocarditis	**Evacuation / Hospitalization according to the technical capacity** ECG, veinous way troponine, haemoculture, echocardiography **- Sample collection (blood and urine)**	Infectious/toxic myocarditis, Peripartum myocarditis	Interview, ECG, CBC, cardiac echography
Unexplained death	Cardiac blood puncture		

	Alert – Autopsy / organ Biopsy on consent		
Unexpected AEFI	**Alert -** Care depends on the diagnosis **Sample collection (blood, CSF and urine** according to the clinical presentation)		

More details about the AEFI case management are included in the NSTGs (National standards Treatment Guidelines)

CHAPTER 4. AEFI SURVEILLANCE IN RWANDA

Surveillance for adverse events following immunization (AEFI) is an integral part of the Expanded Programme on Immunization (EPI) and medicines safety monitoring. It reinforces the safe use of all vaccines in the country while also helping to 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
- 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 stakeholders, regarding the safety of vaccines used in Rwanda.

Fig 4.1 AEFI surveillance cycle

Vaccine recipients themselves and/ or parents of immunized infants/children, health care providers 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 Rwanda FDA using designated reporting tools.

The reportable AEFI include,

- The following AEFIs associated with all vaccines (for routine and non-routine immunization) shall be included in the reporting system; Serious AEFIs, Signals and events associated with a newly introduced vaccines,
- Signal associated with other vaccines used in routine immunization.
- AEFIs caused by immunization error,
- Allergic reactions e.g. anaphylaxis, hives, bronchospasm, edema,
- Clusters of events
- Seizures,
- Any events causing significant parental/caregiver or community concern,
- Swelling, redness, soreness at the site of injection if it lasts more than 3 days or swelling extends beyond nearest joint, inability to move the limb,
- Those that are unexpected and those 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
Injection site abscess	Fluctuant or draining fluid-filled 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

AEFI	Case definition	Vaccine
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 high-pitched 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 capturing the chronology of events following immunization as provided by healthcare providers/families. 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 AEFI reporting Stakeholders

Subnational stakeholders in AEFI reporting

In Rwanda, the subnational stakeholders in AEFI reporting are:

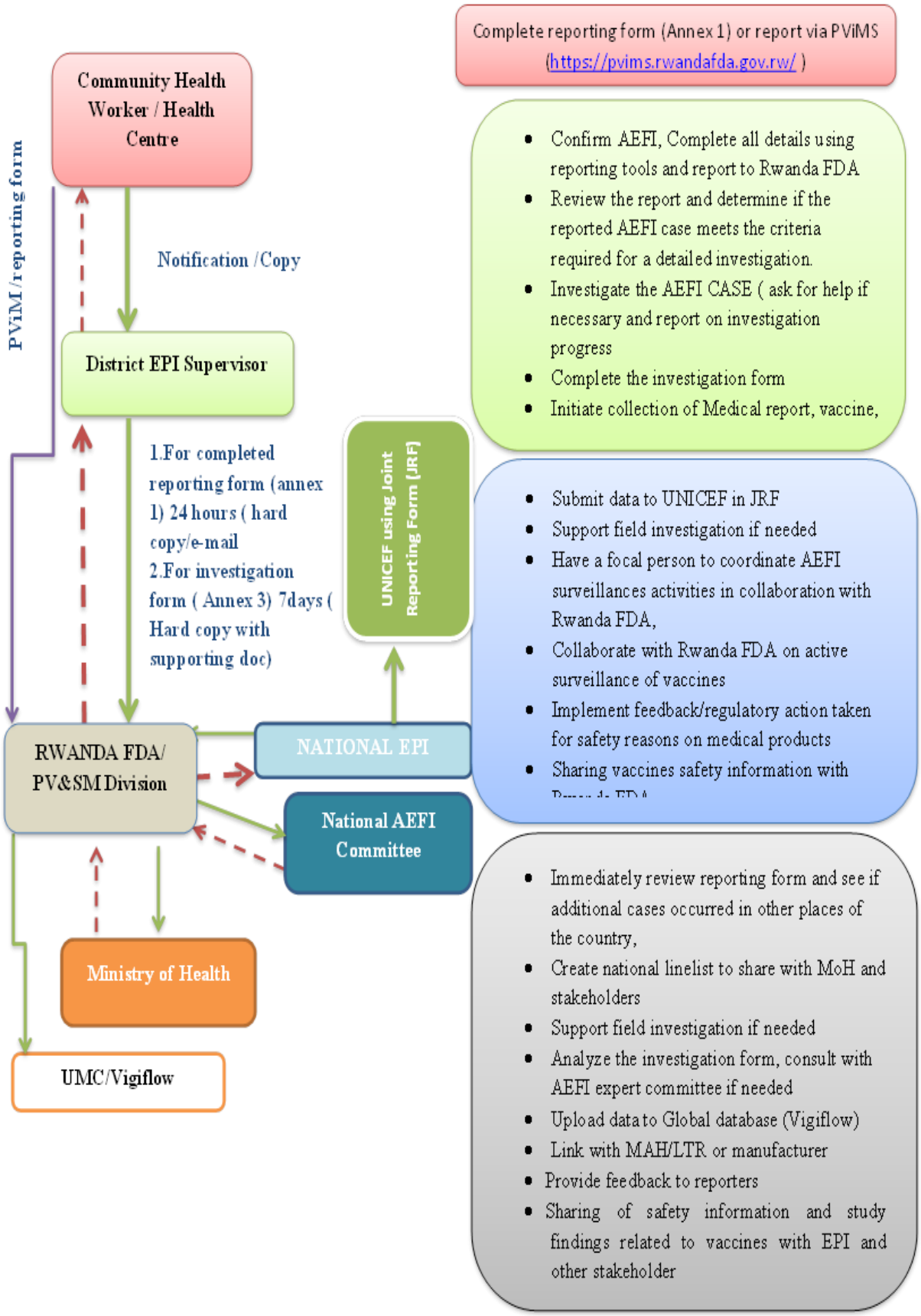
1. Vaccinees/Parents/ guardian
2. Community Health workers
3. All health facilities: Health Post, Health centre, District, Provincial, Teaching and Referral Hospitals, and Private Health Facilities (Clinics, polyclinics and hospitals)

