ADVERSE EVENTS FOLLOWING IMMUNIZATION (AEFI) SURVEILLANCE GUIDELINES

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FOREWORD

The Government of Zimbabwe through the Ministry of Health and Child Care is committed to controlling, eliminating and eradicating vaccine preventable diseases among children under the age of five years. The immunization programmme is a pillar for survival and improvement of child health. The programme aims at reaching every child living in Zimbabwe with safe and potent vaccines. These guidelines will provide an essential platform for monitoring Adverse Events Following Immunization (AEFI) to ensure safety of these vaccines.

Safety of vaccines is an essential part of the successes of immunization programmes, this activity requires the involvement of various stakeholders whose sole mandate is to monitor safety of immunization. The National Pharmacovigilance Centre, Medicines Control Authority of Zimbabwe (MCAZ) in collaboration with the Zimbabwe Expanded Programme on Immunization (ZEPI) are the main drivers of this initiative.

These AEFI guidelines focus on improving the quality of immunization programme through activities that collect, detect, assess, monitor, prevent, and manage AEFIs. Implementation of ZEPI principles outlined in this AEFI guideline will contribute to the realization of Sustainable Development Goals (SDG) 3.3 and 3.8. The Ministry of Health and Child Care urges all health workers in Zimbabwe from both the public and private sector to read and implement the guidelines that are clearly spelt in this important document. I urge all health workers in Zimbabwe to use these AEFI guidelines to safegaurd and protect the health of children.

BRIGADIER GENERAL (DR) G GWINJI
SECRETARY FOR HEALTH AND CHILD CARE

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, WHO 2013 definition. The adverse event may be any unfavourable or unintended sign, abnormal laboratory finding, symptom or disease.

AEFI surveillance: Monitoring, detecting and responding to adverse events following immunization; implementing appropriate and immediate action to correct any unsafe practices detected through the AEFI surveillance system, in order to lessen the negative impact on health of individuals and the reputation of the immunization programme.

Anaphylaxis: It is a reaction after receiving a drug or vaccine.

Anaphylactic shock: A sudden, severe allergic reaction characterized by a sharp drop in blood pressure, urticaria, and breathing difficulties that is caused by exposure to a foreign substance to which a person has an extreme sensitivity, often involving respiratory difficulty and circulation failure.

Causal association/link: An AEFI which is caused by administration of a particular vaccine. Causally associated events are also temporally associated, but events which are temporally associated may not necessarily be causally associated. Causality is usually based on laboratory findings (e.g. isolation of vaccine virus strain), and/or unique clinical syndrome (e.g. anaphylaxis), and/or epidemiological studies showing an increased incidence in vaccinated groups as compared to unvaccinated groups.

Cluster: Two or more cases of the same or similar events, which are related in time, and have occurred within a specific geographical area, or associated with the same vaccine, the same batch number or the same vaccinator.

Coincidental event: An AEFI that is caused by something other than the vaccine product, immunization error or immunization anxiety, but a temporal association with immunization exists.

Immunization anxiety-related reaction: An AEFI arising from anxiety about the immunization.

Immunization error-related reaction: An AEFI that is caused by inappropriate vaccine handling, prescribing or administration and that thus, by its nature, is preventable.

Immunization safety: Includes vaccine safety and quality, safe injection, waste disposal and AEFI surveillance.

Injection safety: Injection safety is the safe handling of all injection equipment, routine monitoring of the availability and use of safe injection equipment, and correct disposal of contaminated injection equipment.

Live viral vaccines: Vaccines containing attenuated (weakened) versions of the disease-causing virus (e.g. poliomyelitis, measles). The vaccine virus causes a mild infection, usually with minimal or no symptoms, that creates immunity against that virus.

Non-serious AEFI: A reaction that is not classified as a serious AEFI.

Serious AEFI: An AEFI that is life-threatening, or results in hospitalization, disability or death.

Temporal association: Two or more events that occur around the same time but are unrelated.

Toxic shock: Toxic shock syndrome is a severe disease that involves fever, shock and problems with the function of several body organs.

Trigger event: A medical incident that stimulates a response, usually a case investigation.

Vaccine: A biological substance that is administered to individuals to elicit immunity (protection) against a specific disease. Combination vaccines (e.g. DTP) protect against more than one disease.

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 such as the adjuvant, preservative or stabilizer.

Vaccine quality defect-related reaction: An AEFI that is caused or precipitated by a vaccine due to one or more quality defects of the vaccine product, including the administration device as provided by the manufacturer.

ABBREVIATIONS

AFP	Acute Flaccid Paralysis
AIDS	Acquired Immuno Deficiency Syndrome
BCG	Bacilli Calmette Guerin
bOPV	Bivalent Oral Polio Vaccine
DTP	Diphtheria Tetanus and Pertussis
DTP-HepB-Hib	Diptheria, Tetanus, Pertussis, Hepatitis B and Haemophillus Influenzae
DT	Diphtheria Tetanus
EDLIZ	Essential Medicines List of Zimbabwe
EPI	Expanded Programme on Immunization
GBS	Guillain-Barre Syndrome
HBV	Hepatitis B Virus
Hep B	Hepatitis B
HIB	Haemophilus Influenza Type B
HIV	Human Immuno-deficiency Virus
HPV	Human Papilloma Virus
IPV	Inactivated Polio Vaccine
MCAZ	Medicines Control Authority of Zimbabwe
MCHIP	Maternal and Child Health Integrated Programme
MR	Measles Rubella
NIDs	National Immunization Days
NNT	Neonatal Tetanus
OPV	Oral Polio Vaccine
PCV	Pneumococcal Conjugate Vaccine
SDG	Sustainable Development Goals
TOPV	Trivalent Oral Polio Vaccine
TD	Tetanus Diphtheria
TT	Tetanus Toxoid
UNICEF	United Nations Children's Fund
WCBA	Women of Child Bearing Age
WHA	World Health Assembly
WHO	World Health Organisation
ZEPI	Zimbabwe Expanded Programme on Immunization

1. INTRODUCTION

Immunization is a successful and cost effective public health intervention that has led to global eradication of diseases like smallpox and has certified large areas of the world polio-free. It is estimated that immunization averts an estimated 2 to 3 million deaths from diphtheria, tetanus, pertussis (whooping cough), and measles every year in all age groups. Zimbabwe attained Universal Child Immunization in 1990 with considerable reduction in morbidity and mortality from vaccine preventable diseases and longer inter-epidemic periods of measles up to 2008. As Zimbabwe continues to adopt WHO recommended vaccination strategies in its population, it is becoming imperative that surveillance of AEFI be increased. The vaccine products and equipment used in immunization undergo intensive World Health Organization (WHO) prequalification exercises to determine quality and approve their uses in countries. These precautionary measures do not necessarily eliminate the risk of adverse events that may arise from the use of products for immunization.Previous experiences have shown that determining causality of an event to a vaccine is a challenge that requires engagement of expert opinion and thorough investigation of the event. Events that occur after vaccinations are called Adverse Events Following Immunization (AEFIs); defined as 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.

The safety of immunization programmes involves a wide spectrum of activities that include regulation, vaccine safety and quality, safe injections, waste disposals, and AEFI surveillance. Effective vaccines (i.e. vaccines inducing protective immunity) may produce some undesirable side effects which are mostly mild and clear up quickly. The majority of events thought to be related to the administration of a vaccine are actually not due to the vaccine itself - many are simply coincidental events or programmatic errors. It is not possible to predict every individual who might have a mild or serious reaction to a vaccine, although there are a few contraindications to some vaccines. Adherence to contraindications minimizes the risk of serious adverse events. During mass immunization campaigns there usually is a general increase in adverse events following immunization. This can be attributed to two factors; the large number of vaccinations performed in a short period of time (from a few days to a few weeks) causes a temporary concentration of adverse events following immunization, and the pressure during the campaigns on vaccination teams means they may fail to observe safe injection practices. Public misconceptions may arise due to occurrence of AEFIs, and these may cause

collective fear of vaccination. It is against this background that standardization and surveillance of adverse events following immunization is critical to enhance effective management of AEFIs. This document is a guide for health workers in the management of Adverse Events Following Immunization (AEFIs), can be adapted to suit each level of health care, and is meant to cover issues of vaccine safety and quality, as well as communication of these events for management.

According to the WHO, 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 health worker, clinic or hospital staff, a volunteer, parent or any other person who detects the AEFI. The WHO recommends that suspicion alone is sufficient for reporting; the primary reporter is not expected to assess causality. In investigating suspected AEFIs, it is important that rapid detection and evaluation of a possible link to vaccines is carried out to ensure the continued safety of vaccines. The WHO Global Manual on Surveillance of AEFIs highlights that in the case of a suspected AEFI, it is preferable to submit a report to a suitable technical authority on time rather than waiting for all aspects of an investigation to be completed; and this is particularly true for serious reports.

To report a suspected AEFI, an AEFI reporting form is to be completed. Five forms are to be fully completed, dated, stamped and signed. One copy of the forms should be filed at the clinic and four submitted to the District level for onward submission of three of the copies to the Provincial level. The Provincial level would then forward two of the three copies to the Zimbabwe Expanded Programme on Immunization Unit at the Head Office and from there one copy would be forwarded to the MCAZ. For serious AEFI a case investigation form is required to be completed, together with an AEFI reporting form, and submitted to the ZEPI-MoHCC and the MCAZ.

All events that are actively notified to the health care system by the parents/guardians or patients themselves or identified by a health care provider that are submitted to the MCAZ are assessed for causality according to the Causality Assessment of an AEFI, User Manual for the revised WHO classification, Aide-memoire 2013.

Zimbabwe documented 80 AEFI cases in 2010, 14 in 2011, 76 cases in 2012, 39 cases in 2013, 48 cases in 2014, 249 cases in 2015 and 11 cases by the 2nd quarter of 2016; most of which were known reactions. Documentation of AEFI cases is an essential part of AEFI management when they occur in children.

Any AEFI that is of concern to parents or health-care workers should be reported. In particular, health workers must report:

a. serious AEFIs

b. signals and events associated with a newly introduced vaccine

c. AEFI that may have been caused by an immunization error

d. significant events of unexplained cause occurring within 30 days after vaccination

e. events causing significant parental or community concern.

WHO assessment tool for AEFI surveillance

The Zimbabwe AEFI surveillance systems is based on the WHO guidelines for AEFI surveillance and WHO assessment tool for AEFI surveillance listed below;

A. Institutional regulations and guidelines for the monitoring and management of Adverse Events Following Immunization (AEFI)

No	Requirements	Status
A1	In the country, is the scope and extent of the AEFI monitoring clearly defined in the legislation (national laws) and national AEFI guidelines?	☑
A2	Does the NRA have the legal basis to enforce the AEFI reporting system and to take actions if needed?	☑
A3	Are there provisions for the establishment of an advisory committee to review AEFI reports?	☑
A4	Does the legislation provide for adequate and proportional sanctions, penalties and prosecution upon conviction of violations?	☑
A5	Are there legal provisions for the NRA to require the manufacturer to perform a specific study of safety in the post-marketing period to assure the safety of authorized products, if needed?	☑

A6	Are there legal requirements for manufacturer to inform NRA of any new safety signal or marketing / regulatory decisions taken in other countries?	☑ Requirement only for Zimbabwe, not other countries
A7	If yes to A6, is this enforced by NRA?	☑
A8	Are there endorsed guidelines explaining the obligation and how, when and what safety issues have to be reported ?	☑
A9	• Objectives of the system • List of AEFI to be reported • Case definitions of AEFI to be reported • Clear definitions of terminology relevant for analysis and response (e.g. adverse event versus adverse reaction; coincidental, immunization error, serious events, cluster events) • Information on how to report (who, how, where, when) • All vaccines to be included in the reporting system (not only EPI vaccines) • Procedure for analyzing data • Feedback procedure back to key players, parents, communities of findings and relevant actions • Procedure for investigating and actions to be taken in case of serious AEFI or cluster events • Definition of the people in charge	☑ ☑ ☑ ☑ ☑ ☑ ☑ ☑ ☑ ☑ ☑

B. Capacity of the AEFI detection and reporting system

No	Requirements	Status
B1	Does the system have satisfactory sensitivity to detect serious adverse events or clusters of events?	☑
B2	List the different systems established within the country that are involved in vaccine safety data collection and transmission.	• Clinic level, central level, MCAZ level • District Health Information System 2 (DHIS2) • Vigiflow • eADR/AEFI Demo

