Republic of Namibia

Ministry of Health and Social Services

NATIONAL GUIDELINES FOR ADVERSE EVENTS FOLLOWING IMMUNIZATION SURVEILLANCE

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Contents

Acknowledgements

The Ministry of Health and Social Services wishes to acknowledge the significant contributions made by stakeholders throughout the development of the National Adverse Event Following Immunisation Guideline.

The stakeholders are the Expanded Programme on Immunization (EPI) - Primary Health Care Directorate; the Therapeutics Information and Pharmacovigilance Centre (TIPC) - Tertiary Health Care and Clinical Support Services Directorate; the national Adverse Event Following Immunisation (AEFI) Committee, the Namibia Medicines Regulatory Council (NMRC) which is technically supported by the United Nations Children Fund (UNICEF) and World Health Organization (WHO).

Special thanks to the numerous individuals and organizations who participated in the development of this guiding document. The implementation of this document is expected to facilitate the work required for AEFI surveillance at all levels of healthcare delivery.

Foreword

Vaccines are preparations that are used to stimulate the immune system's response against diseases. Vaccination is the most effective method of preventing serious diseases.

Vaccines used in national immunization programmes are generally safe and effective when used correctly. However, no vaccine is completely risk-free, and adverse events following immunization can occur infrequently.

The National Adverse Event Following Immunization (AEFI) surveillance has been under the oversight of the national AEFI committee since its inception in 2015. The multi-disciplinary technical committee was placed under the Namibia Medicines Regulatory Council (NMRC) in 2022 in accordance with section 13 of the Medicines and Related Substances Control Act, 2003 (Act No. 13 of 2003). It continues its routine review, assessment, and classification of reported cases, ultimately advising the NMRC and ministerial management team on the causes of AEFI in the country.

The committee is supported by a secretariat comprised of the Therapeutics Information and Pharmacovigilance Centre (TIPC) which falls under the Tertiary Health Care and Clinical Support Services Directorate (THC&CSS) and the Expanded Programme on Immunization (EPI) which falls under the Primary Health Care (PHC) Directorate. Regional and district management teams are tasked with reporting, notifying, investigating, and submitting reports to the National level for assessment and classification.

This AEFI guideline outlines the AEFI Surveillance cycle and is informed by the country context, the most recent global evidence, and operational guidance and recommendations from the World Health Organisation.

I applaud all stakeholders involved in the development of this guideline, which will ensure the effective and efficient implementation of the AEFI Surveillance cycle at all levels of the health system.

DR KALUMBI SHANGULA (MP)
MINISTER OF HEALTH AND SOCIAL SERVICES

Preface

The Namibian government has delegated the Ministry of Health and Social Services the responsibility of providing health and social services to the Namibian population. These services consist of preventive, curative, and rehabilitative services. The Primary Health Care (PHC) Directorate, through the Expanded Programme on Immunization (EPI), is directly responsible for the provision of immunization services in the country.

The operation of the AEFI surveillance system is a collaborative effort between the EPI and the NMRC. The system involves the collection and collation of routine data using health structures. The system ensures that all aspects of the process are addressed thoroughly to ensure high-quality vaccine surveillance. Reporting on all AEFIs is mandatory. Each adverse event should be accurately and promptly reported using the standard AEFI reporting form and in accordance with the standard for data collection, case notification and case reporting procedures.

This guideline outlines the processes and procedures and provides tools for healthcare providers to report, document, and communicate with the media, parents, and caregivers, in order to prevent AEFIs, as well as the roles and responsibilities of stakeholders responsible for the planning and delivery of immunization services in Namibia.

To safeguard vaccine safety in Namibia, I urge all healthcare workers in public and private facilities to implement the AEFI guideline to the best of their abilities.

MR. BEN NANGOMBE
EXECUTIVE DIRECTOR

Glossary

Adverse event following immunization (AEFI)	Any untoward medical occurrence that follows immunisation and 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.
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 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).
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.
Reverse cold chain	Reverse logistics is a widely used term that encompasses numerous processes. In its most general definition, reverse logistics is the process of moving goods backwards through the supply chain, from their final destination to somewhere else.
Safe injection practice	Practices which ensure that the process of injection carries the minimum risk, regardless of the reason for the injection or the product injected.
Serious AEFI	An event that results in death, is life-threatening, requires in-patient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect. Any medical event that requires intervention to prevent one of the outcomes above may also be considered as serious.
Severe vaccine reaction	It refers to the intensity of vaccine reactions. A severe reaction refers to the high-grade intensity of its grading, such as mild, moderate and severe. Severe reactions may include both serious and non-serious reactions.
Signal (safety signal)	Information (from one or multiple sources) which suggests a new and potentially causal association, or a new aspect of an own association, between an intervention and an adverse event or set of related adverse events, that is judged to be of sufficient likelihood to justify verificatory action.
Surveillance	The continuing, systematic collection of data, analysis and dissemination 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.

Abbreviations

ADRs	-	Adverse Drug Reactions
AD	-	Auto- disable syringe
AEFI	-	Adverse Event Following Immunization
ANC	-	Antenatal Care
AIDS	-	Acquired Immune Deficiency Syndrome
BCG	-	Bacillus Calmette-Guerin
CSF	-	Cerebrospinal fluid
CHPO	-	Chief Health Program Officer
CHW	-	Community Health Worker
CIF	-	Case Investigation Form
CIOMS	-	Council for International Organizations of Medical Sciences
COVID 19	-	Corona Virus Disease
CMS	-	Central Medical Stores
DCC	-	District Coordinating Committee
DPHCS	-	District Primary Health Care Supervisor
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
ECG	-	Electro Cardiogram
EPI	-	Expanded Programme on Immunization
GVAP	-	Global Vaccine Action Plan
Hep B	-	Hepatitis B Vaccine
HHE	-	Hypotonic, Hypo responsive Episode
Hib	-	Haemophilus influenza type b vaccine
HIS	-	Health Information System
IPV	-	Inactivated Polio Vaccine
LAV	-	Live Attenuated Vaccine
LP	-	Lumbar Puncture
MMR	-	Measles Mumps Rubella
MR	-	Measles Rubella
mRNA	-	Messenger ribonucleic acid
MoHSS	-	Ministry of Health and Social Services
NITAG	-	National Immunization Technical Advisory Group
NMRC	-	Namibia Medicines Regulatory Council
OPD	-	Outpatient department
OPV	-	Oral Polio Vaccine
PCV	-	Pneumococcal Conjugate Vaccine
QSL	-	Quality Surveillance Laboratory
RCHPO	-	Regional Chief Health Programme Officer
RHMT	-	Regional Health Management Team
SIA	-	Supplementary Immunization Activities
SIDS	-	Sudden Infant Death Syndrome (“cot death”)

THC&CSS	-	Tertiary Health Care and Clinical Support Services Directorate
TIPC	-	Therapeutics Information and Pharmacovigilance Centre
ToR	-	Terms of Reference
TSS	-	Toxic Shock Syndrome
VAPP	-	Vaccine Associated Paralytic Poliomyelitis
VPD	-	Vaccine Preventable Disease
WHO	-	World Health Organization
wP	-	Whole cell Pertussis

Chapter 1. Introduction

Vaccines are biological substances administered to individuals to induce immunity (protection) against specific diseases. Vaccines, like all pharmaceutical products, are composed of adjuvants and/or excipients. Even though vaccines are generally safe when they are administered properly, they rarely cause adverse events in some individuals. The majority of adverse events following immunization (AEFIs) are mild to moderate in severity. AEFI can very rarely be severe enough to necessitate clinical interventions.

A good vaccine provides optimal protection and minimizes adverse events. AEFIs can occur for a variety of reasons including vaccine product related, quality-related, immunization error-related, immunization anxiety-related or coincidental. For this reason, countries must implement a robust vaccine safety monitoring (AEFI surveillance) system in order to prevent their occurrence and take the necessary regulatory or programmatic actions.

The Expanded Programme on Immunization (EPI) unit within family health division of the Primary Health Care Directorate of the Ministry of Health and Social Services (MoHSS) is responsible for establishing procurement guidelines and standards for vaccines and related supplies in the country. EPI has performed well, achieving over 80% immunization coverage for Penta 3, rehabilitating the cold chain system, training healthcare providers, and networking with national and international partners and stakeholders.

The Namibia Medicines Regulatory Council (NMRC) is responsible for authorizing all medicines including vaccines on the Namibian market. In addition, the NMRC monitors the safety of all medical products on the market through pharmacovigilance systems, including spontaneous reporting of any suspected adverse drug reactions experienced by patients. The Therapeutics Information and Pharmacovigilance Centre (TIPC), under the Pharmaceutical Control and Inspection subdivision of Tertiary Healthcare and Clinical Support Services, serves as NMRC's secretariat for medicines safety monitoring. The AEFI committee is the technical committee of the Council that determines whether an AEFI has a causal relationship with vaccines or vaccination.

The reporting of AEFI and subsequent investigation may result in regulatory action, such as the withdrawal of a vaccine's marketing authorization, the instructions to vaccine manufacturers to change the product labelling, the restriction of vaccines use in specific patient groups, or recall of defective vaccine batches from the market.

This guideline describes the processes and procedures healthcare providers must follow when reporting, documenting, and preventing AEFIs, as well as the roles and responsibilities of stakeholders in the planning and delivery of immunization services in Namibia. It describes the surveillance system and provides tools and procedures required to report and manage AEFIs, such as understanding the different types of AEFIs, investigation techniques, specimen collection, managing AEFIs, and communicating with the media and caregivers/parents.

In this manual, a brief introduction to causality assessment is provided.

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 an antigen, an active component of the vaccine which is a modified or partial form of the disease-causing microorganism usually made from either live attenuated or inactivated (killed) forms of the microbe, or its toxin or one of its surface proteins that are incapable of causing the actual disease.

2.1.1 Primary components of vaccines

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

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

The immune system, which is capable of responding to millions of antigens, is not overburdened by the administration of multiple antigens in combined vaccines. Combining antigens does not usually increase the risk of adverse reactions and may lead to a reduction in adverse reactions overall. For instance, it can reduce the frequency of anxiety-related reactions and the likelihood of immunization error-related reactions.

2.1.2 Other components of vaccines

In addition to the primary antigen(s), vaccines contain trace amounts of other substances that may cause AEFIs. They include,

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

Antibiotics: Antibiotics are used during manufacturing to prevent bacterial contamination of the tissue culture cells in which the viruses are grown (e.g. neomycin).

Preservatives: These chemicals are added to inactivated or subunit vaccines in order to inactivate viruses, detoxify bacterial toxins, and prevent serious secondary infections in multi-dose vials caused by bacterial or fungal contamination after they have been opened (e.g. thiomersal, phenol derivatives).

Stabilizers: Stabilizers help the vaccine maintain its effectiveness during storage (e.g. $MgCl_2$, $MgSO_4$)

2.1.3 Classification of vaccines

As previously alluded, there are various types of vaccines: live attenuated, inactivated (killed antigen), subunit (purified antigen), and toxoids (inactivated toxic compounds). The COVID-19 vaccines are composed from messenger ribonucleic acid (mRNA), adenovirus, whole inactivated coronavirus, and protein subunit. These vaccines have distinct properties, which determine how they function.

Table 2.1. Classification of vaccines

Live attenuated vaccines (LAV)	**Bacteria:** BCG vaccine
	Virus: 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 influenza type b (Hib) conjugate vaccine, meningitis A and B conjugate vaccine Pneumococcal conjugate vaccines (PCV-7, PCV-10, PCV-13)
Toxoids	Tetanus toxoid Diphtheria toxoid
mRNA (messenger ribonucleic acid)	Pfizer, Moderna
Adenovirus	(ChAdOx) vector: AstraZeneca, COVISHIELD and Johnson & Johnson
Whole inactivated Coronavirus	Sinopharm Sinovac, Covaxin
Protein subunit	Novavax

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 administered. Ignoring contraindications can result in vaccine reactions that are avoidable. One of the most serious reactions following vaccination is anaphylaxis, 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 steroids treatment, are temporary, and the vaccination can be administered later. These are known as temporary or relative contraindications.

Precautions, are events or conditions that should be considered when determining whether the benefits of the vaccine outweigh its risks (especially if the would-be recipient is immunocompromised or pregnant). Sometimes, the precautions listed on the product's label may be misinterpreted as contraindications, resulting in missed vaccination opportunities.

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. Adverse events that are not due to the vaccine or immunization process but are temporally associated with immunization may also be reported. Table 2.2 describes the five categories of AEFI as defined by CIOMS and WHO.