National stakeholders in AEFI investigation

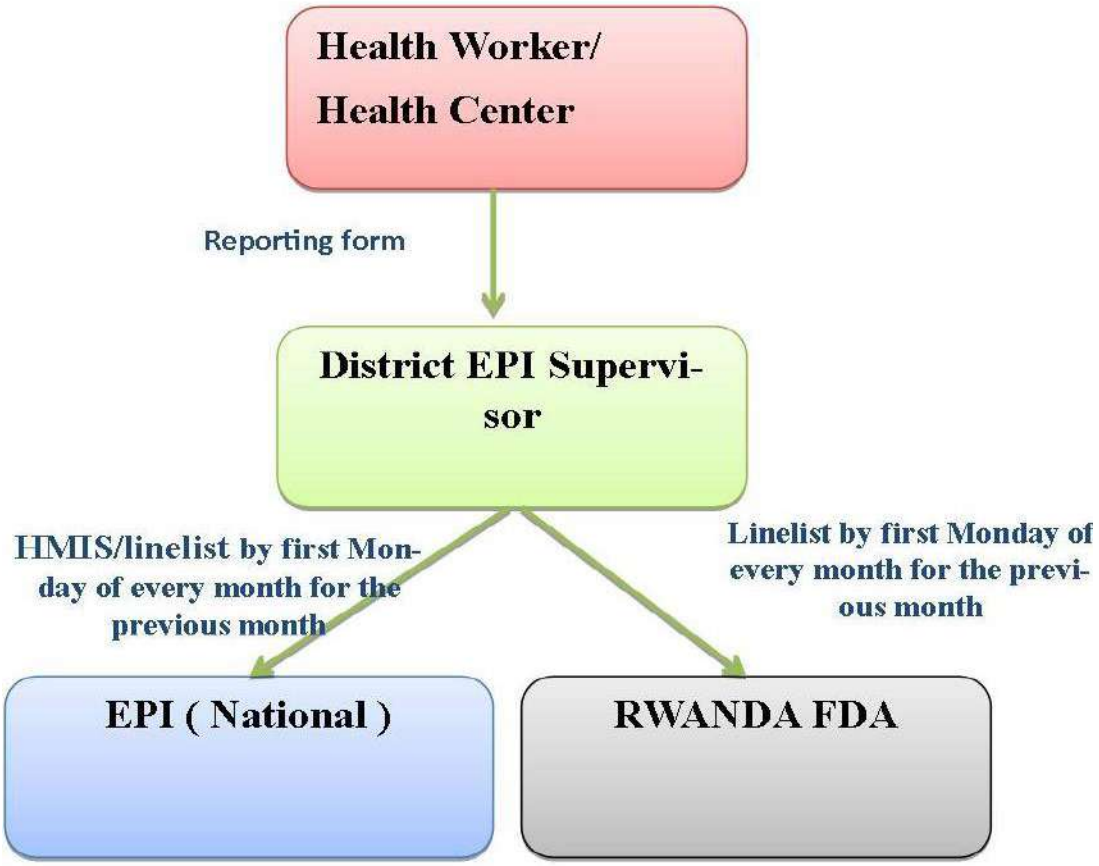
In Rwanda, the national stakeholders in AEFI investigation are:

1. Rwanda FDA, Pharmacovigilance and Food Safety Monitoring Division
2. National AEFI committee
3. Rwanda Biomedical Centre/EPI program
4. Ministry of Health

4.1.2 Rwanda AEFI routing



4.1.3 Routine AEFI reporting in Rwanda



All AEFI that are brought to the notice of the health care system should be reported to Rwanda FDA using reporting form (Annex 1) or online reporting system PViMS and details of each case should be appended into an AEFI line list (Annex 2). On a monthly basis the total number (aggregate) of all AEFI cases (minor and severe) should be reported to national level using the HMIS accompanied by the monthly line list (Annex 2). Any suspected poor quality vaccine should be reported to Rwanda FDA using suspected poor quality product reporting form (Annex 5).

4.1.4 Role of the Subnational stakeholders

4.1.4.1 Role of the vaccinees/ parent/ guardian

At the time of immunization, it is important for health workers to sensitise the parents about expected events such as fever and pain at injection site etc. following immunization. Parents should be advised about simple home remedies (e.g. correct positioning of the child when sleeping, increasing intake of fluids, sponging, breast feeding, antipyretics etc.) in case such events occur; however, at the same time, they should also be instructed to report severe unexpected events (e.g. very high fever, not responding to anti pyretic) or other unusual events to the health worker if they occur.

4.1.4.2 Role of the health worker

If home remedies do not work, vaccine recipients themselves and/ or parents or guardians of immunized infants/children usually notify the event to health care providers at immunization

centre, other health care facilities or Community Health Workers. Sometimes staff in these facilities recognizes or detect AEFIs when they first occur. All such AEFI cases brought to the notice of the health care worker or detected by the health care worker should be reported to Rwanda FDA using the approved tools (Annex 1) and notification sent to District EPI Supervisor. Thus the main role of the healthcare worker is to provide primary medical care and report the basic details about the notified adverse event.

4.1.4.3 Role of stakeholders at the district

When an AEFI notification is received by the District EPI Supervisor, he/she should review the report and determine if the reported AEFI case meets the criteria required for a detailed investigation. If necessary, he/she should contact the primary reporter and visit the locality of the event and interview relevant stakeholders for additional information.

The case may be considered:

1. ***Not warranting detailed investigation:*** if it is a minor AEFI, he/she should record the AEFI and provide guidance on management.
2. ***Warranting a detailed investigation:*** if it is a Serious AEFI (death, hospitalization, significant disability, life threatening, or congenital anomaly/ birth defect) or is a part of a cluster, or a part of a group of events above expected rate/ severity, or a suspected signal.

All serious AEFI should be investigated and a completed AEFI investigation form (Annex 3) routed to the national level. The details of each case should be included in the district and national line list.

He/she should discuss the same with the local experts (or technical expert committee like Drug and Therapeutic Committee) and plan for a detailed field investigation. **(See 4.2 Field investigation of AEFI)**

4.1.4.4 Role of the National stakeholders

When Rwanda FDA receives an AEFI report, causality assessment is conducted.
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 (Annex 2) with information from reporting 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.

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

Rwanda FDA has the responsibility to share the feedback and information with all stakeholders and even the global community by uploading the information into the Global pharmacovigilance

database – VigiBase®, maintained by the Uppsala Monitoring Centre under the WHO International Drug Monitoring Program – using information available in the completed case investigation form (annex 3). Rwanda FDA may provide information on the vaccines and lots distributed in the country when requested by the AEFI committee.

Rwanda FDA links with Marketing Authorisation Holders (MAH) or manufacturer for details on vaccines information related to quality, safety and efficacy or new safety information.

The National AEFI Committee plays a key role in supporting Rwanda FDA and immunization program for AEFI investigation. They also provide recommendations to the Rwanda National Immunization Technical Advisory Group (NITAG), Ministry of Health, Rwanda FDA and EPI on vaccines based on their findings.

EPI and Rwanda FDA constitute the National AEFI committee secretariat and coordinate and provide technical/logistical support to conduct the meetings of the National AEFI Committee (Fig 4.2).

