National Guidelines on Immunization Safety Surveillance:

Surveillance of Adverse Events Following Immunization

Second Edition
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Sri Lanka

National Guidelines on Immunization Safety Surveillance

FOREWORD

National Immunization Programme of Sri Lanka is one of the best performing public health programmes in the region and in the world. Vaccine Preventable Diseases are well controlled in the country and coverage of all infant and early childhood vaccinations is near 100%. The Governments' strong commitment based on the policy to provide free health care services, dedicated staff from national to field level and well literate public is the key to its success.

The Adverse Events Following Immunization (AEFI) Surveillance System in the country has come a long way since its inception in 1996. Intensive efforts are being made by the Ministry of Health to strengthen surveillance of AEFI in the country. Ensuring the quality and safety of vaccines are essential and of paramount importance. Therefore, it is evident that surveillance of AEFI is a challenging task, nonetheless essential.

The first edition of this guideline published in 2012 was to enable the health system to effectively respond to vaccine safety challenges by clear instructions and defining the roles and responsibilities of health staff. It provided a tool for both public health staff and hospital health staff to enable them to respond the adverse events in a timely manner as well as help to prevent AEFIs due to immunization related errors.

This revised second edition is incorporated with updated information on vaccine safety and would further strengthen the AEFI surveillance and response system in the country and would help build public confidence in the National Immunization Programme. It reinforces the commitment of the Government of Sri Lanka to provide quality and safe immunization services in the country as indicated in the National Immunization Policy (2014) of the country.

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PREFACE

The goal of the National Immunization Programme is to protect the individual and the public from vaccine preventable diseases. Vaccines used in the National Immunization Programme are very safe and effective; however no vaccine is entirely free from adverse reactions as for other medicines. The Adverse Events Following Immunization (AEFI) are largely not due to the vaccine or not related to the vaccination and in fact, largely due to other reasons related to immunization or may be coincidental. However, in order to maintain public confidence, it is necessary to strengthen the surveillance of all AEFI for needful action in a timely manner.

Strict regulatory procedures in vaccine registration, procurement, close monitoring and supervision of divisional, district and national level immunization related activities, continued training of staff are in place to ensure quality and safety of the National Immunization Programme.

On par with the National Immunization Policy (2014), Ministry of Health has been making further efforts to ensure Immunization safety of the National Immunization Programme through strengthening the AEFI Surveillance System in the country. The first edition of this guideline for surveillance of AEFI published in 2012 was greatly useful to the health staff to detect report, investigate and monitor the adverse events in a timely manner as well as help to prevent AEFIs due to immunization related errors.

Based on the updated novel information in the fields of vaccine and immunization safety, this guideline is revised and I am thankful to all experts who contributed in the revision of this guideline. It is my fervent hope that this revised document will guide the health staff at all levels to further strengthen the AEFI surveillance in the country and thereby improve quality of the National Immunization Programme in the country.

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GLOSSARY

Adverse Event Following Immunization (AEFI)	Any untoward medical occurrence which follows immunization and which does not necessarily have a causal relationship with the usage of the vaccine. The adverse event may be any unfavourable or unintended sign, abnormal laboratory finding, symptom or disease.
Causal association	A cause-and-effect relationship between a causative (risk) factor and an outcome. Causally associated events are also temporally associated (i.e. they occur after vaccine administration), but events which are temporally associated may not necessarily be causally associated.
Causality assessment	In the context of AEFI surveillance, it is a systematic review of data about AEFI case(s) to determine the likelihood of a causal association between the event and the vaccine(s) received.
Cluster	Two or more cases of the same or similar events related in time, geography (place), and/or vaccine administered. AEFI clusters are usually associated with a particular supplier/provider, health facility, and/or a vial of vaccine or a batch of vaccines.
Coincidental events	An AEFI that is caused by something other than the vaccine product, immunization error or immunization anxiety.
Contraindication	A situation where a particular treatment or procedure, such as vaccination with a particular vaccine, must not be administered for safety reasons. Contraindications can be permanent (absolute), such as known severe allergies to a vaccine component, or temporary (relative), such as an

	acute/ severe febrile illness.
Injection safety	The public health practices and policies dealing with various aspects of the use of injections (including adequate supply, administration and waste disposal) so that the provider and recipient are not exposed to avoidable risks of adverse events (e.g. transmission of infective pathogens) and creation of dangerous waste is prevented. All injections, irrespective of their purpose, are covered by this term.
Immunization safety	The process of ensuring the safety of all aspects of immunization, including vaccine quality, adverse events surveillance, vaccine storage and handling, vaccine administration, disposal of sharps and management of waste.
Immunization safety Surveillance	A system for ensuring immunization safety through detecting, reporting, investigating, and responding to AEFI.
Non-serious AEFI	An event that is not 'serious' and does not pose a potential risk to the health of the recipient. Non-serious AEFIs also should be carefully monitored because they may signal a potentially larger problem with the vaccine or immunization, or have an impact on the acceptability of immunization in general.
Safe injection practice	Practices which ensure that the process of injection carries the minimum of risk, regardless of the reason for the injection or the product injected.
Serious AEFI	An event that results in death, is life-threatening, requires in-patient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect. Any medical event that requires intervention to

	prevent one of the outcomes above may also be considered as serious.
Severe vaccine reaction	It refers to the intensity of vaccine reactions. A severe reaction refers to the high grade intensity of its grading such as mild, moderate and severe. Severe reactions may include both serious and non serious reactions.
Signal *	Information (from one or multiple sources) which suggests a new and potentially causal association, or a new aspect of an own association, between an intervention and an adverse event or set of related adverse events, that is judged to be of sufficient likelihood to justify verificatory action.
Surveillance	The continuing, systematic collection of data those are analysed and disseminated to enable decision-making and action to protect the health of populations.
Trigger event	A medical incident following immunization that stimulates a response, usually a case investigation.
Vaccine	A biological preparation that improves immunity to a particular disease. In addition to the antigen, it contains multiple components (excipients) and each component may have unique safety implications.
Vaccine pharmacovigilance*	The science and activities relating to the detection, assessment, understanding and communication of AEFI and other vaccine- or immunization-related issues, and to the prevention of untoward effects of the vaccine or immunization.
Vaccine product-related reaction *	An AEFI that is caused or precipitated by a vaccine due to one or more of the inherent properties of the vaccine product, whether the active component or one of the other components

	of the vaccine (e.g. adjuvant, preservative or stabilizer).
Vaccine quality defect related reaction	An AEFI that is caused or precipitated by a vaccine that is due to one or more quality defects of the vaccine product, including its administration device as provided by the manufacturer.
Vaccination failure	Vaccination failure may be defined on the basis of clinical endpoints or immunological criteria where correlates or surrogate markers for disease protection exist. Primary failure (e.g. lack of sero-conversion or sero-protection) needs to be distinguished from secondary failure (waning immunity). Vaccination failure can be due to (i) failure to vaccinate, i.e. an indicated vaccine was not administered appropriately for any reason or (ii) because the vaccine did not produce its intended effect (vaccine failure).
Vaccine reaction	An event caused or precipitated by the antigen(s) or one of the other components (Excipients) of the vaccine. It may also relate to a vaccine quality defect.
Vaccine safety	The process, which maintains the highest efficacy of and lowest adverse reaction to a vaccine by addressing its production, storage and handling. Vaccine safety is a part of immunization safety.