Table 2.2 Cause-specific categorization of AEFI Council for International Organizations of Medical Sciences

Cause-specific type of AEFI	Definition
Vaccine product-related reaction	An AEFI caused or precipitated by one or more inherent properties of the vaccine product.
Vaccine quality defect-related reaction	An AEFI 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 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 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

On the basis of cause, seriousness, and frequency, vaccine reactions can be classified 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 if the vaccine has been properly prepared, handled, and administered. Frequently, the precise mechanism of a vaccine product-related reaction is poorly understood. The reaction may be caused by an idiosyncratic immune mediator response (e.g. anaphylaxis) or by replication of the vaccine-associated microorganism (e.g. vaccine-associated poliomyelitis following OPV which contains attenuated live virus).

Vaccine quality defect-related reaction: This is a result of a manufacturing defect in a vaccine or its administration device. Such a defect may affect an individual's response, thereby increasing the likelihood of adverse vaccine reactions. Inadequate inactivation of wild-type vaccine agents (e.g. wild polio virus) during the manufacturing process or contamination introduced during the manufacturing process could result in vaccine quality defect-related reactions.

B. Vaccine reactions by seriousness and frequency

Most vaccine reactions are minor and resolve on their own. Serious reactions are very rare and typically do not result in death or long-term disability. Table 2.3 describes the frequency of occurrence of adverse events that have been reported.

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 occur when the immune system of the vaccine recipient reacts to antigens or the vaccine components such as aluminium adjuvant, stabilizers, or preservatives. Most of the AEFIs are minor and they are self-resolving. Minor AEFIs may be local or systemic in nature. At the injection site, local reactions include pain, swelling, and redness. Systemic reactions include fever, irritability, and malaise. A successful vaccine minimizes these reactions while producing the strongest immunity possible. Table 2.4 describes the common minor vaccine reactions by antigen, as well as their respective treatment.

Table 2.4 Common minor vaccine reactions by antigen and treatment

Vaccine	Local adverse events (pain, swelling, redness)	Fever (> 38^{0}C)	Irritability, malaise and systemic symptoms
BCG[1]	90% - 95%	-	-
Hepatitis B	Adults up to 15% Children up to 5%	1 - 6%	-
Hib	5 - 15%	2% - 10%	
Measles/MR/MMR	~10%	5% - 15%	5% (Rash)
OPV	None	Less than 1%	Less than 1%[2]
Pertussis (DTwP)[3]	up to 50%	up to 50%	up to 55%
†Pneumococcal conjugate	~20%	~20%	~20%
Tetanus/DT/aTd	~ 10%[4]	~ 10%	~ 25%

Treatment	Cold cloth at injection site and Paracetamol*	Give extra oral fluids, wear cool clothing, tepid sponge or bath and Paracetamol*	Supportive treatment

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

Table 2.5 Common minor vaccine reactions by COVID- 19 antigen and treatment

COVID-19 Vaccine	Minor side effects	Rare side effects
Pfizer/ BioNTech BNT162b2 mRNA Comirnaty	At site of injection: pain, swelling, redness Other: tiredness, headache, muscle pain, chills, fever, nausea, swollen lymph nodes	Allergic reaction, myocarditis, pericarditis, swollen lymph nodes, decreased appetite, diarrhea, vomiting, fainting due to shot
Sinopharm Inactivated	Injection site pain, swelling, headache	
Janssen COVID-19 vaccine Ad26.CoV2. S Viral Vector	Injection site pain, headache, fatigue, myalgia, nausea, swollen lymph nodes	Anaphylaxis and severe allergic reaction, blood clots, Thrombosis with Thrombocytopenia syndrome usually occurring in women younger than 50, Guillain-Barré syndrome, capillary leak syndrome, fainting due to shot
Astra Zeneca ChAdOx1-S [recombinant] COVID-19 Viral Vector	Pain where you get the shot, fever, muscle aches, headache	A very rare adverse event called Thrombosis with Thrombocytopenia Syndrome (TTS), involving unusual and severe blood clotting events associated with low platelet counts, has been reported after vaccination with AstraZeneca
Treatment	No specific treatment is recommended	Reported and investigated through treatment on individual client /patient profile

Rare, more severe (and serious) vaccine reactions

These 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); however, the event itself may have relatively minor medical significance. Severe AEFIs can be incapacitating but rarely life-threatening. Examples include seizures, thrombocytopenia, Hypotonic Hypo-responsive Episodes (HHE), persistent inconsolable crying etc.

By definition, AEFIs are considered serious 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 a congenital anomaly/birth defect

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

The frequency of occurrence of rare and serious reactions has been summarized in Table 2.5. Children under six months or older than six years are unlikely to experience febrile seizures. If this occurs, a comprehensive investigation must be conducted to determine the underlying cause(s).

Table 2.6 The onset interval, and frequency of severe vaccine reactions

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 (in Pentavalent)	Persistent (>3 hours) inconsolable screaming	0 - 24 hours	1000 - 6000
	Seizures	0 - 3 days	80 - 570[3]
	Hypotonic, hypo responsive episode (HHE)	0 - 48 hours	30 - 990
	Anaphylaxis	0 - 1 hour	20
	Encephalopathy	0 - 2 days	0 - 1

Notes

1. Reactions (except anaphylaxis) do not occur in those who are already immune (~90% of those who receive a second dose are immune): children aged six years are unlikely to experience febrile seizures.

2. VAPP risk is greater after the first dose (1 in 750,000 versus 1 in 5.1 million for subsequent doses) and for adults and immunocompromised individuals.

3. Seizures are typically caused by fever, and the risk varies with age, with a much lower risk in infants younger than 4 months.

C. Immunization error-related reactions

In this context, the term "Immunization" refers to the "use" of a vaccine to immunize individuals. "Use" includes all processes that take place after a vaccine product has left the manufacturing/packaging site, including handling, prescribing, and administration.

Immunization error-related reactions are usually preventable, and they divert attention away from the benefit of the immunization programme. Several of them are listed in Table 2.6. The timely identification and correction of these errors is, therefore, of utmost 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 Live Attenuated Vaccine (LAV) e.g. Disseminated BCG
	Failure to adhere to vaccine indications or prescription (dose or schedule)	Systemic and/or local reactions, neurological, muscular, vascular or bony injury due to incorrect injection site, equipment or technique
Error in administration	Use of an incorrect diluent or injection of a product other than the intended vaccine	Failure to vaccinate due to incorrect diluent, reaction due to inherent properties of whatever was administered other than the intended vaccine or diluent
	Incorrect sterile technique or inappropriate procedure with a multi-dose vial	Infection at/beyond the site of injection

An immunization error-related reaction may occasionally lead to a cluster of immunization-associated events. These clusters are usually associated with a particular provider or health facility or even a single or multiple vials of contaminated or inappropriately prepared vaccine. For instance, freezing the vaccine during transportation may increase the likelihood of local reactions. The specifics of an investigating strategy for AEFI clusters are described later.

D. Immunization anxiety-related reactions

Individuals and groups may experience anxiety and react in anticipation of and in response to any injection. This reaction is unrelated to the components of the vaccine product. Fainting (vasovagal syncope or syncope) is relatively common, especially among children older than five and adolescents. Some children who faint may experience syncopal hypoxic convulsion. As a result of anxiety about the immunization, hyperventilation causes

specific symptoms such as light-headedness, dizziness, and tingling around the mouth and in the hands. This is also a common occurrence during mass vaccination campaigns.

Breath-holding and vomiting are common anxiety symptoms in young children. Additionally, young children may also scream or flee to avoid the injection. Some individuals may have a fear of needles. During group immunization, mass hysteria is possible, especially if one or more of the vaccines are observed by others to faint or have another reaction, such as itching, limb weakness, etc. Occasionally, an episode of fainting can be misdiagnosed as anaphylaxis. Differentiating between them requires careful observation and clinical judgment.

E. Coincidental events

An event that occurs coincidentally with immunization is sometimes incorrectly attributed to the vaccine, i.e. a chance temporal association is incorrectly attributed to immunization. In a mass immunization campaign such temporal associations are inevitable.

Vaccines are normally administered early in life, when infections and other illnesses are common, including manifestations of congenital or neurological conditions, are prevalent. Therefore, it is possible to encounter many events, including deaths that can be erroneously attributed to vaccines by chance association.

The incidence of sudden infant death syndrome (SIDS or “cot death”), for instance, peaks around the age of early childhood immunization. Consequently, many SIDS cases will occur in children who have recently been immunized. Several well-designed studies have shown, however, that the association between SIDS and immunization is coincidental and not causal.

It is possible to predict adverse events that occur coincidentally. The expected number of events is dependent on the population size and the incidence of disease or mortality rates in the community. Knowledge of these background rates of disease and deaths, particularly age-specific disease incidence rates, allows estimation of the numbers of expected coincidental events.

2.2.2 Key AEFI terminology

Cluster of AEFI

A cluster is defined as two or more cases of the same or similar event that are related in time and have occurred within the same district or geographical area or are associated with the same vaccine, same batch number administered or same healthcare worker.

Signal

Information that arises from one or multiple sources which suggests a new potentially causal association or a new aspect of a known association, between an intervention and an event or set of related events, whether adverse or beneficial, that is deemed sufficient to justify verification.

Chapter 3. Prevention and management of AEFI

3.1 General principles of prevention and management of AEFI

Vaccines are rarely contraindicated. However, it is important to check for contraindications to prevent serious reactions. For example, a vaccine is contraindicated if a previous vaccination resulted in anaphylaxis to a particular vaccine.

Vaccine-induced anaphylaxis is rare. However, it is recommended that emergency treatment for anaphylaxis be available in all clinic settings. All immunization providers must be trained and competent in recognizing and managing anaphylaxis and they must have epinephrine (adrenaline) available.

Parents should be informed on how to manage common minor reactions and instructed to seek appropriate medical care for more severe symptoms. This will help in reassuring parents about immunization and preparing them for common reactions.

Antipyretic drug as directed by the prescriber or manufacturer may be administered in the prescribed dosage and frequency. For example, paracetamol, at a dose of up to 15 mg per kg every 6–8 hours with a maximum of four doses in 24 hours, is useful for treating common minor reactions; it reduces pain and fever. However, it is important to warn against overuse of paracetamol or any other antipyretic drug as overdosing may be harmful to the vaccine recipient. A child with a fever can be cooled with a tepid sponge or bath and light cool clothing. Children with fever must be given extra fluids. For a local reaction, a cold cloth applied to the site may provide pain relief.

For any serious vaccine reaction, provision of prompt medical care by a qualified clinician will minimize the likelihood of negative outcomes, expedite recovery and may save lives.

3.2 Prevention and management of immunization error-related reactions

Immunization error-related reactions are preventable, and prompt identification and correction of these errors are important.

Prior to the introduction of auto-disable (AD) syringes, the most common immunization error was an infection caused by a non-sterile injection due to contamination of the vaccine or diluent vial or the injecting device (syringe and/or needle). The infection could manifest as either a local reaction (e.g. suppuration, abscess) or a severe systemic reaction (e.g. sepsis, toxic shock syndrome (TSS)). In addition, a risk was perceived to exist between immunization and blood-borne infections. However, one must consider the possible infection in mass vaccination cases or disaster situations, especially if there is a shortage of supplies or logistical support. This can be avoided if programme managers plan and prepare adequately.

The symptoms of an immunization error may help in determining the likely cause. For instance, children immunized with a contaminated vaccine (usually *Staphylococcus aureus*) develop an injection site reaction (local tenderness, redness, and swelling) within a few hours, followed by systemic symptoms (vomiting, diarrhoea, high temperature, rigors, and circulatory collapse). If the vial is available, bacteriological examination can confirm the source and type of infection.

Although uncommon (~1 per 100 000 doses), sterile abscesses are local reactions to aluminium-containing vaccines, especially DPT. Along with other local reactions, they are more likely to occur if the vaccine is not adequately shaken before use if the injection is superficial and the vaccine has been frozen. Contamination of vaccine or injection equipment may result in bacterial abscess. Inappropriate injection technique may cause injection (subcutaneous rather than intradermal injection) abscess, a common adverse event of the BCG vaccine.

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

Healthcare workers must have a clear understanding of contraindications and precautions. Precautions are not contraindications, but the decision to vaccinate requires a case-based assessment in which the potential risks and benefits of the vaccine is weighed. The use of live vaccines during pregnancy is a good example of this.

