Adverse Events Following immunization

AEFI Surveillance and Response Operational Guideline

(2021)

Expanded Programme on Immunization (EPI)
Directorate General of Health Services
EPI Bhaban, Mohakhali, Dhaka-1212

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MESSAGE

Immunization is among the most successful and cost-effective public health interventions. It has led to the global eradication of smallpox as well as the elimination of poliomyelitis in regions of the world. Immunization currently averts an estimated 2 to 3 million deaths from diphtheria, tetanus, pertussis (whooping cough), and measles every year in all age groups.

EPI is one of Bangladesh's greatest public health success stories. The Government of Bangladesh's Expanded Programme on Immunization (EPI) envisages to protect all eligible beneficiaries from vaccine preventable diseases by administering life-saving vaccines. Vaccines used in national immunization programme are procured through UNICEF from WHO pre-qualified list of vaccines. These vaccines are very safe and effective. But no vaccine is entirely without risk and adverse events can occur following immunization, most of which are mild and time-limited but can also, in rare cases, have significant impact on health. These adverse events are due to vaccine itself or programmatic error and some are at all not related to vaccination. If any serious adverse events occur it need to be managed quickly not only to prevent mortality and morbidity in the individual recipient but also to ensure there is no disruption by maintaining confidence in vaccines and the EPI.

AEFI surveillance monitors immunization safety, detects and responds to adverse events following immunization; corrects unsafe immunization practices, reduces the negative impact of the event on health and contributes to the quality of immunization services.

I would like to express my thankful gratitude to World Health Organization, Bangladesh for their overall technical support in updating and publishing the fourth edition of the guideline. I am also thankful to my colleagues at EPI, who contributed in the development of the fourth edition of the guideline. Finally, I convey my heartfelt thanks to all who are engaged in providing immunization services to save the life of thousands of children from vaccine preventable diseases.

Prof. Dr. Abul Bashar Mohammad Khurshid Alam

Director & Line Director MNC&AH
Directorate General of Health Services
Mohakhali, Dhaka

FOREWORD

Immunization is one of the most costeffective public health interventions for protecting the individual and the public from vaccine-preventable diseases (VPDs). Modern vaccines are safe and effective. However, like other medicinal products, vaccines are not free from adverse reactions. Vaccine manufacturers develop products with the highest safety and effectiveness possible, given current technology. But some very rare vaccine-related adverse events will always occur.

Vaccines rarely cause serious adverse reactions, and common reactions are minor and self-limited. The safety of vaccines is monitored by looking for adverse events following immunizations (AEFI). An AEFI may be caused by a vaccine reaction but often, particularly if the event is serious, the event is coincidental to vaccination. Other events may be caused by an error in administration or handling of the vaccine. Irrespective of the specific cause, an AEFI may lead to public suspicions of vaccines and parents may refuse further immunization for their children, making them susceptible to VPDs which are disabling and life-threatening.

Surveillance of AEFIs is an effective means for ensuring the quality and safety of immunization services and vaccines used in EPI. Through an effective AEFI surveillance system, cases of AEFI could be detected timely and appropriate and quick response to adverse events could be taken to lessen the negative impact on health of the individuals and maintain public confidence in the immunization programme.

This is the fourth edition of the AEFI surveillance guideline with updated information based on WHO global manual on AEFI surveillance. This document provides a guideline on AEFI detection, reporting, investigation, causality assessment, necessary actions following AEFI and effective communication with parents, community and media.

I sincerely hope that managers at all levels and other concerned personnel will carefully read this document and follow the guideline and strengthen the AEFI surveillance in the country.

Dr Md. Shamsul Haque

Pogramme Manager-EPI
Directorate General of Health Services
Mohakhali, Dhaka

PREFACE

Vaccination is one of the great public health achievements of human history .The mission of the Expanded Programme on Immunization (EPI) in Bangladesh is to reduce morbidity and mortality from vaccine-preventable diseases to a level where they are no longer a public health concern by providing high quality immunization services to all the children. Presently, EPI has been providing vaccines against 10 vaccine preventable diseases by reaching to the community through fixed and outreach sites to protect children.

Vaccines used in Expanded Programme on Immunization (EPI) are considered safe and effective. Vaccines are; however, not risk-free and adverse events will occasionally occur following vaccination. These adverse events are due to vaccine itself or programmatic error and some are at all not related to vaccination.

The benefits of immunization are often not visible, particularly if the target disease incidence is low. In contrast, adverse effects that follow immunization are promptly noticeable and less acceptable, especially when the vaccinee was apparently healthy at the time of immunization Allegations regarding vaccine-related adverse events that are not rapidly and effectively dealt with can undermine confidence in a vaccinee and the immunization programme and ultimately have negative consequences for immunization coverage and disease incidence. To increase immunization acceptance and improve the quality of services, the surveillance of AEFIs must become an integral part of immunization programmes.

The objectives of this guideline are to improve the AEFI surveillance at national and sub national level, improve the quality of immunization services and finally ensure immunization safety of all recipients of vaccines leading to achievements of goal and objectives of the immunization programme in the country.

I would like to thank World Health Organization for their overall technical support in updating and publishing the fourth edition of the guideline. I am also thankful to my colleagues at EPI, who contributed in the development of the fourth edition of the guideline I hope that this guideline would be useful for all concerned persons of the Expanded Programme on Immunization.

Dr Mowla Baksh Chaudhury

LIST OF CONTRIBUTERS (Fourth Edition)

EPI-HQ, DGHS

Dr. Md. Shamsul Haque	Line Director, MNC&AH, DGHS
Dr. Mowla Baksh Chaudhury	Program Manager-EPI, DGHS
Dr. Jesmin Ara Khanom	Deputy Director, EPI & Surveillance, DGHS
Dr. S M Hasibul Islam	Assistant Director, EPI & Surveillance, DGHS
Dr. Md. Monjurul Islam	DPM, Field Service, EPI, DGHS
Dr. Md. Tanvir Hossen	DPM, EPI & Surveillance, DGHS
Dr. Shakila Sultana	DPM, IEC & BCC, EPI, DGHS
Dr. Rajib Sarkar	Medical Officer EPI & Surveillance, DGHS
Mrs Kohinoor Begum	Training Officer, EPI & Surveillance, DGHS

WORLD HEALTH ORGANIZATION (WHO)

Dr Rajendra Bohara	Team Leader, IVD, WHO
Dr Balwinder Singh Chawla	Medical Officer-Immunization System Strengthening
Dr Selina Ahmed	NPO-Vaccine Safety&Quality
Dr Chiranjit Das	NPO Immunization
Dr Jobayer Al Mamun	EPI Divisional Coordinator, Rangpur
Dr AKM Kamruzzaman	EPI Divisional Coordinator, Rajshahi
Dr Md. Arifur Rahman	EPI Divisional Coordinator, Khulna

ABBREVIATIONS AND ACRONYMS

AD	Auto Disable
AEFI	Adverse Event Following Immunization
AFP	Acute Flaccid Paralysis
AHI	Assistant Health Inspector
AHO	Assistant Health Officer
ASO	Antistreptolysin O
BCG	Bacillus Calmette-Guerin
BMA	Bangladesh Medical Association
CC	City Corporation
CERC	Crisis and Emergency Risk Communication
CHO	Chief Health Officer
CHCP	Community Health Care Provider
CIOMS	Council for International Organizations of Medical Sciences
CNS	Central Nervous System
CS	Civil Surgeon
CSF	Cerebro Spinal Fluid
DCS	Deputy Civil Surgeon
DGDA	Directorate General of Drug Administration
DGHS	Directorate General of Health Services
DHIS2	District Health Information System 2
DNA	Deoxyribonucleic Acid
DPT	Diphtheria- Pertussis- Tetanus
DTwP	Diphtheria- Tetanus (whole cell) Pertussis
DTaP	Diphtheria- Tetanus –(acellular) Pertussis
DSFP	Disease Surveillance Focal Person
DT	Diphtheria-Tetanus

ECG	Electrocardiograph
EPI	Expanded Programme on Immunization
ERC	Expert Review Committee
FAQ	Frequently Asked Question
FPI	Family Planning Inspector
FW	Field Worker
FWA	Family Welfare Assistant
GACVS	Global Advisory Committee on Vaccine Safety
GMP	Good Manufacturing Practices
HA	Health Assistant
HHE	Hypotonic Hypo Responsive Episode
HI	Health Inspector
HIV	Human Immune-Deficiency Virus
HO	Health Officer
HPV	Human Papilloma Virus
HQ	Head Quarter
HSO	Hospital Surveillance Officer
HSV	Herpes Simplex Virus
IgG	Immunoglobulin G
IgM	Immunoglobulin M
ILR	Ice-Lined Refrigerator
IM	Intramuscular
IMR	Infant Mortality Rate
IPC	Interpersonal Communication
IPV	Inactivated Polio Vaccine
ITSR	Immunization Triggered Stress Response
IV	Intravenous

LAV	Live attenuated vaccine
LD	Line Director
LSO	Local Surveillance Officer
MDVP	Multi Dose Vial Policy
MgCl2	Magnesium Chloride
MgSO4	Magnesium Sulphate
MMO	Municipal Medical Officer
MMR	Measles-Mumps-Rubella Vaccine
MNC&AH	Maternal Neonatal Child & Adolescent Health
MO	Medical Officer
MO-CS	Medical Officer- Civil Surgeon's Office
MO-DC	Medical Officer Disease Control
MR	Measles-Rubella Vaccine
MT-EPI	Medical Technologist EPI
NCL	National Control Laboratory
NGO	Non Government Organization
NITAG	National Immunization Technical Advisory Group
NRA	National Regularity Authority
OPD	Out Patient Department
OPV	Oral Polio Vaccine
PCR	Polymerase Chain Reaction
PCV	Pneumococcal Containing Vaccine
PM	Programme Manager
PPSV	Pneumococcal Polysaccharide Vaccine
PVV	Pentavalent (DTP-HepB-Hib) Vaccine
Q&A	Question & Answer
SIDS	Sudden Infant Death Syndrome

SIMO	Surveillance & Immunization Medical Officer
tOPV	Trivalent Oral Polio Vaccine
TSS	Toxic Shock Syndrome
TOR	Terms of Reference
TT	Tetanus Toxoid
UHC	Upazila Health Complex
UH&FPO	Upazila Health and Family Planning Officer
UNICEF	United Nations Children's Fund
USC	Union Sub Centre
VAPP	Vaccine Associated Paralytic Poliomyelitis
VPD	Vaccine-preventable Disease
Vit A	Vitamin A
VVM	Vaccine Vial Monitor
VZV	Varicella Zoster Virus
WBC	White Blood Cell
WHO	World Health Organization
ZMO	Zonal Medical Officer

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GLOSSARY

Adverse event following immunization (AEFI)	Any untoward medical occurrence which follows immunization and which does not necessarily have a causal relationship with the usage of the vaccine. The adverse event may be any unfavorable 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, causality assessment is a systematic review of data about AEFI case(s) in order 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.
Immunity	The ability of the human body to tolerate the presence of material "indigenous" to the human "body" (self) and to eliminate "foreign" (non-self) material. This discriminatory ability provides protection from infectious diseases, since most microbes are identified as foreign by the immune system.
Immunization safety	The process of ensuring the safety of all aspects of immunization, including vaccine quality, adverse events surveillance, vaccine storage and handling, vaccine administration, disposal of sharps and management of waste.
Immunization safety surveillance	A system for ensuring immunization safety through detecting, reporting, investigating and responding to AEFI.

Non-serious AEFI	An event that is not "serious" and does not pose a potential risk to the health of the recipient. Non-serious AEFI should also be carefully monitored because they may signal a potentially larger problem with the vaccine or immunization, or may have an impact on the acceptability of immunization in general.
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.
Signal (safety signal)	Information (from one or multiple sources) which suggests a new and potentially causal association, or a new aspect of a known 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 that are analyzed and disseminated to enable decision-making and action to protect the health of populations.
Trigger event	A medical incident following immunization that stimulates a response (usually a case investigation).
Vaccine	A biological preparation that improves immunity to a particular disease. In addition to the antigen, it contains multiple components (excipients) and each component may have unique safety implications.
Vaccine 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).
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 seroconversion or seroprotection) 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 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.
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.

1

Introduction

Immunization is one of the most effective public health interventions to protect the individual and the public from vaccine preventable diseases (VPDs) and vaccinations have saved millions of lives. Globally vaccination saves 2-3 million children each year from the deadly diseases. EPI is one of the greatest public health success stories of Bangladesh. EPI has prevented an estimated 20 lakh (2 million) deaths from 1987-2000 and continues to prevent approximately 200,000 deaths each year. Fully vaccination coverage increased from 2% in 1985 to 83.9 % in 2019 (source CES 2019). Modern vaccines are safe and they effectively protect individuals and public however, vaccines as other medicinal products are not free from occasional adverse reactions.

Adverse events following immunization (AEFI) are usually mild but may on rare occasions be life-threatening. The majority of serious events reported after immunization are coincidences and there is no causal relationship between the vaccine and the reported event. Vaccines rarely cause serious adverse reactions, and common reactions are minor and self-limiting. In majority of serious cases these are merely coincidental and have no relationship with vaccines. At times, however, these are caused by the vaccine or by an error in the administration or handling of the vaccine.

Irrespective of the cause, when AEFI occur, people become suspicious of vaccines and even refuse further immunization for their children, making them susceptible to VPDs which are more disabling and life-threatening. To increase immunization acceptance and improve the quality of services AEFI surveillance must become an integral part of national immunization programme. An effective AEFI surveillance system helps to preserve public confidence in immunization programme.

Increased immunization coverage, mass vaccination campaigns and introduction of new vaccines have increased vaccine use, leading to increase in reporting of AEFIs. Also, public alertness regarding vaccine safety has increased as a result of increased awareness and access to information through the electronic media. Health-care providers have become highly vigilant on vaccine safety and this has led to further strengthening of AEFI surveillance in the country. Increase in coverage will result in seeing less VPDs however any AEFIs occurring at this time will attract more attention in community and media. Therefore, it is essential to report, investigate and assess each AEFI to determine whether a vaccine is causally linked to an AEFI or whether the reported AEFI is a mere coincidence.

This AEFI surveillance guideline is an updated version of the third edition of the AEFI surveillance guideline which was published in December 2014.

This guideline will provide information to the health care providers, mid and senior level immunization programme managers at all levels (national, divisional, district, city corporation, municipalities and upazila level) on the following:

- Strategies and systems for ensuring quality and safety of vaccines in the country;
- Objectives of immunization safety surveillance;
- AEFI surveillance system: reporting, investigation, causality assessment;
- Role and responsibilities of each category of health staff involve in AEFI surveillance;
- Classification of cause-specific AEFI;
- Understanding vaccine reactions for better decision-making;
- Optimal utilization of vaccine safety surveillance data;
- Response process, including a communication strategy on immunization safety for public and media.

The objectives of this guideline are to improve the robustness of AEFI surveillance at national and sub national level, improve the quality of immunization services and finally ensure immunization safety of all recipients of vaccines leading to achievement of goals and objectives of the immunization programme in the country.

2

Basic understanding of principles of immunization and vaccines

2.1 Immunity

Immunity is the ability of the human body to tolerate the presence of material "indigenous" to the human body (self) and to eliminate "foreign" (nonself) material. This discriminatory ability provides protection from infectious diseases, since most microbes are identified as foreign by the immune system. Immunity to a microbe is usually indicated by the presence of antibody to that organism (antigen, immunogen). Immunity is generally very specific to a single organism or to a group of closely-related organisms.

There are two basic mechanisms for acquiring immunity: active and passive.

2.1.1 Active immunity

Active immunity is the stimulation of the immune system to produce antigen-specific humoral (antibody) and cellular immunity for which the protective function of immunization is associated with cells. Usually this lasts for many years, and often for a lifetime. One way to acquire active immunity is to survive infection with the disease -causing form of the organism. Upon re-exposure to the same antigen, the memory cells begin to replicate and produce antibody very rapidly to re-establish protection.

2.1.2 Passive immunity

Passive immunity is the transfer of antibody produced by a human or animal to another. This may be natural (from mother to infant) or artificial (when high levels of human antibodies specific to a pathogen or toxin are transferred to non-immune individuals). The most common form of passive immunity is that which an infant receives from its mother. The antibodies received from the mother protect the infant from certain diseases for up to a year. However, maternal antibodies may inhibit successful immunization against live or attenuated live viral vaccines by interfering with vaccine virus growth. For example, vaccination with the live attenuated measles vaccine needs to be given at the appropriate age (usually after 9 months of age) at which time the presence of maternal antibodies (to measles) in the infants has fallen. Passive artificial immunity provides only temporary protection against infection – as short as 1-6 weeks – because the antibodies degrade over time.

2.1.3 Herd immunity

Herd immunity describes immunity that occurs when the vaccination of a portion of the population (the "herd") provides protection to unprotected individuals. Herd immunity theory proposes that, in diseases passed from individual to individual, it is difficult to maintain a chain of infection when large numbers of the population are immune. Hence, the higher the proportion of immune individuals in a population, the lower the likelihood that a susceptible person will come into contact with an infectious agent. From both theoretical and practical perspective, disease usually disappears before immunization levels reach 100%, as has been seen with smallpox and poliomyelitis. The proportion of immune individuals in a population above which a disease may no longer persist is the "herd immunity threshold". Its value varies with the virulence and transmissibility of the disease, the efficacy and overall coverage of the vaccine, vaccination coverage among the population at risk and the contact parameter for the population.

2.1.4 How does immunization work?

There are several types of vaccines, but they all work in a similar way, by preparing the immune system to attack the infection. Each vaccine has components that are more or less similar to the infecting organism or virus, and so the immune system responds as it would to an infection with that particular organism. The most important consequence of successful vaccination is that it produces long-lived memory lymphocytes that respond more quickly and in a more coordinated way to subsequent infections. As a result, the infectious microbe is destroyed more quickly. Protection is not always complete; an infection might not always be prevented but the severity of the illness is usually reduced.

The first exposure to a vaccine stimulates the immune response (known as priming). The immune system takes time to respond to the antigen by producing antibodies and immune cells. Initially, immunoglobulin M (IgM) antibody is produced but this occurs in small amounts and does not bind very strongly to the antigen. After a few days, the immune response begins to make immunoglobulin G (IgG) antibody which is more specific to the microbe and lasts longer than IgM.

Subsequent administration of the same vaccine stimulates the secondary immune response, which is much faster than the primary response and produces predominantly IgG rather than IgM. The aim of vaccination is to generate enough immune cells and antibodies specific to that vaccine-preventable microbe in order to provide long-lasting protection against the disease.

2.2 Vaccine

Vaccine is a biological product that produces and enhances immunity to a particular VPD. A vaccine contains a disease-causing microorganism or virus, or a portion of it, and is often made from either live attenuated or inactivated (killed) forms of the microbe, or from its toxin or one of its surface proteins.

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

Combined vaccines contain two or more different antigens (e.g. DTwP, DTPa-HepBHib/Pentavalent vaccine). The potential advantages of combination vaccines include reducing the cost of storing and administering multiple vaccines simultaneously, reducing the cost of extra health-care visits, improving timeliness of vaccination, and facilitating the addition of new vaccines into immunization programmes.

Remember

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

2.2.1 Classification of vaccines

There are different types of vaccines, such as: live attenuated, inactivated (killed antigen), subunit (purified antigen) and toxoids (inactivated toxic compounds). The characteristics of these vaccines differ, and these characteristics determine how the vaccines work (Figure 1).

2.2.1.1 Live attenuated vaccines

Live attenuated vaccines (LAVs) are derived from "wild" or disease-causing viruses or bacteria. These wild viruses or bacteria are attenuated, or weakened, in a laboratory, usually by repeated culturing. Live microorganisms provide continuous antigenic stimulus, giving sufficient time for memory cell production in the vaccinated person, and they are also capable of replicating within the host. The immune response to a LAV is virtually identical to that produced by a natural infection.

The first dose of LAV usually provides protection. For instance, 85-90% of recipients will respond to a single dose of measles vaccine at 9 months. The second dose is given as an additional opportunity to induce immunity in those who did not respond to the first dose, and with the second dose more than 95% of persons will be immune. Immunity following live vaccines is long-lasting and booster doses are not necessary, with the exception of OPV which requires multiple doses. LAVs are labile and can be damaged or destroyed by heat and light. They must be handled and stored carefully. Currently used LAVs include vaccines for influenza (intranasal), measles, mumps, OPV, rotavirus, rubella, varicella and yellow fever. Live attenuated bacterial vaccines include BCG and oral typhoid vaccine.

2.2.1.2 Inactivated (killed) vaccines

Inactivated vaccines are produced by growing viruses (e.g. poliomyelitis vaccine) or bacteria (e.g. whole-cell pertussis vaccine) in a culture medium and then inactivating them with heat or chemicals (usually with formaldehyde). Because they are not alive, these viruses cannot grow in a vaccinated individual and therefore cannot cause the disease, even in an immunodeficient person. Inactivated vaccines are generally safer than LAVs, with no risk of inducing the disease. Unlike LAVs, inactivated vaccines are usually not affected by circulating maternal antibodies and do induce an immune response in an infant. They are often more stable than a LAV.

Inactivated vaccines always require multiple doses. In general, the first dose does not produce protective immunity but only "primes" the immune system. A protective immune response is developed only after multiple subsequent doses. In contrast to live vaccines, in which the immune response closely resembles natural infection, the immune response to an inactivated vaccine is mostly humoral with little or no cell mediated immunity. Antibody titres against inactivated antigens diminish with time. As a result, some inactivated vaccines may require periodic supplemental doses to increase, or "boost", antibody titres.

2.2.1.3 Subunit vaccines

Instead of the whole microbe, subunit vaccines include only those antigens that best stimulate the immune response. Because subunit vaccines contain only the essential antigens and not all the other components of the microbes, chances of adverse reactions are lower. Subunit vaccines can be produced in two ways:

- The whole organism is grown in culture media and then is further processed to purify only those components to be included in the vaccine e.g. acellular pertussis and the meningococcal B vaccine.
- Antigen molecules from the microbes can be manufactured using recombinant DNA technology. Vaccines produced in this way are called "Recombinant sub-unit vaccine".

Subunit vaccines are categorized in three groups: protein-based, polysaccharide and conjugate vaccines.

Protein-based vaccines

Subunit vaccines can be protein-based. For example, the hepatitis B vaccine is made by inserting a segment of the hepatitis B virus gene into a yeast cell. The modified yeast cell produces large amounts of hepatitis B surface antigen which is purified and harvested and used to produce the vaccine. The recombinant hepatitis B vaccine antigen is identical to the natural hepatitis B surface antigen but does not contain virus DNA and is unable to replicate and produce infection. Protein based subunit vaccines present an antigen to the immune system without viral particles.

Another protein-based vaccine is the acellular pertussis (aP) vaccine which contains inactivated pertussis toxin (protein) and may contain one or more other pertussis components. The pertussis toxin is detoxified either by chemical treatment or by molecular genetic techniques.

Polysaccharide vaccines

When infecting humans, some bacteria are protected by a polysaccharide (sugar) capsule that helps the organism to evade the human defense systems, especially in infants and young children. Polysaccharide vaccines provoke an immune response against this capsule; however, they are not very immunogenic and induce only short-term immunity, particularly in infants and young children. Examples of these vaccines are the meningococcal and pneumococcal polysaccharide vaccines which contain the polysaccharide coats, or capsules, of encapsulated bacteria which are purified and non-infectious.

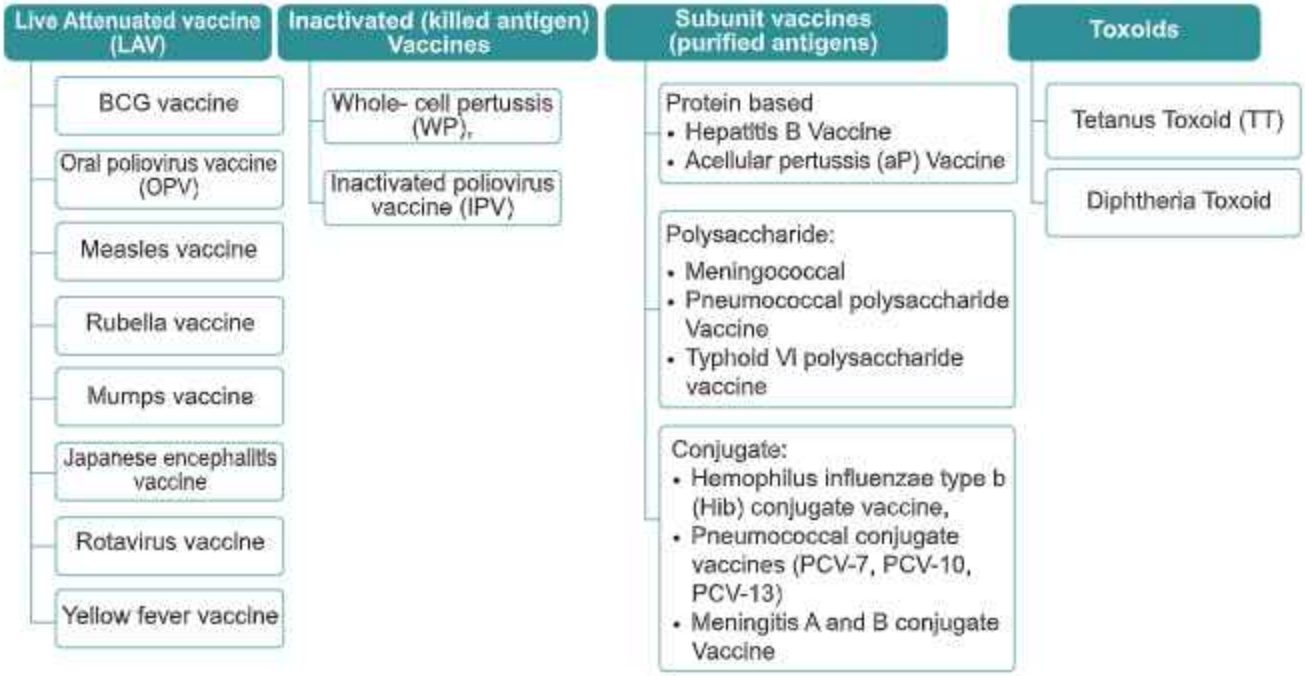
Conjugated vaccines

Many bacteria have a polysaccharide outer wall. The immature immune system of children under 2 years of age does not respond well to polysaccharide antigens, which lead to antibody production via a T-cell independent mechanism. If these polysaccharide antigens are chemically linked (conjugated) to a protein that T-cells recognize, then the conjugated vaccines can elicit strong immune responses and immune memory in young children. Hemophilus influenzae type b (Hib), pneumococcal (PCV-7, PCV-10, PCV-13) and meningococcal A are conjugated vaccines that are widely used and provide longer protection, even among young children.

2.2.1.4 Toxoid vaccines

In some bacterial infections (e.g. diphtheria, tetanus), the clinical manifestations of disease are caused not by the bacteria themselves but by the toxins they secrete. Toxoid vaccines are produced by purifying the toxin and altering it chemically. While they are no longer toxic, the toxoid is still capable of inducing a specific immune response that is protective against the effect of the toxin. To increase immune response, toxoid is combined with an adjuvant (e.g. aluminum salts). Toxoids are not highly immunogenic and require booster doses. They are stable, long-lasting and have a good safety profile.

Figure 1: Types of vaccines



2.2.2 Other components of vaccines (excipients)

Adjuvants

Sometimes a substance is added to a vaccine to enhance the immune response by degree and/or duration, thus making it possible to reduce the amount of antigen (immunogen) per dose or the total number of doses needed to achieve immunity. An adjuvant helps slow escape of the antigen from the injection site to lengthen the duration of contact between the antigen and the immune system. The commonly used adjuvant is aluminium salts (aluminium potassium phosphate or aluminium potassium sulfate) which primarily enhance the immune response to protein. They have been shown to be safe over several decades of use. Oil-in-water emulsions (ASO3 and ASO4) have used as adjuvants in some vaccines developed in recent years. Rarely, adjuvants may cause injection site reactions – including subcutaneous nodules, sterile abscess, granulomatous inflammation and contact hypersensitivity – particularly if the administration technique is wrong (e.g. subcutaneous). Adjuvant-containing vaccines should be administered intramuscularly.

Antibiotics

Antibiotics are used during the manufacturing phase to prevent bacterial contamination of the tissue culture cells in which the viruses are grown. For example, MMR vaccine and IPV each contain less than 25 micrograms of neomycin per dose (less than 0.000025 g). Persons who are known to be allergic to neomycin should be closely observed after vaccination so that any allergic reaction can be treated at once. Neomycin allergy is very rare.

Preservatives

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

Stabilizers

Stabilizers are used to help the vaccine maintain its effectiveness during storage. To confirm product quality (antigenicity) or stability, compounds may be added to vaccines to address problems with acidity, alkalinity (pH), stability and temperature.

Vaccine stability is essential, particularly if the cold chain is unreliable. Instability can cause decreased infectivity of LAVs and loss of vaccine antigenicity. Bacterial vaccines can become unstable due to hydrolysis and aggregation of protein and carbohydrate molecules. Stabilizing agents include MgCl2, MgSO4, lactose-sorbitol and sorbitolgelatine.

Remember

Other components (excipients) are added to vaccines for different purposes and some are removed in subsequent manufacturing steps. However, minute traces may remain in the final product. The amounts present are of consequence only to individuals who are allergic to them.

2.3 Contraindications and precautions

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

Precautions are not contraindications but are events or conditions that should be considered in determining if the benefits of the vaccine outweigh the risks (especially if the would-be recipient is immunocompromised or pregnant). Precautions stated in the product labelling may sometimes be inappropriately interpreted as contraindications, resulting in missed opportunities to vaccinate.

Summary

- Immunity is the body's innate ability to protect itself against disease. There are two basic mechanisms for acquiring immunity: active and passive.
- Active immunity can be either natural, following an infection, and can last for a lifetime, or it can be caused through vaccination which also lasts for a long period.
- Passive immunity can also be either natural or artificial. Both last for a relatively short period.
- Vaccine is a biological product that improves immunity to a given disease and is divided into four types: live attenuated, inactivated (killed), subunit and toxoid vaccines.
- Excipients (antibiotics, and stabilizers) contained in vaccines can very rarely cause reactions.
- Knowledge of what a vaccine contains is important in safety surveillance.

3

Understanding Adverse Event Following Immunization (AEFI)

Vaccines used in national immunization programmes are extremely safe and effective. nevertheless, no vaccine is perfectly safe and adverse reactions may occur. In addition to the vaccines themselves, the process of immunization is a potential source of an adverse reaction.

3.1 What is an AEFI?

An Adverse Event Following Immunization is any untoward medical occurrence which follows immunization, and which does not necessarily have a causal relationship with the usage of the vaccine. The adverse event may be any unfavourable or unintended sign, abnormal laboratory finding, symptom or disease.

Reported adverse events can either be true adverse events, i.e. resulting from the vaccine or immunization process, or coincidental events that are not due to vaccine or immunization process but are temporally associated with immunization.

3.2 Types of AEFI

In 2012, the Council for International Organizations of Medical Sciences (CIOMS) and WHO revised the existing classification relevant to cause-specific categorization of AEFI and a new classification has been introduced.

AEFI is classified into 5 types, depending on the suspected cause of the reaction. These are defined in Table-1.

Table 1: Classification of Adverse Event Following Immunization

Types of AEFI	Definition
1. 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.
2. 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.
3. Immunization error-related reaction	An AEFI that is caused by inappropriate vaccine handling, prescribing or administration.
4.Immunization anxiety-related reaction	An AEFI arising from anxiety about the immunization and fear of injection.
5. Coincidental event	An AEFI that is caused by something other than the vaccine product, immunization error or immunization anxiety.

3.3 Vaccine Reactions

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

(i) Cause specific vaccine reactions:
- (a) vaccine product-related reaction and
- (b) vaccine quality defect-related reactions

(ii) Vaccine reactions by seriousness and frequency:
- (a) common- minor reactions
- (b) rare-serious reactions

3.3.1 Cause specific vaccine reactions

Vaccine product-related reaction is a reaction in an individual's response to the inherent properties of the vaccine, even when the vaccine has been prepared, handled and administered correctly. Most often the exact mechanism of a vaccine product-related reaction is poorly understood. The reaction may be due to an idiosyncratic immune mediate reaction (e.g. anaphylaxis) or to replication of the vaccine-associated microbial agent (e.g. vaccine-associated poliomyelitis following OPV which contains attenuated live virus). However, it is important to note that, among certain high-risk individuals, there is a higher probability of these rare vaccine product-related reactions which do not occur in the majority of vaccinees.