*Source: Definition and Application of Terms for Vaccine Pharmacovigilance. Report of CIOMS/WHO Working Group on Vaccine Pharmacovigilance http://whqlibdoc.who.int/publications/2012/9789290360834_eng.pdf

ABBREVIATIONS

AD	Auto Disable
AEFI	Adverse Event Following Immunization
aTd	adult Tetanus-diphtheria vaccine
BCG	Bacillus Calmette-Guerin - vaccine for tuberculosis
BHT	Bed Head Ticket
CIOMS	Council for International Organizations of Medical Sciences
CHDR	Child Health Development Record
DESC	Drug Evaluation Sub Committee
DGHS	Director General of Health Services
DT	Diphtheria-Tetanus vaccine
DTP	Diphtheria-Tetanus-Pertussis vaccine
DTaP	Diphtheria-Tetanus-Pertussis (acellular) vaccine
DTwP	Diphtheria-Tetanus-Pertussis (whole-cell) vaccine
EPI	Expanded Programme on Immunization
HHE	Hypotonic Hypo-responsive Episode
Hib	*Haemophilus influenzae* type b vaccine
HIV	Human Immunodeficiency Virus
HPV	Human Papilloma Virus Vaccine
IPV	Inactivated Polio Vaccine
JE	Japanese Encephalitis Vaccine
MMR	Measles-Mumps-RubellaVaccine
MOH	Medical Officer of Health
MO MCH	Medical Officer Maternal & Child Health
MRI	Medical Research Institute
NCL	National Control Laboratory
NMRA	National Medicinal Regulatory Authority
NIP	National Immunization Programme
OPD	Out Patient Department
OPV	Oral Poliomyelitis Vaccine
PHI	Public Health Inspector
PHM	Public Health Midwife
PHNS	Public Health Nursing Sister
PvV	Pentavalent (DTP-HepB-Hib) Vaccine
QEB	Quarterly Epidemiological Bulletin
RDHS	Regional Director of Health Services
RE	Regional Epidemiologist
SIDS	Sudden Infant Death Syndrome

SMI	School Medical Inspection
SPHM	Supervisory Public Health Midwife
TT	Tetanus Toxoid Vaccine
UNICEF	United Nations Children's Fund
VAPP	Vaccine Associated Paralytic Poliomyelitis
VPD	Vaccine Preventable Disease
WER	Weekly Epidemiological Report
WHO	World Health Organization

1. Introduction

The goal of immunization is to protect the individual and the public from Vaccine Preventable Diseases (VPD). Although modern vaccines are safe, no vaccine is entirely without risk. Some people experience Adverse Events Following Immunization (AEFI) ranging from mild side effects to rare life-threatening illnesses. In the majority of cases these events are merely coincidences; in others they are caused by vaccine or by an error in the administration process of vaccine or sometimes, there is no causal relationship at all.

The technology continues to improve with time, as do the quality, efficacy (level of protection in clinical trial settings) and effectiveness (level of protection in real life practice; i.e. disease reduction) of the vaccines utilized. New vaccines are adding into the programme and the schedule becomes more tight and congested. Also with emerging diseases demand for new vaccine has increased. An increase in vaccine use (e.g., mass immunization campaigns) will lead to more AEFIs. Surveillance of AEFIs is an effective means of monitoring immunization safety and contributes to safeguard the credibility of the immunization programme. It allows for proper management of AEFIs and avoids inappropriate responses to reports of AEFIs that can create a sense of crisis in the absence of immunization safety surveillance.

Public alert on vaccine safety has increased through awareness and increased access to the information such as through internet. Also, the vigilance of health care providers on vaccine safety has increased, due to strengthening of AEFI surveillance. As a result, more and more concerns on quality and safety of vaccine are highlighted and demanded by both service providers and public. With this complexity, to rule out or rule in causality of true or possible vaccine link and prove coincidence need more detailed investigations, i.e. causality assessment. Causality assessment is an evidence based approach with more scientific analysis of data, often requires a wide ranges of expert's opinions, even further research studies.

Benefits of immunization against diseases such as measles, neonatal tetanus and polio are far outweigh the adverse events caused by immunization. Monitoring of AEFI will enable programme managers to reduce those risks even further.

Irrespective of the cause, when AEFI occurs while reduction of VPD, confusion is created among people to the extent that they may refuse further immunizations for their children leaving them susceptible to vaccine preventable diseases which are more disabling and life threatening. Surveillance of AEFI i.e. systematic collection of data on events following immunization therefore provide information to help developing strategies on regaining public confidence on immunization.

To increase acceptance of immunization and improve quality of services, surveillance of AEFIs must become an integral part of the immunization programme. Thus, a field guide for immunization programme managers at all levels [Regional Directors of Health Services (RDHS) /Regional Epidemiologists (RE) at district level and Medical Officer of Health (MOH) at divisional level] and also hospital staff including both public and private sectors will facilitate achievement of the objectives of AEFI surveillance.

In order to maintain or further improve confidence of public in immunization programme, health staff at all levels, from the field level up to the national level, should be familiarized with all aspects of immunization. Furthermore, they should be equipped to timely respond to any concerns of the public about immunization safety, including vaccine safety concerns. Timely response to public concerns about safety of vaccines as well as prompt communication will protect the public and preserve the integrity of the immunization programme as well.

It is important to note that an AEFI surveillance system is not meant to allot blame/fault to the staff, but to assist and further support them in providing high quality immunization services.

1.1 Vision

To protect the individual and the public from Vaccine Preventable Diseases through ensuring immunization safety.

1.2 General objective

To improve efficiency of surveillance activities of Adverse Events Following Immunization and the quality of immunization services at all levels; thereby

ensure immunization safety of all recipients leading to achievement of goals and objectives of the National Immunization Programme in the country.

1.3 Specific objectives

- To detect and timely identify problems associated with vaccines, which could be attributed to their inherent properties
- To detect, timely correct and prevent immunization related errors
- To identify clustering or unusually high rates of AEFI even if they are considered as mild
- To identify signals of unknown AEFI
- To ensure and facilitate causality assessment of all serious AEFIs and events with public concern ; coincidental, serious and unexpected/unusual AEFIs
- To estimate AEFI rates in the population and its temporal and spatial distribution
- To maintain the confidence of the community and health staff in the immunization programme by appropriately and timely responding to their concerns about immunization safety
- To effectively communicate with parents, community, media and other stake holders including private sector health care providers, to create awareness on AEFIs without jeopardizing the immunization programme

2. Adverse Events Following Immunizations

An adverse event following immunization is **any untoward medical occurrence which follows immunization* and which does not necessarily have a causal relationship with the usage* of the vaccine**. The adverse event may be any unfavourable or unintended sign, abnormal laboratory finding, symptom or disease. Reported adverse events can either be true adverse events, i.e. really a result of the vaccine or immunization process, or coincidental events that are not due to the vaccine or immunization process but are temporally associated with immunization.

(Note: **"Immunization"** as used in these definitions means the usage of a vaccine for the purpose of immunizing individuals. **"Usage"** includes all processes that occur after a vaccine product has left the manufacturing/ packaging site, i.e. handling, prescribing and administration of the vaccine).*

In 2012, Council for International Organizations of Medical Sciences (CIOMS) / World Health Organization (WHO) revised AEFI classification concerning particularly cause-specific categorization of AEFIs. (Table 1)

Table 1: Cause –specific categorization of AEFI (CIOMS/WHO, 2012)

Cause –specific Type of AEFI	Definition
Vaccine product-related reaction	An AEFI that is caused or precipitated by a vaccine due to one or more of the inherent properties of the vaccine product.
Vaccine quality defect-related reaction	An AEFI that is caused or precipitated by a vaccine that is due to one or more quality defects of the vaccine product including its administration device as provided by the manufacturer.
Immunization error-related reaction	Immunization error-related reaction: An AEFI that is caused by inappropriate vaccine handling, prescribing or administration and thus by its nature is preventable.
Coincidental event	An AEFI that is caused by something other than the vaccine product, immunization error or immunization anxiety.
Immunization anxiety-related reaction	An AEFI arising from anxiety about the immunization.

2.1. Vaccine Reaction

The purpose of a vaccine is to induce immunity by causing the recipient's immune system to react to the vaccine. A quality and safe vaccine reduces these vaccine reactions to a minimum while producing the best possible immunity.
A vaccine adverse reaction is an individual's response to the inherent properties of the vaccine, even when the vaccine has been prepared, handled and administered correctly. The new cause-specific categorization is important for decision making on a vaccine product, as it clearly differentiates the two types of possible vaccine reactions;

(i) **Vaccine product related reaction**; a vaccine reaction is an individual's response to one or more of the inherent properties of the vaccine, even when the vaccine has been prepared, handled and administered correctly and

(ii) **Vaccine quality defect-related reaction;** which is important to note that vaccine quality defect during manufacturing process has an impact on individuals response and there by increased risk of adverse vaccine reactions. (*Details are available on the "Report of CIOMS/WHO Working Group on Vaccine Pharmacovigilance, 2012)*

Vaccine reactions may be classified into common, minor reactions and rare, more serious reactions. (Table 2)Most vaccine reactions are minor and settle on their own. More serious vaccine reactions are very rare and in general do not result in long term problems.