The following should be observed to avoid/minimize immunization errors:

- Maintaining the cold chain at all levels is essential.
- Only the diluents provided by the manufacturer may be used to reconstitute the vaccines.
- Reconstituted vaccines should be stored in the recommended cold chain and used within six hours after reconstitution or discarded at the end of each immunization session, they should never be retained.
- Other than vaccines, no other drugs or substances should be stored in the vaccine refrigerator.
- Immunization workers must be adequately trained and closely supervised to ensure that correct procedures are followed.
- It is necessary to conduct a comprehensive epidemiological investigation of an AEFI in order to identify the cause and correct the immunization practices.
- Prior to immunization, adequate attention must be paid to contraindications.

Following immunization error-related reactions, follow-up and corrective measures should be based on the findings of the investigation. Depending on the nature of the immunization error, the measures may be both general (e.g. training and awareness) and specific (e.g. strengthening cold chain maintenance if the problem is found to be related to cold chain issues). Continuous monitoring and supportive supervision can help in the reduction of adverse events.

3.3 Prevention and management of immunization anxiety-related reactions

Training and awareness are important to enable health staff to recognize and appropriately manage medical emergencies. ***Fainting*** does not require clinical management beyond placing the patient in a recumbent position.

When immunizing older children, the possibility of fainting must be anticipated. 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 administration.

Syncopal hypoxic convulsions are brief, generalized tonic-clonic seizures that can be managed by keeping the child lying down and securing the airway by placing the child on one side to prevent aspiration if the child vomits. The seizure will end spontaneously, but if prolonged or focal then further investigations may be required.

Sometimes, ***hysteria*** cases may require hospitalization and may cause public concern. Clear explanations of the immunization and a confident, reassuring delivery will reduce the level of anxiety associated with injections, thereby decreasing the likelihood of occurrence.

Careful observation and clinical judgment to differentiate between ***anaphylaxis and syncope*** is necessary. However, a single dose of adrenaline administered intramuscularly by accident to a vaccine recipient experiencing only syncope does not cause harm.

3.4 Management of suspected anaphylaxis or collapse after vaccination

Sudden and severe events that occur after vaccination, particularly syncope, are mostly reported as anaphylaxis. However, anaphylaxis following vaccination is very rare, and with the risk of 1−2 cases per million vaccine doses.

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

Unpredictable events may occur without warning. Emergency equipment must be readily available whenever immunizations are administered. All health workers must be familiar with the practical steps required to save life in the event of anaphylactic reaction. Each vaccinating facility providing vaccinations must have an emergency kit with adrenaline. The expiry date of the adrenaline should be clearly written on the outside of the emergency trolley and checked weekly. As a part of emergency care, healthcare workers may misdiagnose syncope attacks as anaphylaxis and administer adrenaline. If the correct dose of adrenaline, based on age and weight is administered via the intramuscularly, no harm is likely to occur. However, an overdose of adrenaline administered intravenously or intracardially or repeatedly may be harmful.

In all cases of suspected anaphylaxis, it is important that all symptoms and signs are well documented by healthcare providers. Due to rarity of anaphylaxis, other more common causes of sudden and severe symptoms post-immunization must be considered. The conditions that may be mistaken for anaphylaxis are listed in Table 3.1

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, no tachycardia, no respiratory involvement, spontaneous resolution when prone.
Hypotonic hypo responsive 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 apnoea or aspiration.
Aspiration of oral vaccine (e.g. OPV or rotavirus vaccine)	Immediate respiratory symptoms (cough, gagging, stridor or wheeze) during administration, usually in infants. 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 – unrecognised congenital heart disease or occult infections. May have respiratory or cardiovascular compromise but there are usually symptoms, signs or investigations to indicate alternate causes.
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.

Chapter 4. AEFI surveillance in Namibia

Surveillance for adverse events following immunization (AEFI) is an integral part of the Expanded Program on Immunization (EPI) and helps to maintain public confidence in the immunization programme while promoting the use of vaccines in the country. As shown in Fig 4.1, this is done systematically.

The objectives of AEFI surveillance are to:

1. Detect and respond promptly to the occurrence of an AEFI
2. Notify the different levels within 24 hours and identify, correct, and prevent any immunization error-related reactions.
3. Report both minor and serious cases by completing the AEFI reporting form and inform the next level within 24-48 hours
4. If the case is serious, conduct the investigation within 24-48 hours, provide details to the next level (recognize clustering, identify potential safety signals including previously unknown vaccine reactions), and generate hypotheses that may require further investigation.
5. Collect and analyze relevant information. Compile the report and submit it to the next level.
6. Conduct the causality assessment at the national level, review, assess and classify the case.
7. Provide all levels with feedback and recommendations for corrective action. Provide clients/parents/community/ family/ healthcare workers and other stakeholders with feedback and information regarding the safety of the vaccines used in Namibia.

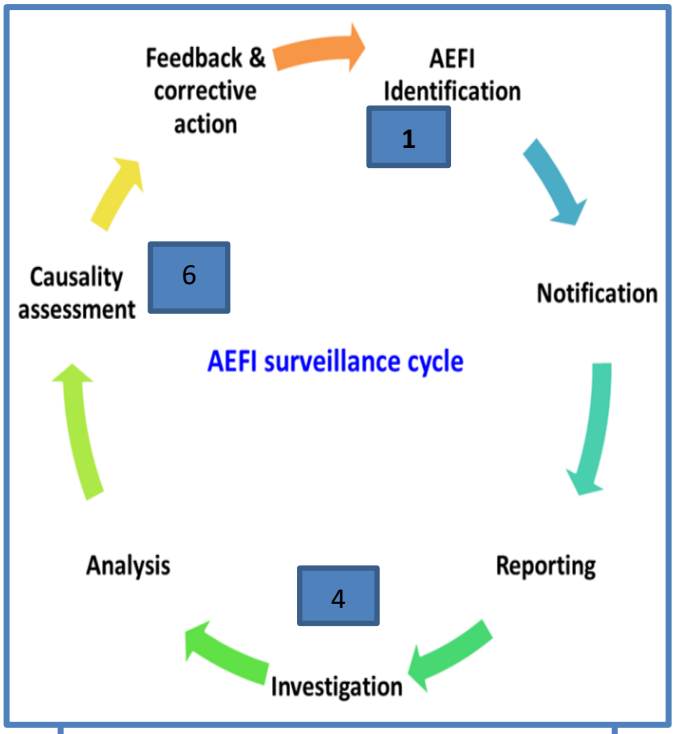


Fig 4.1 AEFI surveillance cycle

Parents of immunized infants/children, healthcare providers and staff at immunization facilities are most likely to recognize or detect AEFIs when they occur for the first time. Any AEFI case notified to healthcare providers should be reported to the District Primary Health Care Supervisor (DPHCS) using the standard reporting form (*Annex 1*). Serious AEFI cases should be promptly reported by telephone to the DPHCS and followed by the completion and submission of the AEFI reporting form.

Serious AEFI cases resulting from potential immunization errors, clusters or AEFI causing parental or community concern, unexpected AEFIs, and known AEFIs must be reported. The case definitions of commonly reportable AEFI are provided in Table 4.1. However, it must be emphasized that all cases notified to health workers must be reported.

Healthcare 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), angio-oedema (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: - 38 to 38.9^{0}C), ▪ Moderate fever: -39 to 40.4^{0}C-and ▪ Severe fever: >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
Lymphadenitis (includes suppurative lymphadenitis)	Either at least one lymph node 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 - 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 centred 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 Acute Flaccid Paralysis (AFP)	Acute onset of flaccid paralysis and neurological deficits, compatible with diagnosis of poliomyelitis, with isolation of vaccine virus and absence of wild virus in stool.	OPV
Serious AEFI: Any AEFI causing • Death • Hospitalization • Disability, congenital anomaly • Other severe and unusual events		No time limit, if they are thought by health workers or the public to be related to immunization

All vaccination staff must be able to recognize AEFIs and report them. However, accurate diagnosis of AEFIs requires trained staff. Healthcare providers are also responsible for managing AEFIs and, if necessary, referring patients for further care.

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

Subnational Stakeholders

The subnational stakeholders involved in AEFI reporting and investigation are:

1. Beneficiaries/parents/ guardian/community
2. Community Health Workers
3. Healthcare workers (medical officers, pharmacists, nurses, etc.)
4. The District Coordinating Committee with the District Primary Health Care Supervisor (DPHCS) as the focal person
5. The Regional Health Management Team (RHMT) with the Chief Health Program Officer (CHPO) for family health as a focal person

National stakeholders in AEFI investigation

The national stakeholders are:

1. EPI, TIPC and NMRC
2. National AEFI Committee
3. Health Information and Research Directorate (Epidemiology and Health Information System divisions)
4. Health professional bodies
5. Partner organizations
6. Central Medical Stores (CMS)

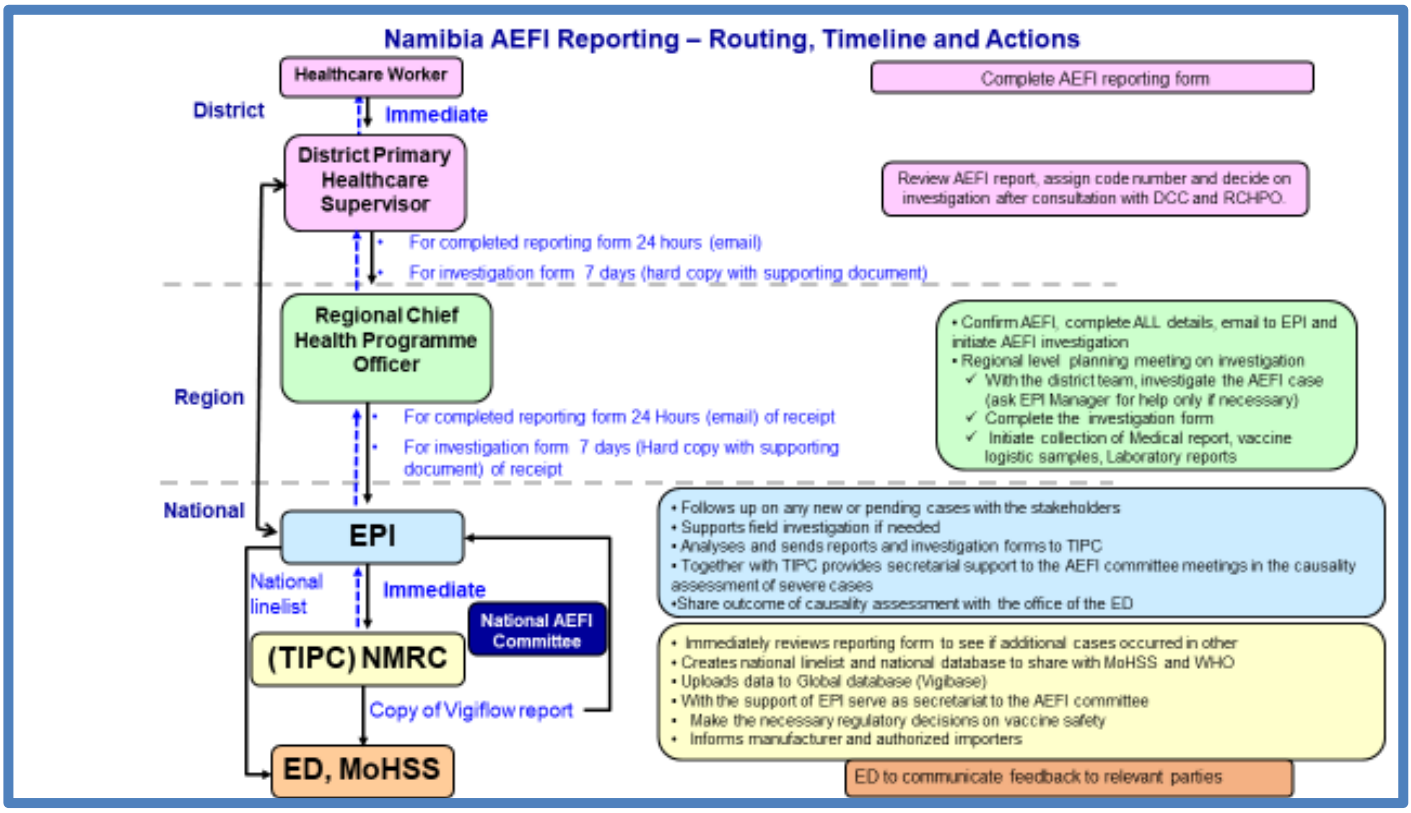


Figure 4.2: Namibia AEFI surveillance flowchart

4.2 Field investigation of AEFI

The ultimate goal of an AEFI field investigation is to identify the cause of the reported AEFI(s) and prevent their recurrence. AEFIs resulting from immunization error-related necessitate prompt corrective action. Even if the cause cannot be identified or the cause of the event was due to a different cause, the fact that staff investigates the incident will increase public confidence in the immunization programme.