Vaccine quality defect-related reaction is the defect in a vaccine that occurred during manufacturing process. Such a defect may have an impact on an individual's response and thus increase the risk of adverse vaccine reactions. Insufficient inactivation of wild type vaccine agent (e.g. Wild polio virus) during the manufacturing process or contamination introduced during manufacturing process could cause the vaccine quality defect-related reactions. In early years of immunization programmes, a few major incidences of vaccine quality defect- related reactions were reported. However, since the introduction of Good Manufacturing Practices (GMP) manufacturing defects are now very rare. Since, vaccine manufacturers have started following GMP, and national regulatory authorities (NRA) have been strengthened, the potential risk of such quality defects are now extremely rare.

3.3.2 Vaccine reactions by seriousness and frequency

Vaccine reactions can be classified into common, minor reactions and rare, more serious reactions. Most vaccine reactions are minor and subside on their own. Serious reactions are very rare and, in general, do not result in death or long-term disability.

Table 2: 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)	≥ 1/1,000 and < 1/100	≥ 0.1% and < 1%
Rare	≥ 1/10,000 and <1/1,000	≥ 0.01% and < 0.1%
Very rare	< 1/10,000	< 0.01%

3.3.2.1 Common, minor vaccine reactions

The purpose of a vaccine is to induce immunity by causing the recipient's immune system to react to the vaccine. Local reaction, fever and systemic symptoms can result as part of the immune response. Some of vaccine's components (e.g. adjuvants, stabilizers and preservatives) can lead to reactions as well. The proportion of reaction occurrences likely to be observed with the most commonly used vaccines are listed in Annex 1.

The occurrence of local reactions such as pain, swelling and/or redness at the injection site varies by the type of antigen. For example, whole cell DPT has reported these local reactions very commonly (>10%), whereas for acellular DPT it is only a common reaction with a frequency of 1-10%. BCG causes a specific local reaction that starts as a papule (lump) two or more weeks after immunization, which becomes ulcerated and heals after several months, leaving a scar. Keloid (thickened scar tissue) from the BCG lesion is more common among Asian and African populations.

The occurrence of systemic reactions also varies by the type of antigen. Fever is a very common (>10%) systemic reaction reported for most antigens. Other common systemic reactions (e.g. irritability, malaise, loss of appetite) can also occur after many antigens and DwPT has more reports of these systemic reactions than DaPT. For live attenuated vaccines such as measles/MR/ MMR and OPV, the systemic reactions arise from vaccine virus infection. Measles vaccine causes fever, rash and/or conjunctivitis, but it is very mild compared to "wild" measles. However, for severely immunocompromised individuals, it can be severe, even fatal. Vaccine reactions for rubella vaccine (joint pains and swollen lymph nodes) are uncommon and affect less than 1% of children. Rubella vaccine causes symptoms very common in adults, with 15% suffering from joint pains. Systemic reactions from OPV are uncommon and affect less than 1% of vaccines with diarrhoea, headache and/or muscle pain.

3.3.2.2 Rare, serious vaccine reactions

"Serious" and "severe" are often used as interchangeable terms but they are different. An AEFI will be considered "serious" if it results in death, is life-threatening, requires in-patient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, or requires intervention to prevent permanent impairment or damage. "Severe" is used to describe the intensity of a specific event (as in mild, moderate or severe). The event itself, however, may be of relatively minor medical significance. For example, fever is a common and relatively minor medical event but, according to its severity, it may be graded as mild fever or moderate fever. Anaphylaxis, on the other hand, is always a serious event and life-threatening.

Serious vaccine reactions may occur in rare cases. Most of these do not lead to long-term effects (e.g. seizures, thrombocytopenia, hypotonic hypo responsive episodes). Anaphylaxis, while potentially fatal, is treatable without leaving any long-term effects.

However, there are few reactions with long-term consequences (e.g. VAPP, BCG osteomyelitis etc.) Case definition and treatment of the serious vaccine reactions are in Annex- 2.

Serious AEFI

An AEFI will be considered serious, if it 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.

Non-serious AEFI

An event that is not "serious" and does not pose a potential risk to the health of the recipient. Non-serious AEFI should also be carefully monitored because they may signal a potentially larger problem with the vaccine or immunization or may have an impact on the acceptability of immunization in general.

Signal (safety signal)

Information (from one or multiple sources) which suggests a new and potentially causal association, or a new aspect of a known 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.

3.3.3 Prevention and treatment

Vaccines are very rarely contraindicated. However, it is important to check for contraindications to avoid serious reactions. For example, vaccines are contraindicated if there is a possibility of serious allergy to a vaccine or its components.

Advice on managing the common, minor reactions should be given to parents, in addition to instructions to seek proper medical care if there are more serious symptoms. Such action will help to reassure parents about immunization and prepare them for common and rare serious reactions.

Table 3: Management of Common Minor Reactions

	Local reaction (pain, swelling, redness)	Fever	Irritability, malaise and non-specific symptoms
Management	- Cold cloth at injection site - Paracetamol*	- Give extra fluids - Wear light cool clothing - Tepid sponge or bath - Paracetamol*	Symptomatic

* Paracetamol dose: up to 15 mg/kg every 6 -8 hours, maximum of 4 doses in 24 hours. Paracetamol eases pain and reduces fever.

Following vaccination, parents should be advised to wait for at least 30 minutes at the vaccination centre. All immunization providers need to be trained to develop confidence in early identification of serious reactions like anaphylaxis. Each service provider should know what to do for managing anaphylaxis. Availability of adrenaline and other basic items for resuscitation is vital. It is also important to ensure a continuous supply of adrenaline and its timely replacement on expiry.

3.4 Immunization error-related reaction

Note

Immunization error-related AEFI reactions were earlier categorized as "programme error"

Immunization error-related reactions are preventable. These occur as a result of inappropriate handling, prescribing and administration of vaccines. It is extremely important that these AEFIs are reported and addressed for early correction. Table-4 provides a list of some immunization errors and types of AEFI.

An immunization error-related reaction may lead to a cluster of events associated with immunization. These clusters are usually associated with a particular provider, or health facility, or even a single vial of vaccine that has been inappropriately prepared or contaminated. Immunization error related reactions can also affect many vials. For example, freezing vaccine during transport may lead to an increase in local reactions.

Sterile abscesses are rare (~1 per 100,000 doses) local reactions from aluminium-containing vaccines, especially DPT. Inadequate shaking of the vaccine before use, superficial injection and use of frozen vaccine increase the risk of sterile abscesses and local reactions. Contamination of vaccine or injection equipment can also lead to a bacterial abscess. For BCG vaccine, injection abscess can result from improper technique of injection (subcutaneous rather than intradermal injection).

Ignoring contraindications can lead to serious vaccine reactions and is considered an immunization error.

Table 4: Immunization Error-related Reactions

Immunization Errors		Related Reactions
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
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
	Failure to adhere to vaccine indications or prescription (dose or schedule)	Systemic and/or local reactions, neurological, muscular, vascular or bony injury due to incorrect injection site, equipment or technique
Error in administration	Use of an incorrect diluent or injection of a product other than the intended vaccine	Failure to vaccinate due to incorrect diluent, reaction due to inherent properties of whatever was administered other than the intended vaccine or diluent
	Incorrect sterile technique or inappropriate procedure with a multidose vial	Infection at/beyond the site of injection

To avoid/minimize immunization error, the following should be noted:

- It is both important and necessary to maintain the cold chain at all levels.
- Vaccines must be reconstituted only with the diluents supplied by the manufacturer.
- Reconstituted vaccine should be used within six hours after reconstitution; it must be discarded at the end of each immunization session and should never be retained.
- Other than vaccines, no other medicines or substances should be stored in the refrigerator of the immunization centre.
- Immunization workers must be adequately trained and closely supervised to ensure that proper procedures are followed.

- Careful epidemiological investigation of an AEFI is needed to pinpoint the cause and to correct immunization practices.
- Prior to immunization, adequate attention must be given to contraindications.

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

3.5 Immunization anxiety-related reactions

Individuals and groups can become stressed and may react in anticipation to, and as a result of, any kind of injection. This reaction is unrelated to the content of the vaccine. Fainting (vasovagal syncope or syncope) is relatively common, particularly in children over five years of age and among adolescents.

Coma Position

Fainting does not require any clinical management beyond placing the patient in a recumbent position. Some children who faint may have a syncopal hypoxic convulsion. This is a short-lived generalized tonic-clonic seizure. The management is to keep the child lying down and secure the airway by placing the child in the "coma" position. The seizure will end spontaneously but, if prolonged or focal, further investigations may be required.

The likelihood of fainting should be anticipated when immunizing older children. It can be reduced by minimizing stress among those awaiting injection, through short waiting times, comfortable room temperatures, preparation of the vaccine outside the recipient's line of vision, and privacy during the procedure.

Hyperventilation as a result of anxiety about the immunization leads to specific symptoms such as light-headedness, dizziness, tingling around the mouth and in the hands. This is also common in mass vaccination campaigns.

Younger children tend to react differently, with vomiting a common symptom of anxiety. Breath-holding may also occur and can result in a brief period of unconsciousness during which breathing resumes. Young children may also scream or run away to avoid the injection.

These reactions are not related to the vaccine, but to the injection process. Some individuals may have needle-phobia, aggravating such reactions. In group immunization, mass hysteria is possible, especially if a vaccinee is seen to faint or have some other reaction such as itching, weakness of limbs and so on. Sometime, these cases may even require hospitalization and can cause public concern. Clear explanations about the immunization and a calm, confident delivery will decrease the level of anxiety about the injections and thus reduce the likelihood of an occurrence.

It is important to note that a fainting episode can be misdiagnosed as anaphylaxis. Health workers need to be able to differentiate between the two conditions. Therefore, it is necessary to promote training and awareness to enable health staff to identify and manage anaphylaxis appropriately (details are outlined in Annex-7)

3.6 Coincidental events

An event may occur coincidentally with immunization and sometimes be falsely attributed to the vaccine. In other words, a chance temporal association (i.e. an event happening after immunization) is falsely considered to be caused by immunization. Such temporal associations are inevitable given the large number of vaccine doses administered, especially in a mass immunization campaign.

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

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

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

A similar calculation is shown in Table 5 for deaths of infants (aged under one year) in selected countries for the number of deaths temporally associated with routine DPT or pentavalent vaccine (PVV) immunization. There will be many coincidental deaths in the day, week and month after immunization which are only temporally related to immunization. The actual number of coincidental deaths depends on the population size, infant mortality rate, number of immunization episodes and immunization coverage.

In general, coincidental events which are clearly unrelated may still require investigation because certain serious events may be blamed on the vaccine by parents, public or media due to the close temporal association with immunization, especially if the child was previously healthy. Such cases need to be investigated in order to allay public fear and maintain credibility. Responding to public concerns about immunization safety is important in maintaining confidence in the immunization programme. Availability of information on background rates of reported coincidental events may be helpful in the investigation of an AEFI.

If the same or similar events affect others in the same age group around the same time but those others did not receive the suspect vaccine(s), then a coincidental event is more likely. There may also be evidence showing that the event is not related to immunization.

Table 5: Estimated Number of Coincidental Infant Deaths that could be Temporally Linked to Immunization (e.g. with DPT/PVV) in the Month, Week and Day after Immunization in Selected Countries

Country	IMR	Number of births	Estimated number of infant's death in			Estimated number of PVV/DPT immunizations in		
		per year (N)	a month	a week	a day	a month	a week	a day
Bangladesh	38	3468365	10983	2745	392	970,919	242,730	34,676
Bhutan	42	15,000	53	12	2	3233	746	106
Canada	5	388,000	162	37	5	86,864	20,045	2,856
China	13	16,364,000	17,728	4,091	583	3,634,035	838,624	119,475
Indonesia	25	4,331,000	9,023	2,082	297	950, 113	219,257	31,237
Iran	21	1,255,000	2,196	507	72	276,445	63,795	9,089
Mexico	13	2,195,000	2,378	549	78	487,455	112,490	16,026
Sudan	57	1,477,000	7,016	1,619	231	313,382	72,319	10,303
United Kingdom	4	761,000	254	59	8	170,540	39,355	5,607

Summary

- Vaccine adverse reactions may occur due to some inherent properties of the vaccine (vaccine product-related reactions) or due to quality defects (vaccine quality defect-related reactions) or due to immunization error-related reactions.
- At times, the event may be unrelated to immunization but may have a temporal association with it (coincidental event).
- Immunization anxiety-related reactions are commoner, resulting from fear of, or pain due to, injection rather than from the vaccine itself.
- Immunization error-related reactions (previously classified as "programme errors") are avoidable.
- Antigen/vaccine-specific rates of vaccine reactions are useful to guide decision-making on vaccine-related reactions
- Minor vaccine reactions are common and do not require special treatment. Rare, serious vaccine reactions need timely treatment by qualified medical personnel

4

AEFI surveillance system

Surveillance of AEFI, i.e. systematic collection of data on events following immunization, provides valuable information to help plan and take necessary actions in order to sustain public confidence and ensure smooth functioning of the immunization programme. Hence, AEFI surveillance becomes an integral part of national immunization programme.

Figure 2: AEFI Surveillance Cycle

Goals

The goal of AEFI surveillance is to:

1. Ensure the quality and safety of immunization services in the country
2. Ensure the quality and safety of vaccines used for immunization in the country
3. Minimize the negative impact of AEFI on public health

Objectives

The objectives of AEFI surveillance are to:

1. Timely detect and report all AEFIs
2. Timely and properly investigation of serious and unexpected/unusual AEFIs
3. Identify unusual high rates of AEFI with specific vaccine lots and brands
4. Promptly address programmatic errors through implementation of corrective measures
5. Ensure that coincidental events are not falsely blamed on immunization
6. Identify events which may indicate a previously unknown and potential vaccine reaction (i.e. a signal)
7. Maintain confidence in the immunization programme by properly responding to Concerns

4.1 Key elements of an effective AEFI surveillance system include:

1. Rapid notification of the basic information
2. Timely and effective evaluation of information received
3. Timely and effective response/action, ensuring appropriate outcome of response/ action
4. Evaluation of the activities of involving officers and train and re-train when it is justified
5. Defining responsibility and avoid duplication of efforts
6. Effective communication with all relevant stake holders

4.2 Type of AEFI surveillance in Bangladesh

The AEFI surveillance in Bangladesh is both facility and community-based passive surveillance. Facility based surveillance refers to the reporting of AEFIs from the health facilities by the doctors or other staff of the health facility. Community based surveillance refers to the reporting of AEFIs by the field workers (e.g HA/FWA/AHI/HI/FPI/CHCP/NGO etc.) from the community.

4.3 Roles and responsibilities of the immunization programme in AEFI surveillance

An effective AEFI surveillance system requires the involvement of health managers and workers at all levels of the immunization programme.

4.3.1 Roles and responsibilities at the level of the immunization service delivery level (Sub-district level)

Detection of AEFI

Reporting of AEFI by the recipient, or by the parent or guardian of the recipient, should be encouraged by the service providers at all levels (community and facility level). It is the responsibility of the community level health workers and the facility-based doctors and other health workers to detect and report cases of AEFI. Any case needing treatment should be referred to the nearest government hospital or any other health facility identified for support.

Recording of AEFI

The AEFI report form (Annex 3) should be used by the reporters (both community and facility-based reporters) to report all AEFIs. All necessary data should be entered in the AEFI report form (physical form) and AEFI form in DHIS2 Tracker Capture App. Regular supply of the AEFI report forms need to be ensured by the supervisors / managers.

Reporting of AEFI

Serious AEFIs (death, hospitalization, persistent or significant disability/incapacity, congenital anomaly/birth defect), AEFI cluster or AEFI causing significant parental/community concern should be immediately notified to the next higher administrative level. Other cases should be reported routinely within 24 hours to the respective level as outlined in chapter 5.

Investigation of AEFI

The service providers will assist the District/City Corporation AEFI Committee during AEFI investigation. The AEFI investigation need to be initiated within 24 hours of notification. The details on AEFI investigation is outlined in chapter 6.

Corrective action

Corrective action, particularly in relation to immunization error-related events, should be taken immediately based on the findings of an investigation as outlined in chapter 8.

Analysis of AEFI data

The mid-level managers at the service delivery level should analyse the AEFI data on regular basis to improve the AEFI surveillance as outlined in chapter 10.

Public education /Communication

Whenever an opportunity is available, the public should be informed of what is being done. People should be educated regarding AEFI. The details on vaccine safety communication is outlines in chapter 9.

AEFI committees at National and Sub national levels

AEFI surveillance in the country is reviewed and implemented through the following committees at national, divisional and districts level.

4.3.2 Roles and responsibilities at the district /city corporation level

Every district and city corporation must constitute and establish a functioning AEFI committee. The Civil Surgeon/Chief Health Officer will form the committee.

District AEFI Committee

Composition of District AEFI committee	
Civil Surgeon (Chairperson)	Upazila Health & Family Planning Officer (UHFPO of concerned upazila)
Paediatrician	MMO of concerned municipality
Medicine Specialist	Asst. Director/Superintendent of Drugs , DGDA
Medical Officer- Disease Control (MO-DC), CS Office	EPI Superintendent
RMO (District Sadar Hospital)	Deputy Civil Surgeon/Medical Officer- Civil Surgeon Office (Member Secretary)

City Corporation AEFI Committee

Composition of City Corporation AEFI committee	
Chief Health Officer	Asst. Director/Superintendent of Drugs , DGDA (local)
Paediatrician	EPI Supervisor
Medicine Specialist	Health Officer/ Medical Officer- City Corporation (Member Secretary)
Zonal Medical Officer/Assistant Health Officer (of concerned zone)	

Respective Surveillance and Immunization Medical Officer (SIMO), WHO will assist the District/City Corporation AEFI committee during AEFI investigation

Terms of Reference (TOR) of the District/City Corporation AEFI Committee

- Investigate serious AEFI cases including clusters and AEFI causing significant parental/community concern. Initiate investigation within 24 hours of notification and complete the investigation within a week.
- Not all committee members need to be part of the investigation. Member Secretary will initiate investigation with the members as advised by the chairperson. Later on, expert opinion can be sought from other members as per need. However, Paediatrician must be included in the investigation team.
- Ensure timely submission of AEFI investigation report to the Divisional AEFI Causality Assessment Committee with a copy to PM-EPI.
- The committee will review the functionality of AEFI surveillance in the district/city corporation/municipality/upazila.
- Analyse and review AEFI data on quarterly basis or earlier as per need
- Review and ascertain the reasons for low or no reporting and take necessary steps to address the issues.
- Collaborate to ensure that the private sector is actively involved in AEFI
- Analyse programme information, media reports and other sources of information on serious AEFI and ensure AEFI reporting and investigation are of the highest standards
- Suggest remedial measures for any programmatic errors reporting
- Communicate and share the conclusions and results of investigation with health workers and the community, where needed
- Participate in the Divisional AEFI Causality Assessment Committee /National AEFI Expert Review Committee meetings for causality assessment, if required
- Support the spokesperson for media communication
- Any other responsibility in context to vaccine safety that the committee would like to add.
- The committee will meet at least once every quarter or earlier when needed.
- The chair of the committee can co-opt members for AEFI investigation or any other technical matter related to AEFI surveillance.

In quarterly review meeting the committee will review the functionality of AEFI surveillance in the district/city corporation. All meetings need to be documented in terms of meeting minutes, attendance of participants.

The committee may also have to meet on very short notices whenever there is a serious AEFI, cluster or AEFI causing significant parental/community concern to do the investigation. During investigation of AEFI, the concerned UHFPO/MMO/AHO/ZMO/NGO Clinic Manager of the respective area where the AEFI occurred will be part of the investigation team.

4.3.3 Roles and responsibilities at the Divisional level

Divisional AEFI Causality Assessment Committee

The Divisional AEFI Causality Assessment Committee will be formed under the leadership of Divisional Director-Health. This committee will conduct causality assessment of serious AEFIs of respective districts/city corporation under the division. Where required the divisional committee will support the District/City Corporation AEFI committee in conducting a high-quality investigation. Key role however will be to timely review and support the causality assessment of the reported cases.

Composition of Divisional AEFI Causality Assessment Committee	
Divisional Director, Health (Chairperson)	Epidemiologist/ public health specialist
Co-Chair Principal of Medical College Hospital (govt)	Pathologist
Paediatrician	Pharmacologist
Medicine Specialist	Forensic Experts
Neurologist	Asst. Director/Superintendent of Drugs , DGDA
Microbiologist/ Virologist	Civil Surgeon of divisional district (member secretary)

The Divisional Director, Health will form the committee as per availability of the above-mentioned experts from his division.

The Divisional Coordinator, WHO will assist the Divisional AEFI Committee during causality assessment of serious AEFI cases.

TOR of the Divisional AEFI Causality Assessment Committee:

- The committee will conduct desk review of the AEFI case investigation reports submitted by the District/City Corporation AEFI committee and undertake causality assessment exercise and classify the event as per guidelines.

- Following causality assessment of the cases, the divisional committee chairperson will forward the report to national AEFI Expert Review Committee for final review and classification of cases with a copy to the PM -EPI and chairperson of District/City Corporation AEFI committee.
- Chairperson of the committee or any person of his/her nominated member will act as a spokesperson for media communication
- The committee will assist AEFI investigation team if required
- Committee will meet quarterly to do the causality assessment or earlier depending on the number of AEFI investigation reports submitted for causality assessment
- In absence of chairperson, Co-Chairperson will preside over the committee meeting.
- The chair of the committee can co-opt members for causality assessment

All divisional review meetings need to be documented in terms of meeting minutes, attendance of participants.

4.3.4 Roles and responsibilities at the national level

4.3.4.1 National AEFI Expert Review Committee

There is a National AEFI Expert Review Committee formed by the MOH&FW. Composition of the committee includes:

Composition of National AEFI Expert Review Committee	
Chairperson	Medicine Specialist
Paediatrician	Neurologist
Microbiologist/ Virologist	Pharmacologist
Epidemiologist	Forensic Experts
Immunologist	Representative from DGDA (NRA)
Pathologist	Programme Manager, EPI and Surveillance, DGHS (Member Secretary)

TOR of the National AEFI Expert Review Committee:

- The committee will play an advisory role in confirming the causality assessment reports of the Divisional AEFI Causality Assessment Committee
- The committee will do the causality assessment and classify the unresolved cases
- The committee will provide technical advice on strengthening the AEFI surveillance system by reviewing AEFI Surveillance Data.
- The committee will monitor reported AEFI data for potential signals of previously unrecognized vaccine-related adverse events and make recommendations for further investigation

- The committee will advise EPI/HQ, NRA/NCL (DGDA) at times of crisis/ emergency and assist the AEFI Investigation Team if needed.
- The committee will meet quarterly or as and when needed
- The chair of the committee can co-opt members for causality assessment or other technical matter related to AEFI surveillance if needed.

4.3.4.2 National AEFI Communication Committee

A national AEFI Communication Committee will be formed to address the media at national level to handle communications pertaining to AEFI, develop risk communication plan, appropriate communication curriculum and communication aids/kits. Composition of the committee includes:

Composition of National AEFI Communication Committee	
Line Director-MNC&AH, DGHS (Chairperson)	Representative from CDC
Programme Manager-EPI and Surveillance, DGHS	Representative(s) from National AEFI Expert Review Committee
Representative from media wing, DGHS	Representative(s) from NITAG
Representative from IEDCR	Representative from WHO
Deputy Programme Manager- BCC, EPI, DGHS (Member Secretary)	Representative from UNICEF

TOR of the National AEFI Communication Committee

- Prepare a database of print and electronic media journalists covering health at national level with their contact details
- Review media coverage reports
- Identify appropriate spokespersons to handle media queries
- Participate in "talk shows" on issues to address mis-information and rumours related to immunization
- Organize press briefing /press conference
- Prepare press statement
- Organize orientation workshop for the journalists
- Develop crisis communication plan
- Crisis management
- Develop a media kit, information package (e.g FAQs, fact sheets) pertaining to AEFI for public awareness on immunization safety
- Organize media training for the spokespersons of different level.
- The chair of the committee can co-opt members if needed.

4.3.4.3 Role of EPI Head Quarter in AEFI surveillance

- Ensure a functioning national AEFI surveillance system in the country for routine immunization programme.
- Ensure detection, reporting (including zero report), recording of AEFIs
- Management of AEFIs
- Investigation and causality assessment of serious AEFIs
- Monitoring of AEFIs to follow up on timeliness and completeness of data reporting on surveillance
- Supply AEFI reporting forms and other logistics at all the levels
- Training and awareness building activities among staff at all levels and encourage AEFI reporting
- Capacity building for the district, divisional and national committees on investigation and causality assessments
- Communicate findings of investigation of serious AEFIs with all stakeholders
- Respond to any crisis due to AEFI
- Communication with media
- Aware public on immunization safety
- Communicate and coordinate with DGDA, the National Regulatory Authority (NRA), NCL and other stakeholders for vaccine safety & quality
- Give access to the online AEFI reports in the DHIS2 tracker capture to DGDA pharmacovigilance cell.
- Provide investigation and causality assessment reports of serious AEFIs and clusters of routine immunization including line lists of passive AEFI reports to DGDA
- Implement recommendations of AEFI Expert Review Committee of EPI and National Advisory Committee of NRA
- Compile and analyze AEFI reports with Line listing, Investigation & Causality Assessment Reports on monthly basis and provide one copy to National Regulatory Authority (NRA) i.e. DGDA
- Summary of the causality assessment done by the AEFI Expert Review Committee of EPI to be placed to DGDA, Adverse Drug Reaction Advisory Committee (ADRAC).
- Identify and allocate resources for the national and sub-national levels to conduct meetings and manage AEFI cases for all the levels
- Support in Monitoring and Evaluation of AEFI Surveillance System

4.4 Roles and responsibilities of the National Regulatory Authority (NRA) in AEFI surveillance

NRAs are responsible for ensuring that any pharmaceutical product, including vaccines, used within the country is (i) of good quality, (ii) effective, and (iii) safe for the purpose for which it is proposed. Strengthening NRA activities is necessary to ensure safe vaccine use and the monitoring of safety events in the pre-licensure and post-marketing phases.

The EPI and NRA have a collective responsibility and play specific roles in immunization safety surveillance. The NRA has the following roles and responsibilities for the AEFI surveillance:

- Ensure participation of DGDA officials to the AEFI surveillance activities for the routine immunization Programme.
- Take part as resource person in the regular training and awareness building activities among staff at all levels and public and to encourage AEFI reporting (including zero report).
- To be a part of the investigation team for any serious adverse events or clusters or any other special reason as necessary.
- Quick respond to work together in any crisis management due to AEFIs at national or sub national level if any request comes from EPI
- Communicate and Coordinate with EPI, DGHS and other stakeholders for vaccine safety & quality.
- Publish and disseminate the EPI Pharmacovigilance updates in PV regular Newsletters
- Take measures for implementing recommendations from AEFI Expert Review Committee for routine Programme on relevant issues.
- Compile AEFI reports with line listing, investigation & causality assessment reports provided by EPI and generate signals (if needed).
- Share reviewed AEFI data with WHO global database i.e. WHO-Uppsala Monitoring Center (UMC) VigiFlow as DGDA is its full member and ADR monitoring Cell of DGDA is working as the National Pharmacovigilance Centre in Bangladesh.

4.5 Monitoring the performance of the AEFI surveillance system

The AEFI surveillance system needs to be regularly reviewed at all levels to ensure that the system is sensitive enough to identify and respond to AEFI rapidly. Key indicators which can be used to monitor the performance of the AEFI surveillance system are outlined in Annex 4.

5

Reporting and Recording AEFIs

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

To improve detection, the primary reporting level should have a good knowledge of AEFI types and the purpose of AEFI surveillance. Regular orientation, training and awareness programmes are necessary to update knowledge and maintain enthusiasm among primary reporters.

5.1 Which events should be reported

All AEFI that was notified by the parent or guardian or reported by the health care provider to the health care system needs to be reported in a standard AEFI reporting form (Annex 3). Any AEFI that is of concern to parents or health-care workers should be reported. In particular, health workers must report:

- serious AEFI (death, hospitalization, disability, congenital anomaly/birth defect)
- signals and events associated with a newly introduced vaccine
- AEFI that may have been caused by an immunization error
- significant events of unexplained cause occurring within 30 days after vaccination
- events causing significant parental or community concern.

Note:

Minor reactions such as pain, mild swelling, mild redness at the injection site and mild fever are common and usually expected. Do not report these mild reactions.

Table 6: List of Examples of Reportable AEFI

AEFI	Time onset following immunization
• Acute flaccid paralysis for OPV recipient • Acute flaccid paralysis for contact of OPV recipient	• 4-30 days following immunization • 4-75 days following immunization
Anaphylaxis (after any vaccine)	Within 2 hours of immunization
Brachial neuritis (after tetanus- containing vaccine)	2-28 days following immunization
Disseminated BCG infection after BCG vaccine	Between 1 and 12 months
Encephalopathy • after measles/MMR vaccine • after DPT vaccine	 • 6-12 days following immunization • 0-2 days following immunization
Hypotonic hyporesponsive episode (HHE) after DPT/PVV vaccine	Median time is 3-4 hours after immunization but ranges from immediate to 48 hours. However, it can occur even after 48 hours
Injection site abscess(bacterial/sterile) after any injectable vaccine	Not specific. However, commonly within first 14 days of immunization
Intussusception (after rotavirus vaccines)	Commonly within 21 days, risk increased after the first 7 days and usually first dose
• Lymphadenitis after BCG vaccine • Osteitis/osteomyelitis after BCG vaccine	Between 1 and 12 months
Persistent (more than 3 hours) inconsolable screaming after DPT/PVV vaccine	Common immediately and up to 48 hours of immunization. However, it can occur even after 48 hours
Sepsis (after any injectable vaccine)	Within 7 days following immunization
Seizures, including febrile seizures • after measles/MMR • after DPT/PVV	 • 6-12 days following immunization • 0-2 days following immunization
Severe local reaction (after any injectable vaccine)	Within 7 days following immunization
Thrombocytopaenia (after measles/ MMR)	Median time is 12-25 days after immunization, but the range is 1-83 days
Toxic shock syndrome (TSS) (after any injectable vaccine)	Commonly within 72 hours following immunization
Death, Hospitalization, Disability, Any other severe and unusual events that, are attributed to immunization by health, workers or the public	No time limit, but in general those within 30 days following any immunization

5.2 AEFI Reporting system

AEFI reporting form has been configured in DHIS2 platform (Tracker Capture App) to facilitate the collection, collation, transmission, analysis and feedback of country's vaccine safety related data (AEFI data). It provides real-time data at all levels. This will help quick access of AEFI data at each level with programmatic analysis and report generation for prompt decision making and programmatic interventions where and when applicable particularly in the events of serious AEFI.

Disease Surveillance Focal Points (DSFP)

For AEFI, like other VPD surveillance, the Disease Surveillance Focal Persons (DSFP) are Civil Surgeon for District, CHO for City Corporation, UH&FPO for Upazila and MMO for municipality. If MMO post is lying vacant then for upazila municipality respective UH&FPO and for district municipality UH&FPO-Sadar will act as DSFP.

Local Surveillance Officer (LSO)

Like other VPD surveillance the Local Surveillance Medical Officer (LSO) will also assist DSFP in carrying out his/her responsibilities in AEFI reporting and investigation.

Table 7: List of DSFP and LSO

Locations	Disease Surveillance Focal Person (DSFP)	Local Surveillance Officer (LSO)
District	Civil Surgeon	MO-CS
City Corporation	Chief Health Officer	HO/ AHO/ZMO
Upazila	UH&FPO	MO-DC
Municipality with Medical Officer	Municipal Medical Officer	MMO
Municipality where MMO post is vacant	Respective UH&FPO (UH&FPO-Sadar for district municipality)	MO-DC of respective UHC

Hospital Surveillance Officer (HSO)

Like VPD surveillance system the RMO/RP/RS/Register/Assistant Register will be designated as Hospital Surveillance Officer (HSO) who will assist the DSFP in carrying out his/her AEFI surveillance responsibilities in the health facilities/hospitals.