2.1.1. Common, minor vaccine reactions

The proportion of vaccine reactions occurrences likely to be expected and observed with the most commonly used vaccines. In addition, some of the vaccine components, excipients (e.g. aluminium adjuvant, stabilizers or preservatives) can also lead to the vaccine reactions.

Fever: Can result as part of the immune response. Fever shall be anticipated in nearly 10% of vaccinees, except with Diphtheria-Tetanus-Pertussis (DTP) vaccine which produce fever in nearly 50% of those vaccinated. Fever is a systemic reaction usually occur within 24-48 hours of immunization except for those produced by measles, mumps and rubella vaccines which may occurs 6 to 12 days after immunization. However, it continues only for 24 – 48 hours.

Local reactions: Include pain, swelling and/or redness at the injection site and can be expected in about 10% of vaccinees. Bacillus Calmette-Guerin – (BCG) vaccine for tuberculosis causes a specific local reaction which starts as a papule (lump) 2-4 weeks after immunization and may get ulcerated and healed after several months, leaving a scar. Keloid (thickened scar tissue) from the BCG lesion is more common among Asian and African populations.

Systemic reactions: Common systemic vaccine reactions are irritability, malaise and loss of appetite. These systemic reactions are relatively common following whole cell Diphtheria-Tetanus-Pertussis (DTwP) vaccination. For Measles/Measles –Mumps-Rubella (MMR) and Oral Poliomyelitic Vaccine (OPV) vaccines, systemic reactions arise due to vaccine virus infection. Measles vaccine may cause fever, rash, and/or conjunctivitis. It is very mild compared to "wild" measles virus, but for severely immuno--compromised individuals, it can be severe, and may be even fatal. Vaccine reactions for Mumps (parotitis; swollen parotid gland) and Rubella (joint pains and swollen cervical lymph nodes) minimally affect the vaccinees.

2.1.2 Rare serious vaccine reactions

It is important to note that there is a difference between the terms "serious" and "severe" adverse events or reactions. "Serious" and "severe" are often used as interchangeable terms but they are not. A serious adverse event or reaction is a regulatory term. "Severe" is used to describe the intensity of a specific event (as in mild, moderate or severe); the event itself, however, may be of relatively minor medical significance.(e.g. Fever is a common relatively minor medical event, but according to its severity it can be graded as mild fever or moderate fever. Anaphylaxis is always a serious event and life threatening.)

A serious adverse event is defined as any untoward medical occurrence following any dose of vaccine that

- results in death or which is life-threatening
- requires hospitalization or prolongation of hospital stay
- results in persistent or significant disability/incapacity, congenital anomaly/birth defect, or requires intervention to prevent permanent impairment or damage

Most of the rare and more serious vaccine reactions [e.g. seizures, thrombocytopaenia, Hypotonic Hyporesponsive Episodes (HHE), persistent inconsolable screaming] do not lead to long term problems. Anaphylaxis, while potentially fatal, is treatable without having any long term effects. Although encephalopathy is included as a rare reaction to measles or DTwP vaccine, it is not certain whether these vaccines in fact cause encephalopathy. Case definitions for these reactions are given in annexure 1.

Table 2: Frequency of Vaccine Reactions

Vaccine	Vaccine Reaction	Expected Vaccine Reaction frequency rate* or %	Frequency category**
BCG Vaccine	▪ Injection site reaction [Papule, mild ulceration or scar]	Almost all vaccinees	Very common
	▪ Suppurative lymphadenitis	1 per 10^3 - 10^4	Uncommon to Rare
	▪ BCG osteitis	1 per 3,333 -10^6	Uncommon to Very rare
	▪ Disseminated BCG disease or systemic BCG-itis	1per 230,000- 640,000	Very rare
	▪ Immunine Reconstitution Inflammatory Syndrome (IRIS)	1 per 640,000	Very rare
Whole cell pertussis vaccines (DTwP)	▪ Fever 37.8^{0}C -39^{0}C	12.4% - 44.5%	Very common
	▪ Injection site Redness	16.4% - 56.3%	Very common
	▪ Swelling	22.4% -38.5%	Very Common
	▪ Pain (Severe-Moderate)	14.3% - 25.6%	Very common
	▪ Fussiness (Severe-Moderate)	12.4% 29.1%	Very common
	▪ Drowsiness	62%	Very Common
	▪ Anorexia	35%	Very common
	▪ Vomiting	13.7%	Very common
	▪ Persistent screaming	3.5%	Common
	▪ HHE	57-250 per100,000	Uncommon to Rare
	▪ Seizures	6 per 100,000	Very rare
	▪ Encephalopathy	0-5.3 per 10^6	Very rare
	▪ Anaphylaxis	1.3 per 10^6	Very rare
Oral Polio virus Vaccine (OPV)	▪ Vaccine Associated Paralytic Poliomyelitis (VAPP)		
	- Recipient VAPP	1 per 6.4 million doses	Very rare
	- Total VAPP	1 per 2.9 million doses [Risk is higher following the first dose(1in750000),and for adults and immune compromised]	Very rare

Inactivated Polio virus Vaccine (IPV)	▪ Injection site erythema ▪ Injection site induration ▪ Injection site tenderness	0.5%-1.5% 3% - 11% 14%- 29%	Uncommon to Common Common to Very common Very Common
Hepaptitis B Vaccine (HepB)	▪ Fever > 37.7^0C ▪ Headache ▪ Injection site pain ▪ Injection site redness ▪ Injection site swelling ▪ Anaphylaxis	1%-6% 3% 3%-29% 3% 3% 1.1 per 10^6	Common Common Common to Very common Common Common Very rare
Hib Vaccine	▪ Fever ▪ Injection site reaction	2% 10%	Common Very common
Tetanus vaccine (TT)	▪ Brachial neuritis ▪ Anaphylaxis	5-10 per 10^6 1-6 per 10^6	Very rare Very rare
Measles Vaccine	▪ Fever ▪ Rash ▪ Injection site reaction ▪ Febrile seizures ▪ Encephalomyelitis ▪ Thrombocytopenia ▪ Anaphylaxis	5% - 10% 5% 17%-30% 1 in 2000-3000 1 per 10^6 1 per 30,000 1 -3.5 per 10^6	Common to Very Common Common Very common Rare Very rare Very rare Very rare
Rubella Vaccine	▪ Fever ▪ Injection site reaction ▪ Acute Arthralgia (adults) ▪ Acute Arthritis (Adults)	2% 17%-30% 25% 10%	Common Very common Very common Very common
Mumps Vaccine	• Injection site reaction • Parotid swelling • Aseptic meningitis		Very common Common Very common
Japanease Encephalitis (JE) vaccine **inactivated Mouse brain vaccine**	▪ Injection site reaction ▪ Systemic reactions [Headache, malaise, myalgia, low-grade fever, nausea, vomiting, abdominal pain, rash, chills and dizziness] ▪ Allergic reaction ▪ Neurological Complications (Convulsions, Encephalitis, Encephalopathy, Peripheralneuropathy, Transverse myelitis ▪ Anaphylaxis	20% 5% - 30% 17 per 10^6 1 -2.3 per 10^6 1 - 2 per 10^6	Very common Common to Very Common Very rare Very rare Very rare