C. Quality management system for pharmacovigilance activities

No	Requirements	Status
C1	Is there an organizational chart and responsibilities to implement the quality management system?	☑
C2	Are the responsibilities, duties and roles of the key persons within the NRA, the NCL, national immunization program or any other authority involved in pharmacovigilance activities well defined, documented and updated?	☑
C3	Is there a management system to ensure traceability of actions?	☑
C4	Is there a well defined auditing system(external & internal),. covering pharmacovigilance activities which is implemented?	☑

D. Human Resource Management

No	Requirements	Status
D1	Are there adequate qualified staff (number, education, training, skills and experience) to perform pharmacovigilance activities?	☑
D2	Is there a staff training plan developed and implemented?	☑
D3	Does the monitoring of acquired skills and competencies of the staff take place after training?	☑

2. IMMUNIZATION SCHEDULE

Table 1: ZEPI NATIONAL IMMUNIZATION SCHEDULE, as of May 2016

Age of Administration	Name of Vaccine	Route of administration
At birth	BCG	Intradermal deltoid muscle of the right arm
6 weeks	OPV 1	Oral
	Pentavalent 1 (DTP-HepB.Hib	Intranuscular antero-lateral aspect of the right mid-thigh
	PVC 1	Intranuscular antero-lateral aspect of the left mid-thigh
	Rotavirus 1	Oral
10 weeks	OPV 2	Oral
	Pentavalent 1 (DTP-HepB.Hib	Intranuscular antero-lateral aspect of the right mid-thigh
	PVC 2	Intranuscular antero-lateral aspect of the left mid-thigh
	Rotavirus 2	Oral
14 weeks	OPV 3	Oral
	Pentavalent 3 (DTP-HepB.Hib	Intranuscular antero-lateral aspect of the right mid-thigh
	PVC 3	Intranuscular antero-lateral aspect of the left mid-thigh
	IPV	Intranuscular antero-lateral aspect of the left mid-thigh 2cm from the PCV 3 site
	MR 1	Subcutaneous of the left upper arm
18 months	DTP Booster	Intranuscular antero-lateral aspect of the right mid-thigh
	OBV Booster	Oral
	MR 2	Subcutaneous of the left upper arm

This is the only national immunization schedule to be used in Zimbabwe, for both private and public sectors. Please refer to future revised schedule, if any, after publication of these guidelines. Children should receive first doses at these stated ages or at first contact after reaching that age. Maximum age limits are: BCG 11 months and Pentavalent (DTP-HepB-Hib) 23 months (these antigens should not be given after these age limits).

Zimbabwe will be part of the global polio endgame countries that will work toward switching from TOPV to BOPV then IPV as stipulated in the Zimbabwe SWITCH plan timelines from 1st May 2016 to 2020.

VITAMIN A SUPPLEMENTATION

Vitamin A supplementation has been integrated in the routine immunization since 2005. Any contact with a health worker is an opportunity to screen mothers and children for eligibility to receive Vitamin A supplementation. The optimal interval between doses for children is every 6 months until 59 months, in Zimbabwe.

Table 2: Vitamin A supplementation schedule

Target for Vitamin A	Immunization Contact	Route	Dose
Infants 6 – 11 months	Routine immunizations/ Campaigns	Oral	100 000 IU
Children 12 – 59 months	Routine immunizations/ Campaigns	Oral	200 000 IU

3. BASICS OF AEFI

Definition

An Adverse Event Following Immunization (AEFI) 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, WHO definition 2013.

a. Types of AEFIs

In 2012, the Council for International Organizations of Medical Sciences (CIOMS) and WHO revised the classification regarding cause-specific categorization of AEFI. There are five cause-specific type AEFI namely; vaccine product-related reaction, vaccine quality defect-related reaction, immunization error-related reaction, immunization anxiety-related reaction and coincidental event.

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

ii. Vaccine quality defect-related reaction:

An AEFI that is caused or precipitated by a vaccine due to one or more quality defects of the vaccine product, including the administration device, as provided by the manufacturer. A vaccine quality defect-related reaction, is a due to a defect in a vaccine (or its administration device) that occurred during the manufacturing process. Such a defect may have an impact on an individual's response and thus increase the risk of adverse vaccine reactions. Insufficient inactivation of wild-type vaccine agent (e.g. wild polio virus) during the manufacturing process or contamination introduced during the manufacturing process could cause the vaccine quality defect-related reactions. In the early years of immunization programmes, some major

vaccine quality defect-related reaction incidents were reported. However, since the introduction of good manufacturing practice (GMP) manufacturing defects are now very rare. Since vaccine manufacturers have started following GMP, and NRAs have been strengthened, the potential risk of such quality defects is now rare.

iii. Immunization error-related reaction:

An AEFI that is caused by inappropriate vaccine handling, prescribing or administration and that thus, by its nature, is preventable. When errors in vaccine handling such as exposure of the vaccines and or diluents, where applicable, to excess heat or cold; use of a vaccine post expiration date, or errors in vaccine prescribing, vaccine administration or non-adherence to recommendations for use occur, immunization error-related reactions result.

iv. Immunization anxiety-related reaction:

An AEFI arising from anxiety about the immunization. These reactions are common, resulting from fear of, or pain due to, injection rather than from the vaccine itself. In some cases the cause of the AEFI remains unknown, however clusters of fainting after immunization are well recognized as anxiety-related reactions during immunization programmes targeting adolescent girls.

v. Coincidental event:

An AEFI that is caused by something other than the vaccine product, immunization error or immunization anxiety, but a temporal association with immunization exists. These require specific domain knowledge for comprehensive investigation and correct interpretation as they may be mistaken for vaccine reactions and could lead to inappropriate suspension of a vaccine programme.

b. Objectives of AEFI Surveillance

i. To ensure patient safety

ii. To detect, investigate and report AEFIs

iii. To analyse AEFI reports and take corrective action

iv. To minimize AEFIs in routine immunization and mass campaigns

4. ROLES AND RESPONSIBILITIES AT VARIOUS LEVELS

Roles and responsibilities are as described below and summarized in the flow chart for AEFI management (appendix 1 on page 32). The flow chart also shows the reporting timelines that should be followed.

a. Community

i. Identification of AEFIs

ii. Reporting to nearest health worker/ health centre

b. Service Delivery Level (hospitals/ clinics - public and private)

i. Identification and/or detection of AEFIs

ii. Clinical management of AEFIs

iii. Reassure the care giver

iv. Completion of AEFI reporting forms and case investigation forms

v. Notify district of any cases of AEFIs (NB. Use fastest means of communication in case of serious or fatal AEFIs; notification to be done within 24 hours)

vi. All fatal cases to be reported to the police for a post mortem

vii. Refer serious cases to district hospital with well completed AEFI reporting and investigation forms

viii. Keep the respective vaccine vial (clearly labeled) under cold chain in cases of severe reaction until investigations are complete

ix. In case of clustering of AEFIs (more than one case) from one batch number of vaccines, stop using that batch and report immediately

x. Maintain line list of AEFIs

xi. Refer all questions to the DMO

XII. Write report and follow up

xiii. Ensure that all fields are completed

c. District Level

i. Ensure all staff are trained on AEFI surveillance

ii. Provide AEFI SOPs to all facilities and ensure adherence

iii. Generate the AEFI report ID number and record it on the submitted AEFI reporting forms

iv. Investigation of all AEFI cases that;

a. are serious cases (death/ resulted in hospitalization/ disability)

b. belong to a cluster of AEFIs

c. are a previously unrecognized event associated with a new introduced vaccine involves an increased number or rates of known cause

d. are a suspected immunization error

e. appear on the list of events defined for AEFI surveillance

f. cause significant parental or public concern.

v. Classify all the AEFIs

vi. Correct programme errors through on job training

vii. Facilitate management of cases

viii. Complete AEFI investigation report

ix. Notify province of any cases of AEFIs (NB. Use fastest means of communication in case of serious or fatal AEFIs)

x. Maintain district line list

xi. Ensure post mortems are done for deaths and reports are submitted timeously to next level, including the AEFI reporting and investigation forms

xii. Refer all questions to the DMO

d. Provincial Level

i. Contact National level focal person for severe and fatal AEFIs

ii. Maintain provincial line list of AEFIs

iii. Investigate or support investigation of serious AEFIs, and forward completed AEFI reporting and investigation forms to the national level

iv. Conduct regular supportive visits to districts

v. Ensure training of staff and provide resources for system

vi. Ensure all reports are submitted to national level in duplicate

vii. Reconcile provincial and national surveillance databases on a quarterly basis

vii. Refer all questions to the PMD

e. National Level

i. Receive and review AEFI case reports from sub-national levels

ii. Conduct investigations when necessary

iii. Submit all AEFI reporting and investigation forms to the Medicines Control Authority of Zimbabwe (MCAZ), within 48 hours of notification

i.v Give regular feedback to lower level and MCAZ

v. Ensure SOPs are compliant to requirements at all times

vi. Provide training to all focal persons

vii. Provide national guidelines on all vaccine management and surveillance issues

viii. Refer all questions to the Public Relations Officer

f. Medicines Control Authority of Zimbabwe – National Pharmacovigilance Center

The process followed by the MCAZ is described as below, and summarised in the MCAZ flow chart for AEFI reports (appendix 2 page 33).

i. On receipt of a completed AEFI reporting and investigation form, assign an in house report reference number.

ii. Check information on the report form for completeness and clarity.

iii. Request for any additional information or clarification from ZEPI where necessary and file the report form in the current AEFIs reports file.

iv. Transfer the information from the AEFI form to the MCAZ in-house report form, and draft the causality assessment and case definition as per the WHO Aide-memoire 2013.

v. The completed in-house report form should be tabled at the next Pharmacovigilance and Clinical Trials (PVCT) Committee meeting for causality assessment. The PVCT Committee is the National AEFI Committee.

vi. During the PVCT Committee meeting endorse on the MCAZ in house report form the Committee decision.

vii. After the Committee meeting proceed as decided by the Committee e.g. seek further information from ZEPI, inform other health care professionals of such AEFIs if necessary as an alert notice, letter or article in the drug information bulletin.

viii. Code report and compute details into the Adverse Drug Reaction (ADR) Vigiflow database as per the SOP.

ix. Complete a letter communicating the causality assessment decision made by the Committee; and send to ZEPI together with additional report forms, and a feedback letter to the reporter.

xi. Conduct further in-depth analysis and risk benefit assessment for serious AEFI and/or cluster AEFI including literature review. Provide feedback to ZEPI and reporter including publication of results in reputable journal.

5. STEPS FOR AEFI REPORTING

i. Receive the report, conduct a quick assessment and inform the next level

ii. Take full socio-medical history

iii. Review available records which the iv. patient might have brought and check any history of previous medication given

iv. Find out if the child had similar episodes prior to immunization or any history of allergies to food and/or medicines e.g. eggs, red meat, injury or any rituals done

v. In case of an abscess refer the child to the next level for probable laboratory tests, incision and drainage

vi. Find out from care giver if anyone in the community had the same problem after being vaccinated

vii. Notify the next level and refer patient to next level when necessary

viii. Compile an incident report of what transpired and submit to the next level with copy of the completed AEFI reporting forms, and AEFI case investigation forms for serious AEFIs.

ix. After results are out dispel myths and misconceptions.

x. In case of a suspected AEFI death offer bereavement counseling and inform the police

xi. Request for post mortem and parents to consent

xii. Refer all questions to the DMO/PMD/ PRO.

xiii. Have a fully equipped emergency tray

xiv. Check the cold chain equipment and temperature records

xv. Keep the used vials under cold chain for investigation

6. PROCEDURE FOR DETERMINING AND REPORTING AN AEFI

An AEFI reporting form should be completed to report an AEFI (appendix 3, page 34). For a serious AEFI an AEFI reporting form and case investigation form (appendix 4, pages 35 to 38) is required to be completed.

a. History talking

i. History taking should include the following:

ii. Vaccination history

iii. Chronic illnesses

iv. Acute infections

v. Medications given before and after vaccination

vi. Allergies to food eg. eggs, red meat etc., medicines

vi. Feeding practices

vii. Growth and development of child, including malnutrition

viii. Previous reactions to medicines

ix. Exposure to HIV

b. Examination and management of AEFI

i. Resuscitate the child and conduct a head to toe examination

ii. Note any abnormalities

iii. Take and record the child's temperature

iv. Confirm type of AEFI e.g. abscess and document findings

v. Counsel and reassure the care giver

vi. Explain procedure to be followed and manage child appropriately

c. Completion of AEFI reporting forms

i. Fill in five (5) AEFI reporting forms

ii. Ensure complete documentation

iii. Sign the forms

iv. Date stamp all the AEFI reporting forms

vi. File 1 copy at clinic

vii. Submit 4 copies to District Level for onward submission of 3 of the copies to the Provincial LevelThe Provincial Level would then forward two of the three copies to the Zimbabwe Expanded Programme on Immunization Unit, and from there one copy would be forwarded to the MCAZ.

viii. A completed AEFI form and case investigation form for serious AEFI are required by ZEPI and MCAZ to enable causality assessment and risk assessment

d. Communication

i. In case of fatal or severe AEFI use the fastest means of communication to inform the next level ie. phone. Fatal cases to be relayed to next level within 24 hours

ii. The communication should follow the normal channel: District, Provincial and ZEPI Head office

iii. Submit a comprehensive report and attach the AEFI reporting forms

7. INVESTIGATION OF AEFIs

Once an AEFI report has been received by the District level, an assessment should be made to determine whether or not an investigation is needed. The reported AEFI must be investigated if it:

i. appears to be a serious event (as defined by WHO) of known or unknown cause;

ii. belongs to a cluster of AEFI;

iii. is a previously unrecognized event associated with an old or newly introduced vaccine

iv. involves an increased number or rates of known cause;

v. is a suspected immunization error;

vi. appears on the list of events defined for AEFI surveillance; and

vii. causes significant parental or public concern.