5.2.1 AEFI reporting system for rural areas

Community

Field workers (HA/FWA/CHCP/NGO field worker) who detect or get information of an AEFI from the community during house visits/EPI session should inform their supervisor (AHI / FPI / HI / NGO Supervisor) and send the filled AEFI report form (Annex- 3) to UH&FPO within 24 hours. The supervisor will ensure reporting of the case to UHC.

Health facility

UHC

Service providers of UHC (both indoor and OPD) detecting AEFI should report to respective HSO within 24 hours using AEFI report form. The HSO will submit these reports to UH&FPO on daily basis .

Other health facility

Service providers of designated AEFI surveillance site (other than UHC) detecting AEFI should report to respective HSO within 24 hours using AEFI report form (Annex-3). The HSO will submit these reports to UH&FPO of the respective Upazila on daily basis.

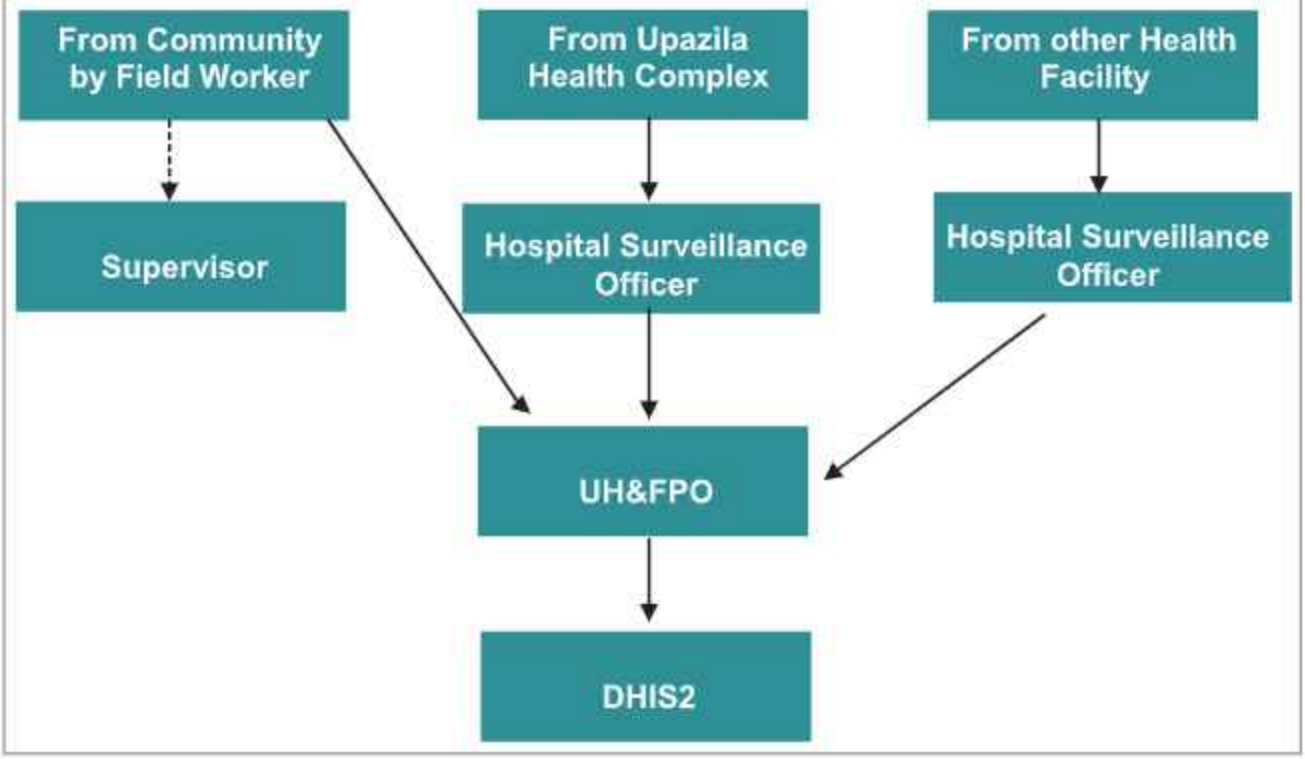
Submission of AEFI reports in DHIS2

All the AEFI reports (AEFI individual case) will be submitted on daily basis in DHIS2 (Tracker Capture App) by MT-EPI/Statistician/Assigned staff. The weekly passive surveillance reports (Aggregate number) must be submitted by following Tuesday of each epidemiological week by the upazila. The UHFPO will supervise timely submission of the AEFI reports in DHIS2.

Immediate reporting

In case of death, hospitalisation, cluster or any event causing significant parental /community concern the AEFI must be reported immediately by telephone to UH&FPO. Once UH&FPO is notified of the above events he/she will immediately notify to Civil Surgeon. Civil Surgeon will notify the serious AEFIs without any delay to Divisional Director (Health) and Programme Manager-EPI. Within 24 hours of detection of such cases, the AEFI report form (Annex-3) should be completed and sent to respective UH&FPO.

Figure 3: Flow Chart of AEFI Reporting for Rural Areas



5.2.2 AEFI reporting system for urban areas

A. Municipality

Community

Field workers of municipalities including NGOs, who detect or get information of an AEFI from the community/EPI session should inform their supervisor and send the filled AEFI report form (Annex- 3) to MMO within 24 hours. The supervisor will ensure reporting of the case to the Municipality.

Health facility

Service providers of health facility detecting AEFI should report to their respective HSO within 24 hours using AEFI report form (Annex-3). The HSO will submit these reports to respective MMO/ In- charge if position is vacant on daily basis.

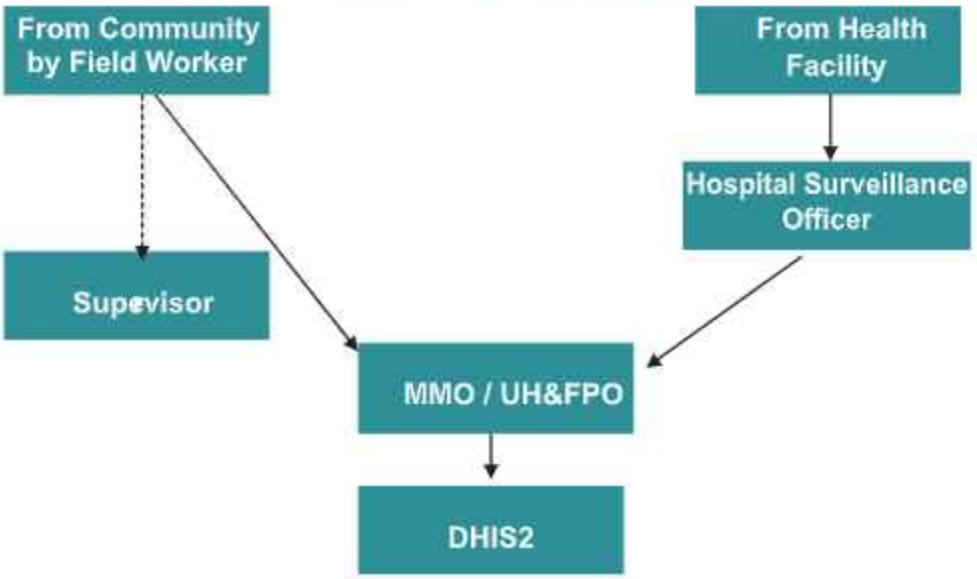
Submission of AEFI reports in DHIS2

All the AEFI reports will be submitted on daily basis in DHIS2 (Tracker Capture App) by EPI Supervisor/ Statistician/assigned staff. The weekly passive surveillance reports (Aggregated number) must be submitted by following Tuesday of each epidemiological week . The MMO/In -Charge will supervise timely submission of the AEFI reports in DHIS2.

Immediate reporting

In case of death, hospitalisation, cluster or any event causing significant parental /community concern the AEFI must be reported immediately by telephone to MMO/In charge. Once MMO/In-charge is notified of the above events he/she will immediately notify to Civil Surgeon. Civil Surgeon will notify the serious AEFIs without any delay to the Divisional Director (Health) and Programme Manager-EPI. Within 24 hours of detection of such cases, the AEFI report form (Annex-3) should be completed and sent to respective MMO/In-Charge.

Figure 4: Flow Chart of AEFI Reporting for Municipality



A. City Corporation

Community

Field workers of City Corporation including NGOs, who detect or get information of an AEFI from the community/EPI session should inform their supervisor and send the filled AEFI report form (Annex- 3) to AHO/ZMO within 24 hours where zone exist otherwise directly to CHO. The supervisor will ensure reporting of the case to City Corporation.

Health facility

Service providers of health facility detecting AEFI should report to their respective HSO within 24 hours using AEFI report form (Annex-3). The HSO will send these reports to AHO/ZMO where zone exist otherwise directly to CHO on daily basis.

Submission of AEFI reports in DHIS2

All AEFI reports will be submitted on daily basis in DHIS2 (Tracker Capture App) by EPI Supervisor/ Statistician/Assigned staff. The weekly reports of passive surveillance (Aggregate number) must be submitted by following Tuesday of each epidemiological week. The AHO/ZMO/CHO will supervise timely submission of the AEFI reports in DHIS2.

Immediate reporting

In case of death, hospitalisation, cluster or any event causing significant parental /community concern the AEFI must be reported immediately by telephone to AHO/ZMO/CHO. Once AHO/ZMO is notified of the above events he/she will immediately notify to Chief Health Officer (CHO). CHO will notify the serious AEFIs without any delay to the Divisional Director (Health) and Programme Manager-EPI. Within 24 hours of detection of such cases, the AEFI report form (Annex-3) should be completed and sent to respective AHO/ZMO/CHO.

Figure 5: Flow Chart of AEFI Reporting for City Corporation (having zone)

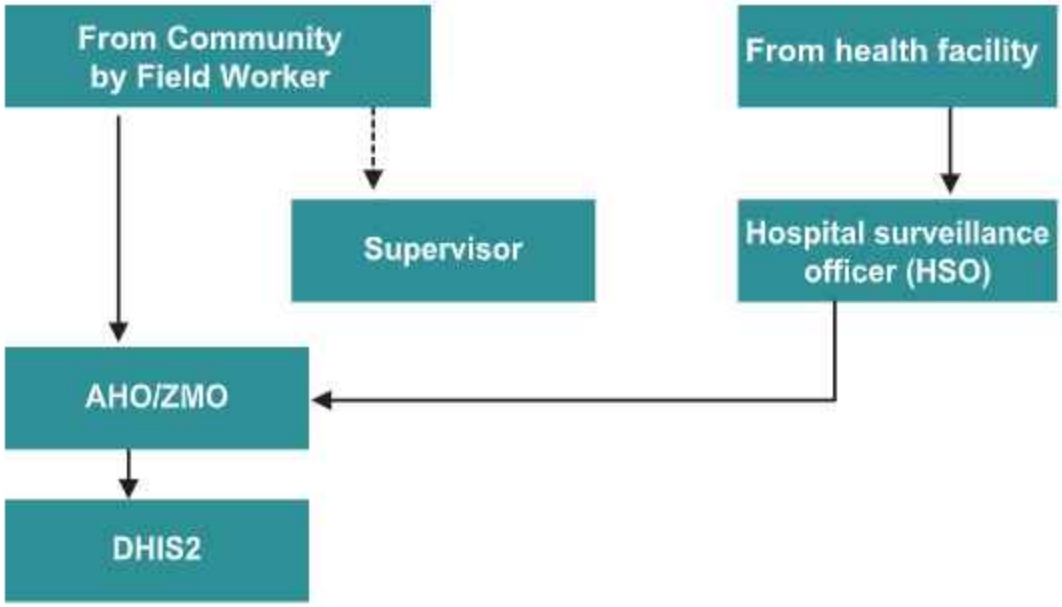


Figure 6: Flow Chart of AEFI Reporting for City Corporation (having no zone)

5.2.3 Who will enter the data in DHIS2 and when?

The AEFI report forms will be submitted to respective upazila/municipality/zone/city corporation from the fields and facilities. These reports should be submitted in DHIS2 (Tracker Capture App) on daily basis. The passive surveillance reports (Aggregate number) must be submitted by following Tuesday of each epidemiological week.

The following staff at different levels will be responsible to enter the AEFI reports in DHIS2.

Table 8: Staff responsible to enter the AEFI report in DHIS2

Level	Staff responsible
Upazila (including UHC)	MT-EPI/Statistician
Health facility (except UHC)	HSO/statistician/assigned staff
Municipality	EPI Supervisor/Statistician/ assigned staff
Zone	EPI Supervisor/Statistician/assigned staff
City Corporation	EPI Supervisor/Statistician/assigned staff

5.2.4 Identification of clusters from the line list

The MO-CS/MO-DC/HO will review the line list from DHIS2 to identify cluster. If any cluster is identified which might be due to programme error, then the respective Civil Surgeon/Chief Health Officer will initiate investigation.

5.3 Barriers to AEFI reporting

Immunization service providers may not report AEFI for several reasons, such as:

- considering that the event did not occur after immunization (however, all events following immunization as per the definition should be reported);
- lack of knowledge about the reporting system and process;
- apathy, lack of interest or time, inability to find the reporting form;
- fear that the report will lead to personal consequences;
- guilt about having caused harm and being held responsible for the event; and
- hesitancy about reporting an event when not confident about the diagnosis.

5.4 Encouraging AEFI reporting

The support of field staff is crucial for the success of any surveillance programme. Field workers are encouraged to report adverse events without fear of any punitive action. The aim is to make surveillance sensitive thereby improving the health care system. This component can be strengthened through periodic capacity building and orientations and not by blaming individuals.

In order to encourage reporting by staff involved in service delivery and others the manager (e.g. UH&FPO, HSO, MMO, HO/ MO/AHO/ ZMO) is responsible to carry out the following activities:

- Train staff on AEFI and its reporting
- Increase awareness of health staff on importance of reporting
- Give positive feedback and appreciate staff reporting such cases.

It is essential that health workers be given feedback about the results of investigations and any actions taken as a result of their reporting.

Managers at all levels should ensure that there is adequate supply of AEFI reporting forms in order to facilitate timely reporting.

Summary

- In Bangladesh, AEFI surveillance is both community and facility-based surveillance
- AEFI need to be reported within 24 hours using the AEFI report form
- Death, hospitalization, cluster or significant community concern need to be notified immediately
- AEFI reports need to be submitted in DHIS2 on daily basis
- Weekly passive surveillance report (aggregated number) need to be submitted on weekly basis by respective upazila/municipality/zone/city corporation
- Identify barriers to reporting and taking appropriate action to address these barriers will improve AEFI reporting

6

Investigation of AEFI

6.1 Why AEFI should be investigated?

The ultimate goal of a case investigation is to find the cause of an AEFI and to implement follow-up actions. Investigation should identify any immunization error-related or vaccine product-related reactions because these are preventable. If coincidental events are recognized, proving them will be important to maintain public confidence in the immunization programme.

The purposes of investigating an AEFI case are the following:

- To identify the details of vaccine(s) administered and to determine the timing between administration of the vaccine and the onset of the event
- To confirm the reported diagnosis or establish a diagnosis
- To document the outcome of the reported adverse event
- To identify the cause of the AEFI
- To determine whether a reported event is a single incident or one of a cluster and, if it is part of a cluster, where the suspected immunizations were given and what vaccines were used
- To examine the operational aspects of the programme and to prevent immunization-related errors
- To determine whether similar events are occurring in individuals who have not received the same vaccine

If the cause is determined to be an immunization error, problem should be corrected quickly. If an AEFI is found to be coincidental, then the community can be reassured about the safety of the vaccine and the immunization programme. The act of investigating AEFI increases the confidence of the community in the health care system and the immunization programme in particular.

6.2 Which AEFI should be investigated?

Not all AEFI reports need investigation. The following AEFIs must be investigated:

- serious AEFI event (death, hospitalization, disability, congenital anomaly/birth defect)
- belongs to a cluster of AEFI
- is a previously unrecognized event associated with an existing or newly introduced vaccine
- involves an increased number or rates of known cause
- causes significant parental/guardian or public concern

Cluster of AEFI

A cluster is defined as 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 vaccine.

For e.g. two or more cases of abscess occurring following one immunization session in a village; repeated abscess cases following immunization by same vaccinator.

6.3 When to investigate AEFI?

AEFIs investigation procedure should start as soon as possible, ideally within 24 hours of notification.

6.4 Who should investigate AEFI?

The District/City Corporation AEFI Committee will be responsible for AEFI investigation in the districts/city corporations. Not all committee members need to be part of the investigation. Member Secretary of the District/City Corporation AEFI committee (DCS/MO-CS at district and HO/Medical Officer at city corporation) with approval of Committee Chairperson (CS/CHO) will initiate investigation with identified members of the AEFI committee. During investigation of AEFI, the concerned UHFPO/MMO/AHO/ZMO /NGO Clinic Manager of the respective area where the AEFI occurred will be part of the investigation team.

The Divisional Coordinator and Surveillance and Immunization Medical Officer (SIMO), WHO will provide technical support to the investigation team.

6.5 How to investigate AEFI?

It is essential to investigate adverse events completely and without any delay. The investigator should search for system problems rather than finding individuals to blame. While an individual may have been at fault, it is more effective to concentrate on changing the system/procedures to avoid such errors than to blame or punish any individuals. Such an approach is essential to ensure that AEFI reports are encouraged.

On receiving information of a serious AEFI, the local manager (UHFPO/MMO/AHO /ZMO/ HO/CHO) will immediately inform CS/CHO and the Member Secretary of the District/City Corporation AEFI committee about the AEFI. The Member Secretary will initiate the investigation with identified members of the AEFI committee as approved by CS/CHO within 24 hours of notification.

In the meantime, the local Manager (UHFPO/MMO/AHO /ZMO/ HO/CHO) should begin an enquiry. He should inform the respective Field Worker/AHI/HI/MT-EPI to collect preliminary data about the patient, vaccine/s administered, immunization session in question and the condition of the other vaccinees. They will also assess whether there is any significant community concern. MT-EPI /equivalent staff of municipality and city corporation will identify the batch/lot number of the vaccines given to the patient and find out where these lots of vaccines were distributed to identify cluster of events.

During investigation the team should be prepared to visit

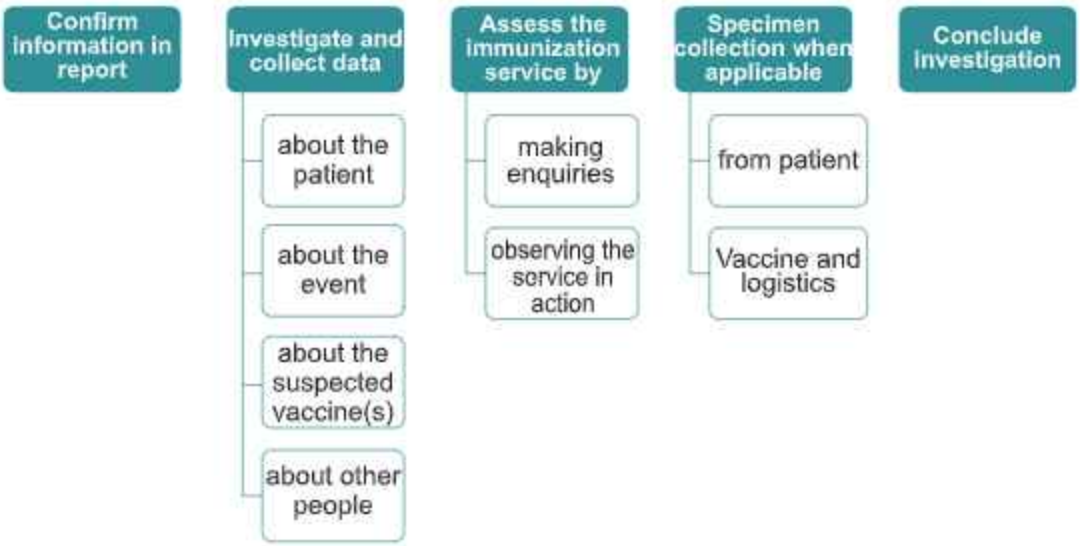
1) the immunization sites
2) vaccine storage points
3) residence and locality of the patients
4) the treatment centres/hospitals/clinic (if applicable).

The investigators will interview the patients (adults), parents or guardian, the treating health staff/clinicians and the staff who administered the vaccine to collect relevant information. Investigators should talk to other parents and guardians who were present during the suspected vaccination session about what they might have seen. Those who received vaccine on the same session should also be interviewed if necessary.

6.5.1 Steps in an AEFI investigation

The following steps to be followed for AEFI investigation:

Figure 7: Steps of AEFI investigation



Step 1: Confirm information in report

- *Obtain patient's medical file (or other clinical records, lab investigation reports etc.)*
- *Check details about the patient and event from the medical records*
- *Verify with AEFI report form, obtain missing details*
- *Identify any other cases that need to be included in the investigation*

Step 2: Investigate and collect data

Step 2a: Investigate and collect data about the patient

Review patient records for

- *immunization history*
- *previous medical history, including prior history of similar reaction or other allergies*
- *family history of similar events.*

Step 2b: Investigate and collect data about the event

- *History of the event in chronological order to explore the underlying factors, if any*
- *Detailed clinical description including sequence of clinical manifestations and the response to treatment*
- *Relevant laboratory tests and other investigations (X-ray, ECG etc.) performed, and results*
- *Details of treatment and outcome.*

Step 2c: Investigate and collect data about the suspected vaccine(s)

- *Storage of vaccines and diluents*
- *Temperature record of ILR*

- *The condition of vaccine vial monitor (VVM)*
- *Lot/batch no of vaccine, manufacturer and expiry dates.*
- *Use of vaccine carriers, condition of ice packs*
- *Conditioning of frozen ice packs*
- *Condition of vaccine labels and date of previous use in case of reuse of previously opened vaccine vials under MDVP*
- *Vaccine handling*
- *Identify where the vaccine(s) were distributed*
- *Transportation of vaccine to the vaccination site*
- *Disposal of vaccine*

Step 2d: Investigate and collect data about other persons

- *Whether others in the community had similar illness; determine the vaccination status of the affected*
- *If possible, try to obtain details of other beneficiaries who received the vaccine from*
  - *the same centre*
  - *the same vial*
  - *the same vaccine lot/batch*

Step 3. Assess the immunization service

Step 3a: Assess the immunization service by making enquiries

- *Use of vaccine and diluent in the correct dosage, person, site and technique*
- *Vaccine handling*
- *Reconstitution procedure and time between reconstituting and administration*
- *Use of AD syringes for vaccination and reconstitution*
- *Other medications (e.g. Vit A) given from the centre on the day*
- *Staff training on immunization*

Step 3b: Assess the immunization service by observing it in action

- *How vaccines are placed in the cold chain*
- *Whether other drugs are stored with vaccines/diluents*
- *Whether any vials have lost their label*
- *Batch numbers and expiry dates*
- *Whether any of the opened vials look contaminated*
- *Directly observe the immunization procedures (reconstitution, drawing up vaccine, injection technique, safety of needles and syringes)*
- *Whether multi dose vial policy (MDVP) is followed as per guideline*
- *Disposal of opened vials.*

Step 4: Specimen collection

Step 4a: Specimen collection: from patient

It is difficult to generalize what specimens will be required in a given situation. It will much depend on symptoms and signs and clinical diagnosis. A good communication between clinician and investigation team is important to make a good decision on what specimens to be collected and where to be sent for investigation etc.

Once a working hypothesis is formulated, it should be apparent whether specimens are required to confirm or rule out the suspected cause. Only appropriate specimens necessary for investigation should be collected, and a clear explanation should be sent to the laboratory of why they were taken and what information is required.

Table 9: Guide to Human Specimen Samples Collection Following Selected AEFI

Hypothesis	Specimen	Reason	Specimen collection
Suspected bacterial sepsis	Whole blood	Bacterial culture	Blood 8-10 ml in each of 2 blood culture bottles.
due to contaminated vial, needle contamination, coincidental	CSF	Differential cell count, biochemistry, bacterial and viral culture, PCR (HSV1/2, enterovirus, other)	Sterile container Viral culture media
	Serum	IgM and IgG antibodies for viral pathogens	Clotted blood 5-10 ml
Suspected viraemia due to vaccine virus or coincidental disease	CSF	Differ ential cell count, biochemistry, bacterial and viral culture, PCR (HSV1/2, enterovirus, other)	Sterile container Viral culture media
	Skin vesicle	Viral culture	Sterile container Viral culture media
	Serum	Mast cell tryptase	Clotted blood 5 –10 ml
Suspected anaphylaxis		Specific IgE	Clotted blood 5 - 10 ml
Suspected toxin or	Urine	Drug screen	Sterile container 1 ml
drug injection/ingestion, either programme error or coincidental	Blood	Chemistry when indicated, liver enzymes, glucose, electrolytes	Clotted blood or in Li Heparin 5-10 ml
Suspected VAPP or coincidental enceph alitis	Stool	Enterovirus and viral culture	Sterile container

The collection and storage of specimens following serious AEFI (e.g. deaths, anaphylaxis, toxic shock syndrome) is important. Therefore, as soon as information is received about a suspected AEFI, the hospital staffs are advised to collect all relevant samples such as blood, urine, cerebrospinal fluid (CSF), vomitus, faeces, sputum, swabs etc. If there is a delay in transport to the laboratory, samples should be stored in a refrigerator at the recommended temperature, depending the type of sample and the facilities available.

Step 4b: Specimen collection: Vaccine and Syringe

Vaccine and Syringes testing should be requested based on clear suspicion and not as a routine procedure, and never before the working hypothesis has been formulated. Laboratory testing is always costly. Determination of which samples to test, if any, depends on the working hypothesis for the cause of the event (Table 10).

The vaccine may be tested for sterility, toxicity and content (e.g. Aluminium content); the diluent for sterility and chemical composition; and the needles and syringe for sterility.

Table 10: Laboratory Testing to Investigate AEFI by Working Hypothesis

Working Hypothesis	Specimens to send	Laboratory Test
Vaccine transportation or storage error	Vaccine vial	Visual test for clarity- presence of foreign matter, discoloration or flocculation
Reconstitution error	Vaccine vial and/or diluents	Chemical composition analysis for abnormal components (e.g. suspect medicine 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. aluminium content) or biological tests for foreign substances or toxins if abnormal toxicity is suspected

Formulate working hypotheses

After collecting enough information, a working hypothesis should be formulated as to what was the probable cause of the AEFI.

The working hypothesis may be a simple statement linking the suspected cause with the reported AEFI. For instance, an abscess following immunization may initially be investigated with the following hypothesis: "An abscess following immunization due to incorrect technique". The working hypothesis may change during the course of the investigation. In this example, additional information may reveal that there are similar cases from more than one clinic and therefore the working hypothesis could be modified as "Abscess following immunization due to cold chain failure in vaccine storage". The focus of the investigation should be to confirm the working hypothesis.

No action should be taken based on the hypothesis, until it is confirmed with reasonable certainty. It is the responsibility of investigation team to form, test and confirm /discard the working hypothesis in a scientific manner.

Step 5: Concluding investigation

- Review epidemiological, clinical and laboratory findings
- Formulate hypothesis on the likely/possible cause (s) of the event
- Test hypothesis if possible
- Reach a provisional conclusion on the cause
- Complete AEFI investigation form

6.6 Preparing and submission of the AEFI investigation report

After collecting all the information, the investigation team members should sit together, discuss on the findings and reach a conclusion. They will fill up the AEFI case investigation form (Annex 5) and sign it.

The AEFI investigation team will submit the investigation report to the Chairperson of the District/CC AEFI Committee (Civil Surgeon/ Chief Health Officer) with the following documents:

- The filled and signed AEFI case investigation form
- Medical record e.g. prescription, treatment sheets, discharge certificates (if patient is hospitalized)
- Laboratory investigation reports (if any)
- Death certificate and Autopsy report (if any)
- AEFI Bangla report form

The Chairperson of the District/CC AEFI Committee (Civil Surgeon/ Chief Health Officer) will send the investigation report with all the documents to the Divisional AEFI Causality Assessment Committee with a copy to the Programme Manager-EPI.

6.7 Investigating AEFI cluster

A cluster of AEFI is defined as two or more cases of the same adverse event related in time, place or vaccine administration. A cluster may occur within the same geographical unit, or be associated with the same vaccine, same batch number administered or same vaccinator.

Cluster investigation begins by establishing a case definition for the AEFI and related circumstances and by identifying all cases that meet the case definition.

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

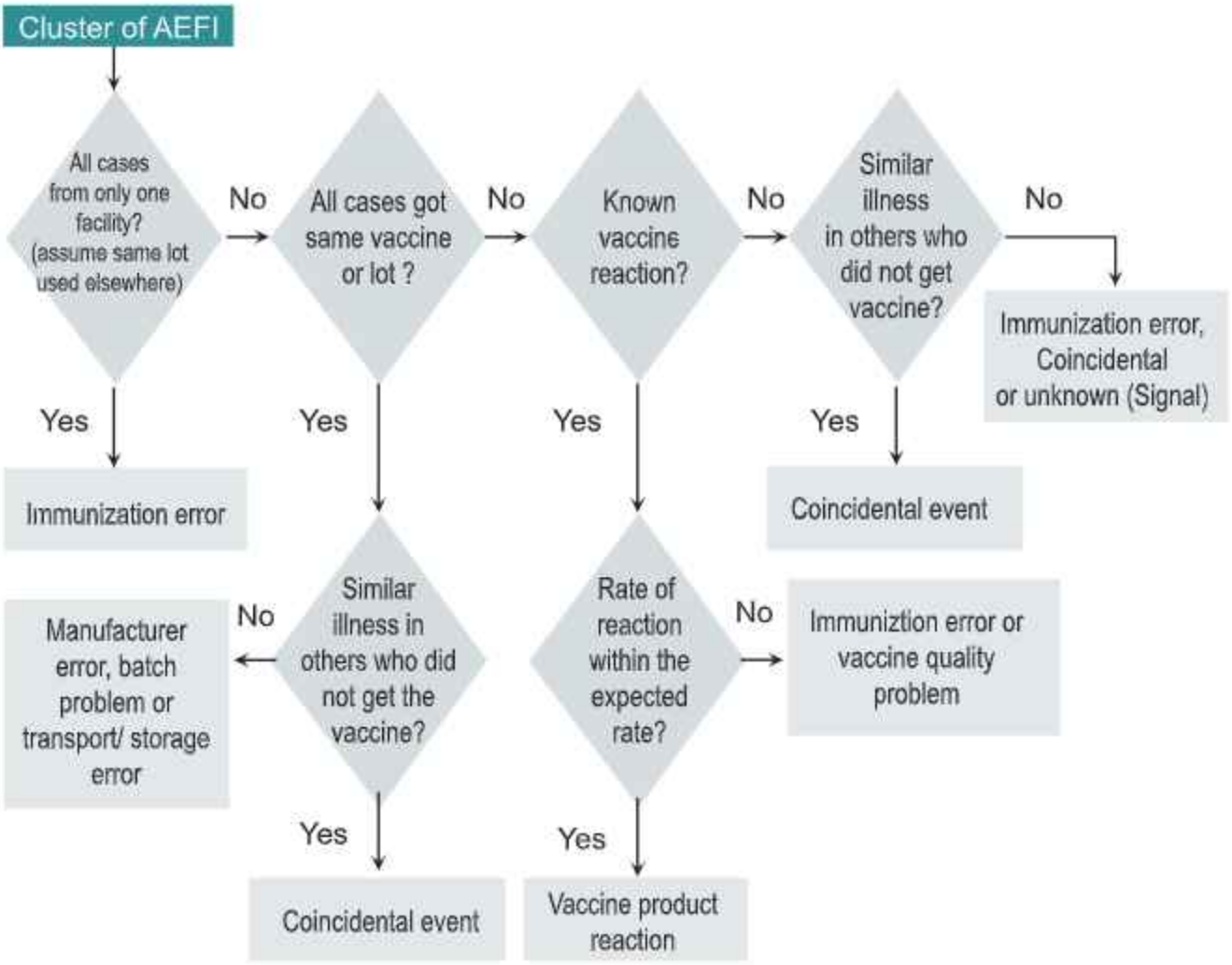
- detailed data on each patient
- programme-related data (storage and handling etc.)
- immunization practices and the relevant health workers' practices

Common exposures among the cases can be identified by reviewing:

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

When an AEFI cluster has been identified, the cause-specific definitions provide a framework for investigation and causality assessment. Usually, the key considerations will be to investigate the possibility of a vaccine quality defect or an immunization error-related AEFI.