Inactivated Cell culture Vaccine	▪ Injection site reaction ▪ Headache, dizziness ▪ Fever > 38^0C ▪ Urticarial rash	4% <1% 12% 6.6 per 10^5	Common Uncommon Very common Very rare
-Live attenuated SA-14-14-2 vaccine	▪ High Fever ▪ Skin rash	5 – 7 per 10^2-10^4 1 per 10^4	Uncommon to Common Uncommon
Human Papilloma virus Vaccine (HPV) - HPV Bivalent vaccine	▪ Fever ▪ Headache ▪ Injection site pain ▪ Redness ▪ Swelling ▪ Rash ▪ Arthralgia ▪ Myalgia ▪ Fatigue ▪ Gastrointestinal disorders	3% 30% 78% 30% 26% 1% 10% 28% 33% 13%	Common Very Common Very Common Very common Very Common Un common Very common Very common Very common Very common
-HPV Quadrivalent vaccine	▪ Fever ▪ Headache ▪ Injection site pain ▪ Redness ▪ Swelling ▪ Urticaria ▪ Arthralgia ▪ Myalgia ▪ Gastrointestinal disorders ▪ Anaphylaxis	13% 26% 5.7% 5.7% 5.7% 3% 1% 2% 17% 1.7-2.6 per10^6	Very common Very Common Common Common Common Common Common Common Very common Very rare
Typhoid Vaccine			
-Ty21a	▪ Fever ▪ Vomiting ▪ Diarrhoea	0.3 % - 4.8% 0.5% - 2.3% 1.2% - 3.9%	Uncommon to Common Uncommon to Common Common
ViCPS	▪ Low grade fever < 39^0C ▪ Local erythema ▪ Soreness ▪ Swelling	Up to 2% 3% - 21% 8% - 33% 2% - 17%	Common Common to Very common Common to Very common Common to Very Common
Vi-TT	▪ Injection site pain ▪ Fever	Data not available Data not available	
Yellow Fever vaccine	▪ Vaccine-associated viscerotropic disease	1 per 10^6	Very rare

*Source : WHO Fact sheets
www.who.int/vaccine_safety/initiative/tools/vaccinfosheets

** Frequency category:

Very Common	Common	Uncommon	Rare	Very Rare
>10%	≥ 1% to ≤10%	≥0.1% to ≤1%	≥0.01% to ≤ 0.1%	<0.01%
≥ 1/10	≥ 1/100 and <1/10	≥1/1000 and < 1/100	≥ 10,000 and 1/1000	< 1/10000

Note:Although encephalopathy is included as a rare possible reaction to measles, JE or DTP vaccines, it is not certain that these vaccines in fact cause encephalopathy. Hence, further scientific evaluation is necessary.

2.2 Immunization error–related reactions

"Immunization" as used here means the usage of a vaccine for the purpose of immunizing individuals. "Usage" includes all processes that occur after a vaccine product has left the manufacturing/ packaging site, i.e. handling, prescribing and administration of the vaccine.

Earlier, this AEFI type was categorised as "Programme errors**"** (*Syn; Programmatic error or Programme operation errors*) result from errors and mistakes in vaccine preparation, handling, or administration (Table 1).

Immunization errors related reactions are preventable and controlled. They reduce the overall benefit of the immunization programme. Identification and correction of these errors are of great importance.(Table 3)

An immunization error related reactions may lead to a cluster of events associated with immunization. These clusters are usually associated with a particular provider or health facility or even a single vial of vaccine that has been inappropriately prepared or contaminated. Immunization errors related reactions can also affect a stock of vaccines (e.g. by freezing vaccines during transport leading to an increase in local reactions in recipients).

Table 3: Immunization Errors leading to Adverse Events Following Immunization

Immunization error	Adverse Event
Non sterile injections: ▪ Contaminated vaccine or diluents ▪ Reuse of reconstituted vaccine at a subsequent session	Infection [e.g. local suppuration at injection site, abscess, cellulitis, systemic infection, sepsis, toxic shock syndrome, transmission of blood borne viruses [Human Immunodeficiency Virus (HIV), Hepatitis B or Hepatitis C]
Vaccine prepared incorrectly: ▪ Vaccine reconstituted with incorrect diluents ▪ Drugs substituted for vaccine or diluents	Effect of other drugs (e.g. Insulin, muscle relaxant), used by mistake, instead of vaccine or diluents
Vaccine injected at wrong site/route: ▪ Use of subcutaneous route instead of intradermal for BCG ▪ Use of subcutaneous route instead of intramuscular for toxoid vaccines (DTP, DT, TT) ▪ Injecting into buttocks	Local reaction or injection site abscess Ineffective vaccination Sciatic nerve damage
Vaccine transported or stored incorrectly	Increased local reactions from frozen vaccine Ineffective vaccination
Contraindications ignored	Avoidable serious vaccine reactions

The most common immunization errors related reactions reported in Sri Lanka are sterile abscesses and nodules due to incorrect technique used in vaccine administration. Infection resulting in non sterile injections was dominant before introducing Auto disable (AD) syringes in many parts of the world. Infection can manifest as a local reaction (e.g. suppuration, abscess) or systemic effect (e.g. sepsis or toxic shock syndrome). Immunization errors related reactions may also result in AEFIs when another chemical or drug, other than the intended vaccine or diluent, is inadvertently used in the reconstitution of freeze dried vaccines (e.g. muscle relaxant given instead of relevant diluent for MMR vaccine) or administered directly in place of liquid vaccines. Immunization

errors related reactions can occur if wrong vaccine is administered to a person or a vaccine was given where it was not indicated (e.g. JE vaccine given instead of DTP vaccine at 2 months of age). These also occur if the contraindications/ precautions are ignored.

An Immunization errors related reaction may lead to a cluster of events associated with immunization. These clusters are usually associated with a particular provider or health facility or even a single vial of vaccine that has been inappropriately prepared or contaminated. Immunization errors can also affect many vials (e.g. by freezing vaccines during transport leading to an increase in local reactions)
Immunization errors related reaction can usually be prevented through properly organized immunization clinic practices, by training of Public Health Midwives, Public Health Inspectors and Nurses, maintaining regular supervision and by providing an adequate supply of equipment for safe injections.

Immunization errors related reactions can be avoided by adhering to following guidance:

- Proper maintenance of cold chain during vaccine storage, transport and until the time of vaccine administration.
- Vaccine must only be reconstituted with the diluent supplied by the manufacturer.
- Reconstituted vaccine should not be used for more than six hours after reconstitution.
- Reconstituted vaccine must be discarded at the end of each immunization session and never retained.
- No other drugs or substances should be stored in the same refrigerator where vaccines are stored.
- Immunization staff must be adequately trained and closely supervised to ensure that proper procedures are being followed including monitoring and supervision of cold chain.
- Careful epidemiological investigation of an AEFI is needed to ascertain the cause and to correct the wrong immunization practices.

2.3 Coincidental Events

Children are usually given vaccines at an age when they are susceptible to many diseases. Thus, situations may arise when an adverse medical event is falsely attributed to the vaccine. In other words a chance of temporal association (i.e. an event occurs after immunization) is falsely considered to be caused by immunization. These are purely temporal associations which are

inevitable when large number of vaccine doses administered, especially in mass campaigns.

Vaccines are normally scheduled early in life, when infections and other illnesses are relatively common, including manifestations of an underlying congenital or neurological condition. It is therefore, possible for many events including deaths, to be falsely attributed to vaccine through chance association. For example, Sudden Infant Death Syndrome (SIDS) incidence peaks around the age of early childhood immunization. Many SIDS cases will be in children who have been recently immunized. Controlled studies have shown that the association of SIDS and immunization is purely coincidental and not causal. Knowledge of Infant mortality rates and, rates of SIDS are helpful when investigating and in causality assessment to make valid conclusions and to rule out vaccine reactions.

Coincidental adverse events are clearly unrelated to vaccination. However, certain serious events may be blamed on the vaccine by parents or community because of its close temporal association with immunization, especially if the vaccinated individual was previously healthy. Therefore, these cases need to be investigated properly to allay public fear and maintain credibility of NIP. Responding to a community's concerns about immunization safety is important in maintaining public confidence in the NIP. If the same event also affected others in the same age group around the same time, who did not receive the suspect vaccine(s), then a coincidental event is more likely. There may also be other evidence showing that the event is not related to immunization.