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. It is important to investigate suspected adverse events promptly and completely. The District level is responsible for carrying out the investigation. The investigation can be a simple assessment or a more rigorous scientific evaluation of the reported AEFI in order to recognize its possible cause(s). The extent of the investigation depends on the nature of the reported AEFI. The WHO's Aide-mémoire on AEFI investigation, 2013 (Appendix 5, pages 39 to 40) should be used as resource material in the investigation of AEFIs. The aide-mémoire proposes a systematic, standardized process to investigate reported serious AEFIs and ascertain the underlying cause.

a. Investigation

The investigation team should fill the AEFI case investigation form and submit the form to the next level, with the AEFI reporting form attached.The following should be checked:

i. Cold chain maintenance

ii. Immunization technique

iii. Vaccine given

iv. Documentation practices

v. Emergency tray

vi. Sharps disposal

b. Composition of Investigation Team

i. Programme Manager

ii. Clinician(Pediatrician/Nurse/ Epidemiologist/Pathologist/Physician

iii. Health Promotion Officer

iv. Pharmacist

v. Surveillance Officer

vi. Logistician

vii. Laboratory and forensic expert

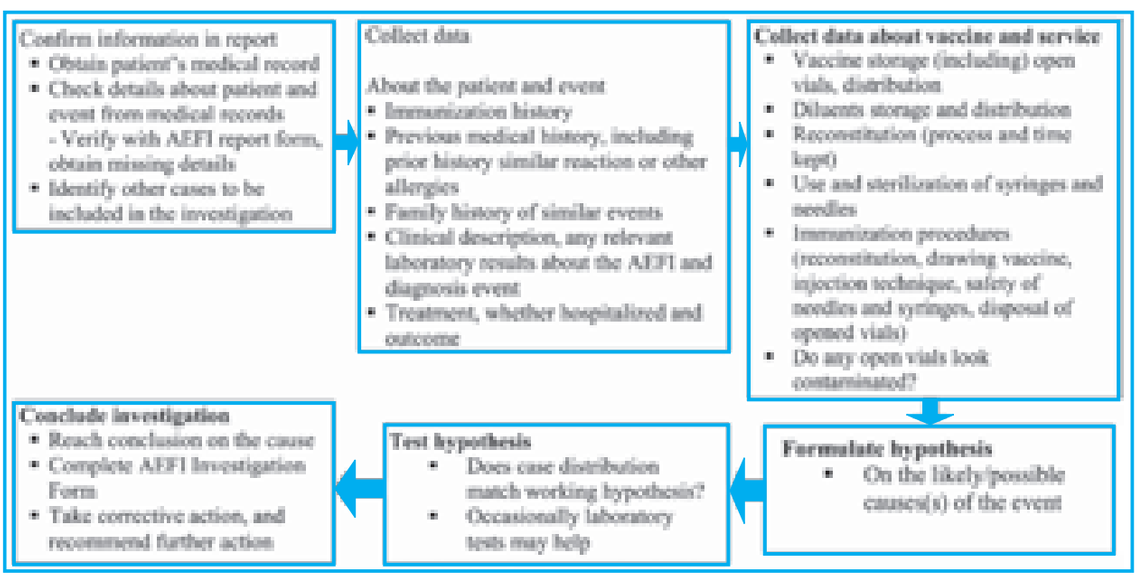
viii. Health Information Officer

Surveillance and investigation of AEFI is important in order to take corrective action and preserve public confidence in ZEPI.

c. How to investigate an AEFI

An AEFI investigation follows standard principles of epidemiologic investigation, as shown below;

Figure 1. Adapted from the WHO Global Manual on Surveillance of AEFIs, 2014.



It is important to investigate suspected adverse events promptly and completely. The investigator will primarily need to focus on the reported reaction as well as gather information from the patient/parent, health workers and supervisors, and community members.

i. Investigation of AEFI Clusters

A cluster of AEFI is defined as two or more cases of the same adverse event related in time, place or vaccine administration. According to the WHO Global Manual on Surveillance of AEFI, 2014 when investigating cluster AEFIs the investigator should look for AEFIs occurring in similar age groups and populations with genetic predisposition or disease. Cluster investigation begins by establishing a case definition for the AEFI and related circumstances and by identifying all cases that meet the case definition.

Cluster identification (i.e. cases with common characteristics) is done by gathering details (who, when and where) of vaccines administered (WHO, 2014). This can be achieved by collecting and recording:

i. detailed data on each patient;

ii. programme-related data (storage and handling, etc.); and

iii. immunization practices and the relevant health workers' practices.

Common exposures among the cases can be identified by reviewing:

i. all data on vaccine(s) used (name, lot number, etc.);

ii. data on other people in the area (also non-exposed); and

iii. any potentially coincident factors in the community.

When an AEFI cluster has been identified, the cause-specific definitions provide a framework for investigation and causality assessment.

The identification of the causes of an AEFI cluster may be investigated as the process flow under Figure 2.

Figure 2. Investigation of AEFI cluster

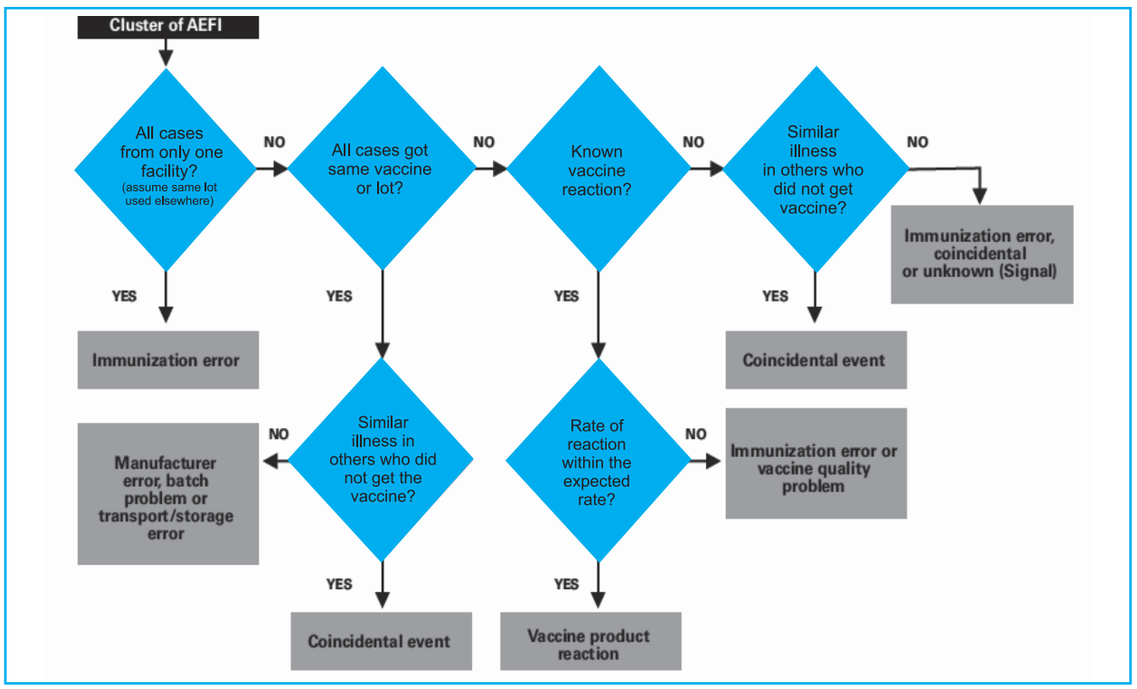


Fig 2. Adapted from the WHO Global Manual on Surveillance of AEFIs, 2014.

ii. 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, and all administrative levels, including the national immunization programme, should be notified of the death (WHO, 2014).

The WHO recommends that death investigation should be carried out by a team comprising clinical, laboratory and forensic experts, and that the team should be supported by the programme managers, as listed under 7(b) above. All relevant information on the event should be available to the investigation team.

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. At the time of autopsy, the autopsy surgeon should be provided documents outlining detailed preclinical and clinical history, including laboratory and radiological findings.

8. ANALYSIS OF AEFI DATA

The analysis of AEFI data is different to the analysis of adverse drug reactions and serious adverse events data. The Global Manual on surveillance of AEFIs by the WHO 2014 details that immunization and vaccine safety surveillance should incorporate inbuilt mechanisms for structured, systematic and continued data collection. Epidemiological 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, and other stakeholders including manufacturers, WHO 2014.

The MCAZ analyses AEFI data as per the WHO Global Manual on surveillance of AEFI and consider the following:

a. reporting source (reports of AEFI by different sources may provide a wider a range of information);

b. completeness of submitted AEFI forms;

c. verification and reassurance of data accuracy;

d. identifying health institutions where AEFI are not reported (determining whether this is due to failure of reporting or whether there are no AEFIs to be reported) and checking on "zero reporting" or "nil reporting";

e. performance of causality assessment to classify the AEFI;

f. estimated AEFI reporting rates (assessing the number of reported AEFI and the rate per 1000, 10 000 or 100 000 doses of vaccine used in a specified time period);

g. estimated rates by type of AEFI and by antigen (assessing the number of causes specific reported AEFI and the rate for 1000, 10 000 or 100 000 doses of vaccine used in a specified time period);

h. comparison of these observable rates with available or expected known events, whether vaccine reactions or background rates or historic reporting trends.

The table below is extracted from the WHO Global Manual on Surveillance of AEFIs, 2014 and explains the purpose of AEFI data analysis at different levels of the immunization safety surveillance system, the extent and purposes of analysis at each level.

Programme implementation level	What data to analyse	Purpose of data analysis at given level
Local level (immunisation provision level)	Number of reports by clinics, hospitals, villages by a given time	These are programmes operation/ surveillance perfomance indicators (timeless,completeness)
	Reported AEFI by place (clinics,hosptals), persons and time	Identification of immunization error related events will lead to corrective action
	Reported by AEFI by antigen	Will also identify vaccine reactions and coincidence
Sublinational Level (regional/ provincial/ district/ town)	Number of reports by local levels	These are programme operation/ surveillance indicators (timeless, completeness) at local level
	Reported AEFI by place (clinics, hospitals), persons and time	Identification of immunization error related events will lead to corrective action
	Cluster analysis	Cluster analysis leads to identification of immunization error related events, coincidence and vaccine reactions
	Reported AEFI by antigen	Will identify vaccine reactions and coincidence
National Level	Number of reports by intermediate levels	These are programme operation/ surveillance indicators (timeless, completeness) at intermediate level
	Reported AEFI by place (clinics, hosptals), personsand time	Cluster analysis leads to identification of immunization error related events, coincidence and vaccine reactions
	Cluster analysis	Will identify vaccine reactions, including detection of signals
	Reported AEFI by antigen	Leads to operational and policy decisions being taken in the country

Adapted from the WHO Global Manual on Surveillance of AEFIs, 2014.

The analysis of AEFI data is carried out by following four steps; as outlined in the Global Manual on surveillance of AEFI;

Step 1: After verification of cases, all reported AEFI data is line-listed and entered into a data base. Line listing aides in the initial identification of clustering or any unusual or significant reporting events that need further analysis.

Step 2: AEFI data is tabulated by place, person, time, antigens and type of event. This step further filters the AEFI by different variables and furthers analysis. It is possible to identify common immunization errors at this step.

Step 3: Calculation of AEFI rates, where the number of doses administered for each antigen is the denominator for calculating reported AEFI rates for each antigen at a given time period.

Step 4: Comparison and interpretation of AEFI rates. Expected vaccine reaction rates that are available for each type of AEFI and antigen (from WHO vaccine reaction information sheets) provide a guide to decision-making on corrective action for reported AEFI.