The Ministry of Health shall develop and review policies and legal framework to strengthen AEFI surveillance activities, ensure effective integration of AEFI surveillance activities within health facilities, mobilize and provide resources for AEFI surveillance activities

4.2 Reporting channels and timelines

Any suspected AEFI should be reported as soon as possible to the Authority via Rwanda FDA toll free number, reporting electronic pharmacovigilance monitoring system (PViMS), pharmacovigilance division email (Pv_sm@rwandafda.gov.rw) or using paper-based reporting forms according to the following timelines:

- Fatal and other serious adverse event following immunization should be notified within 24 hours and an investigation shall be conducted within 48hours.
- Non-serious adverse event following immunization shall be reported within seven (7) calendar days

4.3 Field investigation of AEFI

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.

The purpose of investigating AEFI cases are:

- To confirm the reported diagnosis and/or propose other possible diagnoses as well as clarify the outcome of the medical incident comprising the AEFI.
- 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 reported AEFI.

- To examine the operational aspects of the programme. Even if an event seems to be vaccine product induced or coincidental.
- 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.
- To determine whether unimmunized people are experiencing the same medical conditions.

If the District EPI Supervisor and the experts 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 national level, the EPI and Rwanda FDA should be contacted and assistance for an investigation solicited. National investigations should be led by national AEFI committee, supported by Rwanda FDA and the EPI. During field investigations, the AEFI investigation form (Annex 3) should be used as a guide to collect suitable information.

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:

- Confirm the AEFI, complete all details in the AEFI reporting form (in case any of them were missing when reporting) and initiate AEFI investigation.
- Convene a local expert (or technical expert committee if available) planning meeting prior to the investigation.
- With the experts, the District EPI Supervisor 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.
- Complete the AEFI investigation form (Annex 3).
- 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 investigator should inform Rwanda FDA on the status and progress of the investigation to ensure the media and the public are appropriately informed about the investigation if required. The completed case investigation form (annex 3) along with the supporting documents such as the medical report, vaccine, logistic samples, and laboratory reports e.g. CSF, Serum (or other biological products) should be sent to Rwanda FDA 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 national assistance for an investigation is requested, more accurate information can be obtained by a single coordinated 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.

4.3.1 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 competent authorities. Investigation of the case should be carried out by a team of experts from relevant areas, including clinicians. As a death causally linked to 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 additional 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.

4.3.2 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 similar disease patterns.

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

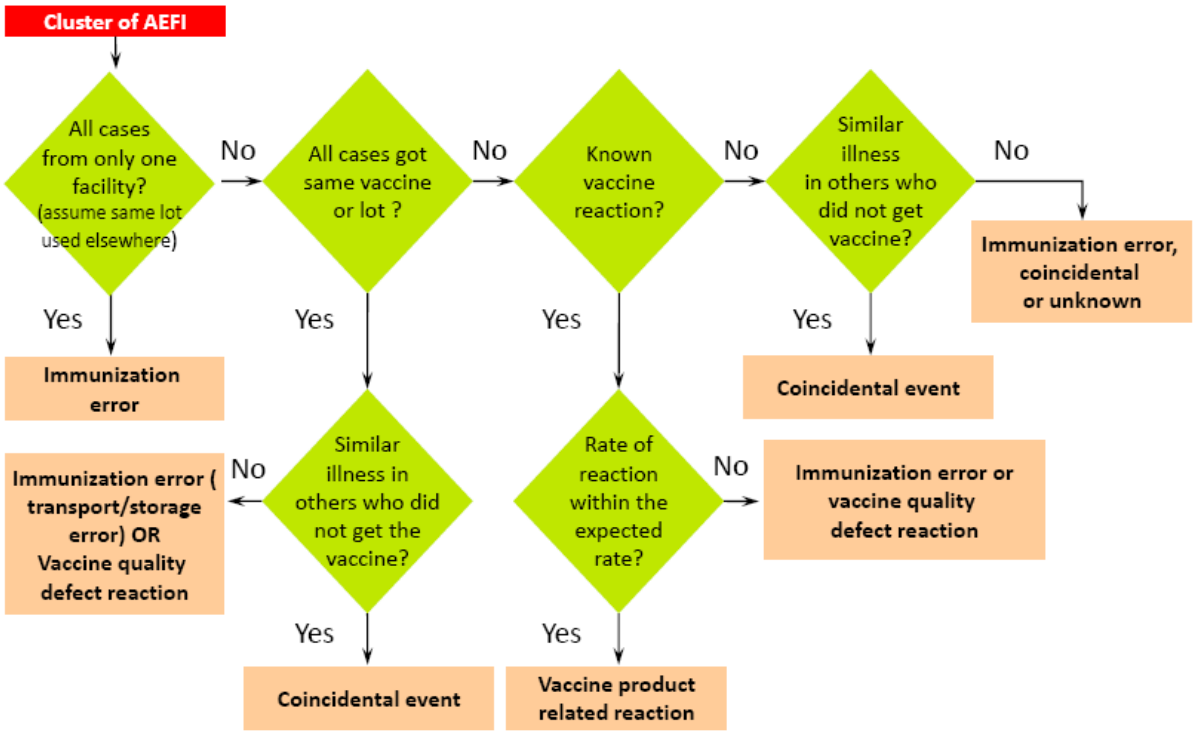
- detailed data on each patient;
- programme-related data (storage and handling, etc.); and
- Immunization practices and the relevant health workers' practices.

Common exposures among the cases can be identified by reviewing:

- All data on vaccine(s) used (name, lot number, etc.);
- Data on other people in the area (also non-exposed); and
- 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 vaccine 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.

4.3.2.1 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).

CHAPTER 5. LABORATORY TESTING OF SPECIMENS

Laboratories have an important role in AEFI case diagnosis and case management. They also have a key role in testing the quality of the samples of vaccines and the logistics used.

Laboratory tests for the purpose of AEFI case diagnosis and case management conducted on the patient (e.g. blood, urine, radiology, ECG etc.) are based on the provisional case diagnosis and recommendations of the treating physician. These tests are considered "routine" and should be performed in clinical laboratories. The results of these tests are important to confirm the case diagnosis and arrive at the "valid diagnosis" for assessing causality as described in section 7.2.

Laboratory testing of samples of vaccines and logistics are 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 of vaccines and logistics are at times required to confirm or rule out the suspected cause.

In the context of AEFI, sometimes additional specific tests on the patient, vaccines and logistics as outlined below may also be necessary to confirm the cause. The testing of additional specimens includes:

Human specimens:

- Histopathology, body fluids etc. can be done at laboratories identified in the local hospitals or approved centres by the Ministry of Health.
- Autopsy specimens at approved and accredited government forensic laboratories as identified by Ministry of Health.