Figure 8: Identifying the Causes of an AEFI Cluster



If all cases received vaccines from the same health worker/facility and there are no other cases, an immunization error is likely. If all cases received the same vaccine or lot, and there are no similar cases in the community, a problem with the vaccine or the respective lot is likely. If the event is a known vaccine reaction but is found to occur at an increased rate, an immunization error or a vaccine quality problem are likely causes. Finally, if cases in the unvaccinated population are occurring at about the same rate/proportion as among the vaccinated from the same area in the same age group, the adverse event was probably coincidental (Table 11).

Table 11: Cause-specific Cluster Characteristics

Cause-specific AEFI	Cluster characteristics
Vaccine reaction (product-related or quality defect-related)	If all cases received the same vaccine or lot, and there are no similar cases in the community If an increased frequency of events is reported from multiple settings
Immunization error-related	If all cases received vaccines from the same health worker/facility and there are no other cases
Coincidental	If cases include people from the same area in the same age group who were not immunized
Immunization anxiety-related reaction	Clusters of fainting after immunization are well-recognized as anxiety-related reactions during immunization programmes targeting adolescent girls

6.8 Investigation of deaths

A field investigation of a death following immunization has to be conducted without delay, as the death can cause significant community concern. All administrative levels, including the national immunization programme, should be notified of the death without delay.

An autopsy is preferred and is recommended following all deaths suspected to be caused by vaccine or immunization. However, the decision to conduct the autopsy should be taken within the context of religious, cultural and the legal framework of the country.

If an autopsy is not possible, a verbal autopsy can be carried out using the verbal autopsy form (Annex-8).

6.9 Investigation of reported sudden unexplained death following vaccination

The sudden and unexpected death of an individual, especially that of a child, is one of the most traumatic and unfortunate events that can happen to a parent/family. Investigation of suspected unexplained deaths following immunization is an issue of great importance regarding the immunization programme, as the proper causality assessment would enable differentiation of vaccine- related deaths from deaths due to other causes.

It is important to understand that in the vast majority of reported sudden unexplained infant deaths, it is possible that the death may be due to natural causes. In a small number of cases, death may be as a result of negligence or a deliberate act.

There are likely to be several factors contributing to sudden and unexpected death. It is important to identify these factors by detailed investigation of the history, circumstances of death, medical examination and postmortem report, if available. Many causes of death from genetic, metabolic or cardiac disorders that were previously unknown have recently come to light.

In order to rule out causes of death such as trauma, crib (in cot)-related deaths including falling from the crib or cot, parents accidentally rolling over the baby during sleep, or other reasons for unexplained deaths, the field worker must examine the site of death, if notified immediately after death. If the child has not been moved, a photograph may be taken immediately for the purpose of documentation.

Investigations of AEFI deaths are multidisciplinary and final collation and interpretation of results would require corroboration with a detailed history that may be forgotten unless documented at the time of the incident.

Table 12: Actions to safeguard the public during an investigation

Stage of investigation	Actions
Incident detected	• Assess and investigate with an appropriate degree of urgency • If needed, quarantine suspect vaccines • Begin communication with all concerned parties
Investigation starts	• Ensure that the investigator has adequate resources, and provide more if needed • Increase surveillance to identify similar cases in and out of area • Define any suspect vaccine • Maintain continued communication on progress of the investigation with all concerned parties
Investigator develops working hypothesis	• Do not communicate the working hypothesis until confirmed (the working hypothesis is for the investigation team only and not for the public since, if the investigation reveals something different from the working hypothesis, this may affect public trust) • If programme-related errors are the working hypothesis, correct them • If a vaccine problem is suspected, quarantine suspect vaccines
Investigator confirms working hypothesis	• Inform the community of the cause and the planned response • Communicate with all concerned parties on findings

Summary

- Investigation should be timely, comprehensive and methodical.
- Testing of vaccine and syringe are important but should not be routine. They should be conducted if only indicated and necessary.
- It is recommended to secure investigational items (vaccine, syringes, blood etc.) in proper condition in case if they may be needed later for laboratory investigations.
- Autopsy investigations are often essential to exclude any coincidental causes of an AEFI

7

Causality Assessment of AEFI

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

Causality assessment is important for:

- 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 comparison of post-marketing surveillance safety data.

The quality of the causality assessment depends on three factors:

1. The quality of case reporting and investigation
2. Availability of adequate medical and laboratory services for the investigation and access to background information on disease/illness rates in the absence of vaccination
3. The quality of the causality review process, including access to appropriate expertise.

7.1 Who should conduct the causality assessment?

The Divisional AEFI Causality Assessment Committee will review the AEFI investigation reports submitted by the district/city corporation AEFI investigation team and do the causality assessment.

The Chairperson of Divisional AEFI Causality Assessment Committee will submit these reports to the National AEFI Expert Review Committee with copy to Programme Manager-EPI.

The National AEFI Expert Review Committee, at the national level will review the causality assessment reports of the Divisional AEFI Causality Assessment Committee and finalize the AEFI classification.

7.2 Case selection for AEFI causality assessment

All AEFI cases investigated need to be subject to a formal causality assessment.

7.3 Steps to be taken before starting a causality assessment

An AEFI should fulfill four prerequisites before causality assessment, namely:

1. The AEFI case investigation should have been completed. Premature assessments with inadequate information could mislead the classification of the event.
2. All details of the case should be available at the time of assessment. They should include documents pertaining to the investigation as well as laboratory and autopsy findings as appropriate.
3. There must be a "diagnosis" for the adverse event, clinical sign, abnormal laboratory finding, symptom and/or disease in question.
4. All vaccines that were administered before the event should be identified.

7.4 Steps in causality assessment

Causality assessment has four steps, as follows:

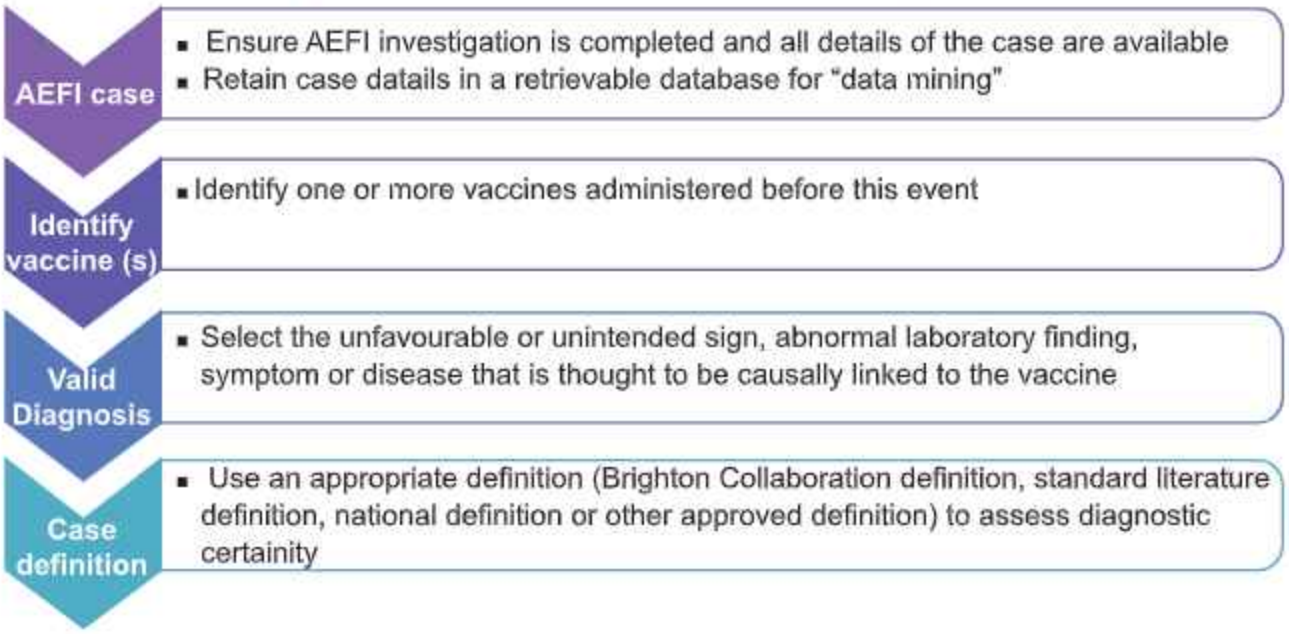
- **Step 1:** Eligibility. The first step aims to determine if the AEFI case satisfies the minimum criteria for causality assessment as outlined below.
- **Step 2:** Checklist. The second step involves systematically reviewing the relevant and available information to address possible causal aspects of the AEFI.
- **Step 3:** Algorithm. The third step obtains a trend as to the causality with the information gathered in the checklist.
- **Step 4:** Classification. The fourth step categorizes the AEFI's association to the vaccine or vaccination on the basis of the trend determined in the algorithm.

The worksheet used for the causality assessment of an individual AEFI case is presented in Annex- 6. WHO has also developed an online tool to do the causality assessment. The casualty assessment tool can be accessed at the link : http://gvsi-aefi-tools.org/

Step 1: Eligibility

The AEFI case need to satisfy the minimum criteria for causality assessment as outlined below in Figure 9.

Figure 9: Causality Assessment: Eligibility



Valid Diagnosis

It is also essential to have a valid diagnosis for the reported AEFI, which could be an unfavourable or unintended sign, an abnormal laboratory finding, a symptom or a disease.

The valid diagnosis should meet a standard case definition (or it could also be a syndromic case definition). If available, it is best to adopt the Brighton Collaboration case definition which can be accessed online. However, when a valid diagnosis exists but a case definition does not; case definitions can be adopted from standard medical literature or national guidelines, or may also be adopted locally by the reviewers. If the reported event does not have a valid diagnosis, the AEFI cannot be classified and additional information should be collected to arrive at a valid diagnosis.

Cases ineligible for causality assessment are those where the amount of information initially available to the assessor is so limited that the assessment cannot be initiated. For example if the name of the vaccine or the valid diagnosis are not available at the time of assessment.

Unclassifiable cases occur in instances where the reviewer is able to initiate an assessment, but during the process, discovers that some key elements are unavailable to permit a logical classification.

In either situation, reasons for not proceeding with the classification have to be provided.

At this stage it is also essential for the reviewers to define the "causality question" (Fig. 10). Examples of causality questions are:

- "Has the vaccine A caused hepatomegaly?" (an example of an unfavourable or unintended sign).
- "Has the vaccine B caused thrombocytopenia?" (an example of a laboratory finding).
- "Has the vaccine C caused itching?" (an example of a symptom).
- "Has the vaccine D caused meningitis?" (an example of a disease).

Figure 10: Causality Question

Create your question on causality here

Has the..... vaccine / vaccination caused ..... (The event for review in step 2 - valid diagnosis)

For a given assessment only one valid diagnosis and one vaccine administered can be assessed at one time. If multiple vaccines are administered to the patient at the same time, each vaccine should be assessed separately; when faced with multiple presumptive diagnoses, the reviewer should consider doing a separate causality assessment for each diagnosis. Likewise, for a cluster of AEFI, each individual case must be assessed separately

At this point of the assessment, the assessor has to make a decision if the information that is available at hand is sufficient to proceed (eligibility for assessment), if not the assessment should be postponed until the basic information is obtained.

Step 2. Checklist

The checklist contains elements to guide the causality assessment committee to collate the evidence for case review (Table 13). It is designed to assemble information on patient-immunization-AEFI relationships in the following key areas:

- Evidence for other causes
- Association of the event and the vaccine/vaccination with the vaccine product(s), immunization error or immunization anxiety (if there is an association, it is also important to find out if the event occurred within a plausible time window)
- Evidence against a causal association
- Other qualifying factors for classification such as previous history of a similar event, the background rate of the event, pre-existing, present and past health conditions, potential risk factors, other medications, exposure to triggering factors etc.

Table 13. The causality assessment checklist

I. Is there strong evidence for other causes?	Y N UK NA	Remarks
1. In this patient, does the medical history, clinical examination and/ or investigations, confirm another cause for the event?	☐☐☐☐	
II. Is there a known causal association with the vaccine or vaccination?		
Vaccine product		
1. Is there evidence in published peer reviewed literature that this vaccine may cause such an event if administered correctly?	☐☐☐☐	
2. Is there a biological plausibility that this vaccine could cause such an event?	☐☐☐☐	
3. In this patient, did a specific test demonstrate the causal role of the vaccine?	☐☐☐☐	
Vaccine quality		
4. Could the vaccine given to this patient have a quality defect or is substandard or falsified?	☐☐☐☐	
Immunization error		
5. In this patient, was there an error in prescribing or non-adherence to recommendations for use of the vaccine (e.g. use beyond the expiry date, wrong recipient etc.)?	☐☐☐☐	
6. In this patient, was the vaccine (or diluent) administered in an unsterile manner?	☐☐☐☐	
7. In this patient, was the vaccine's physical condition (e.g. colour, turbidity, presence of foreign substances etc.) abnormal when administered?	☐☐☐☐	
8. When this patient was vaccinated, was there an error in vaccine constitution/preparation by the vaccinator (e.g. wrong product, wrong diluent, improper mixing, improper syringe filling etc.)?	☐☐☐☐	
9. In this patient, was there an error in vaccine handling (e.g. a break in the cold chain during transport, storage and/or immunization session etc.)?	☐☐☐☐	
10. In this patient, was the vaccine administered incorrectly (e.g. wrong dose, site or route of administration; wrong needle size etc.)?	☐☐☐☐	
Immunization anxiety (Immunization Stress Related Response - ISRR)		

11. In this patient, could this event be a stress response triggered by immunization (e.g. acute stress response, vasovagal reaction, hyperventilation or anxiety)?	□□□□	
II (time). If "yes" to any question in II, was the event within the time window of increased risk?		
12. In this patient, did the event occur within a plausible time window after vaccine administration?	□□□□	
III. Is there strong evidence against a causal association?		
1. Is there a body of published evidence (systematic reviews, GACVS reviews, Cochrane reviews etc.) against a causal association between the vaccine and the event?	□□□□	

IV. Other qualifying factors for classification		
1. In this patient, did such an event occur in the past after administration of a similar vaccine?	□□□□	
2. In this patient did such an event occur in the past independent of vaccination?	□□□□	
3. Could the current event have occurred in this patient without vaccination (background rate)?	□□□□	
4. Did this patient have an illness, pre-existing condition or risk factor that could have contributed to the event?	□□□□	
5. Was this patient taking any medication prior to the vaccination?	□□□□	
6. Was this patient exposed to a potential factor (other than vaccine) prior to the event (e.g. allergen, drug, herbal product etc.)?	□□□□	

Note: Y: Yes; N: No; UK: Unknown; NA: Not applicable.

It is essential that all questions in the checklist be answered with any one of the options, "Yes", "No", "Unknown" or "Not applicable". When there is a positive response to any question, ("Yes" response), it is essential to provide an explanation for the positive response in the corresponding row under remarks. It will be observed that sometimes explanations for other responses ("No", "Unknown" or "Not applicable") are also important to determine causality; therefore, it is essential that the "Remarks" column is used to provide detailed explanation on the reasons.

The checklist and the questions with some suggestive examples are described below. Please note that the list of examples and illustrations provided are not exhaustive.

I. Is there strong evidence for other causes?

In judging whether a reported association is causal, it is necessary to determine the extent to which researchers have taken other possible explanations into account and have effectively ruled out such alternative explanations.

I.1 In this patient, does the medical history, clinical examination and/ or investigations, confirm another cause for the event?

A detailed history, clinical examination and investigations including laboratory tests in the patient may help to identify other conditions such as other diseases and congenital anomalies that could have caused the event. For example:

- The death of a teenage girl in the United Kingdom following vaccination with the human papilloma virus (HPV) vaccine was initially attributed to the vaccine. A post-mortem found it to be due to a malignant mediastinal tumour.

II. Is there a known causal association with the vaccine or vaccination?

To determine if there is a known causal association with the vaccine or vaccination, all relevant information including statements obtained from the patient, parent or guardian, treating physician and health care providers, supervisors, and community members during investigation are invaluable. In addition, hard evidence such as case records, laboratory records, immunization documents, photographs etc. collected by the investigator are very important. The vaccine package insert and the vaccine reaction rate information sheets also provide supporting information. This will help the assessor to determine if the event is vaccine product related, quality defect related, immunization error or anxiety related or if the event was coincidental.

Vaccine product(s)

II.1 Is there evidence in published peer reviewed literature that this vaccine may cause such an event even if administered correctly?

WHO has developed information sheets that provide details on expected adverse reaction rates of selected vaccines, including monovalent, multivalent and combined vaccines. They provide details of minor and severe adverse reactions (local and systemic) following immunization. Expected rates of vaccine reactions have been included if available in published literature. The information sheets are handy references for assessment. The same can be accessed at http://www.who.int/vaccine_safety/initiative/tools/ vaccinfosheets/en/

The package insert of the vaccines provided by the manufacturer also describes the vaccine reactions that are expected to occur.

II.2 Is there a biological plausibility that this vaccine could cause such an event?

Biological plausibility – or biological mechanisms as an additional qualifying factor - can be invoked only when a laboratory finding, or a symptom/sign are similar and consistent with the natural history and physiopathology of the infection or antigen. Evidence regarding biological plausibility, however, can never prove causality. At best, biological plausibility adds an additional piece of supportive evidence. For example:

- Acute cerebellar ataxia is a proven complication of wild type varicella zoster virus (VZV) infection with an estimated incidence of five per 100 000 infections among children aged five years and under. Since the wild virus causes acute cerebellar ataxia, it is biologically plausible that the attenuated vaccine virus could also result in this complication of VZV infection in certain vaccinees. However, existing evidence is still not sufficient to confirm or reject this hypothesis, so it remains a theoretical possibility based on biological plausibility.

II. 3 In this patient, did a specific test demonstrate the causal role of the vaccine?

- As an example, aseptic meningitis has been known to be a complication of mumps vaccination. Among 630 157 recipients of trivalent MMR vaccine containing the Urabe Am9 mumps vaccine, there were at least 311 meningitis cases suspected to be vaccine-related. In 96 of these 311 cases, Urabe Am9 mumps vaccine virus was isolated from cerebrospinal fluid.

Vaccine quality

II. 4 Could the vaccine given to this patient have a quality defect or is substandard or falsified?

A vaccine quality defect-related reaction is an AEFI that is caused or precipitated by one or more quality defects of the vaccine product including its administration device as provided by the manufacturer.

Investigations into an outbreak of suppurative lymphadenitis with a particular brand of BCG vaccine in Singapore showed that of the 283 cases of lymphadenitis identified, 76% were suppurative. A spike in suppurative lymphadenitis cases was seen in the 2011 vaccinated cohort, with an incidence rate of 3.16 per 1000 vaccinees, as compared to 0.71 to 0.85 per 1000 in the 2009, 2010 and 2012 cohorts. Detailed investigations identified the likely cause of the outbreak to be batch-related, arising from manufacturing issues encountered by the manufacturer, after ruling out vaccine administration-related and host-related factors.

Immunization error

Immunization error describes an AEFI that is caused by inappropriate vaccine handling, prescribing or administration and therefore, by its nature, is preventable. An immunization error-related reaction may lead to a solitary event or a cluster of events associated with immunization.

II.5 In this patient, was there an error in prescribing or non-adherence to recommendations for use of the vaccine (e.g. use beyond the expiry date, wrong recipient, etc.)?

It is essential that vaccines are used in accordance with the indications, contraindications, dosage, storage conditions, reconstitution procedures etc. outlined in the package insert. Each vaccine from a different manufacturer may have different specifications and failure to comply with them can result in AEFI. For example:

- systemic and/or local reactions following administration of an incorrect dose;
- systemic and/or local reactions following administration of the wrong product or administration to an individual in an incorrect age group;
- vaccine failure, systemic and/or local reactions following administration of the product that was stored in non-recommended storage conditions;
- vaccine failure if a live attenuated product is given too soon after blood products or at an age when maternally transferred antibody could interfere with the replication required to induce an immune response
- failure to screen and identify absolute contraindication which may have caused an expected AEFI

II.6 In this patient, was the vaccine (or diluent) administered in an unsterile manner?

Poor vaccination technique e.g. touching the hypodermic needle can cause abscess. Children immunized with contaminated vaccine (usually the bacterium Staphylococcus aureus) become unwell within a few hours. Injection site inflammation (redness, swelling and pain) high fever, rigors, vomiting, diarrhoea, rash and septic shock (toxic shock syndrome) may occur. Deaths have been reported due to septic shock. Bacterial culture of the vial contents, if still available, or of local tissue can confirm the source of the infection.

II.7 In this patient, was the vaccine's physical condition (e.g. colour, turbidity, presence of foreign substances etc.) abnormal when administered?

Abnormal colour, turbidity or presence of visible contaminants may be the first indication that the vaccine contents are abnormal or unsterile and may have caused an AEFI such as injection site abscess.

II.8 When this patient was vaccinated, was there an error in vaccine reconstitution/preparation by the vaccinator (e.g. wrong product, wrong diluent, improper mixing, improper syringe filling etc.)?

AEFI including deaths have resulted because of accidental use of the wrong product or the wrong diluent. This may occur because of improper storage and/or improper selection. Vaccine failure can result if the entire content is not dissolved when freeze-dried vaccines are used or if the cold chain is not maintained properly. Errors in drawing up vaccine into syringes may result in AEFI due to excess filling or vaccine failure due to inadequate filling.

II.9 In this patient, was there an error in vaccine handling (e.g. a break in the cold chain during transport, storage and/or immunization session etc.)?

Exposure to excess heat or cold as a result of inappropriate transport, storage or handling of the vaccine (and its diluent where applicable) may result in:

- vaccine failure as a result of inactivation of the active vaccine components;
- 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.

Reconstituted vaccines used beyond the prescribed time and recommended maintenance conditions can result in vaccine failure and/or disease in the recipient (e.g. toxic shock syndrome).

II.10 In this patient, was the vaccine administered incorrectly (e.g. wrong dose, site or route of administration; wrong needle size etc.)?

A variety of AEFI may result from incorrect administration of a vaccine. For example:

- neurological, muscular, vascular or bone injury from the use of an incorrect injection site, equipment or technique;
- systemic and/or local reactions following administration of an incorrect dose;
- sterile abscess following subcutaneous instead of intramuscular injection of alum adjuvanted vaccines – usually a result of using a needle that is too short to reach the muscle layer.

Immunization anxiety (Immunization Stress related response - ISRR)

An "Immunization Stress related response (ISRR)" is the current terminology used to describe a range of signs and symptoms that describe an AEFI arising from anxiety about the immunization. However, this term does not capture all elements of such events and also some AEFIs that may not manifest with typical symptoms of anxiety. WHO has proposed to refer to such events as "Immunization stress related response (ISRR)".

II.11 In this patient, could this event be a stress response triggered by immunization (e.g. acute stress response, vasovagal reaction, hyperventilation or anxiety)?
The types of reactions caused by immunization stress responses include, but are not limited to, acute stress responses, vasovagal reactions and conversion disorders. For example:

Adolescents are more prone to have anxiety-related vasovagal reactions resulting in fainting, sometimes accompanied by tonic-clonic seizure-like movements (not a seizure).

II (time). If "yes" to any question in II, was the event within the time window of increased risk?

II. 12 In this patient, did the event occur within a plausible time window after vaccine administration?

It is important to confirm if the event took place within a "plausible" time window of increased risk. This is applicable to all questions under II. For example:

- The "plausible" time window for VAPP is between 4 and 40 days. Cases with AFP onset less than 4 days or over 40 days after receiving OPV and isolating Sabin virus in the stool are not classified as VAPP.

III. Is there strong evidence against a causal association?

III.1 Is there a body of published evidence (systematic reviews, GACVS reviews, Cochrane reviews etc.) against a causal association between the vaccine and the event?

An AEFI that is initially thought to be due to a vaccine may, after investigation, be found to be explained by a similar manifestation caused by another factor. For example:

- In recent years, some researchers hypothesized that measles vaccine may be associated with autism. A series of studies were reviewed by the GACVS and also the IOM Committee to review adverse effects of vaccines. Both groups concluded that no evidence exists of a causal association between MMR vaccine and autism or autistic disorders.

IV. Other qualifying factors for classification

Sections I to III outline the strong evidence for or against causality for most cases of AEFI. Below are some additional factors that support the above observations. If the AEFI is still unclassified, these qualifying factors provide reviewers with indications on causality.

IV. 1 In this patient, did such an event occur in the past after administration of a similar vaccine?

The occurrence of an AEFI after a previous dose of a similar vaccine should be handled cautiously. For example:

- Revaccinations have to be avoided in patients with a history of anaphylaxis after vaccine injection because of the potential risk of recurrent anaphylaxis.
- Revaccination of children who have a past history of an AEFI appears safe (with the exception of anaphylaxis and encephalopathy).

IV. 2 In this patient did such an event occur in the past independent of vaccination?

It is important to verify if a similar event occurred in the vaccinee and family in the past independent of immunization.

IV. 3 Could the current event have occurred in this patient without vaccination (background rate)?

Knowledge of the background incidence of events which may occur in temporal relationship with a vaccine is essential for assessing a cluster of events in terms of the strength of the signal it may provide.

IV. 4. Did this patient have an illness, pre-existing condition or risk factor that could have contributed to the event ?

During an AEFI investigation, by obtaining a detailed history, clinical examination and laboratory investigation in a patient may identify other inherent pre-existing illness, health conditions or risk factors that may have precipitated the AEFI. For example:

IV. 5 Was this patient taking any medication prior to the vaccination?

Medications are known to cause adverse reactions and, when given concurrently with vaccine(s), must be considered as possible coincidental causes of an observed AEFI.

IV.6 Was this patient exposed to a potential risk factor (other than vaccine) prior to the event (e.g. allergen, drug, herbal product etc)?

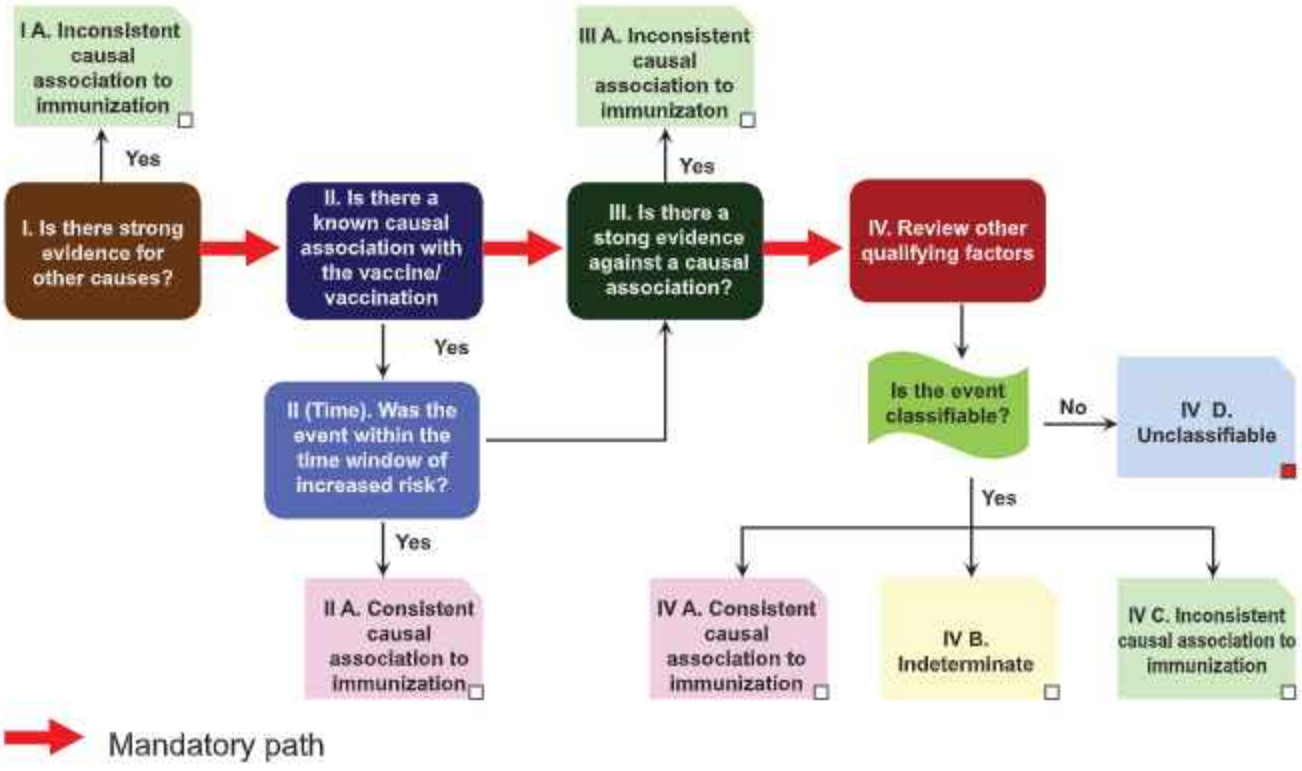
Prior exposure to extrinsic risk factors/toxins may be a clue to the possibility that an AEFI is a coincidental event. One should also consider the possibility of an interaction between a risk factor/toxin and vaccine in causing the AEFI. For example:

- A patient who undergoes a surgical procedure a week prior to vaccination (with an apparently normal post-operative period), may present with fever the day after immunization. One needs to determine if the fever (which is an AEFI) is a coincidental event that occurred as a late complication of surgery or it is due to the vaccine or vaccination (product-related, quality defect-related, or immunization error-related).

Step 3. Algorithm

The algorithm follows the key questions and related answers on the checklist. The stepwise approach of the algorithm helps to determine if the AEFI could be consistent or inconsistent with an association to immunization, an indeterminate outcome or unclassifiable (Figure 11).

Figure 11: Causality Assessment: Algorithm



The algorithm allows the reviewers to focus logically and document their observations to the appropriate conclusions. "Yes" responses in the checklist should have corresponding conclusions in the algorithm. The boxes on the mandatory path (red arrow) correspond to the four major sections in the checklist (I to IV). It is essential that the reviewers evaluate all four boxes using the responses in the checklist.

During the initial stages of the assessment when considering the eligibility (step 1), the reviewer may consider the available information to be sufficient for initiating the causality assessment process. However after completing the checklist (step 2), it may be discovered that the information is insufficient to arrive at a definite conclusion. At this stage of the review, the reviewer may decide to categorize the case as "Unclassifiable" (check-box marked in red in Figure 11). When the conclusion is "unclassifiable", the reviewers should determine the reasons and document why classification was not possible, and all attempts should be made to obtain the necessary supporting evidence for classification.

Step 4. Classification

The final classification is based on the availability of adequate information. After working through the algorithm, a case can be classified as follows:

A. Consistent causal association to immunization

A1. Vaccine product-related reaction; or
A2. Vaccine quality defect-related reaction; or
A3. Immunization error-related reaction; or
A4. Immunization anxiety-related reaction.