The purpose of the AEFI case investigation is to:

- Confirm the reported diagnosis and/or propose alternative possible diagnoses and clarify the outcome of the medical incident comprising the AEFI.
- Determine the specifics, circumstances, and procedures surrounding the vaccine used to immunize the affected recipient. Most importantly, identify any potential vaccine-related association with the given AEFI.
- Examine the operational aspects of the programme. Even if an event appears to be caused by the vaccine product or to be a mere coincidence.
- Determine whether a reported event was a single incident or part of a cluster. If it is a cluster, confirm that the suspected immunizations were administered and identify the specific vaccines used.
- Determine if unimmunized individuals experience the same medical incidents.

4.2.1 Role of the Subnational stakeholders

Beneficiaries/parents/ guardians/community

- At the time of immunization, it is important for healthcare professionals to inform the individual, parents / guardian about expected minor events such as fever and pain at injection site etc.
- Parents should be informed about simple home remedies (e.g. correct positioning of the child when sleeping, increasing intake of fluids, sponging, breastfeeding, antipyretics etc.) for such events ; however, they should be instructed to notify severe expected events (e.g. very high fever, not responding to antipyretic) or other unusual events to the health worker if they occur.
- The community health workers play an important role in notifying and reporting the AEFI to the healthcare workers.

Healthcare worker

The role of the healthcare worker is to educate the individual, parent/guardian about the potential adverse events following immunization. The healthcare worker is responsible for providing primary medical care and report the basic details of the notified adverse event to the district using the AEFI reporting form (*Annex 1*) (preceded with a preliminary report by telephone if it is a serious/severe event).

Role of stakeholders at the district

When the DPHCS receives an AEFI report (*Annex 1*), they should review the report and determine if the reported AEFI case meets the criteria required for a detailed investigation. If necessary, he or she should contact the primary reporter, visit the location of the event and conduct interviews with relevant stakeholders for to obtain additional information. It is possible to consider:

1. If it is a minor AEFI that does not warrant a detailed investigation, the reporter should indicate this on the reporting form and email it to the regional and national levels, using the email: AEFI@mhss.gov.na.
2. If it is a serious AEFI such as death, hospitalization, significant disability, life-threatening, or a congenital anomaly/ birth defect, or is a part of a cluster, or a part of a group of events above the expected rate/ severity, or a suspected signal requires a detailed investigation.
3. Plan for a detailed field investigation after consulting with the technical experts of the District Co-ordinating Committee (DCC) on the matter.
4. Prior to initiating an investigation, they must email the regional and national levels the completed AEFI reporting form (*Annex 1*).

The team conducts an investigation with assistance from the regional and/or national level. The EPI, TIPC, and WHO comprise the national level team. During field investigations, the AEFI investigation form (*Annex 3*) should be used as a guide to collect suitable information.

The investigators should document any deficiencies found in a generic way and suggest corrective measures, rather than blaming individuals. While an individual may have been at fault, it is more effective to focus on identifying systemic and procedural flaws that contributed to the event. This is more effective than blaming or punishing individuals for preventing similar errors in the future. This approach is essential to encourage AEFI reporting for the ultimate benefit of the community and the immunization programme. It is also more likely to improve system performance. Errors provide the opportunity for learning and developing systems that promote continuous improvement. Errors that are concealed will only serve as the foundation for more errors.

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

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

- The DPHCS confirms the AEFI, completes ALL missing details on the AEFI reporting form and initiates the AEFI investigation. Each case will be assigned a unique report identifying case number.
- Prior to the investigation, the DPHCS facilitates the convening of the DCC planning meeting.
- The DPHCS, together with the experts (pharmacists, medical officers, HIS/surveillance officers, infection control focal person, laboratory technicians), should visit the patient, the care provider(s), and the hospital as required; conduct interviews with relevant stakeholders (parents, healthcare worker, treating doctor, vaccine supply focal person); and investigate 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 such as CSF, serum, or other biological products.

Generally, before attributing an AEFI to any vaccine product-related problems, the investigator should rule out any potential immunization errors and obvious coincidental events, as these are more common. Consequently, the investigation should initially attempt to rule out immunization errors associated with storage, handling, reconstitution, or administration of vaccines.

The focus can then shift to other events. Details of coincidental events may be determined by reviewing hospital admissions for similar conditions during the same time 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 consistent with the pattern observed in the previous years. The estimated background incidence of various conditions may be available in the medical published domain.

Once the investigation has been initiated, the District / Regional investigator must update the EPI and the NMRC on the status and progress of the case. This is necessary, as a national-level officer (Public Relations Officer) should be the government spokesperson to the media and the general public regarding the investigation. The completed case investigation form (*Annex 3*), along with the supporting documents such as the medical report, vaccine information, logistic samples, and laboratory reports e.g. CSF, serum, or other biological products, should be sent to the EPI within 7 days of the initial case notification.

Table 4.2 summarizes 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 a patient's medical file (or other clinical record). ☐ Check details about the patient and event from the medical file and document the information. ☐ Obtain any details missing from AEFI Reporting 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/ transported, 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 the health facility, Vaccine Vial Monitor. ☐ The date of manufacture, expiry date, 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). ☐ Number of immunizations done (greater than normal). ☐ Details of training on immunization safe injection practices.
	Observing the service in action:	☐ Refrigerator – what else is stored (note: if similar containers are stored next to vaccine vials, this could cause confusion); which vaccines/diluents are 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 the working hypothesis? ☐ Laboratory tests may help (see chapter 5).

6	**Conclude investigation:**	☐ Complete AEFI Investigation Form. ☐ Take corrective action and recommend further action. ☐ Send the investigation report to EPI which forwards it to the National AEFI Committee.

Role of the Regional stakeholders

The RHMT AEFI Committee is composed of the Chief Medical Officer, Chief Health Programme Officer, Regional Pharmacist, Senior Registered Nurse, and Regional HIS/Surveillance Officer. The primary role of the RHMT is to:

- Assist in responding to AEFI.
- Support the districts in investigations as required.
- Follow up with the DPHCS regarding timely submission of AEFI investigation reports, hospital records, and autopsy reports (where applicable) to the national level for serious AEFI cases.
- Ensure that the reporting and investigation tools for AEFI are accessible at the district and sub-district levels.
- Identify additional training needs and facilitate training at the district and health facility levels.

Role of the National stakeholders

When the national EPI focal person receives the AEFI reporting form, she or he must ensure that the information is shared in a real-time basis with the TIPC at the NMRC.

- EPI should contact the districts reporting serious AEFI cases to follow up, and if necessary, offer support to the investigating team.
    - Compiles AEFI case dossiers for presentation to the AEFI committee.
    - Facilitate provision of feedback to the relevant stakeholders at the regional and district level within 7 days of causality assessment through the existing communication protocols.
    - Following up on and ensuring that they are implementation of actions recommended by the national level (e.g. change in logistics, cold chain, training after program errors etc.). The EPI should also evaluate the AEFI surveillance system periodically and address training needs.

- The TIPC reviews the data in the context of previously received AEFI reports, particularly during the same time frame, to determine if these reports constitute a signal. This can be accomplished by appending data into a national AEFI line list (Annex 2) along with information from the reporting form, reviewing the data, and conducting any necessary analyses. If similar cases have been reported in the past, it is essential to determine whether an epidemiological link or other pattern can be identified.
    - If AEFI cases are received directly at the TIPC, they should be checked for duplication with the cases received from the EPI and compiled.
    - Upload the information to the Global pharmacovigilance database, VigiBase®. This database is managed by the Uppsala Monitoring Centre under the WHO International Drug Monitoring Program. TIPC should provide a line list of cases uploaded on VigiBase® with EPI every month.

- The TIPC and the EPI constitute the National AEFI secretariats. The secretariats coordinate and provide technical/logistical support to the National AEFI Committee's meeting (Fig 4.2).

- When requested by the AEFI committee and EPI Program, Central Medical Stores (CMS) should provide information regarding the vaccines and lots distributed throughout the country. NMRC should provide additional information on AEFI cases from other sources upon request.

4.2.2 Investigation of AEFI with fatal outcome

In the event that a death following immunization is suspected, a field investigation must be initiated immediately. Within 24 hours, the death should be notified to all relevant administrative levels, such as the Regional Director, Chief Health Programme Officer, EPI, and NMRA. The case should be investigated by a team of experts from relevant fields, including clinicians and the national level. Due to the rarity of immunization-related deaths (anaphylactic reactions being one of the only 2-3 known events), major programmatic errors may be involved. Therefore, an investigation must be conducted immediately to rule these possibilities in order to prevent additional cases. A vaccination-related death may cause panic, and the public demand an explanation immediately. A press release or public notice may be issued to calm public and inform them of the next steps to be taken.

For all deaths following immunization or deaths suspected to be caused by a vaccine/immunization, a post-mortem is mandatory and recommended. However, the decision to conduct a post-mortem should be consistent the religious, cultural acceptable practices of the deceased's family and the national legal framework.

4.2.3 Investigating AEFI clusters

A cluster of AEFI is defined as the occurrence of two or more cases of the same adverse event in relation to time, place, or vaccine administration. In addition to these three factors, the investigator should look for AEFI in populations with genetic predispositions or disease, as well as populations of comparable age.

The initial steps of a cluster investigation are establishing a case definition for the AEFI and related circumstances and identifying all cases that meet the case definition. The investigator must define the cluster and identify the cluster's common exposure factors.

Vaccine administration information (when and where) is gathered in order to identify a cluster (i.e. cases with common characteristics). This can be achieved by collecting and recording:

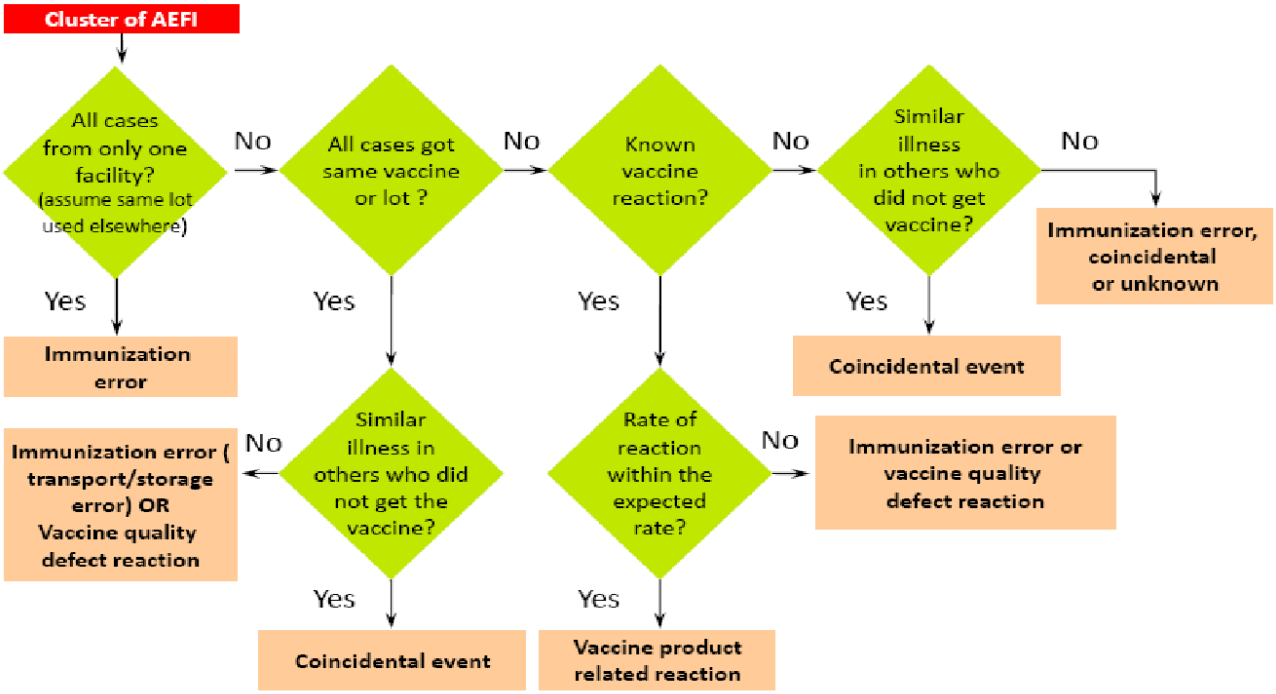
- Detailed data on each patient;
- Programme-related data (storage and handling, etc.); and
- Immunization practices and the practices of the relevant healthcare workers.

Common exposures among the cases may be identified by reviewing:

- All data on the vaccine(s) used (name, lot number, etc.);
- Data on other people in the area (also unexposed); and
- Any potentially coincidental community factors.