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

With increasing awareness of AEFI surveillance, even health staff may report more coincidental events. Also, with introduction of new vaccines, there is a trend of reporting many AEFI including coincidental events. It is crucial to differentiate these reported coincidental events from potential 'signals'[e.g. HHE following introduction of DTP-HepB-HibPentavalent (PvV)vaccine in 2008 in Sri Lanka). Knowledge on background rates of reported coincidental events are also important and helps to determine possible 'signals' and to

correctly categorize them as coincidental events.*(Refer: "signals" is described in section 2.5.3)*

2.4 Immunization anxiety-related reactions

Individuals and groups can react in anticipation to an injection of any kind. This reaction may mimic an AEFI but is unrelated to the content of the vaccine.

Fainting is relatively common, but usually affects children aged over five years. Fainting does not require any management beyond placing the patient in a recumbent position. The likelihood of fainting can be anticipated when immunizing older children and can be reduced by minimizing stress in those awaiting injection through short waiting times, comfortable room temperatures, preparation of vaccine out of recipient view and privacy during the procedure.

Avoiding injury from the fall duet to fainting is important and those at risk should be immunized while seated. However, fainting may also occur sometime after immunization.

Hyperventilation as a result of anxiety about immunization leads to specific symptoms (light headedness, dizziness, tingling around the mouth and in the hands).

Younger children tend to react in a different way with **vomiting**, a common anxiety symptom.
These reactions are not related to the vaccine, but to the injection. Some individuals may be needle-phobic, aggravating such reactions. In a group situation, mass hysteria is possible, especially if a vaccinne has fainted or has had some other reaction following vaccination. Clear explanations regarding the immunization and calm, confident delivery will decrease the level of anxiety about the injection procedure and thus reduce the likelihood of occurrence.

It is important to note, faintish attack (syncope) can be misdiagnosed as anaphylaxis. Health worker need to be differentiating these two statuses and details are given in (Annexure 2: General Circular No: 01-20/2011- Guidelines for initial management of anaphylaxis in field settings). Very careful observation and clinical judgment is necessary in differentiating to prevent misdiagnosis. However, by mistake health care worker may administer a single dose of Adrenaline (intramuscularly) to a vaccinee with just syncope, but it

does not make harm to the vaccinee. To minimize such unnecessary medical emergency interventions, continued training and awareness for health staff is necessary.

2.5. Special Issues

2.5.1 Serious AEFI

Serious AEFIs are defined as those that are life threatening and those that result in hospitalization (or prolonged hospitalization), disability (or have the potential to result in disability) or death.

In addition, it is recommended that certain types of AEFI should be considered serious enough to warrant special attention in order to ensure immediate reporting when they are detected and thereby rapid and prompt response is initiated, including investigation and proper case management. These include AEFIs that may have been caused by immunization errors and occurring in cluster (e.g. bacterial abscess, severe local reaction, high fever or sepsis, BCG lymphadenitis, toxic shock syndrome), serious events of unexplained aetiology occurring within 30 days after a vaccination and events causing significant parental or community concern.

2.5.2 Cluster of AEFI

A cluster is defined as two or more cases of the same or similar event, which are related in time and have occurred within the same geographical unit or associated with the same vaccine, same batch number administered or same vaccinator or which had occurred during the same clinic session.

For example, two or more cases of abscess occurring following one immunization session in a village; repeated cases of abscess following immunization by same vaccinator or same batch of the vaccine will be considered as clusters.

2.5.3 Signals

Signals are defined as possible causal relationship of a reaction/event following a vaccination to which had been previously unknown or incompletely documented. Only a systematic causality assessment based on information/data collected through research methods can detect signals and establish causal

relationships. This is important with new vaccines, particularly if introduced in a mass vaccination approach.
E.g.; Narcolepsy following Pandemic H1NI influenza vaccine *(Pandemrix)*reported in Finland (*Ref: http://www.ema.europa.eu/docs/en_GB/document_library/Press_release/2011/07/WC500109182.pdf)*

2.5.4. Contraindications and precautions

Clear understanding of contraindications and precautions is important and necessary. Contraindications are conditions, when a given vaccine is temporarily or absolutely should not be given due to the past exposure history or present prevailing medical condition(s). Precautions are not contraindications, but decision on vaccination requires an individual case base assessment.

Vaccines are very rarely contraindicated. However, it is important to check for presence of contraindications to avoid serious reactions. For example, vaccines are contraindicated if there is a history of;

- Serious allergy to the index vaccine (anaphylaxis) or its components (excipients)
- Progressive neurological illness
- Immunodeficiency (in the case of live vaccines)

Use of vaccines in pregnancy is limited or mostly not recommended. The vaccines which are recommended in pregnancy would benefit and protect both mother and the newborn. However, the limited use of vaccine in pregnancy is largely due to the potential risk and harm to the foetus. The risk is mostly theoretical and limited to live attenuated vaccines which have demonstrated evidence of potential risk and harm, particularly in animal models. Vaccine manufacturers instruct pregnancy as a contraindication not due to proven evidence, but as a precautionary measure against litigation. The WHO recommends if the benefits of vaccination outweigh the potential 'theoretical risks' use in pregnancy, particularly when the burden of disease is high and, need attention in decision making.
(Ref: http://www.who.int/vaccine_safety/publications/safety_pregnancy_nov2014.pdf)

2.6 Causality Assessment

Causality assessment is the systematic review of data about an AEFI case to determine the likelihood of a causal association between the event and the vaccine/s received. It is a critical part of AEFI monitoring and enhances confidence in the NIP among health staff and public. Steps that need to be taken to address the event would be decided on the fact that it is attributable to the vaccine or the vaccination process.
All reported AEFIs require verification of the diagnosis; coding, review, collation and storage of data; if an AEFI is serious it requires a systematic, standardized causality assessment.

Causality assessment is important for:

- Identification of vaccine related problems
- Identification of immunization related errors
- Testing of hypothesis and research
- A basis for estimation of rates of serious AEFIs
- Comparison of AEFIs between vaccine brands

The quality of the causality assessment process depends on several factors:

- Quality of the investigation process
- Availability of adequate medical and laboratory services for investigations, post mortum facilities (for AEFI deaths) and follow up of cases and access to background information on disease/population and,
- Quality of the causality review process

2.6.1 Levels of causality assessment

Causality assessment of AEFIs may be performed at different levels:

- At the level of the **individual AEFI case report;** in order to estimate the probability that the occurrence of a reported AEFI in a specific individual is causally related to the usage of the index vaccine. It is usually not possible to establish a definite causal relationship between a particular AEFI and a particular vaccine on the basis of a single AEFI case report, if it is a signal (i.e. not previously unknown causality).
- **At the population level;** using surveillance data, investigation reports and appropriate statistical methodology in order to test the hypothesis that there is a causal association between the usage of an index vaccine and a particular AEFI (signal). This may sometimes be combined with

causality assessment at the individual level (of AEFIs collected within that system) whereby some or all of the cases of interest could undergo individual case review and causality assessment before inclusion in a group analysis.

In settings where causality assessment is undertaken it is important to consider all possible explanations for an event and the degree of likelihood for each before addressing the question of whether or not a vaccine product, quality defect, the immunization process or immunization anxiety caused a given event or if it was due to something else such as an infection. This is true whether the assessment is done for one or multiple cases of an expected or unexpected AEFI. Evidence for a causal link exists for some vaccines and AEFIs (e.g. measles vaccine and thrombocytopenia). This does not ensure, however, that causality can be assessed on an individual basis with only on prior knowledge. Most often this is because of missing or imprecise data in the AEFI report(s) resulting in a case being deemed unclassifiable. In other cases the final designation of an AEFI as to causality may be unknown due to lack of evidence for a causal link. It is still important to gather reports on such events because at some point they may be considered a signal and lead to hypotheses regarding a link between a vaccine and the event in question with specific studies designed to test for a causal association.

2.6.2 Criteria for determining the causality

Five criteria by Bradford-Hill will provide logical way to assess the association and test the hypotheses during the causality assessment.

- Strength of the association
- Consistency of the association
- Specificity of the association
- Temporal sequence
- Biologic plausibility (coherence with existing information)

Causality assessment aims to classify the likelihood of a causal association between a vaccine and an adverse event. The National Expert Committee on AEFI plays a critical role in confirming the causality assessments of selected investigations and in determining causality when not established with confidence by the investigator. Expert committee may use WHO Aide Memore on causality assessment as a resource material, which available at www.who.int.immunization_safety/en.