Vaccines and logistics:

- Vaccines and diluents for sterility and chemical composition.
- 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 4) 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.

5.1 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 (State/District) institutions, sending samples to national laboratory or an accredited laboratory abroad need to be considered after discussing with Rwanda FDA.

In case of death suspected to be due to an AEFI, an autopsy recommended 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 Ministry of Health 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.

5.1.1 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 laboratories 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 laboratories conducting tests

Suspected AEFI	Diagnostic Method	Specimen	When to collect	Preparation, Storage and shipment	Referral laboratory for Specimens
Injection site abscesses	Microscopy and Culture/ sensitivity	Pus Swab	At contact	Use Transport media to transport Pus swabs to the next level	**Hospital Laboratories / National Reference lab, Kigali**
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 Reference lab, Kigali**
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	**Hospital Laboratories National Reference lab, Kigali**

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	**Hospital Laboratories / National Reference lab, Kigali**
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	**Hospital Laboratories / National Reference lab, Kigali**
Death	Histopathology Serology	Tissue specimens Venous Blood Vial Batch	Immediate	▪ Never use vials that contained antibiotics ▪ Transport to referral laboratory immediately ▪ Transport sampled vial batch in reverse cold chain	**Hospital Laboratories / National Reference lab, Kigali**

5.2 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 local experts.

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 separately labelled and sent along with unused vials of the same lot.

The District EPI Supervisor will be responsible for the packaging, cold chain maintenance and shipment of samples in the correct temperature to the national laboratory.
All specimens sent to the lab should be accompanied by a laboratory request form (Annex4).

The accredited laboratory will process the specimens and send the laboratory results to Rwanda FDA and National EPI Manager. 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

5.3 Feedback to the reporters

Rwanda FDA shall provide feedbacks on the reported AEFIs to all relevant stakeholders which include: the community, district and national levels.

The feedback is provided within 7 days after the completion of causality assessment or potential signals determined by data review/analysis at the national level.

CHAPTER 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:

- Data collated into a linelist
- Case investigation forms for each reported AEFI case,
- Laboratory information (Human and vaccine related)
- Records about similar events in the community
- Records of the implicated vaccine

6.2 Analysis of AEFI reports

It is essential that all notified cases are reported (serious and non-serious AEFI) using the AEFI reporting form (Annex 1). All reported AEFI cases should be line listed at all levels using the AEFI linelist (Annex 2). 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, national program managers and Rwanda FDA, other key analysis related to the performance of the surveillance system, include:

- Timeliness and completeness of receiving AEFI forms.
- 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.
- Assessing AEFI case reports received during stipulated time period.
- Assessing number of events and reporting rate per 1,000 or 10,000 or 100,000 doses of vaccine used.
- Analyses by the type of AEFI
- Analysing programme errors by number and rates per 100 or 1,000 doses of relevant vaccines used.

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:

- At health center levels the summary reports of all AEFI received should be reported at national level or district level on monthly basis.
- At the district level by District EPI Supervisor and relevant staff and the summary reports of all AEFI received should be reported at national level on quarterly basis.
- All private health facilities, referrals and teaching hospitals shall submit the summary reports of AEFI cases received directly to the Authority on quarterly basis
- At national level by Rwanda FDA and EPI and the summary reports of all received AEFI cases should be done on annual basis.

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.
National level	• Number of reports by district levels • Reported AEFIs by Place (clinics, hospitals), Persons and time • Cluster analysis • Reported AEFIs by antigen	• These are programme operation indicators (timeliness, completeness) at district 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 Rwanda FDA and/or 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 underestimate)

Multiplier: 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 national level, 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 Monitoring and 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 proposed to determine the quality of AEFI surveillance is, "AEFI reporting ratio in surviving infants from a sub-national[1] area/country per year". This is calculated as

It is assumed that a country could have three levels of immunization safety surveillance: national (central), subnational or intermediate (state/province/region/district) and service-provider level 4An estimate of **Surviving Infants** can be calculated by subtracting the number of children who die before they reach their first birthday from the number of children born during that year. Number of children dying during the first year of their life can be estimated by dividing the number of births by 1000 times the infant mortality rate (IMR), where the infant mortality rate is expressed as number of infant deaths per 1000 live births.

$$\text{AEFI reporting ratio per 100,000 surviving infants per year} = \frac{\text{Number of AEFI cases reported from a sub-national area/ country per year X 100,000}}{\text{AEFI reporting ratio per 100,000 surviving infants per year cases reported from a sub-national area/ country per year}}$$

Notes: The target proposed is at least 10 reports per 100,000 surviving infants per year. The sub-national area/country is defined according to the functional requirements and setup of the national AEFI surveillance system.

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

- Timeliness and completeness of AEFI reporting
- Percentage of AEFI cases reported on time (< 24 hours of notification) to the national level
- Percentage of serious AEFI cases investigated on time (< 48 hours of onset) using standard formats.
- Number (%) of AEFI investigation conclusions supported by findings of special tests (clinical specimens, Post-mortem findings (among AEFI deaths), lab findings for vaccine samples)
- Number (%) AEFI cases where final classification including causality assessment by AEFI committee is completed within 30 days of receipt of all documentation from districts
- Number (%) AEFI cases reviewed by National AEFI committee following receipt of reported AEFI cases from district at National level.
- Number (%) AEFI cases reviewed by National AEFI committee and not assessable due to lack of information.
- Response to AEFI by the program particularly those related to programme error

CHAPTER 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 Expanded Programme on Immunization. Causality assessment is important for:

1. identification of vaccine-related problems;
2. identification of immunization error-related problems;
3. excluding coincidental events;
4. detection of signals for potential follow-up, testing of hypothesis and research; and
5. 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

- Serious AEFI
- Clusters & events above expected rate/ severity
- Evaluation of suspected Signals
- Other AEFI (if required) as decided by reviewing team / committee including
    - If immunization error is suspected
    - Significant events of unexplained cause within 30 days of vaccination
    - Events causing significant parental or community concern (e.g. Hypotonic Hyporesponsive Episode (HHE), febrile seizures etc.)