The cause-specific definitions provide a framework for investigation and causality assessment once an AEFI cluster has been identified. Usually, the most important factor will be investigating the possibility of an immunization error or a vaccine quality defect. It is necessary to consider the possibility of an immunization error cluster if events occur in one setting without a similar change in frequency in other settings using the same vaccine. In contrast, if multiple settings report an increase in the frequency of events, the possibility of a vaccine quality defect must be strongly considered. Clusters of fainting after immunization are well-known immunization anxiety-related reactions during school-going children's immunization programmes.

Fig 4.3 Identifying cause of AEFI cluster



For relatively new vaccines or established vaccines administered to new target populations, a cluster may represent a previously unidentified vaccine product-related reaction. Knowledge of the background incidence of events that may occur in a causal relationship with a vaccine is therefore essential for assessing signal strength of a cluster.

Interpretation of results from AEFI clusters

If all cases received vaccines from the same healthcare worker/facility, and there are no additional cases, it is likely that an immunization error occurred. If all cases received the same vaccine or lot, and there are no other similar cases in the community, it is likely that there is a problem with the vaccine or the lot in question. If the event is a known vaccine reaction that occurs at a higher rate than expected, the cause is likely to be an immunization error or a vaccine problem. Finally, if cases in the unvaccinated population are occurring at about the same rate/proportion as among the vaccinated population from the same area and age group, the adverse event was likely coincidental (Fig 4.3).

Chapter 5. Laboratory testing of specimens

Laboratories have an important role in the diagnosis and case management of AEFI cases. In addition, they have an important role in testing the quality of the vaccines samples and the logistics employed.

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 routine and must be performed in clinical laboratories. The results of these tests are important for confirming the case diagnosis and establishing a valid diagnosis for assessing causality, as described in section 7.2.

Laboratory testing of vaccine samples and logistics are rarely required. It is not mandatory to follow an AEFI, especially if the cause is evident, such as a coincidental event or an immunization error. However, sometimes laboratory testing of vaccines and logistics is required to confirm or rule out the suspected cause.

In the context of AEFI, additional patient-specific tests, vaccines, and logistics, as outlined below, may be required. The testing of additional specimens includes:

Human specimens

- Histopathology, body fluids analysis etc., can be performed in MoHSS-approved laboratories.
- The analysis of autopsy specimens is performed at government-approved and accredited forensic laboratories as identified by the MoHSS.

Vaccines and logistics

- Vaccines and diluents tested for sterility and chemical composition.
- Syringes and needles tested for sterility.

Process

- Only the appropriate specimens in the correct quantity required for the investigation should be collected.
- Laboratory specimens should be stored and transported as recommended and should be accompanied by clear supporting documents, reasons for specimen collection, and any other additional information required by the investigators.
- If the laboratory investigation is required, the 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 further investigations 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 patient's symptoms and signs as well as the clinical decisions made by the doctor in charge of the case. Table 5.1 provides a summary of several specimens that may be collected, however it should be noted that the list is not exhaustive. Every sample must include the type, date, and time of its collection. Documentations of clinical investigations and medical records pertaining to the incident will support correct lab investigations. It is recommended to consult the treating doctor(s) before deciding which samples to test.

For biochemical, histo-pathological, and microbiological examination, specimens should be handled at the district hospital and forwarded to the nearest laboratory, which has the required facilities to perform requested laboratory testing. If essential laboratory testing facilities are unavailable at the district level, EPI may recommend sending samples to a national laboratory or an internationally accredited laboratory.

In the event that an AEFI is suspected to be the cause of death, an autopsy must be performed as soon as possible (within 72 hours) to prevent tissue lysis (such as in the adrenal glands), which can alter the diagnosis. An autopsy must be performed by a medical doctor who has received training in autopsy procedures. Samples for both toxicology and pathology examinations should be sent to the reference laboratories identified by EPI as early as possible to prevent the loss of biological samples due to decomposition. It is essential to include a detailed patient history on the autopsy form and submit it to the autopsy team so that any underlying pathologies can be identified.

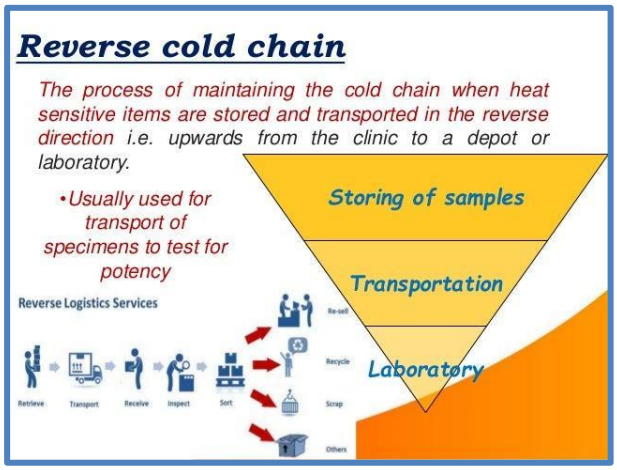
5.1.1 Guide to human specimen sample collection

Table 5.1 provides information on the type of AEFI, the tests to be performed, the specimens to be collected, the method of storage and shipment, and the labs.

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.	National Institute of Pathology
BCG lymphadenitis	Microscopy, Culture and serology	Blood, LN Aspirate or Biopsy and Suspected Vial Batch	At Contact	Wrap in leak proof and waterproof container transport. Vaccine sample should be transported in reverse cold chain	National Institute of Pathology
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	National Institute of Pathology
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	National Institute of Pathology

				Transport to referral laboratory immediately	
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	National Institute of Pathology
Death	Serology	**(1)** Venous Blood **(2)** Vial Batch	Immediate	Never use vials that contained antibiotics Transport to referral laboratory immediately Transport sampled vial batch in reverse cold chain (see figure below)	National Institute of Pathology

Figure 5.1: Reverse Cold Chain Logistics Diagram



5.2 Vaccines and logistics

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

Testing of vaccines and logistics should only be requested on the basis of a strong suspicion and never before a working hypothesis has been formulated (Table 5.2). The determination of samples (if any) to send for testing depends on the working hypothesis for the cause of the event(s). If the used vial of the suspect vaccine is available, it must be labelled and sent alongside unopened vials of the same lot.

The district, regional, and national pharmacists will be responsible for the packaging, cold chain maintenance, and shipment of samples to Quality Surveillance Laboratory (QSL) at the NMRC at the correct temperature. ALL samples sent to the lab must be accompanied by a laboratory request form (*Annex 4*).

The laboratory will process the specimens and send the laboratory results to the requesting doctor, as well as to National EPI Manager and TIPC (National Secretariat).

Table 5.2 Laboratory tests to investigate AEFI according to the working hypothesis

Working hypothesis	Specimens to send For investigation	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

Chapter 6. Data and performance analysis

6.1 Sources of Information on AEFI data

Clinical examinations, interviews with healthcare 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 may provide information on vaccine safety and the possible occurrence of AEFIs. The analysis of data on AEFIs involves reviewing information from the following sources

- Data collated into a line list
- 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

All notified cases (serious and non-serious AEFI) must be reported using the AEFI reporting form (*Annex 1*). All reported AEFI cases at all levels should be AEFI line listed using the AEFI line list (*Annex 2*). This is the initial step of data management. Before conducting analysis, verify and ensure the accuracy of the data. In addition to time, place and person analysis that should be performed by the district and state program managers, other important analyses related to the performance of the surveillance system, include the following:

- Timeliness and completeness AEFI forms submissions.
- Identifying health institutions where AEFIs are not reported by checking on "zero reporting" or "nil reporting." Determine if this due to reporting failure or if there are no AEFIs to be reported.
- Assessing AEFI case reports received within a specified timeframe.
- Assessing the number of events and reporting rate per 1,000 or 10,000 or 100,000 doses of vaccine used.
- Analyses based on the type of AEFI
- Analyzing programme errors by number and rates per 100 or 1,000 doses of relevant vaccines used.
- Compare the rates to 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 the district level by DPHCS and relevant staff
- at the regional level by RCHPO and relevant staff
- at the national level by the EPI and TIPC

Data analysis at the district level is important to identify the programme errors. This allows for prompt corrective action to be taken. The purpose and type of analysis are detailed in Table 6.1.

Table 6.1 Types and purpose of data analysis at different levels

Programme implementation level	Suggested Analysis	Purpose of analysis at this level
District level	• Number of reports by clinics, hospitals, villages by a given time	• These are programme operation indicators such as timeliness and completeness

	• Reported AEFIs by Place (clinics, hospitals), Persons and time • Reported AEFIs by antigen	• Identify immunization errors and thereby will lead to corrective action • Will identify vaccine reactions and coincidence.
Regional level	• Number of reports by district • Reported AEFIs by Place (clinics, hospitals), Person and Time • Cluster analysis • Reported AEFIs by antigen	• These are programme operation indicators (timeliness, completeness) at local level • Identify immunization (programme) errors and thereby will lead to corrective action • Cluster analysis too lead to identify immunization errors, but also coincidence and vaccine reactions too • Will identify vaccine reactions and coincidence
National level	• Number of reports by region • Reported AEFIs by Place (clinics, hospitals), Persons and time • Cluster analysis • Reported AEFIs by antigen	• These are programme operation indicators (timeliness, completeness) at intermediate level • Identify immunization (programme) errors and thereby will lead to corrective action • Cluster analysis too lead to identify immunization errors, but also coincidental events and vaccine reactions • Will identify vaccine reactions including signal detection • Lead to take operational and policy decisions in the country

6.4 Process of data analysis

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

The Vigiflow[@] should be generated Line lists and used sort data by place, person, and time. After stratifying data, analysis should be performed by antigens and by type of reported adverse events (e.g. high fever, abscess) after stratifying data. The best denominator for calculating reported AEFI rates for each antigen in a given time period is the number of doses administered by month, quarter, or year. The limitations of various denominators are described in Table 6.2. When the antigen is administered multiple times, analysis can be expanded to include AEFI rates by first or second or third dose. For this, the total number of doses administered of the given antigen by first, second or third must 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: Using the appropriate multiplier in data analysis is important and varies according to the purpose and level of analysis. At lower levels, the best multiplier is percentage (x100 = %), whereas at national levels, one may use 1000, 100,000, or million. For common, minor vaccine reactions, it is recommended to use percentage, while for rare serious reactions, 10,000, 100,000 or 1,000,000 (million) can be used.

6.5 Interpretation of data

The hyperlink http://www.who.int/vaccine_safety/initiative/tools/vaccinfosheets/en/index.html provides the expected rates for each type of AEFI for a given antigen. This can help to determine the necessary corrective action for AEFIs that have been reported. In addition, it is also important to understand the national background rates of reported medical events. A Comparison between background rates and reported AEFI rates will inform a potential coincidence hypothesis. For example, febrile seizures caused by bacterial or viral infection aetiologies are common in young children and may occur following vaccination with certain vaccines, such as Penta. Therefore, it is important to understand the rate of febrile seizures due to other causes and the expected rates following a exposure to a particular antigen.

If the values exceed the expected background rates, then a true increase or coincidence due to other factor should be considered.

6.6 Monitoring and Evaluating the performance of the AEFI surveillance system

The performance of the AEFI surveillance system must be regularly reviewed at all levels to ensure that it is sensitive enough to rapidly detect and respond to AEFIs. The "standard overall" indicator proposed to determine the quality of AEFI surveillance is the "AEFI reporting ratio in surviving infants from a sub-national area/country per year". This is calculated as:

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

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

Other key performance indicators that help in monitoring 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 in a timely manner (< 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 for which the final classification, including causality assessment by the AEFI committee, is completed within 30 days of receiving all documentation from districts.
- Number (%) AEFI cases reviewed by the National AEFI committee after receiving reports of AEFI cases from the region at National level.
- Number (%) AEFI cases reviewed by the National AEFI committee and not assessable due to lack of information.
- Response to AEFI by the programme, particularly error related to the programme.

Chapter 7 Brief overview of AEFI causality assessment

This section provides a brief introduction and overview of the purpose, process, and classification of AEFI cases after causality assessment. WHO has published a comprehensive guide and background to causality assessment, which can be accessed online via the following link:
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 associated with the vaccine/s administered. In general, causality assessment determines the degree of association between the reported adverse event and the vaccine/vaccination but does not necessarily establish whether a causal relationship exists. However, causality assessment is crucial for AEFI monitoring and improves confidence in the national immunization programme. Causality assessment is important for:

- Identification of vaccine-related problems;
- Identification of immunization error-related problems;
- Excluding coincidental events;
- Detection of signals for potential follow-up, testing of hypothesis and research; and
- Validation of pre-licensure safety data with a 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 and 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.).