The WHO Global Manual on Surveillance of AEFIs, 2014 can be downloaded from the WHO website using this link:

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

9. AEFI CAUSALITY ASSESSMENT

Causality assessment, in the context of AEFI surveillance, 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 (Global Manual on Surveillance of AEFI, WHO 2014). 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. The WHO recommends that the national (central) expert committee for causality assessment and for high-level technical support and decision-making may use the WHO Aide-mémoire on causality assessment as resource material, and is encouraged to use in its investigations the comprehensive case definitions developed by the Brighton Collaboration. To classify AEFI causality, the MCAZ-PVCT Committee, which is the National AEFI Committee, follows these recommendations. To classify causality, the MCAZ-PVCT Committee uses the WHO Aide-memoire on AEFI Causality, 2013 and WHO Causality Assessment worksheet 2013. Appendix 6

9.1 Before AEFI Causality Assessment

9.1.1 The AEFI case investigation should have been completed. Premature assessments with incomplete investigation could mislead the classification of the event. When an investigation is incomplete, follow-up efforts to obtain additional information and documents should be made.

9.1.2 There must be a "diagnosis" using standard or widely accepted criteria for the adverse event, clinical sign, abnormal laboratory finding, symptom and/or disease in question. In other words, it should be clearly understood which vaccine is being associated with what specific event that was reported.

9.2 Causality Assessment Method

The WHO publication, Causality assessment of an AEFI – User manual for the revised WHO classification was developed by WHO as a method for assisting national committees for AEFI case review and causality assessment. It was patterned on an algorithm developed in the USA by the Clinical Immunization Safety Assessment network and with new AEFI definitions proposed by the Council for International Organizations of Medical Sciences (CIOMS).

The revised WHO causality algorithm focuses on two critical questions: "Is there evidence in literature that this vaccine(s) may cause the reported event even if administered correctly?" and "Did the event occur within an appropriate time window after vaccine administration?", WHO 2013.

There are four steps in causality assessment, which are;

Step 1. Eligibility: to determine if the AEFI case satisfies the minimum criteria for causality assessment. It is to be ensured that the AEFI case investigation is completed and that all details of the case are available. One or more vaccines administered before the event are identified and a valid diagnosis selected which is thought to be casually related to the vaccination. An appropriate definition to assess diagnostic certainty is to be used (Brighton Collaboration definition, standard literature, national definition or other approved definition). If an AEFI is reported and appears to not meet the eligibility criteria because of suspected inadequate information, it is important to make attempts to collect the additional information required in order to ensure that the case can be properly assessed for eligibility, WHO 2014.

Step 2. Checklist: to systematically review the relevant and available information to address possible causal aspects of the AEFI. The checklist is used as a guide to assemble information on patient-immunization-AEFI relationships.

Step 3. Algorithm: to obtain direction as to the causality with the information gathered in the checklist. A stepwise approach using the algorithm helps determine if the AEFI could be consistent, or inconsistent, with an association to immunization, or is indeterminate or unclassifiable.

Step 4. Classification: to categorize the AEFI's association to the vaccine/ vaccination on the basis of the direction determined in the algorithm.

The final classification is based on there being available adequate information for the case and the classes are classified as;

a. A: Consistent causal association to immunization

A1 – Vaccine product-related reaction

A2 – Vaccine quality defect-related reaction

A3 – Immunization error-related reaction

A4 – Immunization anxiety-related reaction

b. B: Indeterminate

B1 – Temporary 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. C: Inconsistent causal association to immunization Coincidental

d. Unclassifiable

10. COMMUNICATION

Introduction

Communication with parents, the community, health staff and the media need to be carried out under many circumstances, from launching new vaccines, putting in place mass immunization campaigns, to issuing reminders to maintain vaccinations up to date. When a vaccine safety investigation is underway resulting from one of the reasons outlined in earlier chapters of this manual, communications involve keeping the public informed about the investigation, results and action already taken or going to be taken regarding the AEFI. At the same time it is crucial to highlight the benefits of immunization even while communicating about an investigation.

Trust is a key component in the exchange of information at every level. Any overconfidence about risk estimates that are later shown to be incorrect contributes to a breakdown of trust among people involved. Admit uncertainty of AEFI, investigate fully, and keep the community informed. Avoid making a premature statement about the cause of the event before the investigation is complete. If the cause is identified as immunization related error, it is vital not to lay personal blame on anyone, but to focus on system- related problems that resulted in the immunization error(s) and steps being taken to correct the problem.

In communicating with the community, it is useful to develop links with community leaders and the peripheral health workers so that information can be rapidly disseminated. Maintaining lines of communication with the community is important throughout the investigation. Upon completion of the investigation, the cause of the event(s) needs to be communicated to the community. This communication must include information about the steps being taken to remedy the situation and to prevent a recurrence, if such steps are needed.

In this age of instant communication, as outlined in the WHO Euro manual, "the ease with which information can be disseminated now means that negative comments about vaccines can go "viral" on the internet without balanced professional input. As a result, the media have found rich pickings in vaccine safety issues". Nevertheless, employing strong communication principles and strategies is not a substitute for evidence-based risk analysis. But having a communications plan for rapid implementation may prevent vaccine safety scares from becoming crisis.

10.1 Communication with stakeholders

There are many parties to whom communications should be tailored in order to meet their particular needs. These include:

i. Parents and the community

ii. Health staff

iii. Particular stakeholders such as the ministry of health/ NRA / NCL, politicians, professionals/ academia, international agencies: WHO, UNICEF, and manufacturers.

The media in addition, there are principles of communication that apply to most if not all. These include the need to:

i. Listen empathetically to concerns.

ii. Reassure and support but do not make false promises.

iii. Communicate frequently

iv. Build up and maintain relationship among the stakeholders.

v. Inform about possible common adverse events and how to handle them.

vi. Prepare factsheets on adverse events and other key information for all audiences.

vii. Continuously communicate during the investigation period to assure understanding both the situation and the risk-benefit of vaccination. Do not lay blame, especially not on the health worker(s), but focus on the correction and quality of the EPI system.

While health staff should have some training or at least experience in communication skills by the nature of their work, at the same time communication with them by public health authorities and investigators should be sensitive to their needs. Thus:

i. Communication should be among all levels of health authorities involved.

ii. Reassure the staff of their knowledge, ability, skills and performances.

iii. Do not blame the health worker(s) but focus on the correction and quality of the EPI system.

iv. Keep them updated on investigation process, progress, and findings.

Vaccine safety information needs to be shared with other stakeholders in order to ensure dissemination of correct information and, by doing so, ensure the smooth functioning of national immunization programme in the country. This may be done at two stages: sharing preliminary information at initial stage and sharing the final data/report after completion of investigation/ causality assessment.

10.2 Communicating with the media

The media (newspaper, radio, television and the internet) play an important role in public perception. Understanding what the media want from a story will assist communication with them. In certain situations, media coverage can lead to public concern about immunization. In these situations, it is important to coordinate with professional organizations, health professionals and workers before responding to or addressing the media. The coordination should include preparation on dealing with public concern on this issue, in order to minimize any potential harm to the immunization programme. It is also useful to have other groups and individuals that merit public respect and authority to publicly endorse and strengthen key immunization messages.

Communicating with the media requires particular skills that require training. Reporters are highly trained professionals and their perspective must be properly understood. The media are interested in stories that will attract attention. While the success of a vaccination programme can attract attention, so can a programme that has not gone as planned. Dramatizing and personalizing events can both highlight success as well as create a sense of panic about an AEFI with a particular vaccine product – regardless of whether they are either unrelated to immunization (coincidental) or a localized immunization error. One other important fact is the media want early responses to their questions: therefore waiting for the conclusion of an investigation is rarely possible. Information may need to be disseminated early and often, and it is vital to be honest about what is known and what is not known, and to avoid being evasive and unresponsive.

At the same time, the media can be leveraged positively for the benefit of immunization. Health topics are popular among the public and, therefore, the media like to report about them. The media can be helpful allies in communicating public health messages. They can be helpful allies in reminding the public of the risk benefits of immunization. Building a personal relationship with key health reporters will help them to understand the public health perspective.

Effective communication with the media includes advance preparation. This is part of a communication plan and is particularly important before a new vaccine is introduced or before and during an immunization campaign. A communication plan can also provide ongoing communication support to routine immunization programmes. A good media plan consists of the following:

Table 4: Media plan for communication

A database of journalists	▪ A list of print and electronic media journalists covering health (local, national, international) with contact information. ▪ Always use a database where updating can be done immediately. ▪ Update regularly any changes in the media list.
Information packages	An information package may contain the following documents both in hard copy and e-copies: ▪ Frequently Asked Questions (FAQs) on immunization in general, for specific disease, and AEFI ▪ Fact Sheet or a Technical Brief on a specific vaccine preventable disease: burden of the disease and background rates of AEFI, expected AEFI rates ▪ Recent updates – Statistics, progress made in country, WPR, globally ▪ Contact addresses of spokespersons (experts) in the Ministry. This information package needs regular updating.
The draft media release	Must specifically answer the 6 W's for journalists: ▪ Who is affected/is responsible? ▪ What has happened? What is being done? ▪ Where has it happened? ▪ When did it happen? ▪ Why did it happen? ▪ Will it happen again?
Information specific to media characteristics	▪ Local media: Read and believed by more people in the community than national media. ▪ National media: a wide reach and influences national agendas. ▪ International media: Can influence national agendas.
A spokesperson system:	▪ Identify in advance an appropriate spokesperson (or several spokespersons in the different agencies). ▪ Share contact details of spokesperson(s) with all concerned focal points at different levels of programme implementation. ▪ Ensure spokesperson(s) has experience or some training in dealing with media.

10.2.1. Other tips to keep in mind

Media interest is usually greatest initially when relatively little is known. In this environment, rumours can flourish and the potential for harm is huge. A media conference, convened early even if there is only very limited information to give, can provide a uniform message to all at the same time, thus avoiding any conflicting messages. This will also prevent the circulation of rumours and build a relationship with the reporters. At the end of the press conference, advise that a further conference will be held within a day or so, at which time full details of the event and the investigation will be provided. A media or press conference requires expert planning and expert communications input to ensure that messages are clear, unambiguous and that all expert spokespersons are well prepared.

Professional organizations and other stakeholder parties may have greater credibility than the government, particularly in a crisis situation. Providing them an opportunity for their unified support for immunization and the approach being taken to handle/investigate the problem can help considerably.

10.3 Preparing key messages

Messages need to be as simple as possible. Use simple words and short sentences. It is helpful to tell a story, if possible. Create a 'word picture' (a graphic or vivid description) to get the message across. The key messages should be kept to a minimum and should include some of the facts. The benefit of immunization in preventing certain diseases is well proven. Introduction of vaccines has saved millions of lives.

i. It is risky not to immunize (risk of disease and complications).

ii. Vaccines may/do cause reactions, but these are rarely serious.

iii. Immunization safety is of paramount importance – maintaining confidence in immunization programs is only possible this way.

i.v Any suspicion of a problem is investigated (an advantage of well-establishedimmunization safety surveillance). This investigation is an example of such action being taken.

It is rarely necessary to suspend an immunization programme during an investigation unless it is obvious that there is a problem with the vaccine that warrants such drastic steps. The vast majority of situations prove to be coincidental or due to a very localized problem (depending on type of event), and the immunization programme must continue to keep the population safe from disease.

10.3.1. Preparing a press statement

i. All the information to be conveyed in a media conference should be prepared in advance and included in a press statement.

An effective press statement/ release must specifically answer the six questions ("W's") stated above and include a one page account (400-500 words) written in short sentences outlining:

ii. A complete account of the event, framed in its context (e.g. an isolated event or a cluster of AEFI, or a coincidental event).No technical jargon.

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

iv. A description of the possible cause of the event.

v. An assurance that corrective action will be taken, and what steps have already been taken.

vi. Reference to any relevant publication or web site for further information.

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

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

ix. Repetition of key positive message.

10.3.2. Follow-up actions with communications

Keeping promises:

If it has been promised that updates about the investigation will be disseminated, make sure that this is kept by the promised date. If the findings have been delayed, ensure the delay is communicated.

Providing answers to unanswered questions:

if a question could not be answered for any reason, get back to the requestors with the answers as soon as possible.

Keeping the public informed about subsequent developments:

If any decision or action is taken at the highest levels following AEFI investigations or during the investigations and the public must know about it, keep them informed though a press release to the media or other locally appropriate means.