2. 6.3 Causality assessment method

There are four steps in causality assessment. The steps and their purpose are outlined below:

Step 1 - Eligibility:

To proceed with causality assessment it is necessary first to confirm that the vaccine was administered before the event occurred. This can be ascertained by eliciting a careful history from the relevant stakeholders to ascertain the timing of vaccination and of the onset of any signs and/or symptoms related to the event being assessed. It is also essential to be clear on the "diagnosis" of the reported AEFI. The valid diagnosis could be a clinical sign, symptom, abnormal laboratory finding or disease with clear details regarding onset. The diagnosis should also meet a standard case definition for the disease process that is being assessed. If available, it is best to adopt one of the Brighton Collaboration case definitions. (www.brightoncollaboration.org) However, if this is not possible, case definitions can be adapted from the published medical literature, national guidelines or local clinical practice.

Step 2 – Checklist:

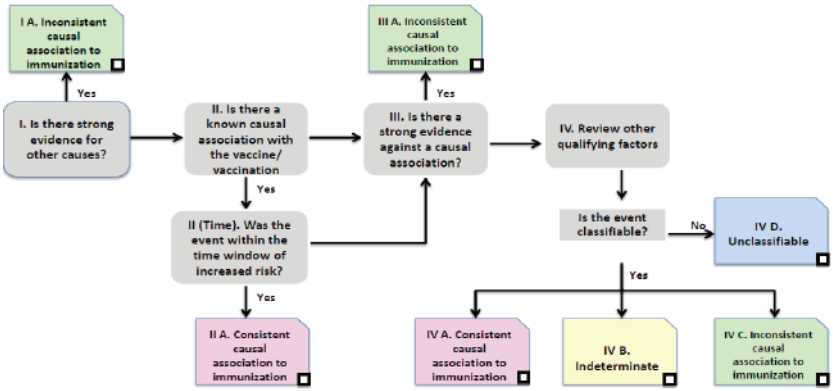
The checklist contains elements to guide the assessor or committee of reviewers to collate systematically the evidence for case review. It is designed to assemble information on patient-immunization-AEFI relationships in the following key areas:

Box 1: Checklist for AEFI causality assessment			
	Yes	**No**	**Un Known**
1. Is there strong evidence for other causes?	☐	☐	☐
2. Is there a known causal association with the vaccine/vaccination? - Relationship with antigen(s) / excipients in vaccines - Immunization error - Injection reaction	☐	☐	☐
3. Was the event within the time window of increased risk?	☐	☐	☐
4. Is there strong evidence against a causal associating?	☐	☐	☐
5. Other qualifying factors	☐	☐	☐

Step 3 - Algorithm:

The algorithm follows the key questions and related answers on 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.

Figure 1: Causality assessment: algorithm

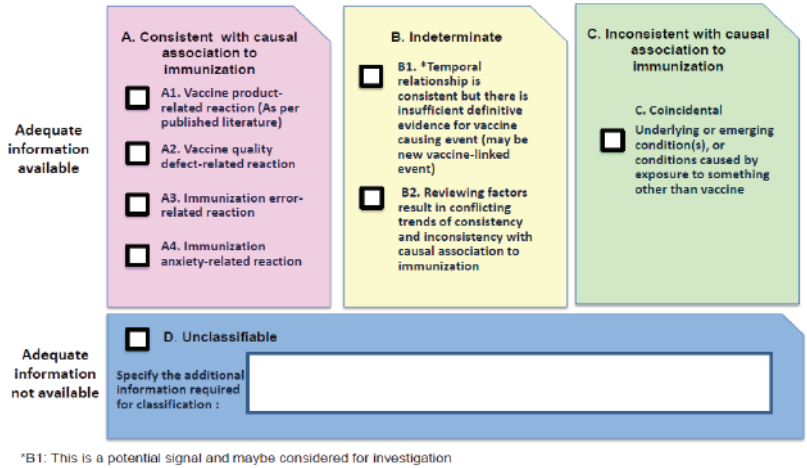


Source: Causality assessment of AEFI: user manual for the revised WHO classification. Geneva: World Health Organization; 2013.

Step 4 - Classification:

To categorize the AEFI's association to the vaccine/vaccination on the basis of the direction determined in the algorithm.

Figure 2: Causality assessment classification



Source: Causality assessment of AEFI): user manual for the revised WHO classification. Geneva: World Health Organization; 2013.

Until the investigation is complete a 'working hypotheses' could be formulated. Later it will be possible to analyze the data and assign a 'cause' and then to further classify into one of the five categories of AEFI. For a few medical events, the diagnosis itself will show the cause whether it is vaccine induced, immunization errors related reaction, coincidental or injection reaction. In others, external evidence may be required to identify the cause.

Recommendations will be made on the findings and conclusions. These recommendations should include the action that should be taken to remedy the problem identified. Action should be taken by the programme managers at each operational level.

3 Surveillance System of AEFI in Sri Lanka

Surveillance of AEFI in Sri Lanka commenced in 1996. All AEFIs are required to be reported irrespective of their nature of either serious or minor cases. However, there is no need to investigate all reported AEFIs. The AEFIs those needs to be investigated are: deaths, all hospitalizations and any AEFI(s) with special interest or public concerns.

3.1. Key elements of an AEFI surveillance system

- Early detection and reporting of AEFIs
- Timely and effective analysis/ evaluation of data/ information received
- Conducting timely and comprehensive investigation and causality assessment
- Dissemination of investigation and causality assessment findings to other responsible persons/units/institutions
- Timely and effective response/ follow up actions based on investigation and causality assessment findings
- Evaluation of the performances of service providers involved and to train and re-train when it is justified
- Defining responsibilities of specific service categories and avoid duplication of efforts
- Effective risk communication

3.2 Reporting events

For the purpose of AEFI surveillance, all adverse medical events following an immunization (irrespective of the cause) occurred within 30 days of administration of vaccine are need to be reported. Thirty (30) days window period is set for the operational purpose of AEFI surveillance. If necessary, any AEFI with an onset beyond 30 days period of date of vaccination still can be reported.

The events that are known to be identified as AEFI (case definitions are given in Annexure 1), events where a change in the nature, severity, frequency could be observed and also event which occur in clusters or cause major public concern should be reported using Notification form for Adverse Events Following Immunization (AEFI Form 1). (Annexure 3)

Any unexplained sudden death of a vaccine recipient temporally linked (**within 30 days**) to immunization, where no other clear cause of death can be established, should be reported. In addition, any unusual events following immunization should be reported.

As soon as health staff is informed of an AEFI or noticed any AEFI, it is important to ensure that recipient has received necessary health care including treatment if it is indicated.

3.3 Case detection and Reporting of AEFI

All reporting should be done using Notification Form for Adverse Events Following Immunization (AEFI Form 1).(Annexure 3) For reporting of Anaphylaxis, a special reporting form is available and need to be used, as it contains additional information. (Annexure 4) AEFI cases detection can be occurred at different places at different times in related to its onset. AEFIs that are required to be reported and their case definitions are given on the reverse side of the AEFI notification form (AEFI Form 1) and the Monthly Surveillance Report on AEFI (AEFI Form 2).(Annexure 5)

3.3.1 Reporting by hospitals

Hospitals (both government and private) and General/Private Practitioners are the first contact for most of the acute AEFIs, when affected patients seek treatment for the said AEFI. Out Patients' Department (OPD) in hospitals, paediatric wards, and surgical wards are potential places where AEFI could be detected. Therefore it is important that relevant health workers in hospitals are made aware of AEFI and AEFI surveillance programme. When a patient is detected as having an A EFI in a hospital, the case should be notified in the prescribed format, Notification Form for AEFI (AEFI Form 1) to the MOH of the area where the patient resides. It is the responsibility of area MOH to ensure that all hospitals are given Notification Forms for AEFI (bind books with triplicate copies). MOH should keep inform General /Private Practitioners also, that reporting of AEFI to MOH is necessary. This AEFI Form 1 is available as a carbonized copy book and each notification form contains 3 copies. The white coloured copy should be sent to the Epidemiology Unit and the pink coloured copy to the RE and the yellow coloured copy should be sent to the MOH. Hospital should maintain Hospital AEFI Register (Annexure 6). It is a responsibility of the head of the institution to designate a responsible officer to maintain this register.