The AEFI reporters and investigation teams are not expected to assess causality of serious AEFI cases.

7.2 Preparation for causality assessment

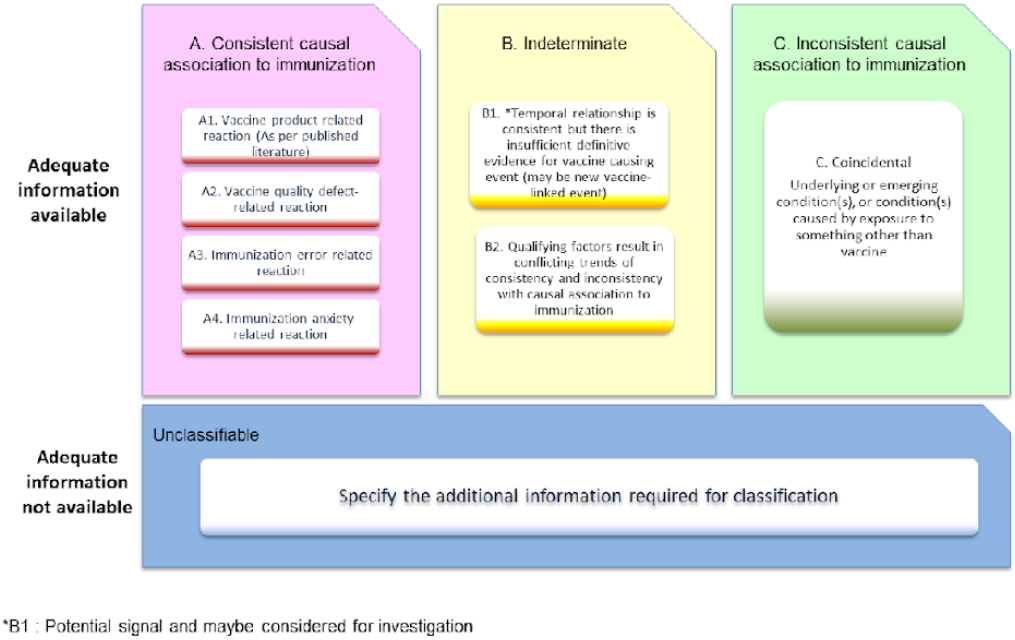
Prior to causality assessment:

- The AEFI case investigation should have been concluded.
- At the time of assessment, all case details, including case report form, case investigation form (*Annex 3*), completed clinical case record, lab reports, autopsy report, details of field investigations, etc., must be accessible.
- There must be a "valid diagnosis," which is the degree to which the unfavourable or unintended sign, abnormal laboratory finding, symptom, or disease is defined.

A causality assessment cannot be performed with inadequate or incomplete case information. If attempted, the AEFI may be deemed unclassifiable or not accessible due to lack of information. Alternatively, even with complete information, the AEFI may be classified as indeterminate due to the absence of clear evidence of a causal link, conflicting external evidence, or other inconsistencies. Nevertheless, these assessments should be

documented because reporting more cases may result in a stronger signal and a plausible hypothesis, or a stronger refutation of any link.

Figure 7.1 Final classification of cases after determining causality



*B1 : Potential signal and maybe considered for investigation

7.3 Causality assessment team

Causality assessment in Namibia is performed by a national AEFI committee that:

- Is independent.
- Is free of real or perceived government and industry conflicts of interest.
- Has a broad range of expertise in the fields of infectious diseases, epidemiology, microbiology, pathology, immunology, neurology, and vaccine program.

The committee's roles and responsibilities have been outlined in a written Terms of Reference (ToR).

In summary, causality assessment of serious cases requires high levels of expertise and will only be performed by an expert committee at the national level. Usually, an assessment will not prove or disprove the association between an adverse event and immunization. It is intended to assist in determining the degree of certainty of such association. A definite causal association or absence of association often cannot be established for an individual event.

7.4 Action and response to AEFI

Responses to AEFI may involve either immediate, short-term 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.

Patients should receive prompt and appropriate care regardless of their diagnosis. Case management and referral will vary depending on the severity of the situation. During immunization, parents can be reassured and educated about how to manage mild symptoms such as fever and pain, which are likely to have a short duration and can be managed by providing reassurance and information. These cases should be documented and reported using the standard form if returning parents seek medical care (*Annex 1*). In the event that patients require hospitalization, a clear referral system should be in place.

Table 7.1 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 state office to consider: ▪ Withdrawing that lot. ▪ Investigating with the manufacturer. ▪ Obtaining a 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 demonstrating that there is no evidence 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 a widespread belief that the event was caused by immunization. Occasionally, it may be useful to enlist further expert investigation to confirm that the event was truly coincidental. The potential for coincidental events to harm the immunization programme through false attribution is enormous.

An investigation may be conducted depending on the nature of the event(s), the number of people affected, and the perceptions of the community. In general, it is not advisable to discontinue the immunization programme while awaiting for the investigation to conclude. Depending on the nature of the event, its extent and whether it is ongoing, a further investigation or epidemiological study may be required if AEFI causality is not established. However, it must be acknowledged that in some instances, the relationship between vaccines and adverse events will never be clear. Communication and training are two important follow-up actions with lasting consequences.

Chapter 8. Communication and media management

8.1 Risk communication

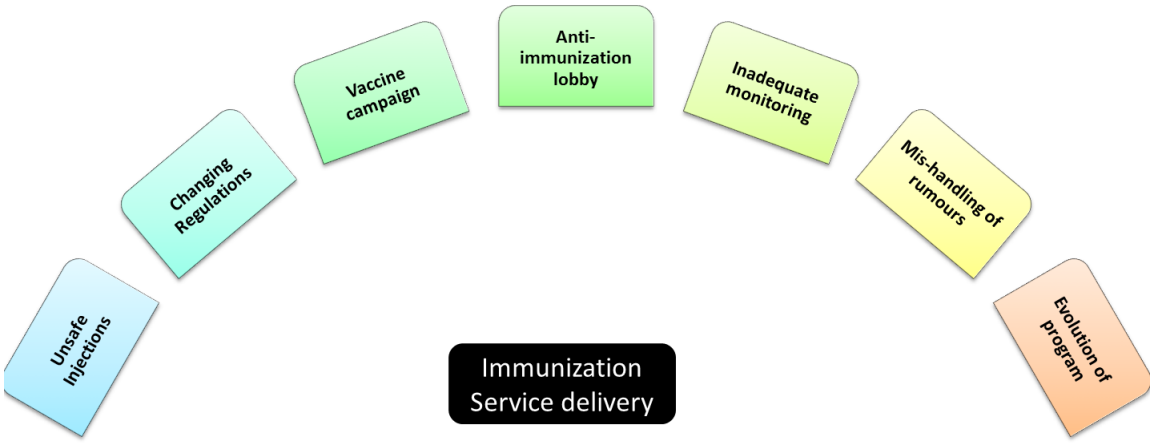
Communication about AEFIs makes stakeholders aware of the process at each stage of the investigation. The identification of specific interest groups and their representatives should be incorporated into communication strategy. A comprehensive communication strategy should include decisions about what, whom, and how, should be part of an overall communication strategy. The existing tools on risk communication strategies should be utilised to ensure effective communication.

Communication to the media and families of the AEFI clients is only done by the Executive Director or a designate.

Need for improved communication

Concerns about vaccines and immunization programmes are frequently voiced by general public and the media. These concerns can be serious and are often unfounded. The graphic below (Fig 8.1) illustrates some of the factors that may trigger public concerns, highlighting the need for increased quantity, quality and targeted communication about vaccine safety.

Fig 8.1 Factors triggering public concerns to immunization



Challenges to effective communication

Among the challenges that must be surmounted through effective communication are:

- Communicating the decline of childhood infections and deaths from VPD
- Parents view infectious disease to be an issue of the past
- Introduction of new vaccines and corresponding knowledge gaps
- Mass campaigns or Supplemental Immunization Activities (SIAs)
- Need for transparency and accountability

8.2 Communication with clients, parents or guardian, and community

Under all circumstances, it is necessary to communicate with parents, other community members, healthcare staff, and the media. Regarding the AEFI, they should be informed of the investigation, its results, and any actions taken or planned. When discussing AEFI with the public and key stakeholders, it is essential to emphasize the advantages of vaccination.

Consider the following when communicating with the vaccine recipient (patient or client), parents or guardians of the patient, community members, and health staff:

- 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, parents, and guardian with hospitalization if necessary.
- Frequent communication with the client, parents, or guardian regarding the progress of the patient.
- Prepare a fact sheet on adverse events for the client, parents or guardian, community, health staff, and media.
- Build up and maintain relationships among health staff, community, and media.
- Inform the 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 ensure an understanding of the risk-benefit of vaccination.

8.3 Role of healthcare worker in community communication on AEFI

AEFI has the potential to affect the entire routine immunization programme and campaigns. When medical interventions are required, they should be carried out as rapidly as possible. Suppressing reports of AEFI or slow reaction may cause significant long-term damage to the immunization programme. Information regarding adverse events must be disseminated swiftly to prevent the spread of rumours.

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

- Communicate immediately with the higher levels and EPI at the national level as per national communication channels.
- Provide the parents with factual information. Remember that some parents may seek information elsewhere, and you may lose credibility if your response is not trustworthy and a technically sound response. The public and the other stakeholders have a right to know exactly what happened.
- Assure parents, caregivers, and adults that necessary measures are being taken to keep community members and caregivers informed of the situation.
- Communicate the results of the investigation to the programme managers and EPI officers at all levels.
- If an immunization error caused the AEFI, the public should be informed of the steps are being taken to prevent future occurrence.
- Broadcast an official statement about the event on radio and television and publish a statement in newspapers.
- Repeat the message to dispel all fears.
- Constantly reassure the public that vaccines are safe.

8.4 Communication with other healthcare staff

- Communicate among all levels of health authorities involved.
- Strengthen their knowledge, ability, skills, and performances.
- Update them on the investigation process, progress, and findings.
- Assure the staff that they can continue to have confidence in the immunization programme; the quality of the vaccine, and the services provided.
- Focus on the correction and quality of the EPI program, as opposed to blaming healthcare workers, instead.

8.5 Communicating with stakeholders

Vaccine safety information must be shared with other stakeholders to ensure the dissemination of accurate information and facilitate the operation of the national immunization programme. Depending on their needs, stakeholders listed below will receive preliminary information at the beginning of the investigation and a final report following the conclusion of the investigation and causality assessment.

- AEFI committee
- Politicians
- Professional associations
- Universities and hospitals
- International agencies and development partners
- Manufacturers

8.6 Communicating with media

The media is an important conduit for informing the public and shaping their perceptions and attitudes towards vaccines and immunization, especially during mass campaigns. Long-term media partnerships are required to keep the public informed about immunization and its benefits and to encourage families and communities to utilize immunization services.

Advance preparedness

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

A database of journalists

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

Information packages

Send periodic updates to the media via email or hard copy regarding all plans, programs, and decisions. Sensitize the media to the health benefits of immunization and its global and national impact. Prepare updates monthly or quarterly. Include frequently asked questions (FAQs) on immunization in general, for specific diseases, and AEFI in a package of updated documents (Factsheet or a technical brief on a specific vaccine-preventable disease, etc.).

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, include the name and contact information of the AEFI focal person(s) and the official spokesperson in case journalists have additional questions (at the end).

A spokesperson system

The national level shall be the ultimate authority in releasing the information to the media. **To this end, the Executive Director's office is responsible for communicating the AEFI to the media, the public, and relevant stakeholders**. This limits the likelihood of conflicting messages from different sources. Ensure the spokesperson has all the pertinent information.

Orientation workshops and field visits for media

Journalists will gain a better understanding of the benefits of immunization and the complexities of an immunization program if they participate in regular orientation workshops and field visits. This will also help in anticipating the types of questions and concerns journalists have.

Media Management during an AEFI crisis

While every AEFI must be thoroughly investigated, not every AEFI case constitutes a crisis. Taking appropriate action on AEFI, inaction often leads to a crisis.

Monitoring of media

When an AEFI occurs, the authenticity of the media's reporting should be monitored. The PRO must act swiftly to rectify any inaccuracies. The PRO could immediately take the following actions:

- Analyze the level, and destructive potential of rumours.
- Anticipate how situations may develop subsequent to a response; prepare before responding.
- Deal with a simple mistake in reporting with a simple solution. If the error is isolated, call the reporter and offer to provide the reporter with correct data and facts immediately and in the future.
- If the rumour is confined to a small audience, it should only be corrected within that group. If the error has been widely reported, it may be necessary to call a media conference to present the correct information before it causes further damage.
- Plan how to prevent future rumours.