10.4 Crisis management

A crisis is a situation in which a real or potential loss of confidence in the vaccine or in the immunization programme is triggered by information about an AEFI. Crises can often be avoided through foresight, care and training. If managed properly, the investigation and management of a vaccine

safety situation will boost public confidence and acceptance and ultimately strengthen the immunization programme.

10.4.1. How to manage a crisis

i. Anticipate: do not wait until a crisis occurs. Prepare for the unavoidable. Develop a good relationship with the media. Good public awareness and understanding of the immunization programme is necessary.

ii. Train staff at all levels to respond adequately: develop confidence responding to the public and the media (particularly to local media) properly and correctly.

iii. Confirm all facts and prepare (see steps for a press conference or press release) before making any public comments.

iv. Prepare a plan to react to a crisis when it occurs. This has to be done in advance, identifying responsible persons to handle the crisis and preparing all supporting documents and information.

Summary

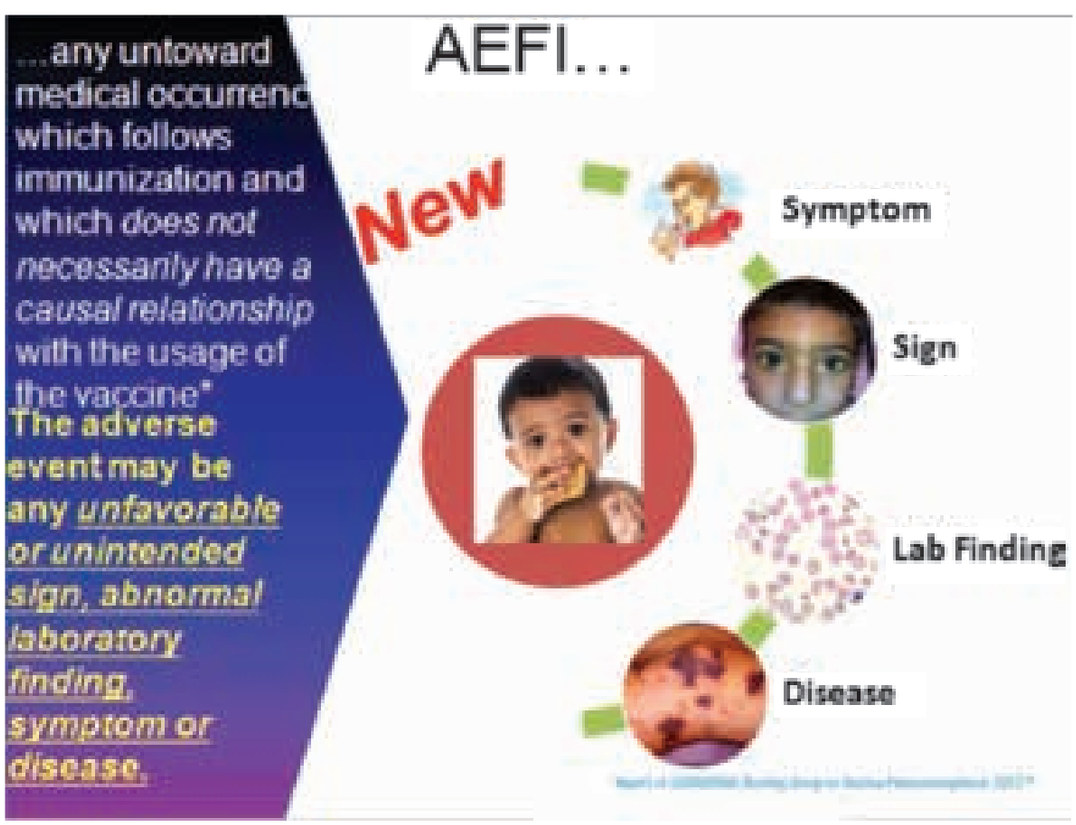
- Communication with parents, community, staff, other stakeholders and the media is necessary and important.
- During communication make sure to build confidence on immunization programme. Be aware of risk-benefits of immunization and the progress and findings of the investigation.
- Communication needs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

11. CONCLUSION

Research has shown that effective AEFI surveillance and management systems result in the minimization of AEFIs and more effective interventions where necessary. This document is expected to strengthen the AEFI surveillance and management in the country, by aligning the current guidelines to ZEPI AEFI surveillance system and the National Pharmacovigilance Plan, including the support and corporation of all health care personnel involved in immunization activities promoting children's health.

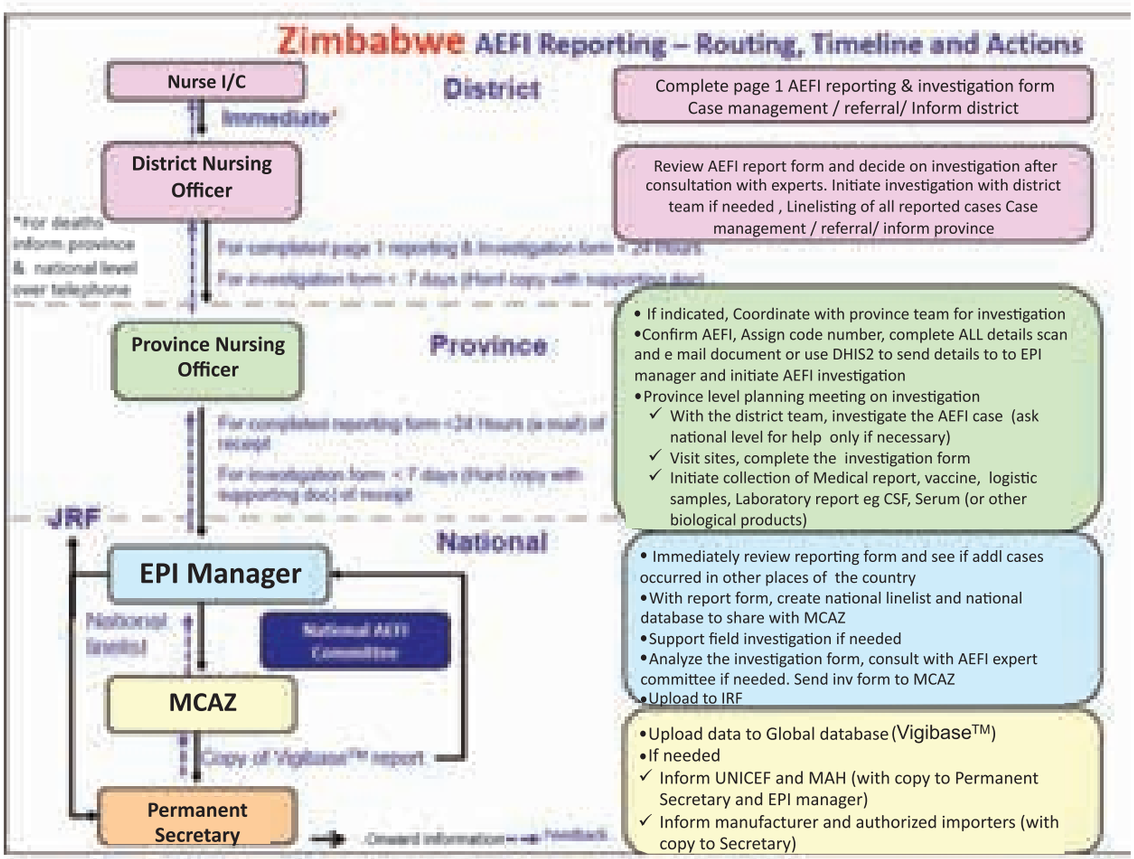
Aligning these national vaccine safety related policies and guidelines ensures that all stakeholders have a clear perspective on the Zimbabwean policy on AEFI surveillance, and ensures that more objective decisions are made.

The support of all stakeholders involved in immunization activities and the care of children would be greatly appreciated.



Appendix 1

Flowchart for AEFI management



Vigibase™ is the WHO Drug Safety database for the WHO International Drug Monitoring Programme, which is also the Zimbabwe National Pharmacovigilance drug safety database.

Joint Reporting Form (JRF): The WHO and UNICEF jointly collect information through a standard questionnaire, the JRF, which is sent to member states. The information collected in the JRF include estimates of national immunization coverage, reported cases of vaccine-preventable diseases, immunization schedules, as well as indicators of immunization system performances,WHO 2016.

Appendix 2

MCAZ FLOWCHART FOR AEFI REPORTS

Appendix 3

AEFI INVESTIGATION FORM

AEFI Report ID Number (ZW-PR-DS-FAC-000-YR): ZW- - - - -

ZIMBABWE REPORTING FORM FOR ADVERSE EVENTS FOLLLOWING IMMUNIZATION (AEFI)

**Patient first name:* Surname *Next of Kin:* **Patient's physical address:* Telephone: Sex: ☐M ☐F **Date of birth (DD/MM/YYYY):* __ __ / __ __ / __ __ __ __ *OR Age at onset :* ☐☐ *Years* ☐☐ *Months* ☐☐☐ *Days*	**Reporter's Name:* Designation, Department & address: District/ Province: Reporting Institution Telephone & e-mail: *Today's date (DD/MM/YYYY):* _ / __ / __ __

Health facility (or vaccination centre) name:

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

**Adverse event (s):* ☐ Severe local reaction ☐ *>1 days* ☐ *beyond nearest joint* ☐ Seizures ☐ *febrile* ☐ *afebrile* ☐ Abscess ☐ Sepsis ☐ Encephalopathy ☐ Toxic shock syndrome ☐ Thrombocytopenia ☐ Anaphylaxis ☐ Fever≥38°C ☐ Other (specify) ..... Date & Time AEFI started (DD/MM/YYYY): __ __ / __ __ / __ __ __ __ ☐☐ Hr ☐☐Min Was the patient hospitalized? ☐Yes ☐No Date patient notified event to health system (DD/MM/YYYY): __ __ / __ __ / __ __ __ __	Describe AEFI (Signs and symptoms):

Treatment provided: yes/ no

**Serious: Yes/ No; If yes,* ☐ *Death* ☐ *Life threatening* ☐ *Disability* ☐ *Hospitalization* ☐ *Congenital anomaly*

**Outcome:*

☐ Recovering ☐ Recovered ☐ Recovered with sequelae ☐ Not Recovered ☐ Unknown

☐ Died. If died, date of death (DD/MM/YYYY): __ __ / __ __ / __ __ __ __ Autopsy done: ☐Yes ☐No ☐Unknown

Past medical history (including history of similar reactions or other allergies), concomitant medications and other relevant information (e.g. other cases). *Use additional sheet if needed :*

First decision making level to complete (District level):

Investigation needed: ☐ Yes ☐ No	If yes, date investigation planned (DD/MM/YYYY) __ __ / __ __ / __ __ __ __

National level to complete:

Date report received at national level (DD/MM/YYYY): __ __ / __ __ / __ __ __ __	AEFI worldwide unique ID :
Comments:	

**Compulsory field*

Appendix 4

AEFI INVESTIGATION FORM

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

Section A — Basic Details

Province: **District:** **AEFI Report ID:**

Name of vaccination site:

Place of vaccination (✓): ☐ Govt. health facility ☐ Private health facility ☐Other (specify) _____
Type of site (✓) ☐ Fixed ☐ Mobile ☐ Outreach ☐ Other _____
Vaccination in (✓): ☐ Campaign ☐ Routine ☐ Other (specify) _____

Name of Investigating Health Worker:

Date AEFI reported: __ __ / __ __ / __ __ __ __
Date investigation started: __ __ / __ __ / __ __ __ __
Date investigation completed: __ __ / __ __ / __ __ __ __

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

Patient Name Sex: ☐M ☐F
(use a separate form for each case in a cluster)
Patient's physical address (*Street name, house number, ward/village, phone number etc.*):

Date of birth (DD/MM/YYYY):	*OR Age at onset:*	*OR Age group:*
___ / ___ / ____	____ years ____ months ____ days	☐ < 1 year ☐ 1-5 years ☐ > 5 years

Complete below table if vaccination information missing on the AEFI reporting form

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

Date of first/key symptom (DD/MM/YYYY): __ __ / __ __ / __ __ __ __ Time of first symptom (hr/min): __ __ / __ __
Date of hospitalization (DD/MM/YYYY) __ __ / __ __ / __ __ __ __

Status on the date of investigation (✓): ☐ Died ☐ Disabled ☐ Recovering ☐ Recovered completely ☐Unknown

If died, date and time of death (DD/MM/YYYY): __ __ / __ __ / __ __ __ __ (hr/min): __ __ / __ __
Autopsy done? (✓) ☐ Yes (date)_____ ☐No ☐Planned on (date)_____ Time_____
Attach report (if available)