7.2 Preparation for causality assessment

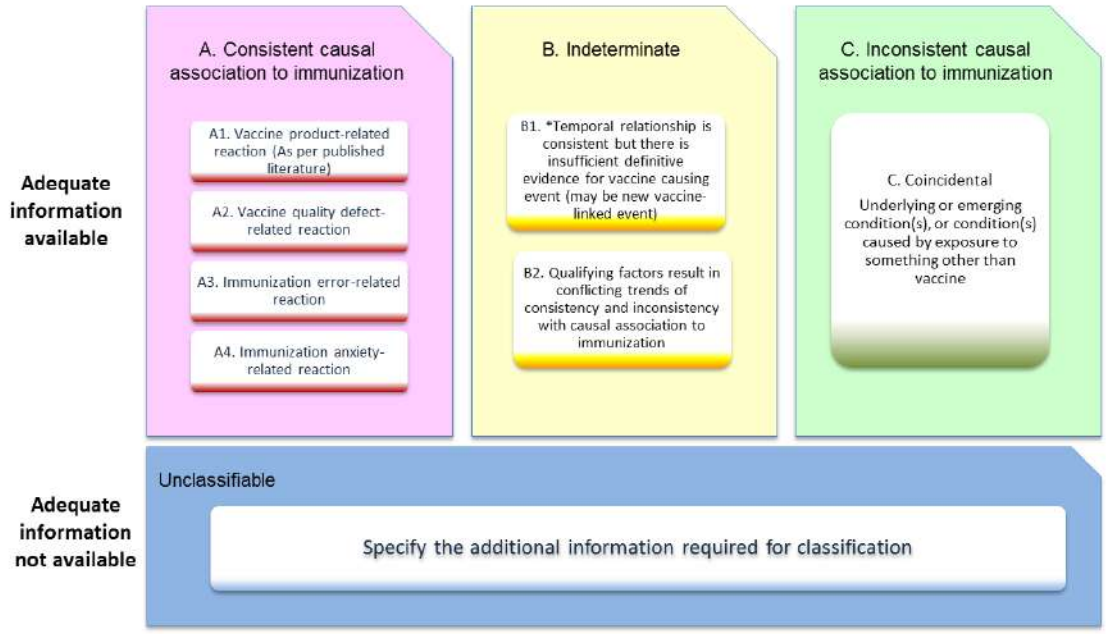
Prior to causality assessment,

- The AEFI case investigation should have been completed
- All details of the case such as case report form, case investigation form (annex 3), completed clinical case record, lab reports, autopsy report, details of field investigations etc. should be available at the time of assessment
- There must be a “valid diagnosis” which is 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 classifications of cases after determining causality



*B1 : Potential signal and maybe considered for investigation

7.3 Causality assessment team

Causality assessment in Rwanda is conducted by Rwanda FDA and can be supported by national AEFI committee.

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.

CHAPTER 8. ACTION AND RESPONSE TO AEFI

After determining the cause, 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 case reporting 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 and UNICEF national offices 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 to the beneficiaries 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.

CHAPTER 9. SIGNAL DETECTION

A signal is information that arises from one or multiple sources (including observations and experiments) 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. Signals can best be identified by pooling of data from multiple sources and analysing if the pooled data points to the occurrence of a new event that could causally related to the vaccine.

When we ascertain or quantify adverse events (AEs), a comparison of the event occurrence is made in vaccinated and non-vaccinated individuals or in exposed versus unexposed time periods for the same individual, using different types of methodologies.

9.1 Source of data used in signal detection

To detect the signal, the observed AE rate is compared with the 'expected' rate which is generally inferred from data from:

- Historical controls using data from the same (or a similar) population during an earlier time period;
- Self-controlled studies, using a case-series, case-crossover or risk interval design, in which all data would be obtained from individuals who received the targeted vaccine, comparing a post-exposure risk window with either a pre-exposure control window or with a post-exposure control window that occurs after the risk window;
- Cohort studies which compare event rates in specific risk windows; controls may be other individuals during the same time period who were no vaccinated with the targeted vaccine but who are otherwise similar to those vaccinated;
- Case-based studies where the vaccination rate among cases who had the AE of interest is compared with that among individuals that did not have the AE of interest, in a case-control or case-coverage design.

CHAPTER 10. MANAGEMENT OF VACCINE SAFETY CRISES

A vaccine safety crisis is caused by an unexpected series of uncontrolled adverse vaccine-related events that result in a situation that has the potential to jeopardize the success of an immunization programme. The crisis may originate from AEFIs caused by vaccine reactions or immunization errors, or it may be triggered by misinformed rumors without any scientific basis. In many cases, the crisis is most commonly related to the identification of an AEFI which is then aggravated by the spread of negative rumors at community level. The magnitude of the crisis is determined by the nature of the rumor, the speed of its spread and the promptness and effectiveness of response actions.

Although a vaccine safety crisis can be challenging, it can also present an opportunity to identify failures to adhere to best practices, improve communication and address issues related to policies and procedures if necessary, in order to strengthen the national immunization programme and vaccine safety surveillance system.

10.1 The goal and objectives

The goal and objectives of vaccine crisis management is to minimize the impact of vaccine safety concerns including AEFIs, misinformation and negative rumors, and maintain the public trust in immunization. A crisis management describes priority interventions and step by step actions to address vaccine misinformation and potential vaccine safety crises.

The specific objectives of the crisis management:

1. Ensuring all serious AEFIs cases are immediately reported, investigated, assessed for causality and documented so as to ensure vigilance and transparency in risk communication
2. Ensuring a well-coordinated response to vaccine safety concerns to maximize its efficiency
3. Strengthening information generation through regular assessments of knowledge, attitudes and practices and community perceptions of routine immunization and new vaccines.
4. Establishing mechanisms to investigate vaccine misinformation and rumours and coordinate the response to anti-vaccine propaganda across all media sources
5. Engaging with national stakeholders, local media, NGOs, social platforms, and others to enhance and sustain public confidence, acceptance and demand for vaccination

10.2 Implementation strategy

The vaccine safety crisis management will necessitate collaboration between national and district stakeholders including the Rwanda FDA, Expanded Programme for Immunization, referral, teaching and district hospitals, development partners, NGOs, social and media platforms.

The implementation strategy will be guided by AEFI surveillance system and information sharing at all levels of the health system and community. It will be vital to integrate risk communication activities in all vaccination plans from central to the district hospital and health center levels as well as ensuring that the community is engaged to support vaccine safety crisis response in case it may arise.

10.3 Intervention areas

The interventions to prepare for and respond to a vaccine safety crisis will be implemented at all levels of the health system and will require engagement of various stakeholders both within and outside of the immunization program. Collaborative initiatives will be critical to ensure a high standard of vaccine safety monitoring and to maintain public confidence in immunization.