B. Indeterminate

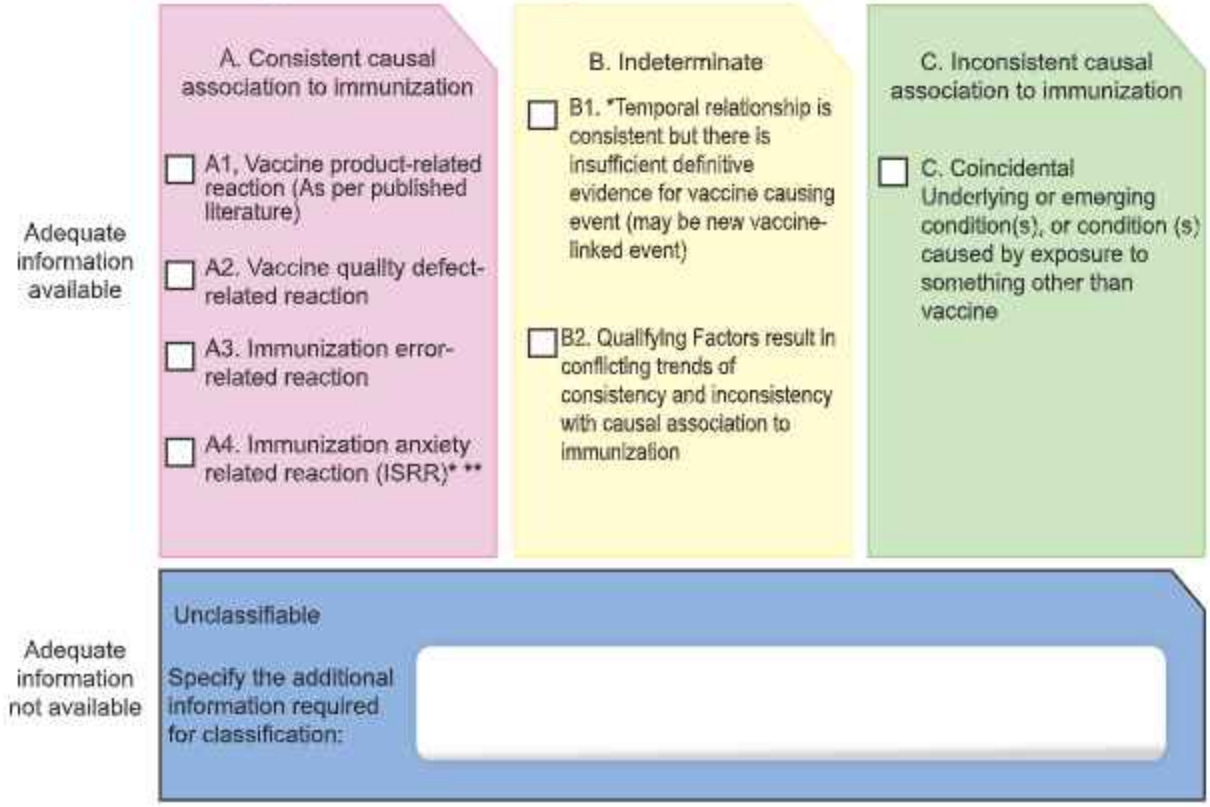
B1. Temporal relationship is consistent but there is insufficient definitive evidence that vaccine caused the event (it may be a new vaccine-linked event). This is a potential signal and needs to be considered for further investigation.
B2. Reviewing factors result in conflicting trends of consistency and inconsistency with causal association to immunization (i.e. it may be vaccine-associated as well as coincidental and it is not possible clearly to favour one or the other).

C. Inconsistent causal association to immunization (coincidental): This could be due to underlying or emerging condition(s) or conditions caused by exposure to something other than vaccine.

Unclassifiable

A Case without adequate information for causality conclusion are categorized as "unclassifiable" and requires additional information for further review of causality. The available information on unclassifiable cases should be placed in a repository or an electronic database which should be periodically reviewed to see if additional information is available for classification and to perform analyses for identifying signals.

Figure 12: Causality Assessment Classification



*B1: This is a potential signal and may be considered for investigation
** Immunization stress related response (ISRR)

7.5 Summarizing the logic of AEFI causality assessment

Causality assessment is performed with the available information and resources that are at the reviewers' disposal at a given point in time. The information and resources may be adequate or inadequate. If a case that is initially evaluated as eligible for classification when assessed is found to have inadequate information, causality assessment is not possible and the case is categorised as unclassifiable. Even with adequate information, the precision of causality is largely determined by the expertise, experience and skill of the assessors (Figure 13).

Figure 13: Summary of classification logic

Summarize the classification logic in the order of priority:
With available evidence, we could conclude that the most likely classification is _____ because:
1.
2.

With available evidence, we could NOT classify the case because _____

Summary

- Causality assessment is the systematic review of individual or population data about an AEFI case to determine the likelihood of a causal association between the event and the vaccine(s) received.
- The quality of the causality assessment depends on factors such as the effectiveness of the reporting system, quality of investigation and the quality of the causality review process.
- Regardless of whether an AEFI is attributable to the vaccine or the vaccination programme, causality assessment determines what steps need to be taken to address the event.

8

Actions and follow-up to AEFI

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

To keep credibility of immunization program high, following actions need to be taken following an AEFI:

8.1 Patient care

It is of utmost importance to ensure that proper and early treatment is received by affected vaccines (patients), regardless of the diagnosis. Mild symptoms such as mild fever and pain are likely to be of short duration and can be managed by assuring and educating parents during immunization. Health workers need to know how to recognize AEFI, how to treat them or refer them to a clinician/ hospital and must report AEFI following the guideline as outlined in chapter 5.

8.1.1 Management of suspected anaphylaxis or collapse after vaccination

Sudden and severe events occurring post-vaccination, especially syncope, are frequently reported as anaphylaxis. However, anaphylaxis following vaccination is considered to be very rare and the risk (in general) is 1-2 cases per million vaccine doses. Recognition and management of anaphylaxis is described in Annex-7.

Events happen without warning. Emergency equipment must be immediately at hand whenever immunizations are given. All vaccinators must be familiar with the practical steps necessary to save life following anaphylaxis. All health facilities must have an emergency kit (AEFI Kit) with adrenaline. The expiry date of the adrenaline should be written on the outside of the emergency kit and the whole kit should be checked three or four times a year.

8.2 Follow up actions

The following table provides a summary of actions that are usually taken when different types of AEFI occur.

Table 14: Actions to be taken upon completion of the investigation/causality assessment

Type of AEFI	Follow-up action
Vaccine -related reaction	If there is a higher reaction rate than expected from a specific vaccine or lot, obtain information from the manufacturer and consult with the WHO regional office to consider: • withdrawing that lot • investigating with the manufacturer • obtaining vaccine from a different manufacturer
Vaccine quality defect related reaction	• If this reaction is related to a particular lot or batch, the distribution of the lot or batch has to be ascertained and specific instructions must be provided on the utilization or non-utilization of the lot or batch. • Inform the national regulatory authority (DGDA) and the marketing authorization holder (the pharmaceutical company) about the AEFI. • WHO-HQ or WHO Uppsala Monitoring Centre should be contacted.
Immunization error-related reaction	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.
Immunization anxiety-related reaction	Assurance to the patients / parents and health (field) staff.
Coincidental	The main objective is to present the evidence showing that there is no indication that the AEFI is a vaccine-related reaction or immunization- error related and, that the most likely explanation is a temporal association between the event and vaccine/vaccination. This communication can be challenging when there is widespread belief that the event was caused by immunization.

In general, it is not advisable to discontinue the immunization programme while awaiting the completion of the investigation. If AEFI causality is not established – depending on the nature of the event, its extent and whether it is ongoing – a further investigation or epidemiological study may be warranted. However, it must be accepted that in some cases the relationship to vaccine will never be clear.

Communication and training are two important follow-up actions. Communication is outlined in detail in Chapter 9.

Summary

- Treating the patient is the priority following an AEFI. Preparedness for managing serious adverse events is important and necessary. Each health facility should have AEFI kit for managing anaphylaxis.
- Anaphylaxis is extremely rare. Syncope/Fainting attacks are common and are often misdiagnosed as anaphylaxis. Administering a single and correct dose of adrenaline by the intramuscular route, even to a patient with syncope but misdiagnosed as anaphylaxis, does not cause harm.
- The response and follow-up to the AEFI will depend on the findings of the investigation.
- Immunization errors will need to be corrected. There should be a checking mechanism to ensure that they do not reappear.
- For coincidental events, the main task is communication to maintain confidence in the immunization programme.
- Training is an important component of the vaccine safety surveillance system and its follow- up activity. Programme managers should use training as an opportunity to strengthen immunization programme in the country.

9

Vaccine safety communication

Vaccines used in Expanded Programme on Immunization (EPI) are extremely safe and effective. But while vaccines are safe, no vaccine is entirely without risk and no immunization programme is entirely free from vaccine safety issues. These issues need to be addressed through proactive communication.

Communication goal

The goal of vaccine safety communication is to maintain public trust in vaccines and immunization safety so as to sustain the immunization programme and achieve a high level of immunization coverage, in order to prevent and control vaccine-preventable diseases in the country.

Specific communication objectives: The communication objectives for different stakeholders are as follows:

Parents and guardians, communities and the public:

- understand and can explain the importance and benefits of vaccines and immunization;
- (after an AEFI episode) have restored confidence in vaccines and immunization and have trust in the national immunization programme; and
- complete the routine immunization schedules, maintaining high immunization coverage.

Health-care providers and other immunization programme implementing stakeholders:

- understand AEFI and risk-benefits of vaccines and immunization;
- can clearly explain vaccine safety issues and related events; and
- demonstrate their enhanced capacities in vaccine safety communication when dealingwith vaccine safety issues and related events.

Media and other partners:

- address vaccine safety issues and related events accurately and objectively;
- are supportive of the national immunization programme; and
- promote the benefits of immunization.

9.1 Communication with families and communities

- Respond in a prompt manner: An immediate response to the bereaved family the moment an AEFI occurs is a good response.
- Disseminate key messages and combat rumours: Timely dissemination of a consistent set of easy to understand key messages to concerned families and communities will help to appease their anxieties and reaffirm their faith in the health system.

Table 15: Key action points for serious AEFI

Serious AEFI such as death/hospitalization/cluster		
Level of intervention		**Follow-up action**
Community level	**HA/ AHI/HI /FWA/FPI/ Vaccinator/ Vaccinator Supervisor**	• Meet the family- parents/ caregivers and empathize with them • Listen patiently to what the parents/public is saying • Ask some elder persons and/or religious leaders/ward counsellor/ward member to accompany you when you go to meet the family • Follow up with the family and ensure their well-being • Respect their space • Assess any community concern and inform the 2nd line supervisors for assistance • Communicate with the parents of other children vaccinated in the same session about their wellbeing • Update the Supervisors
Upz/mun/ zone level	**Local managers: UHFPO, MMO, ZMO/AHO/ HO/MO of the zone**	• Initiate inquiry and communicate with CS/CHO • Take the well-known to the community and most acceptable health staff as appropriate along when you go to meet the family • Get to the source of information and check factual accuracy of the information • Understand the community's perception towards immunization and vaccination history of other children in the family • Take control of the situation and reassure the community without appearing judgmental • Disseminate a consistent set of easy to understand key messages at appropriate times to concerned families and communities to help allay their anxiety and reaffirm their faith on the health system • Identify support groups from within the community who could help convince the community that vaccination at large is beneficial for children

		• Involve school teachers to help in conveying the correct information/message(s) to parents/caregivers of children, and educate them • Review media coverage reports • Keep people and media informed with facts and accurate information • If facts are not yet ready, inform them that the matter is being looked into and the facts will be out soon • Conduct a meeting of opinion leaders and journalists who are supportive to discuss the situation if needed and find possible solutions and a way forward • Assist district AEFI investigation team during investigation
District/CC level	**CS/CHO**	• Initiate AEFI investigation within 24 hours of notification and submit the report on time • Avoid repeated visits to the family • Respect their space • Conduct a meeting of opinion leaders and journalists who are supportive to discuss the situation if needed and find possible solutions and a way forward • Review media coverage reports • Respond to negative media questions with positive answers • Prepare a database of print and electronic media journalists who cover health topics at the District/CC level, with their contact details (before AEFI occurs) • Organize orientation workshops for journalists. • Share feedback with community representatives, when needed
National level	**LD-MNC&AH; PM-EPI, AEFI Focal person, EPI**	• Review media coverage reports • Prepare a database of print and electronic media journalists covering health at the national level with their contact details • handle media queries • Participate in "talk shows" as needed to address rumours and minimize negative impact on immunization • Seek assistance of AEFI Expert Review Committee in crisis • Organize press briefing

9.2 Communication with health-care providers, health workers

Immunization service providers and health professionals at all levels need to be equipped with accurate immunization facts and information about vaccine safety issues/AEFI. They need to have good interpersonal communication (IPC) and counselling skills so that they can explain risks and benefits clearly to parents, guardians and vaccine recipients. Training provides an opportunity to empower health staff with up-to-date information and to discuss the current vaccine safety-related event issues.

When an AEFI occurs, it is crucial for programme managers to encourage and support health-care providers to report adverse events and give them timely feedback on the findings of investigations and causality assessments. This will give health-care providers updated information to communicate to the public, which will help in maintaining public confidence both in the health staff and in the immunization programme.

It is important to be supportive when communicating with frontline health-care providers, and avoid blaming them, particularly in the case of immunization-error related events. This is because due to fear of blame many health workers do not report AEFI.

Whenever a serious AEFI occurs, the security of the local health worker/vaccinator has to be safeguarded, as they might become targets of anger or be confronted by affected community members. The local managers have to be prepared to tackle this situation.

9.3 Communication with community leaders and religious leaders

Community leaders are regarded as credible sources of information. They have the power to shape public opinion and can improve the links between families, communities and health services. Religious leaders also serve as effective communication channels and social mobilizers when it comes to combatting rumours and unfounded negative opinions about vaccine safety and AEFI.

When there is a crisis, early communication with community leaders and religious groups is very important. Provide them an advocacy kit with briefing notes and scripted key messages that they could readily impart to the families and communities.

9.4 Communication with media

The mass media (newspaper, radio, television and social media) plays an important role in the formation of public perception. The media can have a positive or negative influence in the public's views and attitudes towards vaccines and immunization. Build professional relationships with journalists who have a good track record of maintaining high professional standards. If a rumour about vaccine safety begins to circulate, contact these journalists quickly before a crisis around misinformation develops, and give them the facts. The guiding principle for dealing with media must be honesty and building up trust. The effectiveness of our communication is largely determined by whether the audiences perceive us to be trustworthy and believable.

9.4.1 Media management in routine situations

As part of the ongoing communication support to the RI programme, an effective communication plan should be in place.

A good media plan consists of the following:

- Database of journalists: make a list of reporters especially those that deal in health related matters and keep their contact numbers and e mail IDs handy.
- Monitor the media for reports from time to time.
- Develop a media kit: This should contain key messages given in the form of Q&As or frequently asked questions (FAQs), fact sheets.
- Develop spokespersons to respond to media queries from time to time.
- Organize orientation workshops for media personnel.
- Develop a crisis and emergency risk communication plan.

9.4.2 Crisis and emergency risk communication (CERC)

The Crisis and Emergency Risk Communication (CERC) is a tool that helps us provide the public with information to make the best decisions within incredibly challenging time constraints and to accept the imperfect nature of choice. In the EPI, this means responding to vaccine related events, to address public concerns and restore confidence in the vaccine, the vaccinator and the vaccination programme.

Vaccine safety crises are situations in which a real or potential loss of confidence in a specific vaccine or in the immunization programme occurs and are often triggered by identification of Adverse event following immunization (AEFI). A crisis may have a "real" basis arising from genuine vaccine reactions or immunization errors, new study results, temporary suspension or recall of vaccine or vaccine replacement. Alternatively, it may have no legitimate foundation and be initiated and propagated entirely by mistaken rumors. Countries should have in place crisis communication plans at all levels

Six principles of the Crisis and Emergency Risk Communication (CERC)

1. Be the first - crises are time-sensitive: Communicating information quickly is almost always important. For members of the public, the first source of information often becomes the preferred source. Professionals agree that the faster you give up bad news the better, because holding back information implies guilt and ignorance.
2. Be the Right - Information can include what is known, what is not known, and what is being done to fill in the gaps.
3. Be the Credible - accuracy established credibility: Honesty and truthfulness should not be compromised during a crisis. People will believe what you say, need to also tell people what you don't know; you may never have all info when you need it.
4. Express Empathy: Empathy is about bringing yourself into the situation and feeling the same emotions; acknowledging the emotion and feeling the emotion; do not have to feel emotion but need to express that you are; make sure they know you are on their side.

5. Promote Action: People don't care what you know, until they know what action you are asking them to take and care. If you don't' have a specific action, please advise them to stay tuned and stay vigilant, say when should have more info, go about normal activities and ask to check on their neighbours etc.
6. Show Respect: Respectful communication is particularly important when people feel vulnerable, which promotes cooperation and rapport.

Some tips for converting facts into messages during crisis communication

- Concise and focused: When people are scared or anxious, they have a hard time taking in and remembering lots of information.
- Give action steps in positives: Say in case of fire use stairs instead of do not use the elevator. If you repeatedly say, "don't take amoxicillin, don't take amoxicillin, don't take amoxicillin." People eventually are just going to remember amoxicillin.
- Repeat the message: Reach and frequency. Research suggests that messages are more apt to be received and acted upon when the number of people (reach) and the number of times each person hears the message (frequency) go up.
- Personal pronouns: Pronouns personalize the message and help with credibility and identification. "We are committed to…." or "We understand the need for…."
- Use Plain Language: Jargon creates barriers. Instead of "People may suffer morbidity and mortality" say "People exposed may become sick or die." Instead of epidemic or pandemic say Outbreak or Widespread outbreak. Instead of deployed say sent or put in place.
- Avoid speculation and assumptions: Avoid worst case scenario, stick to known facts. Don't' fall for "what ifs."
- Avoid humor: People rarely get joke when are feeling desperate and vulnerable. Remain sensitive

Some frequently asked questions by media person

- Why did this crisis happen?
- Could the situation have been averted had the response been timely and adequate?
- What do you have to say on the occurrence of this incident?
- Who is at fault for this loss and crisis?
- How does the govt plan to handle the situation?
- What compensation being provided to the affected families?
- What are the actions taken so far?

9.4.3 Managing media when an AEFI has occurred

Spokespersons to deal with the media

Media usually appreciate an honest, polite, accurate and authoritative person who can provide them with information they need. Designating the spokesperson(s) to communicate with media limits the possibility of conflicting messages coming from different sources.

The following persons will be the spokesperson at different levels:

- UH&FPO at Upazila and Upazila Municipality
- Civil Surgeon at District and District Municipality
- Chief Health Officer at City Corporation
- Divisional Director-Health at Divisional Level
- Line Director MNC&AH and Programme Manager-EPI & Surveillance at EPI at National level

In addition, prepare a list of potential spokespersons from national level– from AEFI Expert Review Committee, NITAG, Bangladesh Paediatric Association or BMA.

- Spokespersons should be identified, trained and authorized to support media response activities. The upazila, city corporation, districts and divisional level should also identify a second spokesperson to cater for times of need or in an emergency
- All spokespersons are to be notified immediately about any media report and query from all administrative levels using the fastest means of communication, e.g. by e-mail or phone
- If there is a crisis and the reports reach the national media, a press statement should be issued as early as possible (preferably within the first 6 -12 hours). The spokesperson at the national level must respond at the earliest.

Table 16: Actions to be taken on media queries at different level

District Level	
Authority	**Action points**
UHFPO/MMO/ZMO/AHO/ HO	When an AEFI is reported, proactively collects information on the case and note down the details. Spokesperson will address media queries. Share information with CS/CHO.
CS/CHO	Will collect detail information from UHFPO/ZMO/AHO /HO/MO and be prepared to address any media queries. This will help get credible and timely information to the media, killing speculations and building trust as a credible source. When a media query arises, talk to the media and share factual information. The information should be non-speculative. The message should include that the govt is aware of it, is investigating the said AEFI and is also tracking the progress. It is better to give out a written response/press release in case the media report persists, or it is felt that some journalists may misinterpret the message.

CS/CHO	Share the written response with the concerned UHFPO/MMO/AHO/ZMO/HO and the national level simultaneously (since they may get media queries as well). Responses to media have to be time-bound. Factual and timely information will kill speculations. **Recommended timelines/responses to be followed:** • A press release/response statement within 6-12 hours in crisis situation • If queries persist, national level spokespersons to respond at the earliest • Get back to the media with more information/updates as promised. Arrange dialogue with the Divisional AEFI Committee members with media personnel if needed. In case the media did not reach out to the district office but has reported on AEFI cases, Civil Surgeon/ CHO should actively reach out to the reporter who wrote the news and give the correct information. If such media reports continue, ensure that a statement is prepared and mailed to the reporter or the newspaper office or put it up on the website. If the reporter or the newspaper is doing negative stories about the programme without asking for the govt perspective, then a statement with factual information on the AEFI cases and the status of investigation should be prepared and mailed to the editor of the newspaper requesting publishing of the facts or clarifying the issue.
LD-MNC&AH, PM-EPI	**At the national level** Same responses as above If required other technical spokespersons (e.g. NITAG members, Paediatric Association, BMA, AEFI ERC) at the national level should be identified for responses. Ensure there are no conflicting messages by the spokespersons.

9.4.4 Reaching out to Media

There are different ways of reaching out to the media to help communicate with the public. A few of them are listed below:

- Press statement
- Press conference
- Media interview.

Preparing a press statement

Particularly if a severe AEFI is reported, a press statement will be essential. The press statement should include:

- a complete account of the event, specific to its context (e.g. an isolated event or a cluster of AEFI, or a coincidental event)
- an outline of actions taken or planned (such as the AEFI investigation)
- a description of the possible cause of the event (but only when this is known with reasonable certainty and evidence);
- an assurance that corrective action has been taken or will be taken
- Provide information on the five Ws and H of journalism (when, where, who, what, why and how).
- Provide reference to any relevant publication, video material or website
- Provide names and contact details of persons to be reached for additional information or materials.
- Use the Ministry's standard press release format and EPI logo
- Do not use any jargon

Press conference

Press conferences may need to be conducted if an AEFI is reported extensively and widely and there is a need to provide accurate facts and desensationalize the story. A press conference enables all journalists to have the same information, thus there is less likelihood of the event being sensationalized. For press conference everything must be planned well in advance with different stakeholders being present.

How to prepare for a media interview

Before the interview:

- Review the information you communicate – is the data correct? Are the sources reliable?
- Prepare key messages (Annex-10). Key messages used in press releases can be repeated in interviews.

During the interview:

- Maintain eye contact with the interviewer.
- Dress in a professional manner.
- Think before you speak and take time to frame your answers.
- Speak clearly and audibly in simple conversational language.
- Stick to the facts and avoid speculation or personal opinions.
- Make sure you get your key message into the dialogue – more than once if possible.
- Be warm, friendly but determined to get the right message across.
- Be enthusiastic and engaged in the conversation – try not to look nervous, even if you feel uncomfortable about being interviewed.
- Never say, "no comment".

- Remember that there is no such thing as an "off the record" statement that you can be certain the interviewer will keep confidential.
- Try to imagine how the interview will appear to members of the target audience. Will they be persuaded by your message?

Dealing with difficult questions

- Bridge: If you get stuck with a question, move on to your key messages.
- Be assertive, not aggressive.
- Keep calm.
- Take your time and don't let the interviewer interrupt you when giving your key message.
- Make sure you know all the facts.

Facing hostile interviewer

When facing a hostile interviewer, prepare the following techniques:

- **block -** respond to a negative question with a positive answer (e.g. when asked, "How many children have died from immunization?", answer: "Immunization saves lives. Since our immunization programme began X children have been immunized, and of them Y% might have died from one of these diseases. That is the context in which we must consider the tragic, but thankfully rare adverse events which follow immunization."
- **bridge -** having answered a difficult question, move quickly to something linked but positive

Bridge Technique

Question: Does vaccination cause abscesses?
Answer: (Face the element of truth) We know that vaccination can rarely cause abscesses. (here comes the first bridge….) That is why we train staff to avoid them by using sterile Auto Disable (AD) syringe for every child. (Now comes the second bridge) We also purchase only the highest quality vaccines through UNICEF which are WHO prequalified. So we can assure parents/clients that we are providing quality immunization services.

Summary

- Communication with parents, community, staff, other stakeholders and the media is necessary and important.
- During communication make sure to build confidence in the immunization programme. Be aware of the risks and benefits of immunization and the progress and findings of the investigation.
- Communication needs assurance from someone in authority with knowledge and expertise in the subject.
- It is recommended to prepare a communication plan in advance, as this will minimize the negative impact of AEFI-related matters.

10

Analysis of AEFI data

Analysis of data is required to measure the impact of vaccines used in the country immunization programme and to disseminate findings to advise programme managers, the NRA and other stakeholders, including manufacturers.

The number of vaccine product-related reactions will naturally increase with increased vaccine use, so it is essential to calculate antigen (vaccine) specific adverse reaction reporting rates. It is always the rate and not the number of reports that should be evaluated.

Analysis of data on AEFI should consider the following:

- Reporting source (reports received from community and from facility)
- Completeness and timeliness of submitted AEFI report forms;
- Identifying facilities submitting "zero reports";
- AEFI reporting rates (assessing AEFI reporting rate per 100 000 surviving infants; assessing AEFI reporting rate per 100 000 doses of vaccine administered);
- Rates by type of AEFI and by antigen
- Comparison of these observable rates with available or expected known events, or background rates or historic reporting trends.
- Classification of AEFI by cause (number of vaccine product related reactions, number of immunization error, number of coincidences etc.)

10.1 Who should analyse the data

Data analysis could be carried out at different levels of the AEFI surveillance system- the programme implementation level (service delivery level), the subnational level (districts/city corporation) and the national level. The extent and purposes of analysis will vary at each level. Analysis of data at the service provider level is very important for identifying immunization errors and ensuring that corrective action is carried out in a timely manner. Data analysis at higher levels with larger denominators is important to identify rare vaccine safety events and also detect signals.

At the service delivery level

UH&FPO/MMO/AHO/ZMO will analyse the AEFI data on monthly basis. LSO will assist UHFPO in analysing the AEFI data.

At the district /city corporation level

The CS/CHO will analyse the AEFI data on monthly basis. If there is any unusual high rate of AEFI he/she should inform respective UH&FPO/MMO/AHO/ZMO to look into the matter and take appropriate action. LSO will assist CS/CHO in analysing the AEFIs.

At the central level

EPI HQ will also analyse the reports of all AEFIs on monthly/quarterly basis and provide feedback to CS/CHO, NRA, NCL and other partner agencies (WHO, UNICEF etc.)

10.2 How should the data be analysed and interpreted?

Step 1: All reported AEFI data should be line-listed and/or entered into a database. Line-listing will help initial identification of clustering or any unusual or significant reporting events that need further analysis.

Step 2: AEFI data should be tabulated by place, person, time, antigens and type of event (e.g. high fever, abscess). This step further filters the AEFI by different variables and helps programme managers to generate clues for further analysis. Even at this step, it is possible to identify common immunization errors. For example, an increased number of abscesses by one immunization centre/site is more likely to be due to immunization-related error. However, further investigation is necessary to confirm causality.

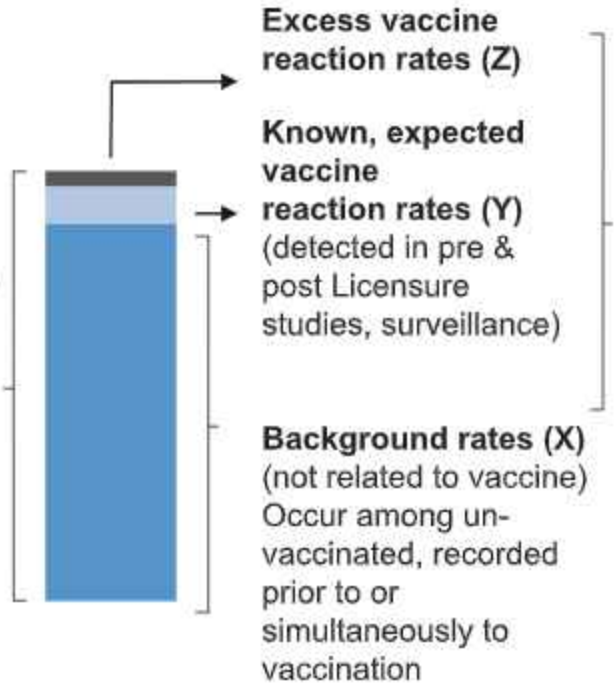
Step 3: AEFI rates should be calculated. The number of doses administered for each antigen is the denominator for calculating reported AEFI rates for each antigen.

For instance, in a hypothetical country X, the registered child population under 1 year of age is 5000. The coverage of MR vaccine is 90%. During the year, 20 febrile seizures were reported following MR vaccination. The numerator for this vaccine reaction (febrile seizures) is 20 and the denominator is number of MR vaccine doses administered. Therefore, denominator = population x coverage = 5000 x 90% = 4500. Thus, the reported rate of febrile seizures is 20 (numerator)/4500 (denominator) x 100 (multiplier) = 0.44%.

Step 4: Rates should be compared and interpreted. Expected vaccine reaction rates that are available for each type of AEFI and antigen (see Annex 1) and WHO vaccine reaction information sheets provide a guide to decision-making on corrective action for reported AEFI. It is also important to know the background rates of reported medical events in the country. Background rates are independent and are not related to the vaccine. Observed (reported) rates include both background rates and vaccine-related rates. Comparison of background rates with reported (observed) rates of AEFI will provide support for a conclusion on the causality of these events being due to a vaccine reaction or not.

Figure 14 shows a comparison of the background rate with the observed rate of an event to determine the vaccine reaction rate (i.e. the rate of events that are actually caused by the vaccine).

Figure 14: Vaccine reaction rate, observed rate and background



*Rates can be expressed per 1000, 10000, 100,000

Vaccine reaction rate= observers (reported) rates-background rates (not related to vaccine)

Vaccine reaction rates are further divided into two subcategories: expected vaccine reaction rates and excess vaccine reaction rates. The WHO vaccine reaction information sheets give the "expected" vaccine reaction rates (the "Y" component in Figure 14), which are based on pre-licensure and post-licensure data. These expected vaccine reaction rates are known rates due to the inherent properties of the vaccines and the response by recipients. If the value exceeds the "expected" vaccine reaction rates, one should consider whether this is a true increase in the vaccine reaction rate or if the values are due to other factors.