Prepare a media release

An effective media release should include a detailed, contextualized account of the event (e.g. an isolated event or a cluster of AEFI or a 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 actions have been taken or will be taken.
- Reference any relevant publication, video material, or website.
- Sender's name and spokesperson's details.
- Content restricted to one page (400-500 words max).
- Brief 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.

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, media conferences may be required. A media conference provides the same information to all journalists; consequently, the event is less likely to be sensationalized. Consider the following steps when preparing for the media conference:

- AEFI Committee takes the lead but may identify who will facilitate the press conference.
- If there are several panelists, agree in advance on the key message(s) in response to the AEFI.
- Determine the roles of each panelist in advance, including the types of questions (media, political, etc.) that they are best suited to answer.
- Panelists must refrain from contradicting each other during the press conference, unless it is absolutely necessary to rectify an incorrect statement.
- Prepare a media kit and share it with journalists. The media kit may include a media release with all the pertinent information, supplementary background information, benefits of immunization, and a list of frequently asked questions.

8.7 Media Management post AEFI

8.7.1 Keeping promises to the media

If it has been promised that the media will be updated on the investigation's findings, it must be done by the promised date. If the results have been delayed, be sure to inform the media, as they are awaiting answers.

8.7.2 Providing answers to unanswered questions:

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

8.7.3 Keeping media informed about subsequent developments:

If a decision or action is made at the highest levels following AEFI investigations or during the investigations that must be communicated to the public, keep the media informed through a press release or hard copy document. The national MOHSS website https://mhss.gov.na is an excellent interface for media updates.

8.8 Dealing with rumours and misinformation

In the context of immunization, rumour is defined as a circulating unverifiable assertion that is or a statement without supporting evidence to confirm its truth. The spread of rumours and misinformation about immunization is one of the serious threats to the success of any immunization programme. Once rumours begin, they can be extremely difficult to stop.

Some examples of rumours:

- “Vaccines are a contraceptive used to control population or to limit the size of a certain ethnic group.”
- “Vaccines are contaminated by the AIDS virus or mad cow disease.”
- “Children are dying after receiving vaccines.”

Unless the rumour can easily be contained and dealt with, you must immediately notify your supervisors. You will be required to work under their direction, as action at national level may be required. The consequences of rumours can be serious, and they can spread quickly beyond your local area if left unchecked.

Common causes of Rumours

- Inadequate information of sharing by healthcare providers or
- Failure to communicate accurate information about vaccine effects and schedules,
- Failure to determine whether caregivers know and understand the information
- Failure to give clients opportunities to ask questions
- Parents/caregivers' negative attitudes towards immunization services

a) What you can do at the health facility

Under the direction of your supervisor:

- Consult with leading opinion leaders (politicians, traditional and religious leaders, community leaders, and other health workers).
- Organize meetings at locations where the individuals/groups are comfortable and feel at ease to ask questions.
- If there is a national media response, encourage your community members to watch and discuss it.
- Report the rumour to the next level immediately.

b) Words of advice

- React swiftly and adapt your ongoing activities to give a quick response.
- Establish strong relationships and trust with your community in advance (religious, social, and media groups).
- Provide clear and consistent messages.
- Meet and encourage leaders to be involved in discussions at the national level.

Annex 1: AEFI Reporting form

AEFI Reporting form V03-250722

MINISTRY OF HEALTH AND SOCIAL SERVICES

ADVERSE EVENT FOLLOWING IMMUNIZATION (AEFI) REPORTING FORM

Submit completed form to the following email address: AEFI@mhss.gov.na

Name of vaccination site is attached to: Name of site where Vaccine is administered (Location):	Outreach / Mobile /Fixed District: Region:	Date of vaccination: (DD/MM/YY) Time of vaccination: (Hour/ Minute) Date AEFI reported: (DD/MM/YY) Time AEFI Reported: (Hour/Minute) Reporter's full name: Reporter's contact number:
Patient First and Last name: Identity no: Nationality:	Next of Kin details First Name and last Name: Contact Nr.	
Unique ID	Patient's Contact Number: Physical Address of Patient:	
Birth Date: (DD / MM / YYYY), if unknown, enter the age Age _____ Months……Years ……..		Patient Gender: Sex: Male □ Female □

Vaccine						Diluent				
Name of vaccine	**Manufacturer**	**Batch/ Lot number**	**Expiry date**	**Dose (1st , 2nd , 3rd, additional**	**Dosage**	**Route**	**Injection Site**	**Batch/ Lot number**	**Expiry date**	**Time of Reconstitution**

Minor or Serious Adverse Event Documentation

□	Severe local reaction	□	>3 days
□	**Seizures**	□ Febrile	□ afebrile
□	Abscess	□	Toxic shock syndrome
□	Sepsis	□	Anaphylaxis
□	Encephalopathy	□	Fever≥38°C
□	Collapse or shock like state within 48 hours	□	Convulsion
□	Thrombocytopenia	□	Other

Date AEFI Started:

Time AEFI started:

Describe AEFI (Signs and symptoms) here:

Action taken: Onsite

Vaccine reaction: Minor or Severe Adverse Event

□ **Minor***(if minor, enter into DHIS2 Tracker/send the form to National level)*	_____ □ Other medically important event (Specify) below:
□ **Severe** *(indicate and complete the form)* □ Hospitalization □ Life-threatening □ Disabling □ Congenital Anomaly □ Death – Date: _ _ / _ _ / _ _ _ _ Autopsy done: □ Yes □ No □ Unknown	Past medical history (including history of similar reaction or other allergies), concomitant medication and dates of administration (exclude those used to treat reaction) other relevant information (e.g., other cases). Use additional sheet if needed:

Outcome of event at the time of the report:

□ Fully recovered	□ Recovered with sequelae	□ Unknown

District level to complete	Investigation needed? □ Yes □ No □ Not done If yes, date investigation planned: If not done: Reason:	If done: Date completed: Date reports submitted electronic to Regional level: Date reports submitted electronic to National level: Date entered into DHIS 2 Tracker:
National level to complete	Date report received at national level	Comments

Annex 2- AEFI Case Line list

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

AEFI CASE LINELIST

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] Immunisation error-related	[A3] Immunisation anxiety-related	[B] Indeterminate	[C] Coincidental	[D] Inadequate information to classify

Annexure 3: AEFI – Investigation form

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

V02-250722: Submit completed form to the following email address: AEFI@mhss.gov.na

Section A	**Basic details**	
Region	**District**	**Case ID**

Place of vaccination *(✓)*: ☐ Govt. health facility ☐ Private health facility ☐ Other (specify) _____

Other (specify) _____

Vaccination in *(✓)*: ☐ Campaign ☐ Routine ☐

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 ☐ ☐

Enter name of all pages Sex: M F

Enter name of patient/client at top on pages 2- 6. Use a separate form for each case in a cluster)

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

***OR** Age at onset: __ __ years __ __ months __ __ __ days*

***OR** Age group: ☐ < 1 year ☐ 1−5 years ☐ > 5 years - 18 years ☐ > 18 years – 60 years ☐ > 60 years*

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

Brand name of vaccines (including manufacturer) /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 / Unkn	
Adverse event after any previous vaccination(s)?	Yes / No / Unkn	
History of allergy to vaccine, drug or food?	Yes / No / Unkn	
Pre-existing comorbidity/ congenital disorder?	Yes / No / Unkn	
Pre-existing acute illness (30 days) prior to vaccination?	Yes / No / Unkn	
Has the patient tested Covid19 positive prior to vaccination?	Yes / No / Unkn	
History of hospitalization in last 30 days, with cause?	Yes / No / Unkn	
Was the patient receiving any concomitant medication? (If yes, name the drug, indication, doses & treatment dates)	Yes / No / Unkn	
Family history of any disease (relevant to AEFI) or allergy?	Yes / No / Unkn	
For adult women • Currently pregnant? 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 m*
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, prescriptions for concomitant medication) 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. colour, turbidity, foreign substances etc.) was abnormal at the time of administration?	Yes☐ / No / Unable to assess
e) Based on your investigation, do you feel that there was an error in vaccine reconstitution/preparation by the 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) Could the vaccine given to this patient have a quality defect or is substandard or falsified?	Yes□ / No / Unable to assess
l) Could this event be a stress response related to immunization (e.g. acute stress response, vasovagal reaction, hyperventilation, dissociative neurological symptom reaction etc.)?	Yes□ / No / Unable to assess
m) Is this case a part of a cluster?	Yes□ / No / Unkn
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 / Unkn
b. If no, number of vials used in the cluster (enter details separately)	

□***It is compulsory for you to provide explanations for these answers separately***

Section E Immunization practices at the place(s) where concerned vaccine was used 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:			
Injection technique in vaccinator(s): (Observe another session in the same locality – same or different place)			
• Correct dose and route?	Yes / No		
• Time of reconstitution mentioned on the vial? (in case of freeze dried vaccines)	Yes / No		
• Non-touch technique followed?	Yes / No		

• Contraindications screened prior to vaccination?	Yes / No
• How many AEFI were reported from the centre that distributed the vaccine in the last 30 days?	
• Training received by the vaccinator? (If Yes, specify the date of last training _____)	Yes / No
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 / Unkn
• Was any other item (other than EPI vaccines and diluents) in the refrigerator or freezer?	Yes / No / Unkn

• Were any partially used reconstituted vaccines in the refrigerator?	Yes / No / Unkn
• Were any unusable vaccines (expired, no label, VVM at stages 3 or 4, frozen) in the refrigerator?	Yes / No / Unkn
• Were any unusable diluents (expired, manufacturer not matched, cracked, dirty ampoule) in the store?	Yes / No / Unkn
Specific key findings/additional observations and comments:	
Vaccine transportation:	
• Type of vaccine carrier used	
• Was the vaccine carrier sent to the site on the same day as vaccination?	Yes / No / Unkn
• Was the vaccine carrier returned from the site on the same day as vaccination?	Yes / No / Unkn
• Was a conditioned ice-pack used?	Yes / No / Unkn
Specific key findings/additional observations and comments:	

Section G Community investigation (Please visit locality and interview parents/others)

Were any similar events reported within a time period similar to when the adverse event occurred and in the same locality?
Yes / No / Unknown If yes, describe:

If yes, how many events/episodes?

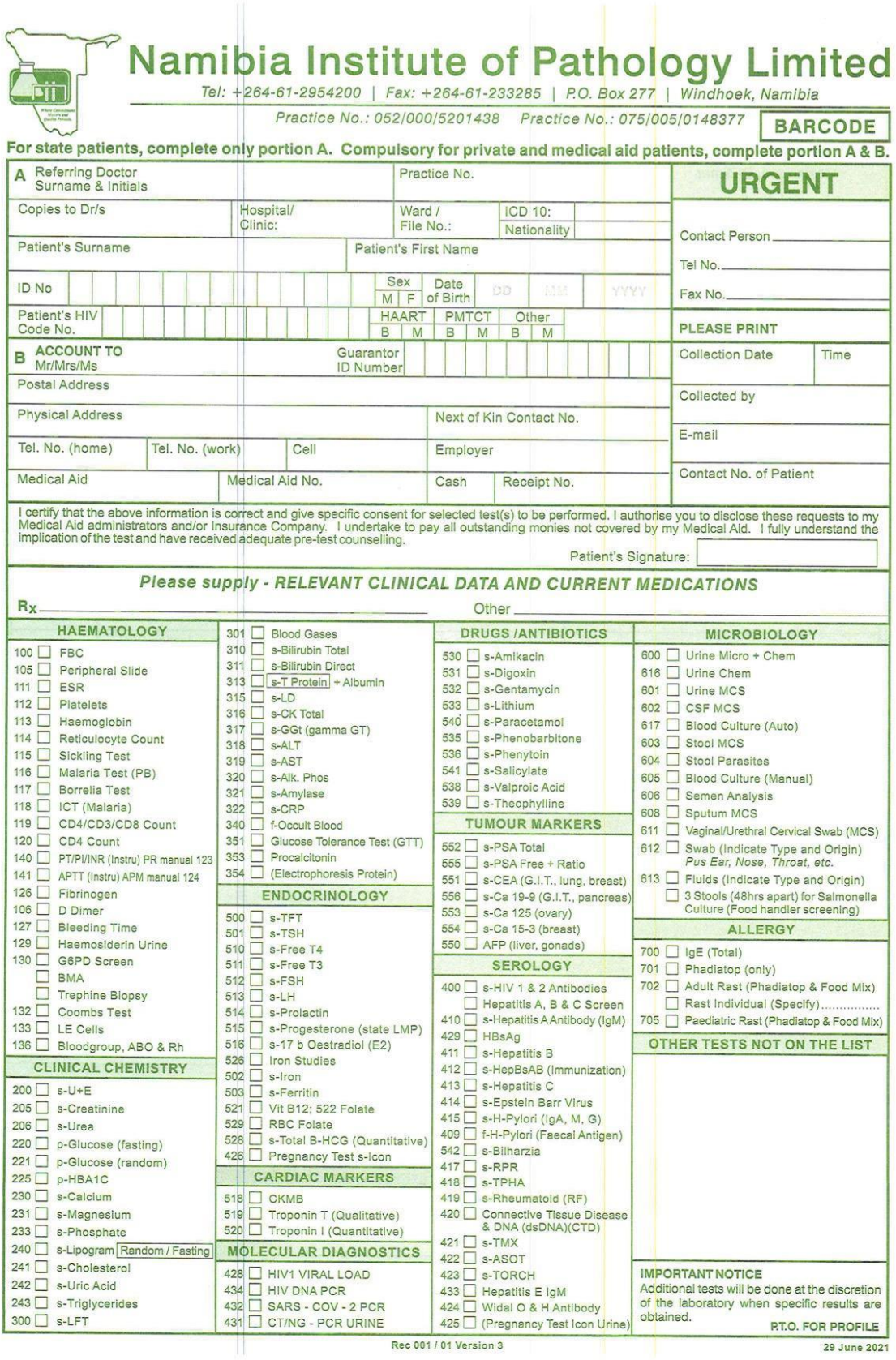
Of those effected, how many are
- Vaccinated:_____
- Not vaccinated:_____
- Unknown:_____