Four areas of interventions have been identified and include:

1. Leadership and coordination
2. AEFIs surveillance and response
3. Risk Communication and community mobilization to promote demand for immunization
4. Data generation and information sharing

CHAPTER 11. COMMUNICATION AND MEDIA MANAGEMENT

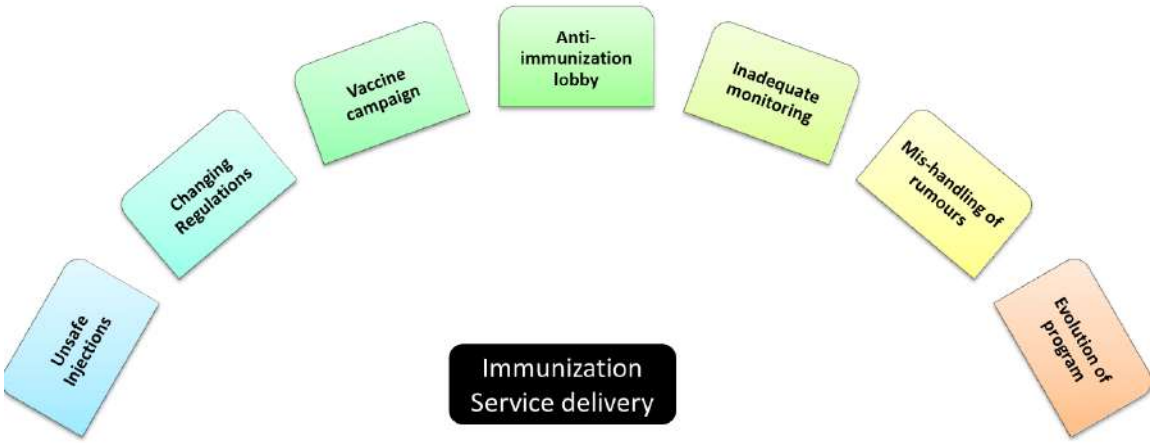
11.1 Risk communication

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.

11.1.1 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 the factors that may trigger public concerns; hence the need for improved quantity, quality and targeted communication about vaccine safety.

Fig 11.1 Factors triggering public concerns to immunization



11.1.2 Challenges to effective communication

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

- Communicating the decline of childhood infections and deaths from VPD
- Parents view that infectious disease is a thing of the past
- Introduction of new vaccines and related information gaps
- Mass campaigns or Supplemental Immunization Activities (SIAs)
- Need for transparency and accountability

11.2 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;

- Listen to the client, parents or guardian and their concerns empathetically.
- Reassure and support the client, parent or guardian but do not make false promises.

- Assist the client (arranging transportation, hospital invoices), parents and guardian for hospitalization if necessary.
- Frequent communication with the client, parents or guardian regarding the progress of the patient.
- Build up and maintain relationship among health staff, community and media.
- Inform the individual client, parent or guardian about possible common adverse events and how to handle them.
- Continuously communicate with the client, parent or guardian and community during the investigation period to assure understanding the risk-benefit of vaccination.

11.3 Role of Community Health workers in Rwanda

The community health workers have an important role for communicating with parents, vaccinees and other stakeholders. They include

- Interpersonal communication before and during vaccination sessions on the benefits and the common AEFI
- Communicating the management of minor ailments after vaccination
- Identification of the severe AEFI and communicating the same to the supervisors through referral notes

11.4 Role of health care provider 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. Refraining from reporting 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:

- Communicate immediately with the District EPI Supervisor.
- 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.
- 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.
- If the AEFI was caused by immunization error, tell the public what steps are being taken to prevent similar events in the future.
- Repeat the message to dispel all fears.
- Constantly reassure the public of the safety of vaccines.

11.5 Communication with other health care staff

- Communicate among all level of health authorities involved.
- Reinforce their knowledge, ability, skills and performances.
- Update them on investigation process, progress and findings.

- Reassure the staff of ongoing confidence in the immunization programme; quality of the vaccine and their services provided
- Do not blame health care worker, instead focus on the correction and quality of the EPI program.

11.6 Communicating with stakeholders

Vaccine safety information needs to be shared by the national program managers with other stakeholders in order to ensure dissemination of correct information and thereby ensuring the smooth functioning of the Expanded Programme on Immunization. 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 by Rwanda FDA:

- EPI
- National AEFI Committee
- Politicians
- Professional associations
- Universities and hospitals
- International agencies and development partners
- Manufacturers

11.7 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.

11.7.1 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.

11.7.2 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.

11.7.3 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.).

11.7.4 Draft media release

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

- Who is affected?
- What has happened?
- What is being done?
- Where has it happened?
- When did it happen?
- Why did it happen?

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).

11.7.5 Spokesperson system

Ministry of Health shall be responsible for communicating the AEFI to media, public and stakeholders if required. This limits the possibility of conflicting messages coming from different sources and unauthorized channels. The Ministry of Health may delegate this responsibility if deemed necessary.

11.7.6 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.

11.7.7 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.

11.7.8 Monitoring of media

Rwanda FDA and EPI shall have the responsibility to monitor all claims and authenticity of publications on AEFI and shall take appropriate measures including but not limited to;

- Analyze rumors, its level and potential to cause damage.
- Anticipate how situations might evolve following response; prepare before responding.
- 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.
- 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.
- Plan how to prevent future rumours.

11.7.9 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;

- An outline of actions taken or planned (such as the AEFI investigation).
- A description of the cause of the event (but only when this is known with certainty).
- An assurance that corrective action has been taken or will be taken.
- Reference to any relevant publication, video material or web site.
- Sender's name and spokesperson's details.
- Limited to one page of matter (400-500 words max).
- 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.

11.7.10 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:

- Rwanda FDA and EPI take the lead but identify who facilitates the press conference.
- If there are several members on the panel, agree beforehand on the key message(s) in response to the AEFI.
- Agree on roles of each panel member beforehand, including the type of questions (media, political etc.) each panel member may best handle.
- Panel members must avoid contradicting each other in the press conference unless it is critical to clarify something incorrect that has been said.
- 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.

11.8 Media Management post AEFI

11.8.1 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.

11.8.2 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.

11.8.3 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.

11.9 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:

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

Common causes of Rumours

- Inadequate information sharing by health care providers or
- Failure to communicate correct information about vaccine effects and schedules,
- Failure to check whether caregivers know and understand information,
- Failure to give clients opportunities to ask questions
- Parents/caregivers' negative attitudes about immunization services

a) What you can do at the health facility

Under the direction of your supervisor:

- Meet with key opinion leaders (politicians, traditional and religious leaders, community leaders, other health workers).
- Organize meetings at sites where the individuals/groups are comfortable and feel at ease to ask questions.
- If there is a national mass media response, encourage your community members to watch and talk about it.

b) Words of advice

- React swiftly and adapt your ongoing activities to give a quick response.
- Develop strong relationships and trust with your community in advance (religious, social and media groups).
- Give clear and consistent messages.