Summary

- Data analysis is important for identifying problems and to take corrective actions
- Compare rates but not absolute numbers
- WHO information sheets on vaccine reaction rates provide rates of reactions to specific vaccines that can be helpful when comparing rates
- Comparison of background rates with reported (observed) rates of AEFI will provide support for a conclusion on the causality of these events

11

Role of Staff

Health Assistant (HA) / Family Welfare Assistant (FWA) / Vaccinator

- Detect and report AEFI timely
- Refer patient to hospital, if possible, accompany
- A good communication: reassure the parents/community
- Prevent AEFI due to programme error through strict compliance to proper and safe vaccine handling and injection safety practices

Assistant Health Inspector (AHI) / Family Planning Inspector (FPI) / Health Inspector (HI)

- Encourage and assist HA/FWA to report AEFI timely
- Ensure HA/FWA has adequate AEFI report form
- Inform UH&FPO of AEFI reported by HA/FWA
- Do supportive supervision in order to prevent programmatic errors
- Support HA/FWA to gain confidence of the community following an adverse event
- Supportive communication with public

Medical Technologist- EPI (MT-EPI)/ Equivalent staff at Municipality and city corporation

- Archive all AEFI reports
- Enter AEFI reports in DHIS2
- Maintain weekly line list
- Notify local managers/ respective SIMO about serious AEFI
- Assist the AEFI investigation team
- Assist local managers to Implement corrective measures as suggested by the investigation team

EPI Superintendent/ equivalent staff at City Corporation

- Archive all weekly line list
- Assist the AEFI investigation team
- Assist local managers to Implement corrective measures as suggested by the investigation team

Upazila Health and Family Planning Officer (UH&FPO) / Municipal Medical Officer (MMO) /Health Officer (HO)/ Medical Officer (MO)/ Assistant Health Officer (AHO) / Zonal Medical Officer (ZMO)

- Ensure appropriate case management of an AEFI
- Encourage HA/FWA/Vaccinators to report AEFI
- Analyse AEFI data and provide feedback to field staff
- Support the District/City Corporation investigation team
- Ensure that the AEFI investigation information has been entered in DHIS2
- Provide feedback to field staff on results of investigation and corrective actions to be taken
- Implement corrective action suggested by the investigation team
- Monitor for clustering of AEFI
- Inform Civil Surgeon/ CHO immediately of deaths, hospitalisation, clusters of events, events causing significant community concern
- Provide AEFI update information to field staff
- Staff motivation in AEFI surveillance
- Reassure the parents/ community
- Handle the media appropriately

Medical Officer in Hospitals

- Detect AEFI and report to HSO within 24 hours
- Assist with diagnosis of AEFI
- Ensure appropriate case management
- Cooperate with the Investigation Team
- Inform HSO immediately of deaths and hospitalisation

Local Surveillance Medical Officer (LSO)

- Assist UH&FPO/MMO/CS/CHO in monitoring weekly AEFIs
- Assist the assigned staff to enter the AEFI investigation information in DHIS2
- Assist DSFP in analyse AEFI data
- Report AEFI to SIMO/Health Officer of UNICEF where further investigation is warranted
- Assist in investigating AEFIs
- Assist spokespersons to deal with media

Hospital Surveillance Officer (HSO)

- Assist UH&FPO/ MMO/ CHO /CS in AEFI surveillance
- Encourage reporting within the facility
- Timely report to UHFPO/AHO/ZMO/CHO
- Report AEFI to SIMO/ Health Officer of UNICEF where further investigation is warranted
- Inform UHFPO/AHO/ZMO/CHO immediately of deaths and hospitalisation following immunization
- Assist spokespersons to deal with media

SIMO (WHO) / Health Officer (UNICEF)

- Encourage reporting of AEFI
- Facilitate timely reporting to appropriate authorities
- Assist local managers to ensure quality of reports
- Facilitate data analysis
- Assist in investigation
- Assist in managing the AEFI case
- Assist spokespersons to deal with media
- Provide need-based assistance to District/ City Corporation AEFI committee

EPI Divisional Coordinator (WHO)

- Monitor and evaluate AEFI surveillance with SIMO
- Support SMO to facilitate AEFI surveillance activities
- Assist in AEFI investigation
- Coordination with CS /CHO and Divisional Director-Health
- Provide need-based assistance to Divisional AEFI committee

Civil Surgeon (CS) / Chief Health Officer (CHO)

- Ensure a functioning AEFI surveillance system in the district/CC
- Notify serious AEFIs to PM-EPI
- Monitor timely reporting of AEFI
- Facilitate investigation of serious AEFI
- Ensure appropriate case management
- Ensure enforcement of corrective action
- Analysis of AEFI data and feed back to Health facilities including UHC/Municipalities/zones
- AEFI Surveillance review with UH&FPO/ zonal officers/cc doctors
- Monitoring of AEFI surveillance in the district /cc
- Communicate with media

Annexures

Annex-1

Frequency of Vaccine Adverse Reactions of Commonly Used Vaccines

BCG Vaccine Summary

Vaccine Adverse Reactions	Frequency category
Injection site reaction - papule, mild ulceration or scar	Very Common
Local abscess, Keloid, Lymphadenitis, Suppuration	Uncommon to Rare
Osteitis	Rare to Very Rare
Disseminated BCG	Very Rare
Immune Reconstitution Inflammatory Syndrome (IRIS)	Very Rare

Hepatitis A Vaccines Summary

Vaccine Adverse Reactions	Frequency category
Soreness- children	Very common
Soreness- adults	Very common
Induration at the injection site	Common
Inj. site erythema and pain after booster doses in children	Common
Inj. site erythema and pain after booster doses in adults	Very common
Headache in children	Common
Headache in adults	Very common
Malaise	Common
Feeding problems	Common
Fatigue, fever, diarrhoea and vomiting	Common

Hepatitis B Vaccines Summary

Vaccine Adverse Reactions	Frequency category
Pain	Very Common to common
Erythema	Common
Swelling	Common
Temperature greater than 37.7°C	Common
Headache	Common
Anaphylaxis	Very rare

DTP Vaccines Summary

Vaccine Adverse Reactions	Frequency category
Whole cell vaccines	
Fever 100.1 to 101	Very Common
Fever 101.1 to 102	Very Common
Fever > 102	Common
Redness 1 - 20 mm	Very Common
Redness > 20 mm	Very Common
Swelling 1 - 20 mm	Very Common
Swelling > 20 mm	Very Common
Moderate Pain	Very Common
Severe pain	Very Common
Moderate fussiness	Very Common
Severe fussiness	Very Common
Drowsiness	Very Common
Anorexia	Very Common
Vomiting	Very Common
Persistent screaming	Common
HHE	Rare
Seizures	Very rare
Encephalopathy	Very Rare
Anaphylaxis	Very Rare

Vaccine Adverse Reactions	Frequency category
Acellular vaccines	
Fever 100.1 to 101	Very Common
Fever 101.1 to 102	Common
Fever :- 102	Uncommon
Redness 1 - 20 mm	Very Common
Redness > 20 mm	Common
Swelling 1 - 20 mm	Very Common
Swelling > 20 mm	Common
Moderate Pain	Common
Severe pain	Uncommon
Moderate fussiness	Very Common
Severe fussiness	Common
Drowsiness	Very Common
Anorexia	Very Common
Vomiting	Very Common
Persistent screaming	Uncommon
HHE	Rare
Seizures	Very Rare
Encephalopathy	No documented risk
Anaphylaxis	Rate undocumented

JE Vaccine Summary

Vaccine type	Frequency category
Inactivated Vero cell-derived	
Vi-TT	
■ Pain, redness, induration, swelling and tenderness at injection site	Very common
■ Rash and other skin lesions	Very common
■ Fever, headache and other mild neurological conditions	Very common
■ Gastrointestinal disorders	Very common
■ Acute disseminated encephalomyelitis (ADEM)	Very rare
■ Neurological events: Encephalitis, encephalopathy, convulsions, peripheral neuropathy, transverse myelitis and aseptic meningitis	Very rare
Inactivated Mouse brain-derived	
■ Injection site reactions; Pain, redness, induration, swelling and tenderness	Very common
■ Headache, malaise, myalgia, low-grade fever, nausea, vomiting, abdominal pain, rash, chills and dizziness	Very common to common
■ Hypersensitivity reactions	Very common
■ Anaphylaxis	Very rare
Live attenuated SA-14-14-2	
■ Injection site reactions	Very common
■ Fever, vomiting, abnormal crying, drowsiness, appetite loss and irritability	Very common
■ Hypersensitivity reactions	No reports
Live recombinant	
■ Injection site reactions	Very common
■ Fever, vomiting, abnormal crying, drowsiness, appetite loss and irritability	Very common
■ Hypersensitivity reactions	No reports

Varicella Zoster Vaccines Summary

Vaccine Adverse Reactions	Frequency category
Monovalent varicella vaccine	
■ Fever	Very common
■ Injection site reactions	Very common to common
■ Skin rash at injection site	Common
■ Skin rash generalised	Common
Combination MMRV	
■ Fever	Very common
■ Skin rash	Very common
Monovalent varicella vaccine	
■ Febrile seizures (with MMR via sesparate injection)	Rare
Combination MMRV (age 12-23 months)	
■ Febrile seizures	Rare

Hib Vaccines Summary

Vaccine Adverse Reactions	Frequency category
■ Fever	Common
■ Injection site reactions	Very common

Pneumococcal (conjugated & unconjugated) vaccines Summary

Vaccine Adverse Reactions	Frequency category
■ Injection site reactions	Very common
■ Fever	Uncommon

Polio Vaccines Summary

Vaccine Adverse Reactions	Frequency category
Oral Polio Vaccine (OPV)	
■ VAPP	
- Recipient VAPP	Very Rare
- Total VAPP	Very Rare
Inactivated Polio Vaccine (IPV)	
■ Injection site erythema	Common
■ Induration	Common to Very common
■ Tenderness	Very common

Human Papilloma Vaccines (HPV) Summary

Vaccine Adverse Reactions	Frequency category
Bivalent HPV Vaccine	
■ Injection site reactions, erythema, swelling	Very common
■ Pyrexia	Common
■ Urticaria	Common
■ Headache	Very common
■ Myalgia	Very common
■ Arthralgia	Very common
■ Gestrointestinal disorders	Very common
■ Fatigure	Very common
■ Rash	Common
Quadrivalent HPV Vaccine	
■ Injection site reactions, erythema, swelling	Common to very common
■ Pyrexia	Very common
■ Urticaria	Common
■ Headache	Very common
■ Myalgia	Common
■ Arthralgia	Common
■ Gestrointestinal disorders	Very Common
■ Anaphylaxis	Very Rare

Typhoid Vaccine Summary

Vaccine type	Frequency category
Ty21a	
■ Fever	Uncommon to common
■ Vomiting	Uncommon to common
■ Diarrhoea	Common
ViCPS	
■ Low grade fever [<39c)	Common
■ Local erythema	Common to very common
■ Soreness	Common to very common
■ Swelling	Common to very common
Vi-TT	
■ Injection site pain	Only clinical trial data available
■ Fever	Only clinical trial data available

Rotavirus Vaccines Summary

Vaccine Adverse Reactions	Frequency category
■ Intussusception	Very rare with first dose; none after subsequent doses

Measles Vaccines Summary

Vaccine Adverse Reactions	Frequency category
■ Injection site reactions	Very common
■ Fever	Common to very common
■ Rash	Common
■ Febrile seizures	Rare
■ Encephalomyelitis	Very rare
■ Thrombocytopenia	Very rare
■ Anaphylaxis	Very rare

Rubella Vaccines Summary

Vaccine Adverse Reactions	Frequency category
■ Fever	Common
■ Injection site reactions	Very common
■ Acute Arthralgia	very common
■ Acute Arthritis	very common

Mumps Vaccines Summary

Vaccine Adverse Reactions	Frequency category
■ Injection site reactions	Very common
Parotid swelling	Common
Aseptic meningitis	Very common
Orchitis, Sensorineural deafness, acute myositis	Case reports

Key

Very common	> 1/10	> 10%
Common	> 1/100 and < 1/10	> 1% and < 10%
Uncommon	> 1/1,000 and < 1/100	> 0.1% and < 1 %
Rare	> 1/10,000 and < 1/1,000	> 0.01% and < 0.1%
Very rare	< 1/10,000	< 0.01%

Annex-2

Case Definitions and Treatments for AEFI

Adverse event	Case definition	Treatment	Vaccines Involved
Acute flaccid paralysis (Vaccine associated paralytic poliomyelitis)	Acute onset of flaccid paralysis within 4 to 30 days of receipt of oral poliovirus vaccine (OPV), or within 4 to 75 days after contact with a vaccine recipient and neurological deficits remaining 60 days after onset, or death.	No specific treatment available; supportive care.	OPV
Anaphylactoid reaction (acute hypersensitivity reaction)	Exaggerated acute allergic reaction, occurring within 2 hours after immunization, characterized by one or more of the following: ▪ Wheezing and shortness of breath due to bronchospasm ▪ Laryngospasm/laryngeal oedema ▪ One or more skin manifestations, e.g. hives, facial oedema, or generalized oedema	Self-limiting Anti-histamines may be useful	All
Anaphylaxis	Severe immediate (within 1 hour) allergic reaction leading to circulatory failure with or without bronchospasm and/or laryngospasm/laryngeal oedema.	Adrenaline injection (See Annex- 7)	All
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 immunocompromised individuals.	Should be treated with anti-tuberculous regimens including isoniazid and rifampicin.	BCG
Encephalopathy	Acute onset of major illness characterized by any two of the following three conditions: ▪ seizures ▪ severe alteration in level of consciousness lasting for one day or more ▪ distinct change in behaviour lasting one day or more Needs to occur within 48 hours of DPT vaccine or from 7 to 12 days after measles vaccine, to be related to immunization.	No specific treatment available; supportive care.	Measles, Pertussis

Adverse event	Case definition	Treatment	Vaccines Involved
Fever	The fever can be classified (based on rectal temperature) as: ▪ Mild fever: 100.4°F to 102°F (38 to 38.9°C), ▪ High fever: >102°F to 104.7°F (39 to 40.4°C) and ▪ Extreme fever (hyperpyrexia): 104.8°F or higher (>40.5°C)	Symptomatic; paracetamol.	All
Hypotonic hypo responsive 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	The episode is transient and self-limiting, and does not require specific treatment. It is not a contraindication to further doses of the vaccine.	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, culture), Sterile abscess if no evidence of bacterial Infection on culture. Sterile abscesses are usually due to the inherent properties of the vaccine.	Incise and drain; antibiotics if bacterial.	All
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).	Heals spontaneously (over months) and best not to treat unless lesion is sticking to skin. If so, or already draining, surgical drainage and local instillation of anti-tuberculous drug. Systemic treatment with anti-tuberculous drugs is ineffective	BCG

Adverse event	Case definition	Treatment	Vaccines Involved
Osteitis/ Osteomyelitis	Inflammation of the bone with isolation of Mycobacterium bovis BCG strain.	Should be treated with anti-tuberculous regimens including isoniazid and rifampicin.	BCG
Persistent inconsolable screaming	Inconsolable continuous crying lasting 3 hours or longer accompanied by high pitched screaming.	Settles within a day or so; analgesics may help.	DPT
Seizures	Occurrence of generalized convulsions that are not accompanied by focal neurological signs or symptoms. Febrile seizures: if temperature elevated >100.4°F (rectal) Afebrile seizures: if temperature is normal	Self-limiting; supportive care; paracetamol and cooling if febrile; rarely anticonvulsants.	All, especially DPT and Measles
Sepsis	Acute onset of severe generalized illness due to bacterial infection and confirmed by positive blood culture (if possible). Needs to be reported as possible indicator of programme error.	Critical to recognize and treat early. Urgent transfer to hospital for intravenous antibiotics and fluids.	All
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 duration ▪ requires hospitalisation. Local reactions of lesser intensity occur commonly and are trivial and do not need to be reported.	Settles spontaneously within a few days to a week. Symptomatic treatment with analgesics. Antibiotics are inappropriate.	All
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. Needs to be reported as possible indicator of programme error.	Critical to recognize and treat early. Urgent transfer to hospital for intravenous antibiotics and fluids.	All

Annex-3

এইএফআই (AEFI) রিপোর্ট ফরম

সেকশন ১ : রোগীর তথ্য

রোগীর নাম : ..... লিঙ্গ: ☐ ছেলে ☐ মেয়ে জন্ম তারিখ (দিন/মাস/সাল): ...../...../..... অথবা বয়স : .....

মাতার নাম : ..... পিতার নাম : ..... স্বামীর নাম (প্রযোজ্য ক্ষেত্রে) : .....

ফোন নম্বর : ..... জন্মনিবন্ধন নং (যদি থাকে) : ..... জাতীয় পরিচয় পত্র নং (যদি থাকে) : .....

বাড়ি/জিআর নম্বার: ..... মহল্লা/গ্রাম : ..... ওয়ার্ড : ..... ইউনিয়ন : .....

উপজেলা/পৌরসভা/জোন : ..... জেলা/ সিটি করপোরেশন : ..... বিভাগ: .....

সেকশন ২ : রিপোর্টারের তথ্য

রিপোর্টারের নাম : ..... পদবী : ..... প্রতিষ্ঠান : .....

উপজেলা/পৌরসভা/জোন : ..... জেলা/ সিটি করপোরেশন : ..... বিভাগ : .....

টেলিফোন : ..... ইমেইল (যদি থাকে) : ..... স্বাক্ষর : .....

সেকশন ৩ : টিকাদান কেন্দ্রের তথ্য

টিকাদান কেন্দ্রের নাম : ..... টিকাদান কেন্দ্রের ঠিকানা: সাব ব্লক/ মহল্লা..... ওয়ার্ড .....

ইউনিয়ন ..... উপজেলা/পৌরসভা/জোন ..... জেলা/ সিটি করপোরেশন ..... বিভাগ .....

সেকশন ৪ : টিকা ও ডাইলুয়েন্ট প্রদানের তথ্য

টিকা						ডাইলুয়েন্ট				
টিকার নাম	প্রদানের তারিখ	প্রদানের সময়	ডোজ (১ম, ২য়, ইত্যাদি)	ব্যাচ/লট নং	মেয়াদোত্তীর্ন তারিখ	ডাইলুয়েন্টের নাম	ব্যাচ/লট নং	মেয়াদোত্তীর্ন তারিখ	মেশানোর তারিখ	মেশানোর সময়

ব্যাচ/লট নং এবং মেয়াদোত্তীর্ণ তারিখ জেলা, উপজেলা, মিউনিসিপালিটি, সিটি করপোরেশন, জোন ও ওয়ার্ড (শুধুমাত্র ডিএনসিস ও ডিএসসিসির ক্ষেত্রে প্রযোজ্য) লেভেলের রিপোর্টিং ফ্যাসিলিটি পুরন করবে।

সেকশন ৫.(i) : টিকা পরবর্তী বিরূপ ঘটনা		
☐ ফোঁড়া	☐ খিঁচুনি ☐ জ্বর সহ খিঁচুনি ☐ জ্বর ব্যতীত খিঁচুনি	☐ ইনজেকশনের জায়গায় অনবরত রক্তক্ষরন
☐ জ্বর- ১০২° ফা, এবং এর বেশি	☐ গলা (Cervical) এবং/অথবা বগলের (Axillary) গ্রন্থি ফুলে যাওয়া	☐ এএফপি
☐ ইনজেকশনের জায়গায় মারাত্মক প্রতিক্রিয়া: যেমন লাল হওয়া, ফুলে যাওয়া ☐ তিন দিনের বেশি ☐ নিকটবর্তী অস্থিসন্ধি (জয়েন্ট) ছাড়িয়ে যাওয়া	☐ অজ্ঞান হয়ে যাওয়া	☐ এনাফাইলেক্সিস
☐ ইনজেকশনের জায়গায় শক্ত হওয়া	☐ সাময়িকভাবে মূর্ছা যাওয়া	☐ টক্সিক শক সিনড্রম
☐ লালচে দানা/ ফুসকুরি	☐ ক্রমাগত জোরে জোরে চিৎকার দেওয়া	☐ এনকেফালোপ্যাথি
☐ অন্যান্য (নির্দিষ্ট করে লিখুন) :		

সেকশন ৫. (ii) : হাসপাতালে ভর্তি হলে ভর্তির তারিখ : ...../...../....	☐ মৃত্যু হলে মৃত্যুর তারিখ : ...../...../....	☐ জনসাধারনের মধ্যে মারাত্মক উদ্বেগ

সেকশন ৬ : এইএফআই শুরু ও রিপোর্টের তারিখ	
এইএফআই শুরু হওয়ার তারিখ :...../..../.... শুরু হওয়ার সময় :...../..../.... এইএফআই রিপোর্ট করার তারিখ: ...../...../.....	কোথা থেকে রিপোর্ট করা হয়েছে ☐ মাঠ পর্যায় ☐ হাসপাতাল

সেকশন ৭ : এইএফআই তদন্ত এবং প্রকারভেদ (জেলা, উপজেলা, মিউনিসিপালিটি, সিটি করপোরেশন ও জোন লেভেলের রিপোর্টিং ফেসিলিটি পুরন করবে)

রিপোর্ট গ্রহণ করার তারিখ(দিন/মাস/সাল): ..... /..... /			আজকের তারিখ (কম্পিউটারে ডাটা এন্ট্রির তারিখ): ..... /..... / .....
মারাত্মক এইএফআই ?: ☐ হ্যাঁ ☐ না হ্যাঁ হলে ☐ মৃত্যু ☐ জীবন আশংকাজনক ☐ বিকলঙ্গতা ☐ হাসপাতালে ভর্তি ☐ জন্মগত ত্রুটি ☐ অন্যান্য গুরুতর স্বাস্থ্য সংক্রান্ত ঘটনা (নির্দিষ্ট করে লিখুন).....			
তদন্তের প্রয়োজন কি-না?: ☐হ্যাঁ ☐না	উত্তর হ্যাঁ হলে তদন্ত শুরু করার তারিখ (দিন/মাস/সাল): ..... / ..... /	তদন্ত শেষ হয়েছে ? ☐ হ্যাঁ ☐ না	তদন্ত শেষ হবার তারিখ (দিন/মাস/সাল): -----/------/--------
পরিনতি (শুধুমাত্র মারাত্মক এইএফআই-এর ক্ষেত্রে): ☐ সুস্থ হচ্ছে ☐ সুস্থ হয়েছে ☐ সুস্থ হয়েছে তবে কিছু সমস্যা রয়ে গেছে ☐ সুস্থ হয়নি ☐ মৃত্যু ☐ অজানা			
কেস আইডি নং:			
কর্মকর্তার নাম:	পদবী :		স্বাক্ষর : .....
ইপিআই-প্রধান কার্যালয়, ঢাকা পূরন করবে। বিশেষজ্ঞ পর্যালোচনা কমিটি দ্বারা সম্পাদিত চূড়ান্ত প্রকারভেদ:			

AEFI REPORT FORM

(English Translation)

Section 1: Patient's detail

Name of the Patient: ..... **Sex:** ☐ M ☐ F **Date of birth (DD/MM/YYYY) :** ...../...../..... **OR Age :** .....

Name of Mother :.....	Name of Father :	Name of Husband (if applicable)	Telephone number :	
Birth ID (if available) :	National ID (if available):	House/ GR No. :	Mahalla/ Village:	Ward : .....
Union :	Upz./Mun./Zone	District/CC	Division.....	

Section 2: Reporter's detail

Reporter's name: ..... Designation : ..... Institution/organization: .....

Upz/Mun/Zone: ..... Dist/CC: ..... Division : .....

Phone: ..... Email (if available): ..... **Signature:** .....

Section 3: *Vaccination centre* detail

Name of vaccination centre: ..... *Address: Sub-block / Mahalla* ..... Ward.....

Union..... *Upz/Mun/Zone*..... *Dist/CC* ..... *Division*.....

Section 4: Details of vaccines/diluents administered

Vaccine						***Diluent***				
Name of vaccine	Date of vaccination	Time of vaccination	Dose (1st, 2nd, etc.)	Batch/ Lot number	Expiry date	Name of diluent	Batch / Lot number	Expiry date	Date of reconstitution	Time of reconsti-tution

Note: Batch/Lot number and expiry date to be filled up by the reporting facility

Section 5 (i) : Types of adverse event			
☐ Abscess		☐ Unconscious	☐ AFP
☐ Fever (≥ 102⁰ F)	☐ Rash	☐ Fainting	☐ Anaphylaxis
☐ Severe local reaction ☐ > 3 days ☐ beyond nearest joint	☐ Convulsion/Seizure ☐ febrile ☐ afebrile	☐ Persistent screaming	☐ Toxic shock syndrome ☐ Encephalopathy
☐ **Nodule**	☐ BCG lymphadenitis	☐ Continuous bleeding from injection site	
☐ **Other (specify):**			
Section 5 (ii) Hospitalised: Date ...../...../..... ☐ Died: Date ...../...../..... ☐ Significant community concern			
Section 6: Date of AEFI onset and reporting			
Date of AEFI onset: ...../...../.....	Time of onset: AM/ PM	Date of Reporting :.....	AEFI is reported from: ☐ Community ☐ Health Facility

Section 7 : AEFI investigation and classification Reporting facility of District, Upazila, Municipality, City corporation or Zone level to complete:

Date report received (DD/MM/YYYY): ..... / ..... /		Today's Date (DD/MM/YYYY): ..... / ..... /	
Serious AEFI ?: ☐ Yes ☐ No, If Yes ☐ Death ☐ Life threatening ☐ Disability ☐ Hospitalization ☐ Congenital anomaly ☐ Other important medical event (specify)			
Investigation required?: ☐ Yes ☐ No	If yes, date investigation started (DD/MM/YYYY): ..... / ..... /	Investigation completed ☐ Yes ☐ No	Date investigation completed (DD/MM/YYYY): ..... / ..... / .....
Outcome (only for serious AEFI): ☐ Recovering ☐ Recovered ☐ Recovered with sequelae ☐ Not recovered ☐ Died ☐ Unknown			
Case ID Number:			
EPI-Head Quarter, Dhaka to complete Final classification by the Exert Review Committee:			
Officer in charge Name: .....**Designation :** .....**Signature :**			

Annex-4

AEFI Surveillance Monitoring Indicators

Monitoring all AEFI reports

1. AEFI reporting rates per 100,000 surviving infants

No. of total AEFI / total No. of surviving infants X 100,000 (Minimum Target 10)

2. AEFI reporting rate per 100,000 doses administered

No. of total AEFI / total No. of dose administered X 100,000 (No Target)

3. Completeness of Reporting

No. of reporting units submitted the passive reports (including zero reports) weekly/ No. of reporting units expected to submit the passive reports in the same time period x 100 (Target 80%)

4. Timeliness of Reporting

No. of reporting units submitted the passive reports (including zero reports) weekly on time / No. of reporting units expected to submit the passive reports in the same time period x 100 (Target 80%)

5. Percentage of reporting units submitting "zero reports"

No. of reporting units submitted "zero reports"/ Total No. of reporting units submitted reports in the same time period x 100 (No Target)

6. Percentage of serious AEFI cases

No. of serious AEFI cases/ Total No. AEFI cases x 100 (No target)

Monitoring serious AEFI reports

7. Percentage of serious AEFI case investigation initiated on time

No. of serious AEFI case investigation initiated within 24 hours of notification / Total No. of serious AEFI cases x 100 (Target ≥ 80%)

8. Percentage of serious AEFI cases investigation completed on time

No. of serious AEFI cases investigated and submitted to the divisional AEFI ERC within 7 days of case notification/ No. of serious AEFI cases x 100 (Target≥80%)

9. Percentage of serious AEFI cases classified by the Divisional AEFI ERC on time

No. of serious AEFI cases reviewed and classified by the divisional AEFI ERC within 3 months of completion of investigation / No. of serious AEFI case investigation completed x 100 (Target ≥ 80%)

10. Percentage of serious AEFI cases classified by the National AEFI ERC on time

No. of serious AEFI cases reviewed and classified by the national AEFI ERC within 3 months of submitting the report by the divisional AEFI ERC committee/ No. of serious AEFI cases reviewed and classified by the divisional AEFI ERC x 100 (Target ≥ 80%)

Annex-5

AEFI CASE INVESTIGATION FORM

An AEFI case investigation should be initiated within 24 hours of notification.
This form to be completed by the AEFI Investigation Team

Investigation ID: BAN AEFI _ _ ___ __ ___	Date AEFI reported: _____
	Date investigation started: _____

Demographic data of the patient:

Name of the child/woman: _____ Date of Birth/Age: _____

Sex: ❑ Male ❑ Female

Name of Mother/Father/Husband: _____

Address: House/GR No. _____Para/Village: _____ Mahalla/Rural Ward: ____

Union/Urban Ward _____ Upazila/Mun/Zone: _____ District/CC: _____

Most Recent Immunization history:

Date and time of vaccination	Vaccine & dose number	Site of administration	Vaccination centre	Vaccinated by

Information about the vaccines and diluents administered to the patient:

Vaccines	Manufacturer	Lot no/ batch no	Expiry Date
Diluents			

Suspected vaccine which caused AEFI:

Describe the adverse event in detail:

H/O present illness:

Date of onset of AEFI: _____ Time of onset of AEFI: _____

Date of hospitalization: _____ Time of hospitalization: _____

Date of death: _____ Time of death: _____

Examination Findings:

Pulse	:	/min	Temp	:	°F
BP	:	mm of Hg	Heart Rate	:	/min
Resp. Rate	:	/min	Lungs (wheeze, creps, ronchi)	:	
Skin change	:		Size of skin lesion	:	cm
Cyanosis	:		Pupil (reaction to light)	:	
Kernig's sign	:		Neck stiffness	:	
Level of Consciousness			Lymph Node	:	
Jerks	:				
Cranial nerve abnormality	:				

Other Abnormal Signs (if any):

Treatment:

Provisional Diagnosis:

Outcome:

Additional information about the patient: (write yes or no, if yes specify)

Past H/O similar event	:
Reaction after previous vaccination	:
H/O allergy	:
Pre-existing illness/ disorder	:
Current medication (for other than AEFI)	:
H/O hospitalization in last 30 days with cause	:
Recent H/O trauma with date, time, site and mode	:
Family history of any disease or allergy	:

Community investigation:

No. of cases immunized with suspected vaccine in same session	:
No. of cases of same adverse events found in immunized children/women	:
No. of cases of same adverse events found in non- immunized population	:

EPI Management Practice (fill up this section by asking and observing practice):
Write yes or no where applicable, if yes specify

EPI store:

Temp inside ILR (°C)	:
Temp of freezer (°C)	:
Correct procedure of storing vaccines, diluents and syringes followed	:
Any other object (other than EPI vaccines and diluents) in the ILR or freezer	:
Partially used reconstituted vaccines in the ILR	:
Unusable vaccines (expired, no label, VVM stage 3 & 4, frozen) in the ILR	:
Unusable diluents (expired, manufacturer not matched, cracked, dirty ampoule) in the store	:

Transportation:

Type of vaccine carrier used	:
Vaccine carrier packed properly	:
Vaccine carrier sent to the EPI site on the same day of vaccination	:
Vaccine carrier returned from the EPI site on the same day of vaccination	:
Conditioned ice-pack used	:

Reconstitution:

Correct procedure followed	:
Correct amount of diluent used	:
Used separate syringe for each vial	:
Matching diluent used	:

Injection technique:

Correct dose and route	:
Non-touch technique followed	:
Vial shaked before each injection	:
Contraindication assessed	:
How many AEFI reported from vaccination sites of the same worker in the last 30 days?	:
Training on EPI received by the vaccinator: (specify the last training including date)	:

Laboratory investigation(s) conducted?: Yes❑ No❑ If yes, mention the tests (attach copy of the reports)

Assessment:

Conclusion about cause of AEFI: tick categories, rank if more than one cause:				
Immunization error	**Vaccine product - related reaction**	**Vaccine quality defect -related reaction**	**Immunization anxiety - related reaction**	**Coincidental**
❑ Non-sterile injection ❑ Vaccine prepared incorrectly ❑ Faulty administration technique/site ❑ Faulty vaccine transportation ❑ Faulty vaccine storage ❑ Other:	❑	❑	❑	❑
Reason(s) for conclusion:				

Corrective Actions:

Recommendations:

Additional Notes (attach additional paper):

Investigation Team Details:

1. Name: _____ Designation: _____ Signature: _____
2. Name: _____ Designation: _____ Signature: _____
3. Name: _____ Designation: _____ Signature: _____
4. Name: _____ Designation: _____ Signature: _____
5. Name: _____ Designation: _____ Signature: _____
6. Name: _____ Designation: _____ Signature: _____
7. Name: _____ Designation: _____ Signature: _____

Date Investigation Completed: ____/____/_____

Notes:

1) Investigation team will submit the filled AEFI investigation form to the Chairperson of the District/CC AEFI Committee. Attach copy of all medical records e.g. prescription, treatment sheet (if patient is hospitalised), laboratory investigation reports (if any), death certificate & autopsy report (in case of death, if any) etc. with the investigation form. Copy of the AEFI report form should also be attached with the investigation report.
2) Chairperson of the District/CC AEFI Committee will send the investigation report with all attachment to the Divisional AEFI Committee with a copy to Programme Manager-EPI & Surveillance.
3) In case of cluster, use separate investigation form for each of the case.

Step 1 (Eligibility) Worksheet for AEFI causality assessment

Annex-6

Patient ID/ Name : PQ **DoB/ Age: 5 Months** **Sex: ✓ Male/ Female**

Name one of the vaccines administered before this event	What is the Valid Diagnosis?	Does the diagnosis meet a case definition?