Other comments:

Section H Other findings/observations/comments

Submit the completed form to the following email address: AEFI@mhss.gov.na
Email Subject: AEFI Minor/Serious: Name of District

Annexure: 4 Laboratory Request Form



Namibia Institute of Pathology Limited

Tel: +264-61-2954200 | Fax: +264-61-233285 | P.O. Box 277 | Windhoek, Namibia

Practice No.: 052/000/5201438 Practice No.: 075/005/0148377 **BARCODE**

For state patients, complete only portion A. Compulsory for private and medical aid patients, complete portion A & B.

A Referring Doctor Surname & Initials | Practice No.

Copies to Dr/s | Hospital/ Clinic: | Ward / File No.: | ICD 10: | Nationality

Patient's Surname | Patient's First Name

ID No | Sex M F | Date of Birth DD MM YYYY

Patient's HIV Code No. | HAART B M | PMTCT B M | Other B M

B ACCOUNT TO Mr/Mrs/Ms | Guarantor ID Number

Postal Address

Physical Address | Next of Kin Contact No.

Tel. No. (home) | Tel. No. (work) | Cell | Employer

Medical Aid | Medical Aid No. | Cash | Receipt No.

URGENT

Contact Person

Tel No.

Fax No.

PLEASE PRINT

Collection Date | Time

Collected by

E-mail

Contact No. of Patient

I certify that the above information is correct and give specific consent for selected test(s) to be performed. I authorise you to disclose these requests to my Medical Aid administrators and/or Insurance Company. I undertake to pay all outstanding monies not covered by my Medical Aid. I fully understand the implication of the test and have received adequate pre-test counselling.

Patient's Signature:

Please supply - RELEVANT CLINICAL DATA AND CURRENT MEDICATIONS

Rx _____ Other _____

HAEMATOLOGY

- 100 ☐ FBC
- 105 ☐ Peripheral Slide
- 111 ☐ ESR
- 112 ☐ Platelets
- 113 ☐ Haemoglobin
- 114 ☐ Reticulocyte Count
- 115 ☐ Sickling Test
- 116 ☐ Malaria Test (PB)
- 117 ☐ Borrelia Test
- 118 ☐ ICT (Malaria)
- 119 ☐ CD4/CD3/CD8 Count
- 120 ☐ CD4 Count
- 140 ☐ PT/PI/INR (Instru) PR manual 123
- 141 ☐ APTT (Instru) APM manual 124
- 126 ☐ Fibrinogen
- 106 ☐ D Dimer
- 127 ☐ Bleeding Time
- 129 ☐ Haemosiderin Urine
- 130 ☐ G6PD Screen
- ☐ BMA
- ☐ Trephine Biopsy
- 132 ☐ Coombs Test
- 133 ☐ LE Cells
- 136 ☐ Bloodgroup, ABO & Rh

CLINICAL CHEMISTRY

- 200 ☐ s-U+E
- 205 ☐ s-Creatinine
- 206 ☐ s-Urea
- 220 ☐ p-Glucose (fasting)
- 221 ☐ p-Glucose (random)
- 225 ☐ p-HBA1C
- 230 ☐ s-Calcium
- 231 ☐ s-Magnesium
- 233 ☐ s-Phosphate
- 240 ☐ s-Lipogram Random / Fasting
- 241 ☐ s-Cholesterol
- 242 ☐ s-Uric Acid
- 243 ☐ s-Triglycerides
- 300 ☐ s-LFT
- 301 ☐ Blood Gases
- 310 ☐ s-Bilirubin Total
- 311 ☐ s-Bilirubin Direct
- 313 ☐ s-T Protein + Albumin
- 315 ☐ s-LD
- 316 ☐ s-CK Total
- 317 ☐ s-GGt (gamma GT)
- 318 ☐ s-ALT
- 319 ☐ s-AST
- 320 ☐ s-Alk. Phos
- 321 ☐ s-Amylase
- 322 ☐ s-CRP
- 340 ☐ f-Occult Blood
- 351 ☐ Glucose Tolerance Test (GTT)
- 353 ☐ Procalcitonin
- 354 ☐ (Electrophoresis Protein)

ENDOCRINOLOGY

- 500 ☐ s-TFT
- 501 ☐ s-TSH
- 510 ☐ s-Free T4
- 511 ☐ s-Free T3
- 512 ☐ s-FSH
- 513 ☐ s-LH
- 514 ☐ s-Prolactin
- 515 ☐ s-Progesterone (state LMP)
- 516 ☐ s-17 b Oestradiol (E2)
- 526 ☐ Iron Studies
- 502 ☐ s-Iron
- 503 ☐ s-Ferritin
- 521 ☐ Vit B12; 522 Folate
- 529 ☐ RBC Folate
- 528 ☐ s-Total B-HCG (Quantitative)
- 426 ☐ Pregnancy Test s-Icon

CARDIAC MARKERS

- 518 ☐ CKMB
- 519 ☐ Troponin T (Qualitative)
- 520 ☐ Troponin I (Quantitative)

MOLECULAR DIAGNOSTICS

- 428 ☐ HIV1 VIRAL LOAD
- 434 ☐ HIV DNA PCR
- 432 ☐ SARS - COV - 2 PCR
- 431 ☐ CT/NG - PCR URINE

DRUGS /ANTIBIOTICS

- 530 ☐ s-Amikacin
- 531 ☐ s-Digoxin
- 532 ☐ s-Gentamycin
- 533 ☐ s-Lithium
- 540 ☐ s-Paracetamol
- 535 ☐ s-Phenobarbitone
- 536 ☐ s-Phenytoin
- 541 ☐ s-Salicylate
- 538 ☐ s-Valproic Acid
- 539 ☐ s-Theophylline

TUMOUR MARKERS

- 552 ☐ s-PSA Total
- 555 ☐ s-PSA Free + Ratio
- 551 ☐ s-CEA (G.I.T., lung, breast)
- 556 ☐ s-Ca 19-9 (G.I.T., pancreas)
- 553 ☐ s-Ca 125 (ovary)
- 554 ☐ s-Ca 15-3 (breast)
- 550 ☐ AFP (liver, gonads)

SEROLOGY

- 400 ☐ s-HIV 1 & 2 Antibodies
- ☐ Hepatitis A, B & C Screen
- 410 ☐ s-Hepatitis A Antibody (IgM)
- 429 ☐ HBsAg
- 411 ☐ s-Hepatitis B
- 412 ☐ s-HepBsAB (Immunization)
- 413 ☐ s-Hepatitis C
- 414 ☐ s-Epstein Barr Virus
- 415 ☐ s-H-Pylori (IgA, M, G)
- 409 ☐ f-H-Pylori (Faecal Antigen)
- 542 ☐ s-Bilharzia
- 417 ☐ s-RPR
- 418 ☐ s-TPHA
- 419 ☐ s-Rheumatoid (RF)
- 420 ☐ Connective Tissue Disease & DNA (dsDNA)(CTD)
- 421 ☐ s-TMX
- 422 ☐ s-ASOT
- 423 ☐ s-TORCH
- 433 ☐ Hepatitis E IgM
- 424 ☐ Widal O & H Antibody
- 425 ☐ (Pregnancy Test Icon Urine)

MICROBIOLOGY

- 600 ☐ Urine Micro + Chem
- 616 ☐ Urine Chem
- 601 ☐ Urine MCS
- 602 ☐ CSF MCS
- 617 ☐ Blood Culture (Auto)
- 603 ☐ Stool MCS
- 604 ☐ Stool Parasites
- 605 ☐ Blood Culture (Manual)
- 606 ☐ Semen Analysis
- 608 ☐ Sputum MCS
- 611 ☐ Vaginal/Urethral Cervical Swab (MCS)
- 612 ☐ Swab (Indicate Type and Origin) *Pus Ear, Nose, Throat, etc.*
- 613 ☐ Fluids (Indicate Type and Origin)
- ☐ 3 Stools (48hrs apart) for Salmonella Culture (Food handler screening)

ALLERGY

- 700 ☐ IgE (Total)
- 701 ☐ Phadiatop (only)
- 702 ☐ Adult Rast (Phadiatop & Food Mix)
- ☐ Rast Individual (Specify).....
- 705 ☐ Paediatric Rast (Phadiatop & Food Mix)

OTHER TESTS NOT ON THE LIST

IMPORTANT NOTICE

Additional tests will be done at the discretion of the laboratory when specific results are obtained.

P.T.O. FOR PROFILE

Rec 001 / 01 Version 3 29 June 2021

PROFILES

DIC Screen
FBC, Blood Film, PI, PTT, Fibrinogen, D-Dimer

Haemolytic Screen
FBC, Blood Film, Coombs, Bili, Retics, LDH (Optional), Haptoglobin

Bleeding Screen
FBC, INR, APTT, Factor Assays

Thrombotic Screen
(Arrange with lab)

IRON Studies
S-Iron, Transferrin Saturation, Transferrin, Ferritin

Arthritis Screen
FBC, ESR, CRP, RF, Uric Acid, ANF (If ANF positive, Anti-DNA and ENA will be done)

Antenatal Screen
FBC Blood Group, Rh, RPR, Rubella, HepSAg, CRP, HIV

STD Screen
RPR, Herpes, HBsAg, Chlamydia (Blood/Urine) HIV, Gonorrhea (Urine)

Menopausal Screen
FSH, LH, Oestradiol (E_2)

Infertility Female
FSH, LH, Prolactin, Oestradiol, Progesterone, Total Testosterone, SHBG, TSH, DHEAS
(Take specimen on day 21)

Infertiltiy Male
(Abnormal semen analysis assumed): FSH, LH, Prolactin, Total Testosterone, SHBG

COLOUR CODE CHART FOR BLOOD COLLECTION CONTAINERS

Colour of stopper	Additive	Tests	Draw size
YELLOW	Gel to separate serum	Clinical chemistry, Immunochemistry, Serology, i.e. all tests that require clotted blood	5 ml
RED	No additive	All tests requiring clotted blood, e.g. RPR and Blood groups	4 ml
PURPLE	EDTA	Haematology FBC, CD4, Hb electrophoresis, DNA-HIV, PCR, Lead, HBA1C	4 ml & 3 ml
GREEN	Lithium Heparin	Special tests e.g. LE cells, Chromosomes etc. (Refer to collection table in specimen and information booklet)	10 ml
GREY	Potassium oxalate, Sodium flouride	Glucose determination / Lactate	4 ml
BLUE	Sodium Citrate	Coagulation tests: PI, PTT, D-Dimer, Factor assays, etc.	4 ml
CLEAR	Gel with EDTA	Only for viral load	5 - 10 ml

FOR NIP USE ONLY

Date received:_____ Time: _____ Received by:_____

NA Number:_____ Logged by:_____

Container types: _____ Check Logged by: _____

COMMENTS: _____

MEDICAL AID DETAILS

Receipt No.: _____ **Amount:** N$ _____

Payment Method: Medical Aid ☐ Cash ☐ Credit Card ☐ Account ☐

prime press 102021

ZA

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