Section B — Relevant patient information prior to immunization

Criteria	Finding	Remarks (If yes provide details)
Past history of similar event	Yes / No / Unkn	
Adverse event after previous vaccination(s)	Yes / No / Unkn	
History of allergy to vaccine, drug or food	Yes / No / Unkn	
Pre-existing illness (30 days) / congenital disorder	Yes / No / Unkn	
History of hospitalization in last 30 days, with cause	Yes / No / Unkn	
Was patient on medication at time of vaccination?	Yes / No /	

AEFI INVESTIGATION FORM

Name of patient: **AEFI Report ID:**

(If yes, name the drug, indication, dosen & treatmont dates)	Unkn	
Did patient consult faith healers before/after vaccination? *specify	Yes/ No / Unkn	
Family history of any disease (relevant to AEFI) or allergy	Yes / No / Unkn	

For adult women
- Currently pregnant? Yes (weeks) _____ / No / Unknown
- Currently breastfeeding? Yes / No

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

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

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

Source of information (✓ *all that apply*): ☐ **Examination by the investigator** ☐ **Documents** ☐ **Verbal autopsy**
☐ **Other**_____ *If from verbal autopsy, please mention source* _____

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

Other sources who provided information (specify): _____

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

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

****Instructions – Attach copies of ALL available documents (including case sheet, discharge summary, case notes, laboratory reports and autopsy reports) and then complete additional information NOT AVAILABLE in existing documents, i.e.**
- ***If patient has received medical care*** – attach copies of all available documents (including case sheet, discharge summary, laboratory reports and autopsy reports, if available) and write only the information that is not available in the attached documents below
- ***If patient has not received medical care*** – obtain history, examine the patient and write down your findings below (add additional sheets if necessary)

Provisional / Final diagnosis:

Section D **Details of vaccines provided at the site linked to AEFI on the corresponding day**

Number vaccinated for each antigen at session site. Attach record if available	Vaccine name									
	Number of doses									

a) When was the patient vaccinated? (✓ the ☐ bellow and respond to ALL questions)

☐ Within the first vaccinations of the session ☐ Within the last vaccinations of the session ☐ Unknown

AEFI INVESTIGATION FORM

Name of Patient: AEFI Report ID:

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

It is compulsory for you to provide explanations for 'yes' answers separately

Section E Immunization Practices at the place(S) where concerned vaccine was used
Complete this section by asking and/or observing practice)

Syringes and needles used:			
• Are AD syringes used for immunization?	Yes / No / Unkn		
If no, specify the type of syringes used: ☐ Glass ☐ Disposable ☐ Recycled disposable ☐ Other _____			
Specific key findings/additional observations and comments:			
Reconstitution: (complete only if applicable, ✓ NA if not applicable)			
• Reconstitution procedure (✓)	Status		
Same reconstitution syringe used for multiple vials of same vaccine?	Yes	No	NA
Same reconstitution syringe used for reconstituting different vaccines?	Yes	No	NA
Separate reconstitution syringe for each vaccine vial?	Yes	No	NA
Separate reconstitution syringe for each vaccination?	Yes	No	NA
• Are the vaccines and diluents used the same as those recommended by the manufacturer?	Yes	No	NA
Specific key findings/additional observations and comments:			

Section F Cold chain and transport
(Complete this section by asking and/or observing practice)

Last vaccine storage point:	
• Is the temperature of the vaccine storage refrigerator monitored?	Yes / No
○ If "yes", was there any deviation outside of 2–8° C after the vaccine was placed inside?	Yes / No
○ If "yes", provide details of monitoring separately.	
• Was the correct procedure for storing vaccines, diluents and syringes followed?	Yes / No / Unkn
• Was any other item (other than EPI vaccines and diluents) in the refrigerator or freezer?	Yes / No / Unkn
• Were any partially used reconstituted vaccines in the refrigerator?	Yes / No / Unkn

AEFI INVESTIGATION FORM

Name of patient: AEFI Report ID:

• Were any unusable vaccines (expired, no label, VVM at stages 3 or 4, frozen) in the refrigerator?	Yes / No / Unkn
• Were any unusable diluents (expired, manufacturer not matched, cracked, dirty ampoule) in the store?	Yes / No / Unkn
Specific key findings/additional observations and comments:	
Vaccine transportation from the refrigerator to the vaccination centre:	
• Was cold chain properly maintained during transportation?	Yes / No / Unkn
• Was the vaccine carrier sent to the site on the same day as vaccination?	Yes / No / Unkn
• Were conditioned coolant-packs used?	Yes / No / Unkn
Specific key findings/additional observations and comments:	

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

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

If yes, how many events/episodes?

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

Other comments:

Section H Other relevant findings/ observations/ comments

Appendix 5

WHO's Aide-me'moire, 2013 on AEFI Investigation

World Health Organization

ADVERSE EVENT FOLLOWING IMMUNIZATION

AIDE-MÉMOIRE ON AEFI INVESTIGATION

Purpose: This aide-mémoire proposes a systematic, standardized process to investigate reported serious adverse events following immunization (AEFI) and ascertain the underlying cause of the AEFI by:

- confirming a diagnosis and timing
- identifying details of vaccine(s) administered
- documenting the outcome of the reported adverse event
- determining whether the reported event is solitary or part of a cluster
- reviewing the operational aspects of the programme

DETECTION AND REPORTING

Vaccine recipients themselves and/or parents of vaccine recipients who identify AEFI should notify the same to the health care provider. All notified AEFI cases should be documented and reported in a simple standard reporting form by the health care provider.

WHICH OF THE REPORTED AEFI SHOULD BE INVESTIGATED IN MORE DETAIL?

A detailed AEFI investigation to assess causality is necessary if:

- it is serious*
- it is part of a cluster*
- it is part of a suspected signal*
- it is a suspected immunization error*
- it appears on the list of events defined for AEFI investigation or
- it causes significant parental or public concern

WHO SHOULD INVESTIGATE AEFI?

Detailed AEFI field investigation can be done based on the program's operational structure and the expertise available. A basic preliminary investigation by local programme managers may be sufficient if the cause of the reported AEFI is very clear; otherwise, investigation should be done by next/higher administrative level, by a trained/skilled person/ team, depending on the nature of event, its seriousness and impact to the programme.

WHEN TO INVESTIGATE AEFI

If a detailed investigation is warranted, it should be initiated as soon as possible, ideally within 24 to 48 hours of the case being first reported.

CHECKLIST FOR AEFI INVESTIGATION

1. PRELIMINARY STEPS

- ☐ Develop national guidelines with case definitions for reportable AEFIs, reporting forms, investigation procedures, roles and responsibilities
- ☐ Develop resource documents and training material on reporting, management and investigation of AEFIs
- ☐ Designate and train staff to conduct an AEFI investigation using the investigation form and guidelines
- ☐ Train staff on how to collect and store specimens
- ☐ Have a functioning National AEFI Review Committee with suitable representation
- ☐ Establish procedure, criteria and designate focal persons for notifying and communicating with WHO and UNICEF (if UN- supplied vaccine) or other relevant party depending on procurement mechanism
- ☐ Identify a spokesperson for public communications

2. RECEIVING A REPORT

- ☐ Provide rapid attention to all reports received and immediate response to serious events
- ☐ Verify the information in the report, confirm the diagnosis, classify and assess the AEFI using established case definitions. Decide whether it needs further detailed investigation.
- ☐ If investigation is warranted, travel to the location of the AEFI, or delegate responsibility to another trained person

3. INVESTIGATE AND COLLECT DATA

- ☐ Obtain information from patient or relatives directly/ use available records
- ☐ Obtain information from immunization service providers and medical care service providers (hospital staff)/ use available records
- ☐ Ask about the vaccine(s) administered and other drugs potentially received
- ☐ Establish a more specific case definition if needed
- ☐ Ask about other vaccinees who may have received the same or other vaccines
- ☐ Observe the service in action
- ☐ Ask about cases in unvaccinated persons
- ☐ Formulate a hypothesis as to what may have caused the AEFI (see table below)
- ☐ Collect specimens (if indicated by investigation, but not as a routine):
  - ✓ from the patient
  - ✓ the vaccine and diluent if applicable
  - ✓ the syringes and needles

WHO's Aide-me'moire, 2013 on AEFI Investigation

World Health Organization

ADVERSE EVENT FOLLOWING IMMUNIZATION

- ☐ Dispatch specimens to appropriate testing facility (laboratory, regulatory authority, etc.)

4. ANALYSE THE DATA

- ☐ Review epidemiological, clinical, and laboratory findings
- ☐ Share findings with national AEFI committee for expert advice
- ☐ Summarize and report findings

5. TAKE ACTION

The local response after an AEFI investigation should be based on findings (data/information) and local practices. The highest priority is to treat patient. Suspending vaccination at the locality of the event temporarily pending investigation outcome may be necessary but is uncommon. Broader suspension of vaccination is only very rarely necessary. When taking action, it is important to:

- ☐ Provide feedback to health staff
- ☐ Communicate findings and action to the parents and public – during all stages of the investigation
- ☐ Correct problem (based on the cause) by improving training, supervision and/or distribution of vaccine/injection equipment
- ☐ Replace vaccines if indicated

INVESTIGATING DEATHS AFTER IMMUNIZATION

After informing higher authorities, field investigation should be conducted by a team of clinical, laboratory and forensic experts supported by programme managers. A decision on autopsy should be taken within the local sociocultural, religious, political context. Autopsies should be done with adequate information of the circumstances of the event using standard autopsy protocols. Appropriate specimens should be collected for testing.

If an autopsy is not possible, a verbal autopsy can be carried out using established guidelines and protocols.

OUTCOME OF AEFI INVESTIGATION

On concluding the investigation, the documents and evidence collected should be compiled, a report prepared and submitted to a group of experts to determine/evaluate causality.

POSSIBLE CAUSES OF AEFI

Related to vaccine or vaccination

- Vaccine product-related
- Vaccine quality defect-related
- Immunization error-related
- Immunization anxiety-related

Coincidental adverse event

KEY RESOURCES FOR AEFI INVESTIGATION

- WHO standard AEFI reporting form
- WHO standard AEFI investigation form
- Global manual on surveillance of AEFI
- User manual for the revised WHO AEFI causality assessment classification
- Brighton Collaboration standard case definitions
- Verbal autopsy standards: ascertaining and attributing causes of death

[i] An AEFI 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.

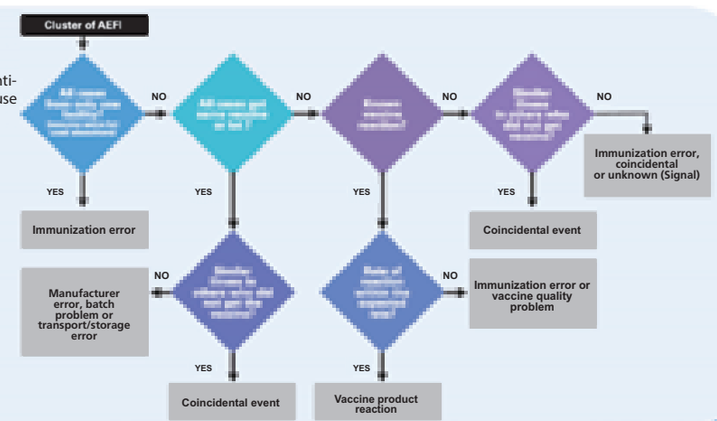
[ii] Serious AEFI include death, hospitalization or prolongation of existing hospitalization, persistent or significant disability or incapacity, congenital anomaly/birth defect or is life-threatening

[iii] A cluster of AEFIs is two or more cases of the same adverse event related in time, place or vaccine administered

[iv] 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.

INVESTIGATING AEFI CLUSTERS

Suggested steps for identifying the most likely cause of a cluster of AEFI



Appendix 6

WHO's Aide-me'moire, 2013 on AEFI Casuality Assessment

World Health Organization

ADVERSE EVENT FOLLOWING IMMUNIZATION

AIDE - MEMOIRE ON CAUSALITY ASSESSMENT

Purpose: This aide-mémoire serves as a guide to a systematic, standardized process of assessing whether serious adverse events following immunization (AEFI[1]) are causally linked to vaccines/immunization or not.

Definition: AEFI causality assessment determines if a causal relationship exists between a vaccine (and/or vaccination) and an adverse event.

Rationale: Safety requirements for vaccines are stricter than those for drugs since vaccines are biological products that are more prone to lot variation and instability, they are used in healthy populations and the target groups are vulnerable. Vaccines therefore require a causality assessment process that responds in a timely manner and with scientific rigour to AEFI.

WHO SHOULD ASSESS AEFI CAUSALITY?