ENDORSEMENT OF THE GUIDELINES

	Author	Checked by		Approved by
Title	**Division manager PVSM**	**Head of Department FDISM**	**Quality Assurance Analyst**	**Director General**
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Signature				
Date	23/09/2022	23/09/2022	03/10/2022	03/10/2022

APPENDICES

ANNEX 1: FORM No. FDISM/PVSM/FOM/014

Format: QMS/FMT/002 Revision No: 1 Effective Date: 20 June 2022	Department/Division/Office/Unit	FDISM/PVSM
Document Type: **Form**		Doc. No : FDISM/PVSM/FOM/014
RWANDA FDA Rwanda Food and Drugs Authority	**ADVERSE DRUG REACTION / ADVERSE EVENT FOLLOWING IMMUNIZATION REPORTING FORM**	Revision Number : 02 Revision Date: : 25/07/2022 Effective Date : 13/08/2022 Review Due Date : 12/08/2025 Ref Doc. :FDISM/PVSM/GDL/002

Type of Report	**Seriousness of ADR/AEFI**	**Category of Suspected Product**
Initial☐ Follow up☐	Serious☐ Not Serious☐	Medical product☐ Vaccine☐

I.PATIENT INFORMATION

Patient ID/initials: _____**Gender**: Male ☐ Female ☐ **Weight**(kg)_____ **Height** (m): _____ Pregnancy Status: **YES** ☐ **NO** ☐ **Date of birth**: _____/____/_____ **Patient Address:** Village _____ Cell: _____Sector: _____ District: _____ Phone N° _____	**Patient's Medical History** (Provide any relevant medical history and laboratory results including dates (if done): …… …… …… …… …… …… …… ……

II. INFORMATION ON ADVERSE EVENT(S)

Brief description of the ADR/AEFI:

(a) Information on Onset: **Date of ADR/AEFI onset:** ____ /_____/_____(dd/mm/yyyy) **Time of onset:** _____/___ _/_____ (hours, Min, Sec) **Date ADR/AEFI stopped:** _____ / ____/_____(dd/mm/yyyy)	**(d) Adverse Event Evolution/ Outcome:** Recovered ☐ Recovering ☐ Recovered with sequelae ☐Not recovered ☐ Congenital abnormality ☐ Death ☐ Unknown ☐
(b)Severity of the ADR/AEFI: Mild ☐ Moderate ☐ Severe ☐ Unknown ☐ **Reason for seriousness:** hospitalization☐ Prolonged hospitalization☐ Disability ☐ Congenital abnormality☐ Life threatening ☐	**(e)Causality of the ADR/AEFI (If performed):** Certain☐ Probable/Likely☐ Possible☐ Unlikely☐ Unclassifiable ☐
(c) Action Taken: Drug withdrawn ☐Dose increased ☐ Dose reduced ☐Dose not changed ☐Substituted ☐Antidote ☐**Other**☐ ***(Specify):*** …… …… …… …… ……	**(f) Optional information:** ☐Therapeutic Failure *(Provide information on medicine (s) or vaccine (s) that showed lack of efficacy*……. ☐Medication errors *(Provide details of medication errors)* …… ……

III. INFORMATION ON SUSPECTED PRODUCT

A. Details of suspected medicinal product Source/Supplier:……							
Product brand name & manufacturer	**Generic name/ /Strength/ Dosage form**	**Route of Administration**	**Dose and frequency**	**Starting Date and Time**	**Stopping Date and Time**	**Batch Nº. & Expiry date**	**Indications (Reason for use)**
Other medicines used at the same time and/ or in the last one month (including herbal medicines)							

B. Details of Suspected Vaccine					**Diluent (if applicable)**		
Name of vaccine	**Date of vaccination**	**Time of vaccination**	**Dose (1st, 2nd, 3rd etc.)**	**Batch/Lot Nº &Expiry date**	**Name of diluent**	**Batch/Lot Nº& Expiry date**	**Date & time of re- constitution**

IV. REPORTER INFORMATION							
Name of reporter:		Qualification:		Phone number			
Health Facility Name:		District:		Report Reference Nº			
E mail Address of Reporter:		Contact/Tel Nº:		Date of report:			

Note: Reporters and patients' identity are held in strict confidentiality by Rwanda FDA and protected to the fullest extent of the Law. Once this form is completed please send it to Rwanda FDA via the following email: pv_sm@rwandafda.gov.rw

ANNEX 2: FORMAT No. FDISM/PVSM/FMT/002

Rwanda Food and Drugs Authority
Nyarutarama Plaza, KG 9 Avenue
P.O. Box: 1948 Kigali - Rwanda
Email: info@rwandafda.gov.rw
website: www.rwandafda.gov.rw

QMS N°: FDISM/PVSM/FMT/002
Revision No: 2
Effective Date: 10/10/2022

ADVERSE EVENT FOLLOWING IMMUNIZATION (AEFI) LINE LIST

													Name/ID
													Village/Cell/Sector/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

													Time interval between vaccination and onset of symptoms (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-related	[A3] Immunization anxiety-related	[B] Indeterminate	[C] Coincidental	[D] Inadequate information to classify

ANNEX 3: FORM No. FDISM/PVSM/FOM/024

Format: QMS/FMT/002 Revision No: 1 Effective Date: 20 June 2022		Department/Division/Office/Unit	FDISM/PVSM
Document Type: **Form**		Doc. No	:FDISM/PVSM/FOM/024
RWANDA FDA Rwanda Food and Drugs Authority	Title: **ADVERSE EVENT FOLLOWING IMMUNIZATION (AEFI) INVESTIGATION FORM**	Revision Number	: 2
		Revision Date:	: 23/09/2022
		Effective Date	: 10/10//2022
		Review Due Date	: 09/10/2025
		Ref Doc.	:FDISM/PVSM/GDL/007

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

Section A:	**Basic details**			
Province/District	**Sector**	**Cell**	**Village**	**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 filling this form:__ __ / __ __ / __ __ __ __

Designation / Position:

This report is: ☐ *First* ☐*Interim* ☐*Final*

Telephone # landline (with code): Mobile: e-mail:

Patient Name Sex: ☐M ☐ F

(usea 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 (e. g. 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 symptom (*hh/mm):* __ __ / __ __
Date of hospitalization*(DD/MM/YYYY)*: __ __ / __ __ / __ __ __ __
Date first reported to the health authority *(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 (If yes provide details)**
Past history of similar event	Yes / No/ Unknown	
Adverse event after previous vaccination(s)	Yes / No/ Unknown	
History of allergy to vaccine, drug or food	Yes / No/ Unknown	
Pre-existing illness (30 days) / congenital disorder	Yes / No/ Unknown	
History of hospitalization in last 30 days, with cause	Yes / No/ Unknown	
Patient currently on concomitant medication? (If yes, name the drug, indication, doses &treatment dates)	Yes / No/ Unknown	
Family history of any disease (relevant to AEFI) or allergy	Yes / No/ Unknown	
For adult women • Currently pregnant? Yes (weeks) _____ / No/ Unknown • Currently breastfeeding? Yes / No		