3.3.2 Reporting by Immunization Clinic/Field Settings

Most minor cases, without need of medical care may not report to the above reporting sources. Information of such cases is obtained during the next clinic visits or during home visits by area Public Health Midwife (PHM).

At every immunization clinic, screening of all children for AEFI following previous immunization is mandatory and a separate column for this is available in the immunization record section of the Child Health Development Record (CHDR)(Annexure 7).In this format the last column is specifically to record any adverse events which occurred following a previous immunization. For example, when a mother brings her infant for the first dose of PvV/OPV the PHM responsible for screening must specifically inquire about any adverse events following BCG vaccination. If no AEFI are reported a "0" must be marked in the relevant column against the particular vaccine. In the event of reported AEFI it must be recorded briefly in the relevant column against the particular vaccine. In addition these cases are to recorded in the Clinic AEFI Register (Annexure 8), which is kept in the immunization clinic. However, for these retrospective reported cases to be reported in the clinic, there is no need to fill Notification Form for AEFI.

When a supervising officer [(MOH, Public Health Nursing Sister (PHNS) or Supervisory Public Health Midwife (SPHM)] inspects the CHDR when a six month old infant is brought to the immunization clinic for the third dose of PvV/OPV and notices that the AEFI column is blank against previous vaccinations, it indicates that the PHM has not screened the child regarding AEFI during subsequent clinic immunization visits.

3.3.3 Reporting by MOH Office

Some acute cases may directly report to the MOH by recipients/parents or guardians. Some private hospitals or private practitioners also may report directly to MOH office by phone/by SMS/ by email, without filling and sending Notification Form for AEFI (AEFI Form 1). In such cases MOH shall complete Notification Form for AEFI (AEFI Form 1) for given reported AEFI. Each MOH should maintain "MOH Office AEFI Register' (Annexure 9) and information coming from any other source (Hospital, General Practitioners, direct reported cases to MOH). should be recorded in this register. AEFI cases recorded in "Clinic AEFI Register' should be transferred into the MOH Office AEFI Register at the monthly conference in the MOH office. For this purpose,

PHM in charge of the field clinic should bring with her Clinic AEFI Register to the monthly conference. It is also important to avoid duplicating of AEFI cases, while entering AEFI information in the MOH Office AEFI Register.

AEFI reported to the MOH office either directly or through clinics AEFI registers during the month must be consolidated in the prescribed format (Monthly Surveillance Report on AEFI/ Annexure 5). This is a printed book in a carbonized triplicate copy; one copy must be sent to the Epidemiology Unit (white colour) and another to the RE (pink colour). Office copy (yellow colour) should be kept in the printed book as an institutional record for any follow up references. With this report, duly completed investigation form for each AEFI case that was investigated should be attached and sent to the Epidemiology Unit.

3.3.4 Reporting by Private sector institutions

As in government institutions, all private sector medical institutions and General Practitioners (full time and part time) handling immunization services and treating AEFI cases should report all AEFIs to the respective MOH, where vaccine was given, preferably using Notification form for AEFI (which is available at www.epid,gov.lk) or by telephone or by fax or by email.

Reporting from private sector is encouraged for two reasons: (i) Public commonly seek out patient medical care from the private sector, for AEFI following vaccines received at public institutions. (ii) It is important to monitor vaccine use in private sector

Specialist/Medical Officer who treats the patient at the private hospital is responsible for sending information. Each private hospital should identify an officer to coordinate this mechanism. The responsibility and coordination could delegate to a senior nursing officer too. The reporting from private sector does not different from practice by government hospital; it is a case base reporting to the respective MOH.

For vaccines which are used only in the private sector: All serious AEFI from any vaccine should be reported to the Epidemiology Unit immediately by the relevant private hospital / General Practitioner by using any means specified. All AEFIs following vaccines exclusively being used in private sector should be reported to the National Medicinal Regulatory Authority

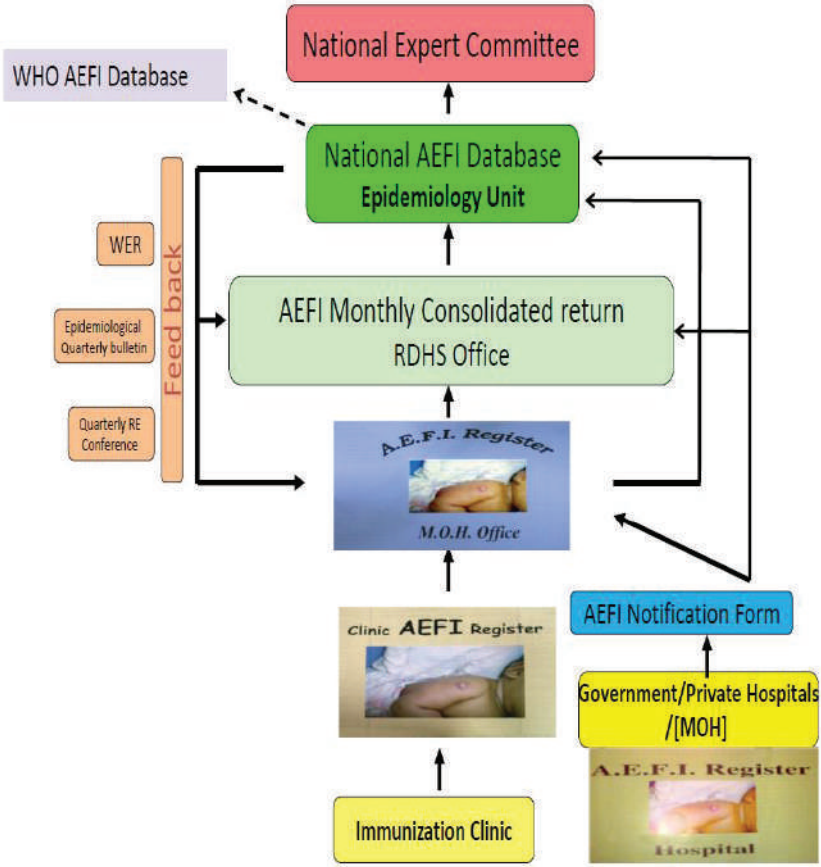
(NMRA) in a quarterly basis with a copy to Epidemiology Unit by the local agent of the relevant vaccine.

3.3.5 How can reporting be encouraged?

Support of field staff is crucial for the success of any surveillance programme. Field staff should be encouraged to report adverse events without fear or penalty. Available AEFIs should be reported even if there is a delay in the submission of information by the field staff.

It is important that field staff should be given a feedback about the results of investigations and action taken. This has to be carried out at each level of the surveillance process and should include positive feedback such as an acknowledgement for reports received. Feedback also should include sharing information on management of child/recipient especially concerning future vaccination and the outcome of investigations or causality assessment when these are carried out.

Figure 3: AEFI surveillance system in Sri Lanka



4. Investigating of AEFI

Ultimate goal of a case investigation is to find the cause of an AEFI and to prevent the occurrence of similar events in future and to ensure safety of vaccines and immunization. Therefore reporting and investigation of AEFIs related to all vaccines used in both government and private sectors are important and necessary. If the cause is identified as an immunization related error, remedial action can be taken promptly and public can be assured of the integrity of the immunization services through appropriate risk communication strategies. Even if the cause cannot be identified or the cause of the event was attributed to some other reason, the fact that health workers had investigated the incident itself will increase public confidence towards immunization.

Purpose of investigating AEFI cases are:

- To confirm the reported diagnosis or propose other possible diagnoses and clarify the outcome of the medical incident.
- To identify details of specifications of the vaccine used to immunize the affected recipient and most importantly to identify any vaccine related link for the given AEFI.
- To examine the operational/performance aspects of the programme.
- To determine whether a reported event was a single incident or one of a cluster and if it is a cluster where/by whom the suspected immunizations were given and what vaccines were used.
- To determine whether unvaccinated people are experiencing the same medical incidents.