Ideally an AEFI review committee should be in place backed by written terms of reference. It should consist of independent experts who have no conflicts of interest. As far as possible, the experts should cover a broad range of expertise: infectious diseases, epidemiology, microbiology, pathology, immunology, neurology, forensics and vaccine programming. The committee should be supported by a secretariat (usually the national regulatory authority [NRA] and the immunization programme) that can provide supporting evidence and investigation findings to enable causality to be determined.

WHAT ARE PREREQUISITIES FOR AEFI CAUSALITY ASSESSMENT?

- AEFI case investigation should be completed. Premature assessments may mislead classification.
- All relevant information should be available, including documents of investigation, laboratory and postmortem findings (if applicable).
- Valid diagnosis (unfavourable or unintended sign, abnormal laboratory finding, symptom or disease) for the AEFI must be defined, be well-founded and correspond accurately to the event being assessed.
- Information that could bias results (patient name, hospital name, etc.) should be anonymized.

POSSIBLE CAUSES OF AEFI

Related to vaccine or vaccination

- Vaccine product-related
- Vaccine quality defect-related
- Immunization error-related
- Immunization anxiety-related

Coincidental adverse event

AT WHAT LEVELS IS AEFI CASUALITY ASSEESSED?

AEFI causality assessment could be performed:

- **At population level** (is there a causal association between usage of a vaccine and a particular AEFI in the population?)
- **For an individual** (is the adverse event in the individual patient causally linked to the vaccine/vaccination?)

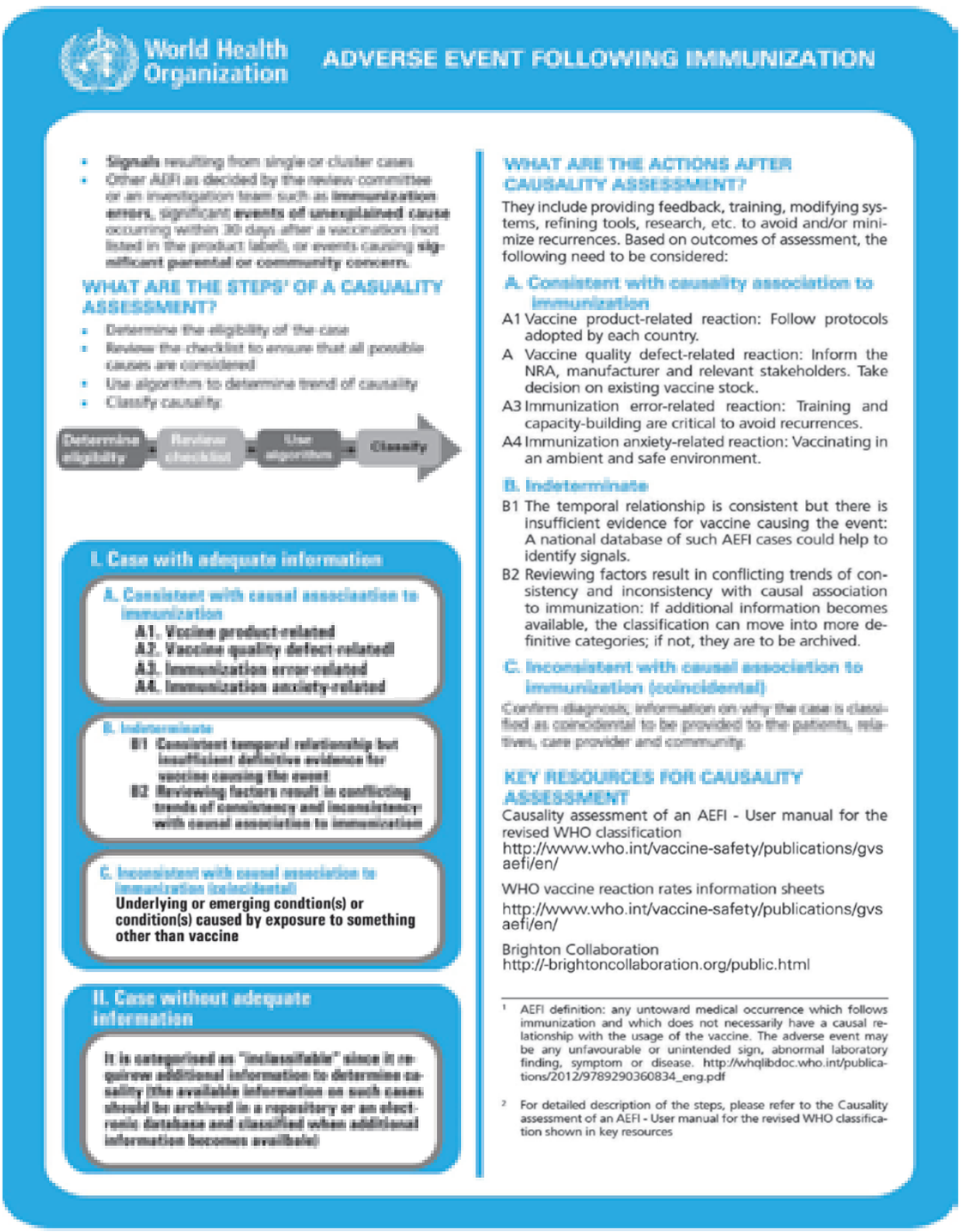
CONSIDERATIONS FOR ASSESSING CASUALITY OF A SOLITARY AEFI:

- **Temporal relationship:** is it certain that the vaccination preceded the adverse event?
- **Alternate explanations:** is the event coincidental, i.e. is it due to something other than the vaccine product, immunization error or immunization anxiety?
- **Proof of association:** is there clinical or laboratory proof that the vaccine caused the event?
- **Prior evidence:** has a similar AEFI been previously reported in studies/literature or other sources?
- **Population-based evidence:** does the rate of event occurrence exceed the expected rate of the event in the population? (Refer to WHO information sheets on observed rates of known vaccine reactions.)
- **Biological plausibility:** can the association be explained by the natural history, biological mechanisms of the disease, laboratory evidence or animal studies? However this is not an important consideration.

WHICH AEFI TO SELECT FOR CASUALITY ASSESSMENT?

All reported AEFI require verification of diagnosis, coding, review, information collation and storage. Causality assessment needs to be done for:

- **Serious AEFI** (i.e. events that are life-threatening or lead to death, hospitalization, significant disability or congenital anomaly)
- **Clusters of AEFI** (the cause for each case in the cluster should be determined separately). Line-listing of data may identify patterns that could constitute a signal
- Occurrence of **events above the expected rate** or of **unusual severity**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ADVERSE EVENT FOLLOWING IMMUNIZATION
Signals resulting from single or cluster cases
Other AEFI as decided by the review committee or an investigation team such as immunization errors, significant events of unexplained cause occurring within 30 days after a vaccination (not listed in the product label), or events causing significant parental or community concern.
WHAT ARE THE STEPS[1] OF A CASUALITY ASSESSMENT?
Determine the eligibility of the case
Review the checklist to ensure that all possible causes are considered
Use algorithm to determine trend of causality
Classify causality
Determine eligibility
Review checklist
Use algorithm
Classify
I. Case with adequate information
A. Consistent with causal association to immunization
A1. Vaccine product-related
A2. Vaccine quality defect-related
A3. Immunization error-related
A4. Immunization anxiety-related
B. Indeterminate
B1 Consistent temporal relationship but insufficient definitive evidence for vaccine causing the event
B2 Reviewing factors result in conflicting trends of consistency and inconsistency with causal association to immunization
C. Inconsistent with causal association to immunization (coincidental)
Underlying or emerging condtion(s) or condition(s) caused by exposure to something other than vaccine
II. Case without adequate information
It is categorised as "inclassifable" since it requires additional information to determine causality (the available information on such cases should be archived in a repository or an electronic database and classified when additional information becomes available)
WHAT ARE THE ACTIONS AFTER CAUSALITY ASSESSMENT?
They include providing feedback, training, modifying systems, refining tools, research, etc. to avoid and/or minimize recurrences. Based on outcomes of assessment, the following need to be considered:
A. Consistent with causality association to immunization
A1 Vaccine product-related reaction: Follow protocols adopted by each country.
A Vaccine quality defect-related reaction: Inform the NRA, manufacturer and relevant stakeholders. Take decision on existing vaccine stock.
A3 Immunization error-related reaction: Training and capacity-building are critical to avoid recurrences.
A4 Immunization anxiety-related reaction: Vaccinating in an ambient and safe environment.
B. Indeterminate
B1 The temporal relationship is consistent but there is insufficient evidence for vaccine causing the event: A national database of such AEFI cases could help to identify signals.
B2 Reviewing factors result in conflicting trends of consistency and inconsistency with causal association to immunization: If additional information becomes available, the classification can move into more definitive categories; if not, they are to be archived.
C. Inconsistent with causal association to immunization (coincidental)
Confirm diagnosis; information on why the case is classified as coincidental to be provided to the patients, relatives, care provider and community.
KEY RESOURCES FOR CAUSALITY ASSESSMENT
Causality assessment of an AEFI - User manual for the revised WHO classification
http://www.who.int/vaccine-safety/publications/gvsaefi/en/
WHO vaccine reaction rates information sheets
http://www.who.int/vaccine-safety/publications/gvsaefi/en/
Brighton Collaboration
http://-brightoncollaboration.org/public.html
[1] AEFI definition: 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. http://whqlibdoc.who.int/publications/2012/9789290360834_eng.pdf
[2] For detailed description of the steps, please refer to the Causality assessment of an AEFI - User manual for the revised WHO classification shown in key resources

World Health Organization

ADVERSE EVENT FOLLOWING IMMUNIZATION

STEP 1 (ELIGIBILTY

Name of the patient	Name of one or more vaccines administered before this event	What is the Valid Diagnosis? (The case diagnosis of the AEFI)	Does the diagnosis meet a case definition?

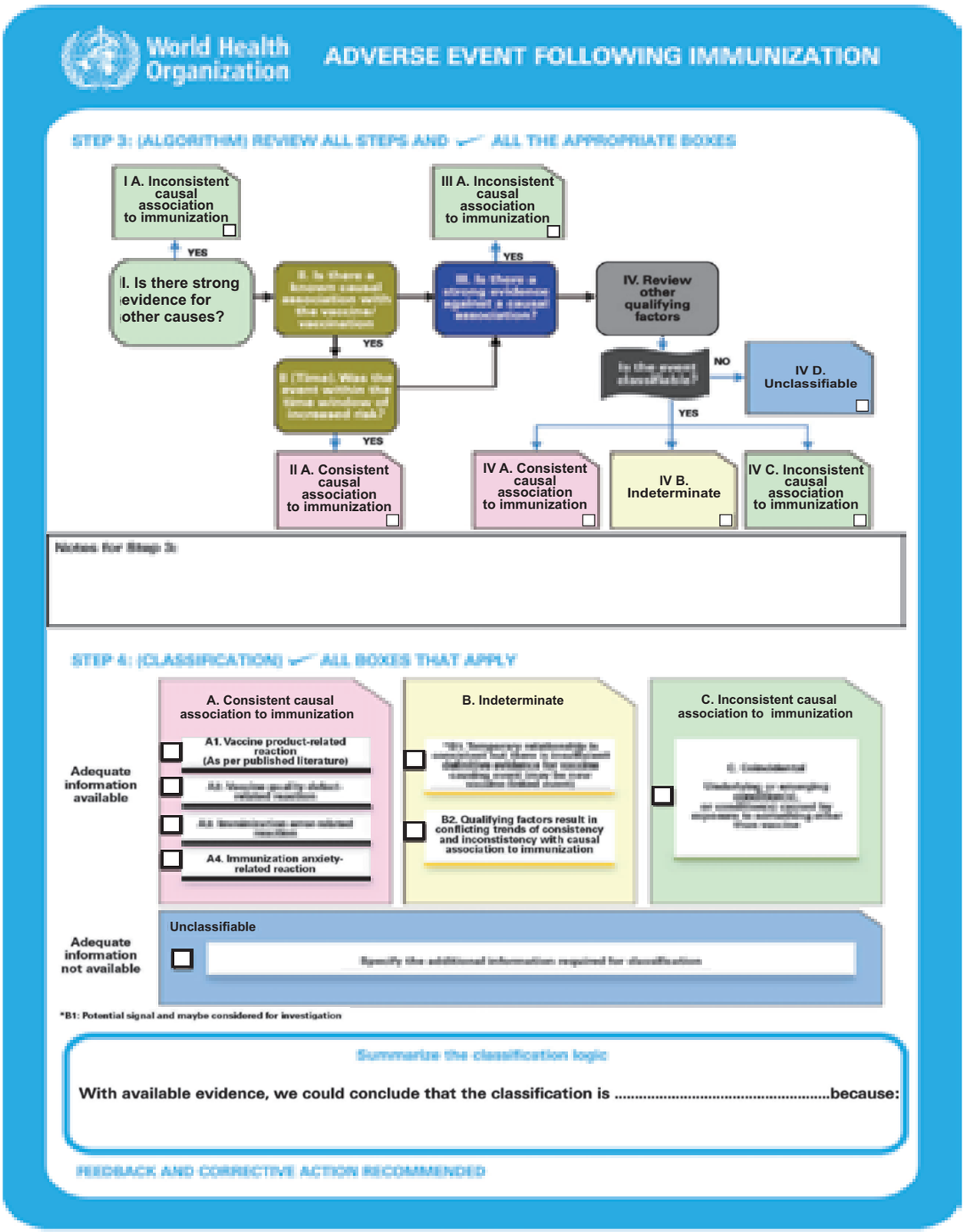
Create your question on causality here

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

STEP 2 (EVENT CHECKLIST) [✓ check all boxes that apply]