Create your question on causality here

Has the _____vaccine / vaccination caused _____(The event for review in step 2)

Is this case eligible for causality assessment? ✓ Yes/ No; If, "Yes", proceed to step 2

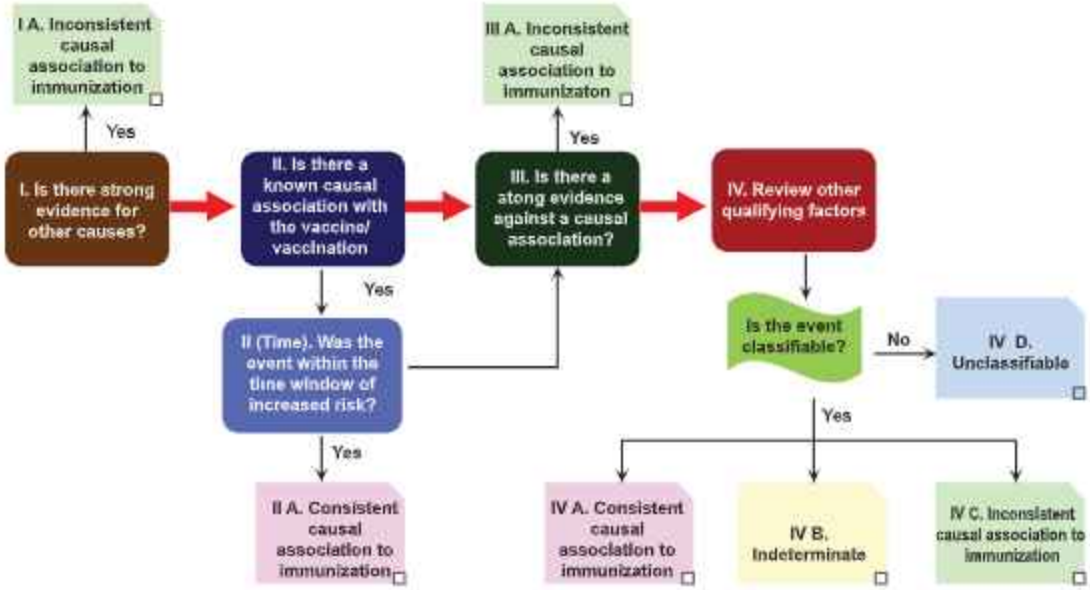
Step 2 (Event Checklist) ✓ (check) all boxes that apply

I. Is there strong evidence for other causes?	Y N UK NA	Remarks
1. In this patient, does the medical history, clinical examination and/ or investigations, **confirm** another cause for the event?	☐☐☐☐	
II. Is there a known causal association with the vaccine or vaccination?		
Vaccine product		
1. Is there evidence in published peer reviewed literature that this vaccine may cause such an event if administered correctly?	☐☐☐☐	
2. Is there a biological plausibility that this vaccine could cause such an event?	☐☐☐☐	
3. In this patient, did a specific test demonstrate the causal role of the vaccine?	☐☐☐☐	
Vaccine quality		
4. Could the vaccine given to this patient have a quality defect or is substandard or falsified?	☐☐☐☐	
Immunization error		
5. In this patient, was there an error in prescribing or non-adherence to recommendations for use of the vaccine (e.g. use beyond the expiry date, wrong recipient etc.)?	☐☐☐☐	
6. In this patient, was the vaccine (or diluent) administered in an unsterile manner?	☐☐☐☐	

7. In this patient, was the vaccine's physical condition (e.g. colour, turbidity, presence of foreign substances etc.) abnormal when administered?	☐☐☐☐	
8. When this patient was vaccinated, was there an error in vaccine constitution/preparation by the vaccinator (e.g. wrong product, wrong diluent, improper mixing, improper syringe filling etc.)?	☐☐☐☐	
9. In this patient, was there an error in vaccine handling (e.g. a break in the cold chain during transport, storage and/or immunization session etc.)?	☐☐☐☐	
10. In this patient, was the vaccine administered incorrectly (e.g. wrong dose, site or route of administration; wrong needle size etc.)?	☐☐☐☐	
Immunization anxiety (Immunization Triggered Stress Response - ITSR)		
11. In this patient, could this event be a stress response triggered by immunization (e.g. acute stress response, vasovagal reaction, hyperventilation or anxiety)?	☐☐☐☐	
II (time). If "yes" to any question in II, was the event within the time window of increased risk?		
12. In this patient, did the event occur within a plausible time window after vaccine administration?	☐☐☐☐	
III. Is there strong evidence against a causal association?		
1. Is there a body of published evidence (systematic reviews, GACVS reviews, Cochrane reviews etc.) **against** a causal association between the vaccine and the event?	☐☐☐☐	
IV. Other qualifying factors for classification		
1. In this patient, did such an event occur in the past after administration of a similar vaccine?	☐☐☐☐	
2. In this patient did such an event occur in the past independent of vaccination?	☐☐☐☐	
3. Could the current event have occurred in this patient without vaccination (background rate)?	☐☐☐☐	
4. Did this patient have an illness, pre-existing condition or risk factor that could have contributed to the event?	☐☐☐☐	
5. Was this patient taking any medication prior to the vaccination?	☐☐☐☐	
6. Was this patient exposed to a potential factor (other than vaccine) prior to the event (e.g. allergen, drug, herbal product etc.)?	☐☐☐☐	

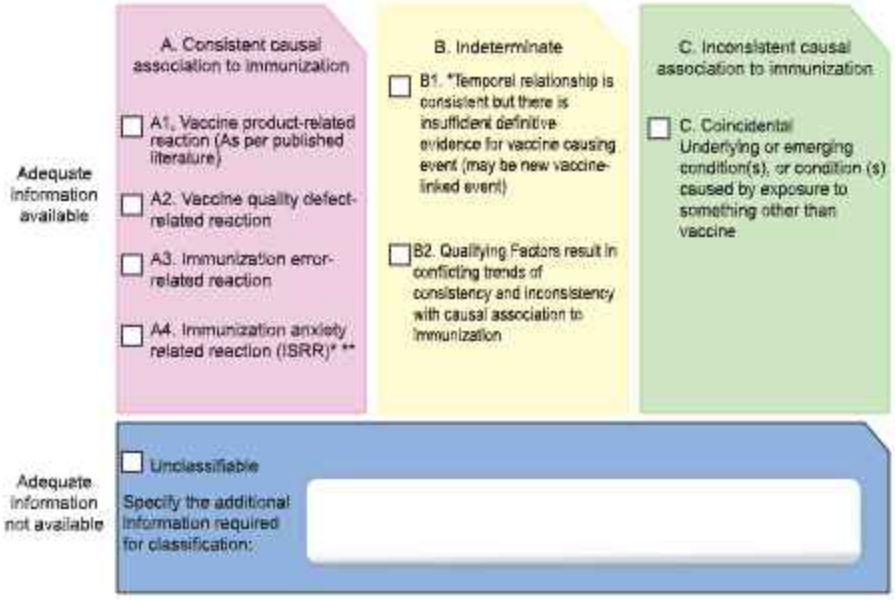
Y: Yes N: No UK: Unknown NA: Not applicable

Step 3 (Algorithm) review all steps and ✓all the appropriate boxes



Notes for Step 3:

Step 4 (Classification) ✓all boxes that Apply



*B1: This is a potential signal and may be considered for investigation
** Immunization stress related response (ISRR)

Summarize the classification logic in the order of priority:
With available evidence, we could conclude that the classification is _____because:

With available evidence, we could NOT classify the case because: _____

Examples

Example 1: Meningococcal Conjugate Vaccine and Seizures

Presenting problem: A five-month-old male (name PQ), given a second dose of Menjugate vaccine (first dose at age three months); two days post-immunization reported onset of fever – not documented. Five days post-immunization the infant had a right focal seizure and altered level of consciousness. The documented temperature was 39° C. The patient was treated with anticonvulsants and was admitted to hospital. He had persistent seizure activity on the third and fourth days in hospital. He was transferred to a tertiary-care referral paediatric hospital and admitted to the intensive care unit with status epilepticus. Seizures were controlled within 24 hours.

Past medical history: unremarkable good general health; no evidence of immune deficiency

- no prior history of seizures.

Investigations:

- CSF: 61 RBC; 144 WBC; 57% PMN; and 26% lymphocytes;
- protein 1.2; glucose 3.1;
- culture of CSF, pharynx and stool all negative;
- PCR positive for herpes simplex virus;
- MRI showed extensive inflammation of right frontal, parietal and temporal lobes, and a small amount of bleeding into the left temporal lobe;
- EEG showed paroxysmal lateral epileptiform discharges.

An investigation at the immunization session site confirmed the quality, application of correct procedures and technique in vaccine administration.

Treatment and course of illness: Treated with antibiotics and antiviral (acyclovir). The former was discontinued once PCR results were known; the latter was continued for 21 days. Good recovery in hospital on treatment. At discharge the infant was alert and active with normal tone. Home on anticonvulsants.

Note: *The case meets the Brighton Collaboration case definition for encephalitis - at a level 2 of diagnostic certainty (evidence of encephalopathy with decreased level of consciousness and associated seizures; multiple indicators of CNS inflammation [temp 39C; CSF pleocytosis; EEG findings consistent with encephalitis; neuroimaging consistent with encephalitis]).*

Step 1 (Eligibility)

Patient ID/ Name : PQ **DoB/ Age: 5 Months** **Sex: ✓ Male/ Female**

Name one of the vaccines administered before this event	What is the Valid Diagnosis?	Does the diagnosis meet a case definition?
Menjugate (Meningococcal Gr C conjugate vaccine)	Meningoencephalitis	Yes (level 2 of Brighton Collaboration)

Create your question on causality here
Has the Menjugate vaccine / vaccination caused Meningoencephalitis (The event for review in step 2)

Is this case eligible for causality assessment? ✓ Yes/ No; If, "Yes", proceed to step 2

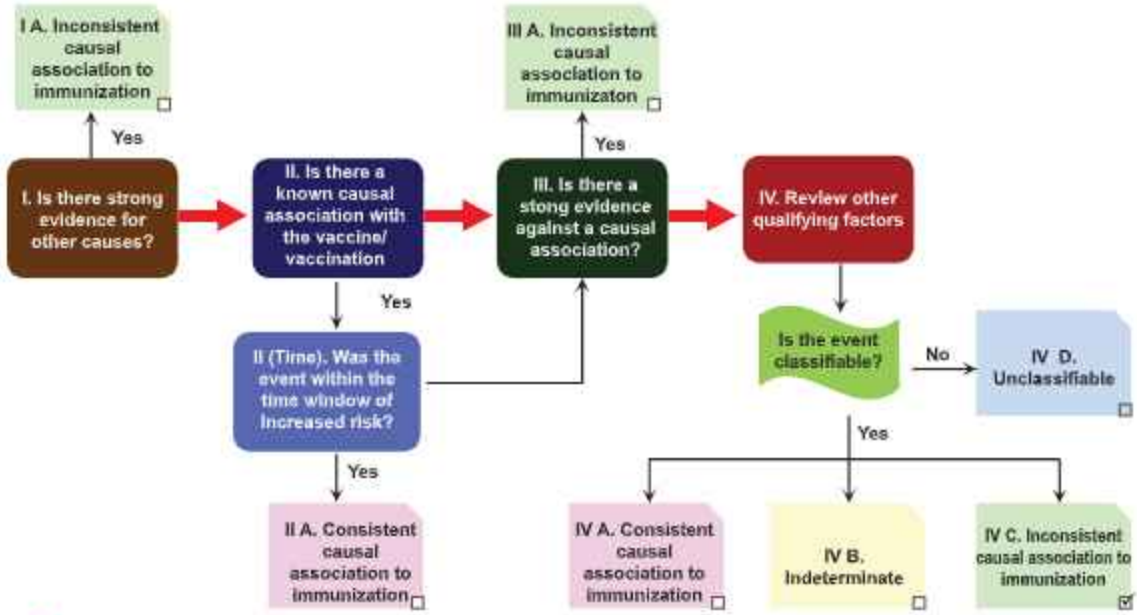
Step 2 (Event Checklist) ✓ (check) all boxes that apply

I. Is there strong evidence for other causes?	Y N UK NA	Remarks
1. In this patient, does the medical history, clinical examination and/ or investigations, **confirm** another cause for the event?	☑ ☐ ☐ ☐	*Yes – CSF PCR positive for herpes simplex virus*
II. Is there a known causal association with the vaccine or vaccination?		
Vaccine product		
1. Is there evidence in published peer reviewed literature that this vaccine may cause such an event if administered correctly?	☐ ☑ ☐ ☐	*Unknown – not reported so far in literature*
2. Is there a biological plausibility that this vaccine could cause such an event?	☐ ☐ ☑ ☐	*Contains inactivated extracts of Neisseria meningitidis group C bacteria*
3. In this patient, did a specific test demonstrate the causal role of the vaccine?	☐ ☑ ☐ ☐	*No – CSF PCR positive for herpes simplex virus*
Vaccine quality		
4. Could the vaccine given to this patient have a quality defect or is substandard or falsified?	☐ ☑ ☐ ☐	*As per investigation report*
Immunization error		
5. In this patient, was there an error in prescribing or non-adherence to recommendations for use of the vaccine (e.g. use beyond the expiry date, wrong recipient etc.)?	☐ ☑ ☐ ☐	*As per investigation report*
6. In this patient, was the vaccine (or diluent) administered in an unsterile manner?	☐ ☑ ☐ ☐	*As per investigation report*

7. In this patient, was the vaccine's physical condition (e.g. colour, turbidity, presence of foreign substances etc.) abnormal when administered?	☐ ☑ ☐ ☐	*As per investigation report*
8. When this patient was vaccinated, was there an error in vaccine constitution/preparation by the vaccinator (e.g. wrong product, wrong diluent, improper mixing, improper syringe filling etc.)?	☐ ☑ ☐ ☐	*As per investigation report*
9. In this patient, was there an error in vaccine handling (e.g. a break in the cold chain during transport, storage and/or immunization session etc.)?	☐ ☑ ☐ ☐	*As per investigation report*
10. In this patient, was the vaccine administered incorrectly (e.g. wrong dose, site or route of administration; wrong needle size etc.)?	☐ ☑ ☐ ☐	*As per investigation report*
Immunization anxiety (Immunization Triggered Stress Response - ITSR)		
11. In this patient, could this event be a stress response triggered by immunization (e.g. acute stress response, vasovagal reaction, hyperventilation or anxiety)?	☐ ☑ ☐ ☐	*Anxiety cannot cause Meningoencephalitis*
II (time). If "yes" to any question in II, was the event within the time window of increased risk?		
12. In this patient, did the event occur within a plausible time window after vaccine administration?	☐ ☐ ☐ ☑	*Because there are no, "Yes" responses in II.*
III. Is there strong evidence against a causal association?		
1. Is there a body of published evidence (systematic reviews, GACVS reviews, Cochrane reviews etc.) **against** a causal association between the vaccine and the event?	☐ ☐ ☑ ☐	*Unknown – hasn't been studied*
IV. Other qualifying factors for classification		
1. In this patient, did such an event occur in the past after administration of a similar vaccine?	☐ ☑ ☐ ☐	*Child fine after first dose*
2. In this patient did such an event occur in the past independent of vaccination?	☐ ☑ ☐ ☐	*Was in good health previously*
3. Could the current event have occurred in this patient without vaccination (background rate)?	☑ ☐ ☐ ☐	*Several causes for infant meningoencephalitis*
4. Did this patient have an illness, pre-existing condition or risk factor that could have contributed to the event?	☐ ☐ ☑ ☐	
5. Was this patient taking any medication prior to the vaccination?	☐ ☐ ☑ ☐	*"No" is also ok here*
6. Was this patient exposed to a potential factor (other than vaccine) prior to the event (e.g. allergen, drug, herbal product etc.)?	☐ ☐ ☑ ☐	

Y: Yes N: No UK: Unknown NA: Not applicable

Step 3 (Algorithm) review all steps and ✓all the appropriate boxes



Notes for Step 3: I A: Because PCR positive for herpes simplex virus. IV C: Because several causes of meningoencephalitis in infants. Could be one of several different infections.

Step 4 (Classification) ✓all boxes that apply

Adequate information available

A. Consistent causal association to immunization

- ☐ A1, Vaccine product-related reaction (As per published literature)
- ☐ A2. Vaccine quality defect-related reaction
- ☐ A3. Immunization error-related reaction
- ☐ A4. Immunization anxiety related reaction (ISRR)* **

B. Indeterminate

- ☐ B1. *Temporal relationship is consistent but there is insufficient definitive evidence for vaccine causing event (may be new vaccine-linked event)
- ☐ B2. Qualifying Factors result in conflicting trends of consistency and inconsistency with causal association to immunization

C. Inconsistent causal association to immunization

- ☑ C. Coincidental Underlying or emerging condition(s), or condition (s) caused by exposure to something other than vaccine

Adequate information not available

- ☐ Unclassifiable

Specify the additional information required for classification:

*B1: This is a potential signal and may be considered for investigation
** Immunization stress related response (ISRR)

Summarize the classification logic in the order of priority:
With available evidence, we could conclude that the classification is **inconsistent (coincidental)** because: There is a clear alternative explanation for the meningoencephalitis (Herpes simplex virus confirmed

Example 2: OPV and Acute Flaccid Paralysis

MA, a male child, was born on 29 December 2006 to a farmer couple in a polio endemic country. On 1 July 2009, he suddenly developed inability to use the left upper limb. This was reported by the local health worker to the medical officer on the same day and was investigated on 2 July 2009.

The medical officer obtained the details of the present illness from the parents. MA had a sudden onset of flaccid paralysis in the left arm on 1 July 2009. On the day of paralysis, there was no fever. The paralysis was static (neither ascending nor descending). There was no sensory loss. He did not travel outside his locality for 35 days preceding his illness. There was no history of trauma, no loss of consciousness and no convulsions. Within 30 days prior to the paralysis onset, he had injections in the gluteal region.

MA had a BCG scar. The health worker mentioned that MA had received three doses of OPV through routine immunization and the parents mentioned that he had over 10 doses of OPV through mass immunization campaigns (SIA). The last OPV before paralysis onset (and stool sample collection) was administered on 7 June 2009 as a part of SIA.

On clinical examination the medical officer observed that the tone was markedly diminished in the left upper limb. There was power of 0/5 in the muscles of the wrist, forearm and upper arm. The biceps, triceps and supinator jerks were diminished. Examination also showed that all other limbs were clinically within the normal range of expected findings. Using a measuring tape, he determined and recorded the circumference of all the limbs.

To test for the presence of enterovirus, two stool specimens were collected on 2 July 2009 and 4 July 2009. Both specimens were of adequate volume and were sent to a WHO-accredited laboratory in good condition (i.e. without desiccation or leakage, with adequate documentation, and with evidence that the cold chain was maintained). The second stool sample isolated Sabin type 1 and Sabin type 2 strains of poliovirus.

The medical officer re-examined MA on 9 September 2009 and observed that that the tone was diminished in the left upper limb compared to the right. There was improvement in the power in the muscles of the wrist (4/5), forearm (2/5) and upper arm (2/5). The biceps, triceps and supinator jerks were still diminished. Examination also showed that all other limbs were clinically within the normal range of expected findings. On measuring the limbs, the medical officer determined that there was wasting in the left upper arm.

Patient ID/ Name :MA **DoB/ Age: 29.12.2006** **Sex: ✓ Male/ Female**

Step 1 (Eligibility)

Name one of the vaccines administered before this event	What is the Valid Diagnosis?	Does the diagnosis meet a case definition?
OPV	AFP	Yes*

Create your question on causality here
Has the OPV vaccine / vaccination caused AFP (The event for review in step 2)

Is this case eligible for causality assessment? ✓ Yes/ No; If, "Yes", proceed to step 2

Step 2 (Event Checklist) ✓ (check) all boxes that apply

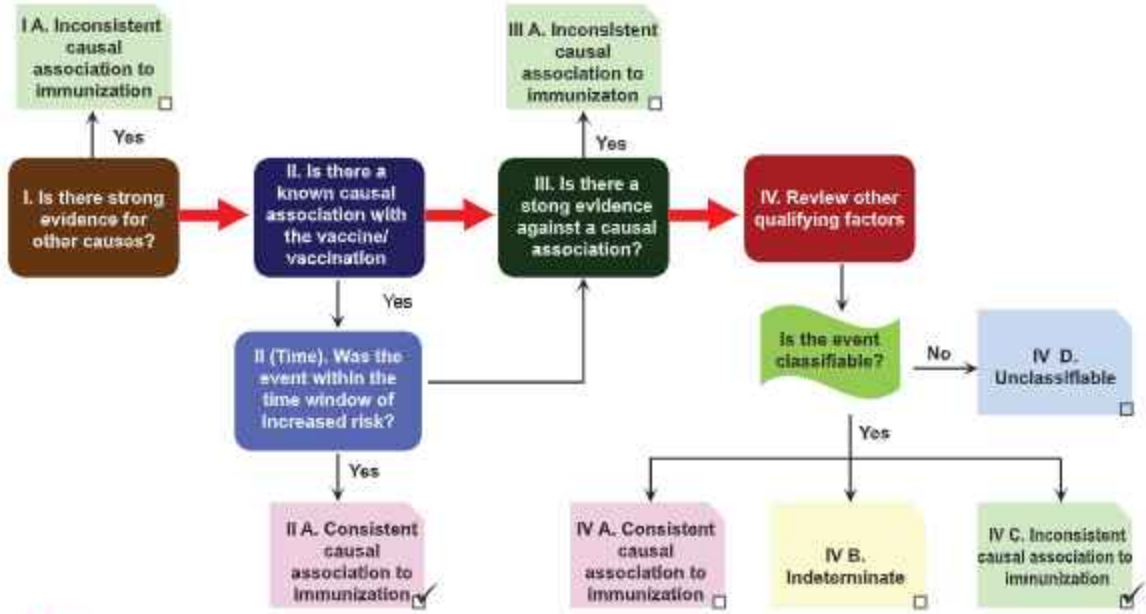
I. Is there strong evidence for other causes?	Y N UK NA	Remarks
1. In this patient, does the medical history, clinical examination and/ or investigations, **confirm** another cause for the event?	☐ ☐ ☑ ☐	*No details available on the other tests conducted on this child*
II. Is there a known causal association with the vaccine or vaccination?		
Vaccine product		
1. Is there evidence in published peer reviewed literature that this vaccine may cause such an event if administered correctly?	☑ ☐ ☐ ☐	*VAPP is a recognized event*
2. Is there a biological plausibility that this vaccine could cause such an event?	☑ ☐ ☐ ☐	*Sabin OPV can cause AFP*
3. In this patient, did a specific test demonstrate the causal role of the vaccine?	☑ ☐ ☐ ☐	*Sabin 1 and 2 isolated from stool*
Vaccine quality		
4. Could the vaccine given to this patient have a quality defect or is substandard or falsified?	☐ ☑ ☐ ☐	*Very unlikely in OPV SIA*
Immunization error		
5. In this patient, was there an error in prescribing or non-adherence to recommendations for use of the vaccine (e.g. use beyond the expiry date, wrong recipient etc.)?	☐ ☐ ☑ ☐	*Details unavailable*
6. In this patient, was the vaccine (or diluent) administered in an unsterile manner?	☐ ☐ ☑ ☐	*Details unavailable*

7. In this patient, was the vaccine's physical condition (e.g. colour, turbidity, presence of foreign substances etc.) abnormal when administered?	☐ ☐ ☑ ☐	*Details unavailable*
8. When this patient was vaccinated, was there an error in vaccine constitution/preparation by the vaccinator (e.g. wrong product, wrong diluent, improper mixing, improper syringe filling etc.)?	☐ ☐ ☐ ☑	*OPV is not reconstituted*
9. In this patient, was there an error in vaccine handling (e.g. a break in the cold chain during transport, storage and/or immunization session etc.)?	☐ ☐ ☑ ☐	*Details unavailable*
10. In this patient, was the vaccine administered incorrectly (e.g. wrong dose, site or route of administration; wrong needle size etc.)?	☐ ☐ ☑ ☐	*Details unavailable*
Immunization anxiety (Immunization Triggered Stress Response - ITSR)		
11. In this patient, could this event be a stress response triggered by immunization (e.g. acute stress response, vasovagal reaction, hyperventilation or anxiety)?	☐ ☑ ☐ ☐	
II (time). If "yes" to any question in II, was the event within the time window of increased risk?		
12. In this patient, did the event occur within a plausible time window after vaccine administration?	☑ ☐ ☐ ☐	*Yes, 24 days after OPV*
III. Is there strong evidence against a causal association?		
1. Is there a body of published evidence (systematic reviews, GACVS reviews, Cochrane reviews etc.) **against** a causal association between the vaccine and the event?	☐ ☑ ☐ ☐	
IV. Other qualifying factors for classification		
1. In this patient, did such an event occur in the past after administration of a similar vaccine?	☐ ☑ ☐ ☐	
2. In this patient did such an event occur in the past independent of vaccination?	☐ ☐ ☑ ☐	
3. Could the current event have occurred in this patient without vaccination (background rate)?	☑ ☐ ☐ ☐	*There are many causes for AFP*
4. Did this patient have an illness, pre-existing condition or risk factor that could have contributed to the event?	☑ ☐ ☐ ☐	*Unknown illness < 30 days*
5. Was this patient taking any medication prior to the vaccination?	☑ ☐ ☐ ☐	*Unknown injection < 30 days previously*
6. Was this patient exposed to a potential factor (other than vaccine) prior to the event (e.g. allergen, drug, herbal product etc.)?	☑ ☐ ☐ ☐	*IM injections 30 days prior: A risk factor for VAPP*

Y: Yes N: No UK: Unknown NA: Not applicable

*http://www.who.int/immunization_monitoring/diseases/poliomyelitis

Step 3 (Algorithm) review all steps and ✓all the appropriate boxes



Notes for Step 3: *II A: With available information, it seems likely that the vaccine caused the event. This is because OPV is known to cause AFP and the time window is suitable. IV C: There are other causes of flaccid paralysis and the child was treated for an illness 30 days prior to paralysis; however, this information is inadequate.*

Step 4 (Classification) ✓ all boxes that apply

	A. Consistent causal association to immunization	B. Indeterminate	C. Inconsistent causal association to immunization
Adequate information available	☑ A1, Vaccine product-related reaction (As per published literature) ☐ A2. Vaccine quality defect-related reaction ☐ A3. Immunization error-related reaction ☐ A4. Immunization anxiety related reaction (ISRR)* **	☐ B1. *Temporal relationship is consistent but there is insufficient definitive evidence for vaccine causing event (may be new vaccine-linked event) ☐ B2. Qualifying Factors result in conflicting trends of consistency and inconsistency with causal association to immunization	☑ C. Coincidental Underlying or emerging condition(s), or condition (s) caused by exposure to something other than vaccine
Adequate information not available	☐ Unclassifiable Specify the additional information required for classification:		

*B1: This is a potential signal and may be considered for investigation
** Immunization stress related response (ISRR)

Summarize the classification logic in the order of priority:
With available evidence, we could conclude that the classification is **consistent** because: With available information, it seems likely that the vaccine caused the event. (But we need to keep in mind that VAPP is more likely to occur after the first dose than after later doses.)
However, even though the trend is consistent we cannot completely rule out **inconsistent, since information available on other causes is inadequate.**

Example 3: AEFI After MR Vaccine

XX, a South Asian girl child was born on 1December 2010 through LSCS (gestational age 38 weeks + 2 days). She was the first child to the parents. Birth weight was 3200g and Apgar at birth was 10.

On 22 May 2012 (at 18 months) between 9.30 and 10 a.m. she received 0.5ml MR vaccine in the left arm with a 25nm 23G needle. She died 10 days after immunization.

She was not on any simultaneous medication. She had no antenatal complications, she had no food allergies, and her feeding and activities were normal. She had no history of hospitalization, no underlying congenital or acquired diseases or disorders, and no evidence of abuse, harm, neglect, accidental injury or previous need for child protection.

Previously she had the following immunizations: Penta (DTP Hep B and Hib) 1/OPV 1 on 9 August 2011, Penta 2/OPV 2 on 25 October 2011, and JE on 10 January 2012.

Prior to immunization, her feeding and activity were normal. She had an attack of fever one week prior which resolved. She was not receiving any medication at the time of vaccination.

After immunization with MR, she developed mild fever on the same day (22 May 2012). On the third day after immunization (25 May 2012), she developed cough, high fever, vomiting and flushed face. On day 8 after immunization (30 May 2012), she was admitted to the local district hospital where tentative diagnosis of lower respiratory tract infection was made. Full blood examination showed that the initial WBC count was 3800 and platelets 152 000. The prescribed medications included Paracetamol, chlorpheneramine maleate, Cefaloxine, Salbutamol, Theophyllin, and Diclofenac sodium suppository.

She was later transferred to the district general hospital on 30 May 2012. The next day she developed fever, right hypochondrial tenderness and tenderness of the liver (1cm). Although she was haemodynamically stable, her WBC was 1300 and platelets 112 000. The condition was diagnosed as probable dengue illness. She further developed watery diarrhoea and convulsions and was treated for acute gastroenteritis with IV antibiotics and IV fluids. In the evening, the platelet count dropped from 112 000 (at 5:00 a.m.) to 77 000 (at 5:00 p.m.). Clinicians considered probable entry into the critical phase of dengue haemorrhagic fever, even though evidence of haemorrhages was not detected. At 8.00 p.m., there was a further drop in platelet count to 54 000 which clinicians considered as entry into the critical phase with haemodynamic instability (HR- >200; systolic BP – 60mmHg). She was then placed on IV fluids over six hours, exceeding the fluid quota (1330 ml given – 90.5%).

On day 10 following immunization, she was transferred to the intensive care unit. Her heart rate remained high and she continued to be haemodynamically unstable, with pupils wide, tachypnoea, peripheral cyanosis and fluid overload. She died at 9 a.m. on 1 June 2012.

Diagnosis of dengue illness was considered but no objective confirmation of dengue haemorrhagic fever was made (ultrasound, chest X-ray or virological examination). The primary cause of death was considered to be both prolonged shock and fluid overload. Her body was sent for autopsy.

No written autopsy report was available. The case (at the time of writing this report) was awaiting the pathological report. The medical officer who performed the autopsy unofficially communicated to the immunization programme manager that the appearance was compatible with a viral infection; however, there was no macroscopic evidence of bleeding or fluid leakage.

Field investigation by the immunization programme

Investigation on vaccine cold chain and vaccination technique at the Ministry of Health showed that the MR vaccine, Batch number 065004 and expiry date February 2014 was given. It was manufactured by the manufacturer xyz. There was no breakdown in the cold chain after receipt of the stocks of vaccine at national level according to the daily temperature record. The VVM status was stage 1.

Further investigation showed that, of the 30 other children vaccinated on the same day at the same clinic, three were vaccinated with the same vaccine and there were no similar events.