For infants

The birth was ☐full-term ☐pre-term ☐post-term. Birth weight:

Delivery procedure was ☐ Normal ☐ Caesarean ☐ Assisted (forceps, vacuum etc.) ☐ with complication (specify)

Section C: Details of first examination of serious AEFI case**

Source of information (✓ *all that apply*): ☐**Examination by the 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 reports and autopsy reports, if available) and write only the information that is not available in the attached documents below
- ***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 recommendations 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. color, 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 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 etc.)?	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 locations: _____	
k) Is this case a part of a cluster?	Yes* / No/ Unknown
i. If yes, how many other cases have been detected in the cluster?	
a. Did all the cases in the cluster receive vaccine from the same vial?	Yes* / No/ Unknown
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/ Unknown		
If no, specify the type of syringes used: ☐Glass ☐Disposable ☐Recycled disposable ☐ Other _____			
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 different vaccines?	Yes	No	NA
Separate reconstitution syringe for each vaccine vial?	Yes	No	NA
Separate 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°C after the vaccine was placed inside?	Yes / No
○ If "yes", provide details of monitoring separately.	
• Was the correct procedure for storing vaccines, diluents and syringes followed?	Yes / No/ Unknown
• Was any other item (other than EPI vaccines and diluents) in the refrigerator or freezer?	Yes / No/ Unknown
• Were any partially used reconstituted vaccines in the refrigerator?	Yes / No/ Unknown
• Were any unusable vaccines (expired, no label, VVM at stages 3 or 4, frozen) in the refrigerator?	Yes / No/ Unknown
• Were any unusable diluents (expired, manufacturer not matched, cracked, dirty ampoule) in the store?	Yes / No/ Unknown
Specific key findings/additional observations and comments:	
Vaccine transportation:	
• Type of vaccine carrier used	

• Was the vaccine carrier sent to the site on the same day as vaccination?	Yes / No/ Unknown
• Was the vaccine carrier returned from the site on the same day as vaccination?	Yes / No/ Unknown
• Was a conditioned ice-pack used?	Yes / No/ Unknown
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 occurred and in the same locality? Yes / No/ Unknown If yes, describe:
If yes, how many events/episodes?
Of those effected, how many are • Vaccinated:_____ • Not vaccinated:_____ • Unknown:_____

Other comments:

Section H: Other findings/observations/comments

ANNEX 4: FORM No. FDISM/PVSM/FOM/006

Format: QMS/FMT/002 Revision No: 1 Effective Date: 20 June 2022		Department/Division/Office/Unit	FDISM/PVSM
Document Type: **Form**			Doc. No :FDISM/PVSM/FOM/006
RWANDA FDA Rwanda Food and Drugs Authority	**AEFI LABORATORY REQUEST FORM (LRF)**		Revision Number : 2
			Revision Date: : 23/09/2022
			Effective Date : 10/10/2022
			Review Due Date : 09/10/2025
			Ref Doc. :FDISM/PVSM/GDL/007

(Raised by…….. LRF should be accompanied with specimens)
(For Serious Adverse Events Following Immunization)
AEFI category (Encircle): **Death / Hospitalized / Cluster / Disability**

Province		**Case ID**
District		
Sector		
Name of person sending the specimen: Date of filling LRF : Designation: Phone Number :		

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

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

1. Specimen:
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				
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 5: FORM No. FDISM/PVSM/FOM/016

Format: QMS/FMT/002 Revision No: 1 Effective Date: 20 June 2022	Department/Division/Office/Unit	FDISM/PVSM
Document Type: **Form**		Doc. No : FDISM/PVSM /FOM/016
RWANDA FDA Rwanda Food and Drugs Authority	**SUSPECTED POOR QUALITY PRODUCT REPORTING FORM**	Revision Number : 2 Revision Date: : 05/08/2022 Effective Date : 12/08/2022 Review Due Date : 05/08/2025 Ref Doc. :FDISM/PVSM/GDL/003

I. PRODUCT CATEGORY (Tick as appropriate)							
Medicinal product Vaccine Other Biological Products Herbal Product Other *(Please Specify):* ……							
II. PRODUCT DETAILS							
Brand name				Generic Name			
Batch/ Lot Nº		Manufacturing Date		Expiry date		Date of receipt	
Name of manufacturer				Physical Address and Country of Origin			
Name of Distributor/Supplier				Distributor/ Supplier's Address			

III. PRODUCT FORMULATION	**IV. DESCRIPTION OF PRODUCT COMPLAINT**
Tablets /capsules	Color/odor change
Suspension/Syrup	Molding
Injectable/Infusions	Turbidity
Creams/Ointment/Liniment/Paste	Mislabelling
Pessaries	Poor Packaging/ lack of patient leaflet/ lack measuring devices
Suppository	Therapeutic ineffectiveness
Powder for reconstitution of oral suspension	Particulate matter
Powder for reconstitution of injection	Seal Integrity of packs and/ or Leakage
Ear/Eye drops	Caking
Diluents	Separating
Nebulizing solutions	Incomplete packs
Other *(Please Specify)* …… ……	Powdering/crumbling

	Suspected falsified/ Substandard Others*Specify)* ……

Describe the Complaint in details:

……
……
……

V. PRODUCT STORAGE CONDITIONS	
Does product require refrigeration? **YES NO** Does product require protection from light? **YES NO** Does product require protection from Moisture? **YES NO** Was it stored following manufacturer/Rwanda FDA guidelines? **YES NO**	***Other Storage details*** *(if necessary):*

VI. CIRCUMSTANCE AND TIME OF THE POOR-QUALITY DETECTION		**VII. ACTION TAKEN**
When did you notice the poor-quality problem? Before taking/administering the product While taking/administering the product After taking/administering the product When the patient returned the product	After a complaint of the patient After Visual inspection After quality control Other(specify)…….	Stop Taking/Administration of the product Quarantining the product Returning the product to the supplier Other (specify):…….

Have you experienced any adverse event after taking this medicine? **YES NO** If **YES,** please complete the ADR/AEFI Reporting Form.

VIII. REPORTER INFORMATION					
Name of reporter:		Qualification:		Phone number:	
Name of Health Facility		District:		Report Reference No:	
E-mail Address:		Contact/Tel No:		Date of report:	

All information is held in strict confidentiality and will not disclose reporter's identity in response to any public request. Information supplied will contribute to the improvement of safety and vigilance of Medical Products in Rwanda. Once this form is completed please send it to Rwanda FDA via the following email: pv_sm@rwandafda.gov.rw