I. Is there strong evidence for other causes?	Y N UK NA	Remarks
Does clinical examination, or laboratory tests on the patient, confirm another cause?	☐☐☐☐	
II. Is there a known causal association with the vaccine or vaccination?		
Vaccine product(s)		
Is there evidence in the literature that this vaccine(s) may cause the reported event even if administered correctly?	☐☐☐☐	
Did a specific test demonstrate the causal role of the vaccine or any of the ingredients?	☐☐☐☐	
Immunization error		
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.)?	☐☐☐☐	
Was the vaccine (or any of its ingredients) administered unsterile?	☐☐☐☐	
Was the vaccine's physical condition (e.g. colour, turbidity, presence of foreign substances etc.) abnormal at the time of administration?	☐☐☐☐	
Was there an error in vaccine constitution/preparation by the vaccinator (e.g. wrong product, wrong diluent, improper mixing, improper syringe filling etc.)?	☐☐☐☐	
Was there an error in vaccine handling (e.g. a break in the cold chain during transport, storage and/or immunization session etc.)?	☐☐☐☐	
Was the vaccine administered incorrectly (e.g. wrong dose, site or route of administration; wrong needle size etc.)?	☐☐☐☐	
Immunization anxiety		
Could the event have been caused by anxiety about the immunization (e.g. vasovagal, hyperventilation or stress-related disorder)?	☐☐☐☐	
II (time). If "yes" to any question in II, was the event within the time of increased risk?		
Did the event occur within an appropriate time window after vaccine administration?	☐☐☐☐	
III. Is there strong evidence against a causal association?		
Is there strong evidence against a causal association?	☐☐☐☐	
IV. Other qualifying factors for classification		
Could the event occur independently of vaccination (background rate)?	☐☐☐☐	
Could the event be a manifestation of another health condition?	☐☐☐☐	
Did a comparable event occur after a previous dose of a similar vaccine?	☐☐☐☐	
Was there exposure to a potential risk factor or toxin prior to the event?	☐☐☐☐	
Was there acute illness prior to the event?	☐☐☐☐	
Did the event occur in the past independently of vaccination?	☐☐☐☐	
Was the patient taking any medication prior to vaccination?	☐☐☐☐	
Is there a biological plausibility that the vaccine could cause the event?	☐☐☐☐	

Y. Yes. N. No UK: Unknown. NA: Not applicable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ADVERSE EVENT FOLLOWING IMMUNIZATION
STEP 3: (ALGORITHM) REVIEW ALL STEPS AND ✓ ALL THE APPROPRIATE BOXES
I A. Inconsistent causal association to immunization
III A. Inconsistent causal association to immunization
YES
I. Is there strong evidence for other causes?
IV. Review other qualifying factors
NO
IV D. Unclassifiable
YES
II A. Consistent causal association to immunization
IV A. Consistent causal association to immunization
IV B. Indeterminate
IV C. Inconsistent causal association to immunization
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)
A4. Immunization anxiety-related reaction
B2. Qualifying factors result in conflicting trends of consistency and inconsistency with causal association to immunization
Adequate information not available
Unclassifiable
*B1: Potential signal and maybe considered for investigation
Summarize the classification logic
With available evidence, we could conclude that the classification is .....because:
FEEDBACK AND CORRECTIVE ACTION RECOMMENDED

Appendix 7

WHO 2013 Work sheet for causality Assessment

Step 1 (Eligibility)

Name of the Patient	Name of one or more 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)

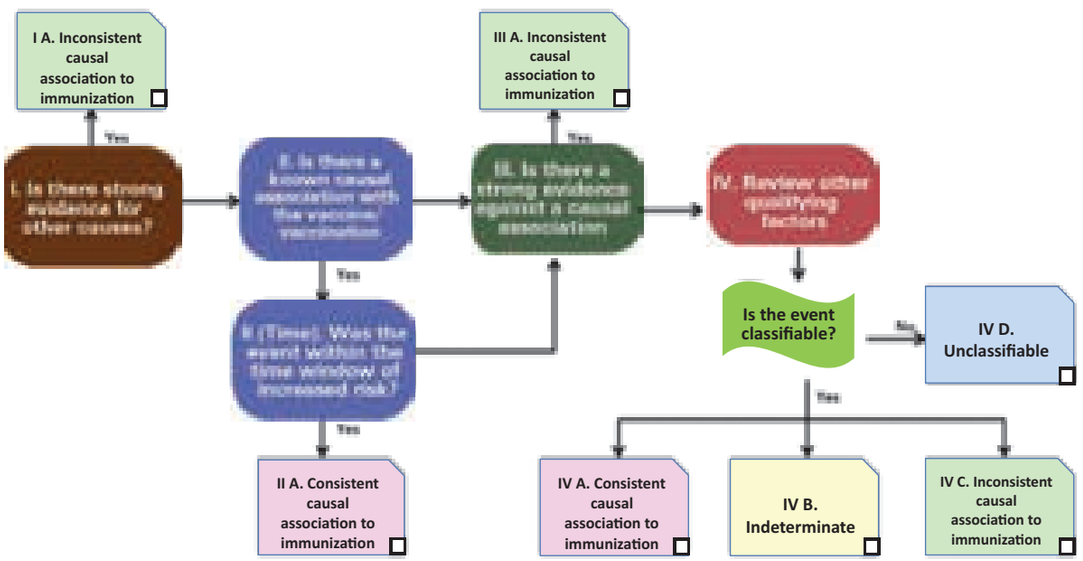
Step 2 (Event Checklist) *(check all boxes that apply)*

I. Is there strong evidence for other causes?	Y N UK NA	Remarks
Does a clinical examination, or laboratory tests on the patient, confirm another cause?	☐☐☐☐	
II. Is there a known causal association with the vaccine or vaccination?		
Vaccine product(s)		
Is there evidence in the literature that this vaccine(s) may cause the reported event even if administered correctly?	☐☐☐☐	
Did a specific test demonstrate the causal role of the vaccine or any of the ingredients?	☐☐☐☐	
Immunization error		
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.)?	☐☐☐☐	
Was the vaccine (or any of its ingredients) administered unsterile?	☐☐☐☐	
Was the vaccine's physical condition (e.g. colour, turbidity, presence of foreign substances etc.) abnormal at the time of administration?	☐☐☐☐	
Was there an error in vaccine constitution/preparation by the vaccinator (e.g. wrong product, wrong diluent, improper mixing, improper syringe filling etc.)?	☐☐☐☐	
Was there an error in vaccine handling (e.g. a break in the cold chain during transport, storage and/or immunization session etc.)?	☐☐☐☐	
Was the vaccine administered incorrectly (e.g. wrong dose, site or route of administration, wrong needle size etc.)?	☐☐☐☐	
Immunization anxiety		
Could the event have been caused by anxiety about the immunization (e.g. vasovagal, hyperventilation or stress-related disorder)?	☐☐☐☐	
II (time). If "yes" to any question in II, was the event within the time window of increased risk?		
Did the event occur within an appropriate time window after vaccine administration?	☐☐☐☐	
III. Is there strong evidence against a causal association?		
Is there strong evidence against a causal association?	☐☐☐☐	
IV. Other qualifying factors for classification		
Could the event occur independently of vaccination (background rate)?	☐☐☐☐	
Could the event be a manifestation of another health condition?	☐☐☐☐	
Did a comparable event occur after a previous dose of a similar vaccine?	☐☐☐☐	

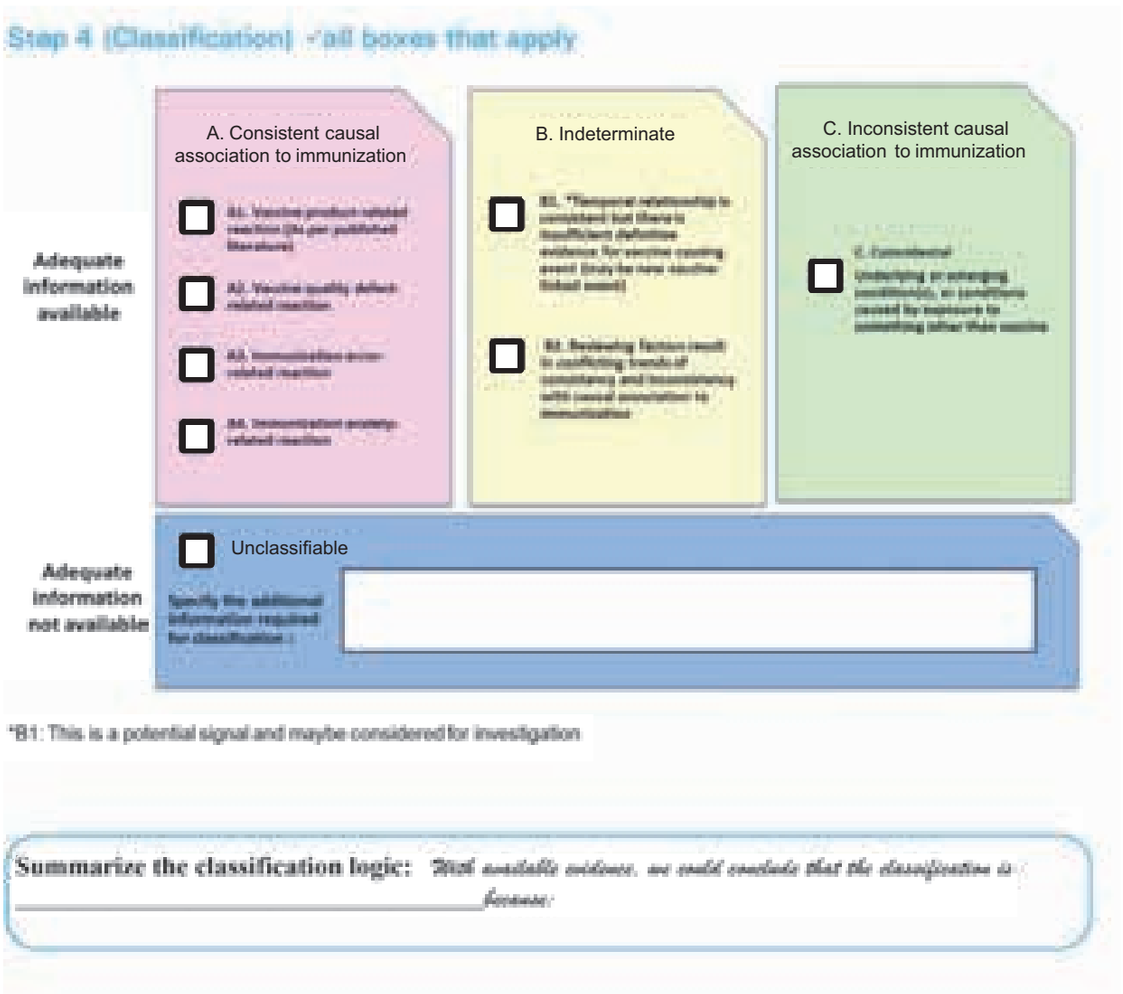
Was there exposure to a potential risk factor or toxin prior to the event?	☐☐☐☐	
Was there acute illness prior to the event?	☐☐☐☐	
Did the event occur in the past independently of vaccination?	☐☐☐☐	
Was the patient taking any medication prior to vaccination?	☐☐☐☐	
Is there a biological plausibility that the vaccine could cause the event?	☐☐☐☐	

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
A. Consistent causal association to immunization
B. Indeterminate
C. Inconsistent causal association to immunization
Adequate information available
Adequate information not available
Unclassifiable
*B1: This is a potential signal and maybe considered for investigation
Summarize the classification logic:

13. REFERENCES

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