Step 1 (Eligibility) Option 1 – MR vaccine and thrombocytopenia

Patient ID/ Name : XX **DoB/ Age: 01.12.2010** **Sex: Male/ ✓ Female**

Name one of the vaccines administered before this event	What is the Valid Diagnosis?	Does the diagnosis meet a case definition?
MR	Thrombocytopenia	Yes, Brighton level 2

Create your question on causality here
Has the MR vaccine / vaccination caused Thrombocytopenia (The event for review in step 2)

Is this case eligible for causality assessment? ✓ Yes/ No; If, "Yes", proceed to step 2

Step 2 (Event Checklist) ✓ (check) all boxes that apply

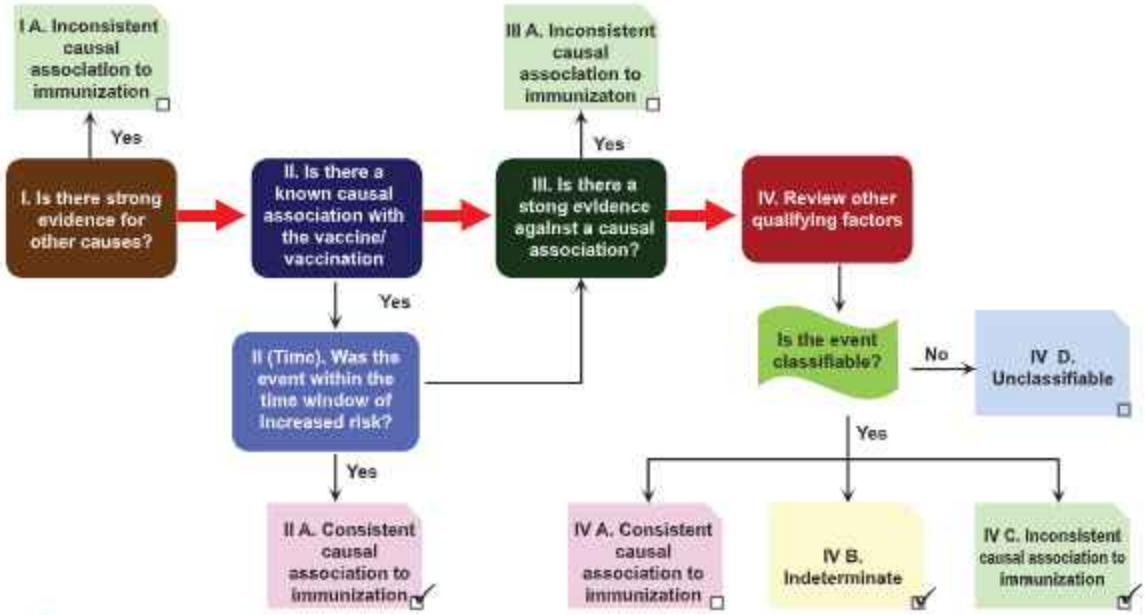
I. Is there strong evidence for other causes?	Y N UK NA	Remarks
1. In this patient, does the medical history, clinical examination and/or investigations, **confirm** another cause for the event?	☐ ☐ ☑ ☐	*With platelet count ↓, Liver enlarged, TWBC ↓ the tests may support dengue as a dx but unable to confirm it*
II. Is there a known causal association with the vaccine or vaccination?		
Vaccine product		
1. Is there evidence in published peer reviewed literature that this vaccine may cause such an event if administered correctly?	☑ ☐ ☐ ☐	*Measles vaccine can cause thrombocytopenia*
2. Is there a biological plausibility that this vaccine could cause such an event?	☑ ☐ ☐ ☐	*Many viral infections cause thrombocytopenia*
3. In this patient, did a specific test demonstrate the causal role of the vaccine?	☐ ☑ ☐ ☐	
Vaccine quality		
4. Could the vaccine given to this patient have a quality defect or is substandard or falsified?	☐ ☑ ☐ ☐	*As per investigation report*
Immunization error		
5. In this patient, was there an error in prescribing or non-adherence to recommendations for use of the vaccine (e.g. use beyond the expiry date, wrong recipient etc.)?	☐ ☑ ☐ ☐	*As per investigation report*
6. In this patient, was the vaccine (or diluent) administered in an unsterile manner?	☐ ☑ ☐ ☐	*As per investigation report*

7. In this patient, was the vaccine's physical condition (e.g. colour, turbidity, presence of foreign substances etc.) abnormal when administered?	☐ ☐ ☑ ☐	
8. When this patient was vaccinated, was there an error in vaccine constitution/preparation by the vaccinator (e.g. wrong product, wrong diluent, improper mixing, improper syringe filling etc.)?	☐ ☑ ☐ ☐	*As per investigation report*
9. In this patient, was there an error in vaccine handling (e.g. a break in the cold chain during transport, storage and/or immunization session etc.)?	☐ ☑ ☐ ☐	*As per investigation report*
10. In this patient, was the vaccine administered incorrectly (e.g. wrong dose, site or route of administration; wrong needle size etc.)?	☐ ☑ ☐ ☐	*As per investigation report*
Immunization anxiety (Immunization Triggered Stress Response - ITSR)		
11. In this patient, could this event be a stress response triggered by immunization (e.g. acute stress response, vasovagal reaction, hyperventilation or anxiety)?	☐ ☑ ☐ ☐	
II (time). If "yes" to any question in II, was the event within the time window of increased risk?		
12. In this patient, did the event occur within a plausible time window after vaccine administration?	☑ ☐ ☐ ☐	*< 6 weeks - see Ref[1] below*
III. Is there strong evidence against a causal association?		
1. Is there a body of published evidence (systematic reviews, GACVS reviews, Cochrane reviews etc.) **against** a causal association between the vaccine and the event?	☐ ☑ ☐ ☐	
IV. Other qualifying factors for classification		
1. In this patient, did such an event occur in the past after administration of a similar vaccine?	☐ ☐ ☐ ☑	
2. In this patient did such an event occur in the past independent of vaccination?	☐ ☑ ☐ ☐	*She had an attack of fever one week prior*
3. Could the current event have occurred in this patient without vaccination (background rate)?	☑ ☐ ☐ ☐	*Dengue endemic country*
4. Did this patient have an illness, pre-existing condition or risk factor that could have contributed to the event?	☑ ☐ ☐ ☐	*Other viral infection (H/o prior febrile illness +, present illness - fever, flushing cough and vomiting, diarrhoea)*
5. Was this patient taking any medication prior to the vaccination?	☐ ☑ ☐ ☐	
6. Was this patient exposed to a potential factor (other than vaccine) prior to the event (e.g. allergen, drug, herbal product etc.)?	☐ ☐ ☑ ☐	

Y: Yes N: No UK: Unknown NA: Not applicable

[1] Idiopathic thrombocytopenic purpura and MMR vaccine: E. Miller et al http://adc.bmj.com/content/84/3/22

Step 3 (Algorithm) review all steps and ✓ all the appropriate boxes



Notes for Step 3: *II A: Because measles vaccine can cause thrombocytopenia (but is not severe enough to cause death by bleeding). The time window fits. However, there is no evidence for bleeding on autopsy. IVB: Because other viral infection (H/o prior febrile illness +,present illness - fever, flushing cough, vomiting and diarrhea). IVC: Because we need to consider other viral infections (dengue cannot be ruled out).*

Step 4 (Classification) ✓all boxes that apply

	A. Consistent causal association to immunization	B. Indeterminate	C. Inconsistent causal association to immunization
Adequate information available	☑ A1. Vaccine product-related reaction (As per published literature) ☐ A2. Vaccine quality defect-related reaction ☐ A3. Immunization error-related reaction ☐ A4. Immunization anxiety related reaction (ISRR)* **	☐ B1. *Temporal relationship is consistent but there is insufficient definitive evidence for vaccine causing event (may be new vaccine-linked event) ☑ B2. Qualifying Factors result in conflicting trends of consistency and inconsistency with causal association to immunization	☑ C. Coincidental Underlying or emerging condition(s), or condition (s) caused by exposure to something other than vaccine
Adequate information not available	☐ Unclassifiable Specify the additional information required for classification:		

*B1: This is a potential signal and may be considered for investigation
** Immunization stress related response (ISRR)

Summarize the classification logic in the order of priority:
With available evidence, we could conclude that the classification could be indeterminate / inconsistent because: It is not possible to come to a conclusion as to whether the thrombocytopenia was caused by the vaccine, by dengue or by another viral disease. However, there is no evidence of bleeding on autopsy. Therefore, even if the MR contributed to thrombocytopenia, it did not contribute to death. Death could have occurred by fluid overload.

Step 1 (Eligibility) Option 2 – MR vaccine and sepsis

Patient ID/ Name : XX **DoB/ Age: 01.12.2010** **Sex: Male/ ✓ Female**

Name one of the vaccines administered before this event	What is the Valid Diagnosis?	Does the diagnosis meet a case definition?
MR	Sepsis	*Yes* weblink: http://www.bmj.com/content/335/7625/879

Create your question on causality here

Has the MR vaccine / vaccination caused Sepsis (The event for review in step 2)

Is this case eligible for causality assessment? Yes/ No; If, "Yes", proceed to step 2

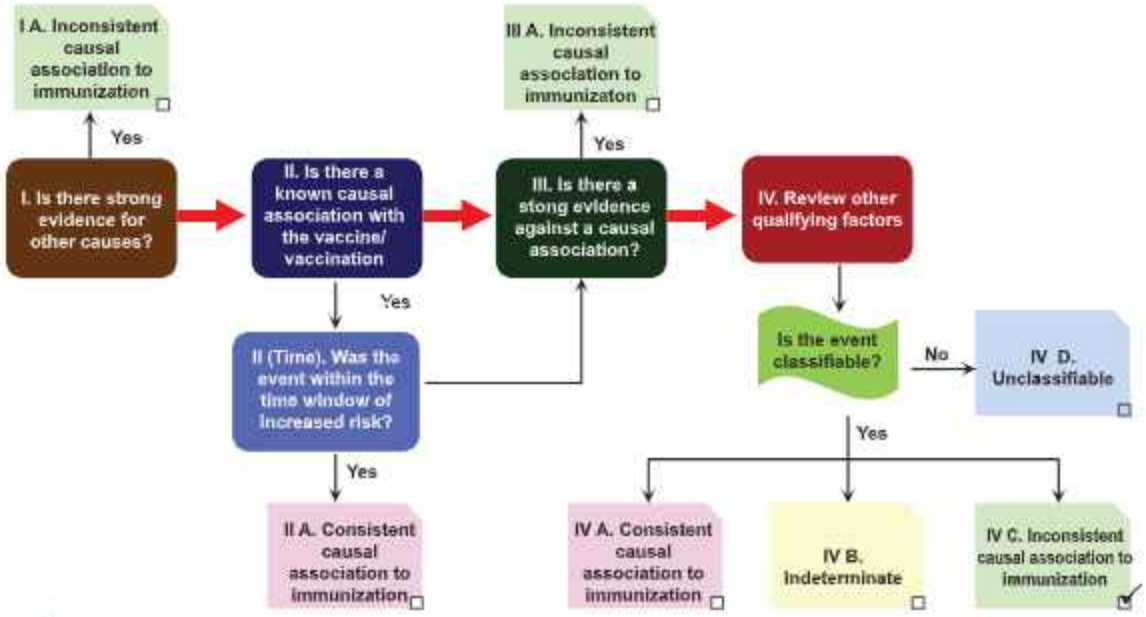
Step 2 (Event Checklist) ✓ (check) all boxes that apply

I. Is there strong evidence for other causes?	Y N UK NA	Remarks
1. In this patient, does the medical history, clinical examination and/or investigations, **confirm** another cause for the event?	☐☐☑☐	*Dengue is suspected but not confirmed. (Platelets ↓, TWBC ↓, liver ++). But X ray, Culture, IgM and virus isolation not done*
II. Is there a known causal association with the vaccine or vaccination?		
Vaccine product		
1. Is there evidence in published peer reviewed literature that this vaccine may cause such an event if administered correctly?	☐☑☐☐	
2. Is there a biological plausibility that this vaccine could cause such an event?	☐☑☐☐	
3. In this patient, did a specific test demonstrate the causal role of the vaccine?	☐☑☐☐	
Vaccine quality		
4. Could the vaccine given to this patient have a quality defect or is substandard or falsified?	☐☑☐☐	*As per investigation report*
Immunization error		
5. In this patient, was there an error in prescribing or non-adherence to recommendations for use of the vaccine (e.g. use beyond the expiry date, wrong recipient etc.)?	☐☑☐☐	*As per investigation report*
6. In this patient, was the vaccine (or diluent) administered in an unsterile manner?	☐☑☐☐	*As per investigation report*

7. In this patient, was the vaccine's physical condition (e.g. colour, turbidity, presence of foreign substances etc.) abnormal when administered?	☐☐☑☐	
8. When this patient was vaccinated, was there an error in vaccine constitution/preparation by the vaccinator (e.g. wrong product, wrong diluent, improper mixing, improper syringe filling etc.)?	☐☑☐☐	*As per investigation report*
9. In this patient, was there an error in vaccine handling (e.g. a break in the cold chain during transport, storage and/or immunization session etc.)?	☐☑☐☐	*As per investigation report*
10. In this patient, was the vaccine administered incorrectly (e.g. wrong dose, site or route of administration; wrong needle size etc.)?	☐☑☐☐	*As per investigation report*
Immunization anxiety (Immunization Triggered Stress Response - ITSR)		
11. In this patient, could this event be a stress response triggered by immunization (e.g. acute stress response, vasovagal reaction, hyperventilation or anxiety)?	☐☑☐☐	
II (time). If "yes" to any question in II, was the event within the time window of increased risk?		
12. In this patient, did the event occur within a plausible time window after vaccine administration?	☐☐☐☑	*Because there are no, "Yes" responses to questions in II*
III. Is there strong evidence against a causal association?		
1. Is there a body of published evidence (systematic reviews, GACVS reviews, Cochrane reviews etc.) **against** a causal association between the vaccine and the event?	☐☑☐☐	
IV. Other qualifying factors for classification		
1. In this patient, did such an event occur in the past after administration of a similar vaccine?	☐☐☐☑	
2. In this patient did such an event occur in the past independent of vaccination?	☐☐☑☐	
3. Could the current event have occurred in this patient without vaccination (background rate)?	☑☐☐☐	*In this situation, it is possible that sepsis could be a complication of the respiratory tract infection*
4. Did this patient have an illness, pre-existing condition or risk factor that could have contributed to the event?	☑☐☐☐	*Fever one week prior to immunization*
5. Was this patient taking any medication prior to the vaccination?	☐☑☐☐	
6. Was this patient exposed to a potential factor (other than vaccine) prior to the event (e.g. allergen, drug, herbal product etc.)?	☑☐☐☐	*Other infections, (unconfirmed)*

Y: Yes N: No UK: Unknown NA: Not applicable

Step 3 (Algorithm) review all steps and ✓ all the appropriate boxes



Notes for Step 3: IV C: In this situation, it is possible that sepsis that may have caused the death is a complication of the respiratory tract infection. Other infections, probably dengue (unconfirmed)need to be considered as the fever one week prior to Immunization is suggestive that she was probably unwell at the time of vaccination.

Step 4 (Classification) ✓all boxes that apply

	A. Consistent causal association to immunization	B. Indeterminate	C. Inconsistent causal association to immunization
Adequate information available	☐ A1. Vaccine product-related reaction (As per published literature) ☐ A2. Vaccine quality defect-related reaction ☐ A3. Immunization error-related reaction ☐ A4. Immunization anxiety related reaction (ISRR)* **	☐ B1. *Temporal relationship is consistent but there is insufficient definitive evidence for vaccine causing event (may be new vaccine-linked event) ☐ B2. Qualifying Factors result in conflicting trends of consistency and inconsistency with causal association to immunization	☑ C. Coincidental Underlying or emerging condition(s), or condition (s) caused by exposure to something other than vaccine
Adequate information not available	☐ Unclassifiable Specify the additional information required for classification:		

*B1: This is a potential signal and may be considered for investigation
** Immunization stress related response (ISRR)

Summarize the classification logic in the order of priority:
With available evidence, we could conclude that the classification is **coincidental / inconsistent** because: sepsis that caused the chain of events leading to the death of the child could have been due to a complication of respiratory tract infection or other viral disease (dengue suspected). The autopsy findings will give a better picture. MR is not the cause of death

Annex-7

Recognition and Management of Anaphylaxis

Anaphylaxis is a very rare, unexpected, and occasionally fatal allergic reaction. When anaphylaxis does occur, the patient must be diagnosed properly, treated and managed urgently by trained staff and transferred to a hospital setting (if not already in a hospital setting).

There is a high risk that health workers who lack training will misdiagnose faints (vasovagal syncope) and dizziness following immunization for the onset of anaphylaxis. Most episodes of feeling ill or faint, or actual fainting that occur immediately after immunization are not due to the onset of anaphylaxis. The vaccinators, paramedics and physicians should be adequately trained so that they are able to distinguish anaphylaxis from fainting, anxiety and breath-holding spells, which are common benign reactions.

During fainting, the individual suddenly becomes pale, loses consciousness and collapses to the ground. Fainting is sometimes accompanied by brief clonic seizure activity (i.e., rhythmic jerking of the limbs), but this requires no specific treatment or investigation. Fainting is relatively common after immunization of adults and adolescents, but very rare in young children. It is managed by simply placing the patient in a recumbent position. Recovery of consciousness occurs within a minute or two, but patients may take some more time to recover fully.

An anxiety spell can lead to pale, fearful appearance and symptoms of hyperventilation (light-headed, dizziness, tingling in the hands and around the mouth). Breath holding occurs in young children and will lead to facial flushing and cyanosis. It can end in unconsciousness, during which breathing resumes.

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

The onset of anaphylaxis can occur after several minutes (>5minutes) but rarely up to two hours following vaccination. The progression of symptoms is rapid and usually involves multiple body systems, almost always with skin involvement (generalized erythema and/ or urticaria), as well as signs of upper and/or lower respiratory tract obstruction and/or circulatory collapse. In young children (though anaphylaxis occurs at any age) limpness, pallor or loss of consciousness may reflect hypotension. In general, the more rapid the onset, the more severe is the reaction. Symptoms limited to only one system can occur, leading to delay in diagnosis. Biphasic reactions where symptoms recur 8-12 hours after onset of the original attack, and prolonged attacks lasting up to 48 hours, have been described.

Distinguishing Anaphylaxis from Fainting (Vasovagal Syncope)

	Fainting (Vasovagal Syncope)	Anaphylaxis
Onset	Occurs suddenly, before, at the time of or soon after injection	Seconds to minutes after exposure, almost all cases within 1 hour
System		
Skin	Pale, cold, sweaty/clammy	Red, raised itchy rash; swollen eyes and face; generalized rash
Respiratory	Normal to deep breaths	Noisy breathing, wheeze or stridor, persistent cough
Cardiovascular	Slow pulse, transient hypotension	Fast pulse, hypotension
Gastrointestinal	Nausea, Vomiting	Abdominal cramps, vomiting, nausea
Neurological	Transient loss of consciousness reversed by supine position, dizziness, numbness, tingling around lips, spasms in hand and feet	May develop loss of consciousness not relieved by supine position

Conditions that may be mistaken for Anaphylaxis Post Immunization

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

Early recognition of anaphylaxis

Because anaphylaxis requires immediate treatment, diagnosis is primarily made based on recognition of clinical signs and symptoms,including:

- ***Respiratory:*** *sensation of throat closing, stridor (high-pitched sound while breathing), shortness of breath, wheeze,cough*
- ***Gastrointestinal:*** *nausea, vomiting, diarrhea, abdominal pain*
- ***Cardiovascular:*** *dizziness, fainting, tachycardia (abnormally fast heart rate), hypotension (abnormally low bloodpressure)*
- ***Skin/mucosal:*** *generalized hives, itching, or swelling of lips, face,throat*

Symptoms often occur within 15-30 minutes of vaccination, though it can sometimes take several hours for symptoms to appear.

Early signs of anaphylaxis can resemble a mild allergic reaction, and it is often difficult to predict whether initial, mild symptoms will progress to become an anaphylactic reaction. In addition, not all symptoms listed above are necessarily present during anaphylaxis, and not all patients have skin reactions. Symptoms are considered generalized if there are generalized hives or more than one body system (e.g.cardiovascular, gastrointestinal) is involved. If a patient develops itching and swelling confined to the injection site, the patient should be observed closely for the development of generalized symptoms.

If symptoms are generalized, adrenaline should be administered as soon as possible, emergency medical services should be contacted, and patients should be transferred to a higher level of medical care.

Every health facility should have health staff trained in treatment of anaphylaxis and should have rapid access to an AEFI Kit with adrenaline and be familiar with its dosage and administration. Adrenaline has a short expiry life, the expiry date need to be monitored on regular basis.

Management of Anaphylaxis

If anaphylaxis is suspected, take the following steps:

- Rapidly assess airway, breathing, circulation, and mentation (mentalactivity).
- Place the patient in a supine position (face up), with feet elevated. If the patient vomits or unconscious, lie the patient in left lateral position.
- Give injection adrenaline (1mg/ml aqueous solution [1:1000 dilution]) intramuscular (IM) immediately at the midpoint of the anterolateral aspect of the middle third of the thigh (preferable) or midpoint of deltoid muscle
  - Dose of Adrenaline (1 mg/ml) is 0.01 ml/kg. If the weight of the patient is unknown, follow the age specific dosage chart
  - The maximum adult dose is 0.5 mg per dose.
  - Adrenaline dose may be repeated every 5-15 minutes if symptoms do not improve
  - Because of the acute, life-threatening nature of anaphylaxis, there are no contraindications to epinephrine administration.

Antihistamines (e.g., H1 or H2 blockers) and bronchodilators do not treat airway obstruction or hypotension, and thus are not first-line treatments for anaphylaxis. However, they can help provide relief for hives and itching (antihistamines) or symptoms of respiratory distress (bronchodilators) but should only be administered after epinephrine in a patient with anaphylaxis. Because anaphylaxis may recur after patients begin to recover, monitoring in a medical facility for at least several hours is advised, even after complete resolution of symptoms and signs.

Dosage chart of Inj. Adrenaline (1mg/1ml) IM

Age	Dose in ml	Volume in 100 unit insulin syringe
0-1 year	0.05	05 units
>1-6 years	0.1	10 units
>6-12 years	0.2	20 units
>12-18 years	0.3	30 units
Adults	0.5	50 units

Management of Anaphylaxis at the Outreach Immunization Sessions

Anaphylaxis is to be managed as a medical emergency. It should be suspected and recognized early so that it can be managed immediately by trained staff and the patient is transferred to the nearest hospital. The national AEFI Expert Review Committee and the National Immunization Technical Advisory Committee (NITAG) constituted by the Ministry of Health and Family Welfare reviewed scientific literatures and asserted that immediately administering a single dose of adrenaline by the health worker (HA/FWA/other vaccinator) is safe. It further recommended that the case should be then immediately transported to the nearest hospital for further management.

Annex-8

Verbal autopsy form for interviewing family of reported AEFI

Case ID NO .....

To be filled only in cases where inadequate information is available (brought dead/home death/insufficient medical records/not hospitalized/ clinical diagnosis not possible)

Section 1. Basic details

A) Demographic data of the patient

Name of the child/ woman: _____ Date of Birth: _____

Age (in months/years): _____ Sex: ☐ Male ☐ Female

Name of Mother/Father: _____

Complete address:

House No.: _____ Para/Village: _____ Mahalla/Rural Ward: _____

Union/Urban ward: _____ Upazila/Mun/Zone: _____ Dist/CC: _____

B) Details of respondent

SL No	Name of respondent	Relation with deceased
1		
2		
3		
4		
5		
6		

Name of the main respondent:

Relation of main respondent with the deceased:

Did the respondent live with the deceased during the events that led to death? Yes/No

Did the respondent witness the event that led to death? Yes/No

Note the time of Event: _____

Place at which event occurred: home/govt facility/private facility/others (please specify: _____

Section 2. For cases of children (from 0 to 5 years)

If weight not available, ask whether the child looked weaker/smaller as compared to babies of similar age Yes/No

A) Birth details (Check records if available)

Birth weight:

Child's size, if weight is unknown (small/average/larger than average/unknown):

Place of delivery:

Type of delivery (normal/caesarian/forceps):

Was s/he born premature? (less than 37 weeks): Yes/No;

If yes, please specify _____

Was the child part of a multiple birth? Yes/No; ☐ ☐ ☐

Was the child the first, second, or later in the birth order? First Second or later

History of any birth defects/ malformation? Yes/No

If yes specify_____

B) Feeding history:

Exclusive Breast fed- (Yes/No):

Other foods (Yes/No; if yes, specify_____

What foods and liquids was the child fed in the past 24 hours?

Breast milk: Yes/No (If yes, frequency _____and when last fed_____)

Animal milk: Yes/No (if yes, frequency _____and when last fed_____,

Water: Yes/No (If yes, frequency _____and when last fed_____)

Other liquids (give details): Yes/No If yes, specify _____ frequency _____and when last fed_____

Solids: Yes/No (If yes, specify _____and when last fed_____) frequency _____and when last fed_____)

On what day and at what approximate time was the child last fed?

Date: Time:

With what the child was last fed? Specify _____

Who last fed the child: _____

C) Medical conditions

What condition(s) did the child have? (see the options below)

Condition	Unknown	No	Yes	Remarks
Fever				
Diarrhoea				
Excessive sweating				
Lethargy				
Sleeping more than usual				
Difficulty in breathing				
Irritable				
Excessive crying				
Apnea (Stopped breathing)				
Reluctant to feeding				
Cyanosis (turned blue/ grey)				
Vomiting				
Seizures or convulsions				
Skin rash				
Choking				
Unconscious				
Others (specify)				

D) Development status

Appropriate for age ☐ Delayed ☐ If delayed, give details: .....

.....

E) In case of death at home:

Where was the child last known to be alive? .....When?.....

In what position was the child placed? .....

Face position when last placed (Face down on surface/ face up/ face to a side)

In what position was the child placed? .....

Face position when child found (Face down on surface/ face up/ face to a side)

What was the child wearing? _____

What was the temperature in child's room? (Hot/cold/normal/other. Please specify _____)

Was anyone sleeping with the child? (Yes/No):

Which of the following items were within the child's reach?

(Toys/pillows/polythene bangs/blankets/sheet/others. Please specify _____ _____)

Describe the infant's appearance when found:

Appearance	Unknown	No	Yes	Describe and specify location
Discoloration a round face/nose/mouth				
Secretions (foam, froth)				
Skin discoloration				
Pressure marks (pale areas/ blanching)				
Rash or petechiae (small red blood spots on skin, membranes, or eyes)				
Marks on body (scratches or br uises)				
Other				

What did the infant feel like on touching when found?

(Sweaty/warm to touch/ cool to touch/limp/flexile/rigid/stiff/unknown/others. Please specify_____

At which of the following places or facilities did the child/ person receive treatment for the event?

Home ☐ traditional healer ☐ government hospital ☐ private clinic/ hospital ☐ pharmacy any other place or facility ☐ (specify _____)

Please collect copy of prescription/ discharge notes if available)

Section 3: Family history

Number of people staying in the house and relation to the child/ person:

Socioeconomic status:

Health status of siblings:

Consanguinity: Yes/No (If yes, specify _____),

Yes/ No: If yes, specify _____

Occupation of father/ mother:

History of similar illness to any child in family:

Presence of adverse family circumstances:

(family relationships/economics/behavioral/addictions/circumstantial evidence):

Yes/No: (If yes, specify _____) Any other significant factor:

_____

Section 4: Interviewer's observations (Case summary)

(Emphasis should be placed on establishing the exact chronology of events from point of vaccination of occurrence of event)

Name of interviewer:

Designation : .....

Address : .....

Contact No. : .....

Email : .....

Annex-9

District AEFI response template for press briefing

District_____ Date_____

As a part of the Expanded Programme on Immunization (EPI), _____District Vaccinated _____ (number of) children against vaccine preventable diseases including polio, childhood TB, diphtheria, pertussis, tetanus, hepatitis B, Hib, measles and rubella during the year _____ (from and to). The District _____, through its ongoing efforts, has achieved an immunization coverage rate of _____% in _____(year).

___ (number of) doses of Penta/IPV/BCG/OPV/MR (choose the vaccine in question) have been administered to _____number of children between (the dates). _____and_____

As a part of routine surveillance, _____(number of) AEFI have been reported during the period _____(date) in district (name of district), including_____ (details of case/s e.g. 4 deaths, 3 Hospitalizations). The AEFI surveillance system records all minor adverse events (such as rashes, swelling at the injection site, fever) and investigates the serious cases (such as death and hospitalization) to strengthen the immunization programme.
(please add particulars of the relevant investigation/s).

The District AEFI Committee is investigating the above cases. The investigation team composed of_____ (mention the designation with name of the members).

AEFI surveillance is a reporting system to report and investigate the potential side effects after vaccination. Reporting an AEFI does not mean that the vaccine has caused it. The cause can be determined only after proper investigation and Casualty Assessment.

Vaccination has been recognized as the most effective public health intervention for child health, preventing disease mortality and morbidity. Every year,_____(number of) infants/ under 5 years suffer from (diseases specific to antigen in question, depending on the available data) in the district.

Manufacturing of vaccines is a tightly monitored process with multiple checks at different stages of production. Post production, each batch goes through tests to ensure quality and safety before they are released for use. Moreover , the vaccines used in EPI are WHO prequalified vaccines.

Annex-10

Key messages for spokespersons on immunization and vaccines

Spokespersons should repeat these messages consistently during interviews:

Key Messages on Importance of A Sustained Immunization Programme

- Immunization is key to achieving the goal of reducing vaccine preventable deaths among children under five years old.
- In the past, millions of people died or were disabled from diseases that we can now prevent with vaccines. If we do not continue to vaccinate, these diseases will return and claim more lives.
- Immunization currently prevents an estimated 2-3 million deaths every year. But, an estimated 22 million infants worldwide are still missing out on basic vaccines.
- Vaccines save lives.
- It is more hazardous not to vaccinate, because of the potential serious complications of the disease.
- It is much safer to be vaccinated than to contract the disease.
- Vaccines can cause reactions, but mostly they are mild, do not last long and self-limited; very rarely do they lead to serious or long-term problems.
- The safety of vaccines is of fundamental concern to health-care providers, and if there are any perceived or real problems with safety, these are investigated and corrected.
- The safety of vaccines is closely monitored by surveillance, and thereby safety of vaccine and immunization is ensured.
- All vaccines have a safety profile, meaning they have expected minor reactions, but these are usually mild and temporary.

Investing in Immunization

- Immunization remains one of the most cost-effective health interventions, even with newer, more expensive vaccines.
- By keeping children healthy, immunization helps to extend life expectancy and time spent on productive activities. Immunization therefore helps to reduce poverty.
- A fully immunized child is more likely to attend school, have greater cognitive abilities, and be a more productive member of society and less likely to be disabled as result of serious disease.

Annex-11

Frequently asked questions (FAQs)

Are vaccines safe ?

Vaccines are very safe. They prevent dangerous, deadly diseases that can lead to blindness, deafness, brain damage, heart problems, pneumonia, and paralysis and carry a risk of life-long disability or death. Vaccines have saved millions of lives.

How can we be sure that vaccines are safe?

Remember that there is nothing in life that is 100% safe – not even water, since you can drown in it. No medicinal product is 100% safe, although some are lifesaving. Similarly, although vaccines are very safe, there is the possibility of adverse events.

Vaccine development is a costly process. A vaccine has to pass a lengthy testing process before it comes on to the market for public use. Vaccines also have to be licensed for use by the National Regulatory Authority (NRA). This means that vaccines have to undergo extensive additional safety and quality checks before they can be brought into the country. In addition, they are also monitored for safety after licensure. WHO prequalification of vaccines is another option for assuring vaccine safety.

UNICEF assists countries in the purchase of vaccines that are WHO prequalified for the EPI. This means the vaccines we use are safe, as they have passed and meet global safety and quality standards.

If any adverse reaction does occur, this is usually minor and self-limited, lasting only for a few days. Such side effects do not disrupt daily activities. Serious adverse reactions from vaccines are extremely rare. Vaccine safety is closely monitored by EPI so that any problems can be dealt with quickly and timely through the AEFI surveillance system .

At what rate do AEFI occur in a vaccination campaign?

During a mass vaccination campaign or supplementary immunization activity, millions of doses of vaccine may be given. That means that even if AEFI occur at the same rate as for the rest of the year, we can expect that this would result in a more concentrated occurrence of AEFI than usual. For instance, if the expected rate of high fever following administration of measles vaccine is 2% of vaccines and a country gives on average 100 000 doses of measles vaccine in one year, then it would be expected that over the year 2000 children would be reported with high fever following administration of measles vaccine. This works out as approximately 40 children per week (2000 over 52 weeks = around 40).

If a campaign were to be carried out in which 100 000 doses of measles vaccine were given in one week, we would expect 2000 children with high fever to be reported in that week. The rate remains the same, and it is only the number of high fever cases reported during that one week of vaccination campaign that is causing concern. Parents and guardians need to be reassured that vaccines are safe and that the reported AEFI numbers are still within the expected, low rate of 2%.

What is a coincidental death?

Every year a certain number of children under 1 year and under 5 years will die, due to various causes. This is expressed as a rate per 1000 live births for every country. Because we give many vaccines to children at this age, it is possible that death might occur after any of these vaccinations, although caused by another condition, such as pneumonia, meningitis etc. These are called 'coincidental child deaths' and should not be attributed to immunization. In these cases a proper causality assessment, particularly supported with postmortem findings, can prove that the vaccine has no link to the death.

What is being done by national EPI to monitor the safety of vaccines and quality of the vaccination programme?

AEFI surveillance system is in place to monitor safety of vaccines and the quality of the immunization programme. There are District/ City Corporation AEFI Committee, divisional AEFI causality assessment committee and National AEFI Expert review Committee to review AEFIs data, investigate serious AEFIs and do causality assessment to find out the cause of AEFIs and take appropriate action as required.

What is the difference between the whole cell Pertussis vaccine (DTwP) and acellular Pertussis vaccine (DTaP)?

Whole cell Pertussis vaccine (DTwP) contains the whole cell, killed of the bacteria (germ) responsible for this disease and the acellular Pertussis vaccine (DTaP) contains only parts of a cell.

The acellular pertussis vaccine is more expensive because its production costs are high. The difference between the two vaccines is that acellular pertussis vaccines have fewer side effects (mainly minor ones) but the vaccines are both of good quality and offer good and higher protection. New evidence even suggests that in terms of longer term protection, the whole-cell killed vaccine is better.

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