Box 2: AEFI to be investigated

- **All deaths** that occur within one month of an immunization and attributed to that particular immunization
- **All cases requiring hospitalization** that occurs within one month of an immunization which are attributed to that particular immunization; this includes *Anaphylaxis, Central Nervous System adverse events, HHE, Injection sites abscess, Lymphadenitis, Osteitis/Osteomyelitis, Persistent screaming, Severe local reactions and Toxic Shock Syndrome*
- **All medical events** that are believed to have been caused by an immunization and for **which people are concerned**.

4.1 Steps in AEFI investigation

Immediately after any serious, unusual AEFI or death is reported, MOH and the field staff should re-assure the affected recipient/ parents/guardian that an investigation would be carried out. The investigation should begin as soon as possible.

Box 3 - Steps in investigation of an AEFI

- Confirm information in reported AEFI
- Ensure that patient is properly and timely treated
- Planning and preparation for investigation
- Visit to site of immunization
- Investigate and collect data using AEFI Investigation Form
    - About the patient :examine the patient-see/touch/record vitals
    - About the event
    - About the suspected vaccine(s)
    - About other people
- Assess immunization service by
    - Conducting interviews : patients, parents, service providers including hospital staff
    - Observing the service in action
- Specimen collection
    - From Patient
    - Vaccine vials and injection equipment
- Conclude Investigation

It is important to initiate an investigation urgently whenever it is deemed necessary so that the cause may be determined (where possible) and in some events additional cases are prevented. MOH, RE, MO/MCH or Epidemiology Unit may conduct the investigation depending on its seriousness and significant impact on immunization and NIP. Investigation of AEFI is a responsibility of the area MOH. However, in case of a death, the district team should conduct the investigation and MOH shall assist the district team. If the event is of national interest, a team from Epidemiology unit will conduct the investigation with participation of the district team. Whoever initiates the investigation should immediately notify the event to the relevant supervising officers. AEFI case investigation form (AEFI Form 3) is used for this purpose. (Annexure 11)

On completion of the investigation, cause of the event needs to be communicated to the relevant health officials (MOH, RE and Epidemiology Unit), parents/relatives and the community. This must include information about the steps being taken to remedy the situation and to prevent a recurrence, if such steps are needed.

4.2 Information to be collected during the investigation

- Inquire from the recipients (if possible)/parents or guardians about the health condition of the affected
- Check about the vaccine that is attributed and other drugs received
- Inquire about other vaccines received
- Question about the quality of immunization services
- Observe the immunization sessions in action
- Inquire about similar events in unvaccinated persons
- Support case definition or establish a more specific case definition if needed
- Seek information from other recipients/community regarding any similar events

4.3 Collection of specimens

Laboratory testing are useful to confirm or rule out the suspected cause: the vaccine and diluent may be tested for safety, sterility and chemical composition and the needles and syringes for sterility. Testing should only be requested on a clear suspicion and not as a routine procedure.

Collect specimens if relevant (i) from the patient (ii) the vaccine/diluents (iii) syringes and needles and (iv) post mortem samples

For histo-pathological examination and microbiological examination specimens should be handled at the local hospital or forwarded to MRI. Specimens for toxicological examination are performed at the Government Analyst Department. Above activities could be coordinated through Epidemiological Unit and RE of the district. If facilities for essential laboratory testing are not available at national institutions, sending samples to an accredited laboratory abroad need to be considered.

On clear suspicion samples from vaccine and diluent should be sent for testing to the MRI and if necessary to the international laboratories. The manufacturer should be informed. During transport of samples cold chain (2-8 ^{o}C) conditions should be maintained and have to be sent to the laboratory as quickly as possible. Relevant information should be clearly written on the request of the sample. It is important that the used vial with remaining vaccine and diluent (if applicable and available) is sent for testing along with the unused 1-2 vials of the same batch. Ensure that the label of the vaccine is intact and the used vial is packed in polythene and kept upright in the vaccine carrier to avoid contamination and leakage.

Information regarding the identity of the deceased and the details of authorization (postmortem order by coroner) should be obtained and included in the report. Samples should be taken and investigated in cases such as alleged intoxications, allergy related incidents etc. Therefore, as soon as information is received clinical staff should be advised to preserve samples such as blood, urine, CSF, vomitus, faeces, sputum, swabs etc., that have already been obtained. Samples (blood) for immunological studies in an anaphylactic reaction should be collected immediately after the reaction and also at 3 hrs and 6 hrs following the event optimally. Ward staff should be advised to document all therapeutic interventions.

Table 4: Types of specimens to be collected and purpose of laboratory investigations

Event	Specimen from the patient	Purpose of testing
Severe local reaction	Blood	Immunological assessment
Abscess	Swab of abscess fluid, Blood	Microbiological assessment
Lymphadenitis	Blood	Microbiological assessment
CNS symptoms with no paralysis	Cerebrospinal fluid, blood	Microbiological assessment: viral serology , cell counts, protein
CNS symptoms with paralysis	Stool	For Polio virus*

Respiratory symptoms	Blood, Nasopharyngeal swabs	Microbiological: particularly of influenza and other respiratory viruses
Toxic shock syndrome	Blood	Microbiological assessment and CBC, blood culture, blood glucose, blood gas, lactate, electrolytes, BUN and creatinine, LFT
Anaphylaxis	Blood	Immunological assessment: for Tryptase*(blood to be collected within 6 hours of the onset of anaphylaxis)*
Death	Postmortem tissue specimen (*Refer to the guideline on paediatric autopisies on deaths following immunization)*	Microbiological, Chemical, Histopathological, Immunological and Toxicological assessment

Date and time of collection of each sample and type of preservative used in each should be recorded. Reports of clinical investigations and medical records related to the incident such as microbiology, biochemistry, immunology, histopathology, haematology, radiology etc. should be collected and documented. A detailed history which includes past medical history, drug history, immunization history, history of allergies and findings of medical records etc of the patient should be obtained.

The area MOH, where the child was vaccinated needs to preserve empty vials, diluents, syringes and needles used at the incriminating event along with control samples of the same batch, if those need for further investigation to be done at MRI or NMRA or Government Analyst department or any other designated institution/laboratory. RE should coordinate this activity with the consultation of Epidemiology Unit.

4.4 Investigation of a Death

In the event of a death following immunization, it should be notified to the Regional Epidemiologist and Epidemiological Unit immediately over the phone and the field investigation has to be initiated promptly by the RE with the participation of MOH and also preferably with MO MCH.

Following information should be obtained during the investigation and format for investigation of death following immunization has to be completed. (Annexure 12)

- Detailed history from the parents/guardian
  - Pre immunization health status
  - Significant past medical problems of the child
- Sequale of the AEFI following administration of the vaccine(s)
- Details of all medical interventions; preferably copies of Bed Head Tickets (BHT) and reports of laboratory investigation should be collected for subsequent causality assessment.
- Information on storage conditions, maintenance of cold chain and handling of vaccines, diluents and syringes
- Information on similar events among other recipients of vaccine in the same clinic setting and the neighborhood.
- A post mortem examination is preferred following all deaths suspected to have been caused by vaccine/immunization. It should be performed by a consultant Judicial Medical Officer or a medical officer qualified with a diploma in legal medicine. Guidelines on conducting paediatric autopsies on deaths following immunization (Annexure 13) is available at the Epidemiology Unit website www.epid.gov.lk
- During such postmortem examinations macroscopic examination, histo-pathological examination and relevant microbiological and toxicological examinations has to be conducted as is deemed necessary. Specimen collection and storage has to be done according to the guidelines provided for paediatric autopsies on deaths following immunization.
- Post mortem specimens have to be preserved at the Judicial Medical Officer's office at least for a period of one year, in case further investigation is required.
- Detailed death investigation report has to be forwarded by the RE to the Epidemiological Unit for evaluation.

* If paralysis follows administration of OPV, specimens of stools are important. Samples of syringes and needles may be irrelevant since it is an oral vaccine. Stools are to be collected as according to the guidance given for AFP surveillance (refer "Eradication of Poliomyelitis – A comprehensive guide for Medical officers', Epidemiology Unit, 2005, available at www.epid.gov.lk)

4.5 Investigation of AEFI cluster

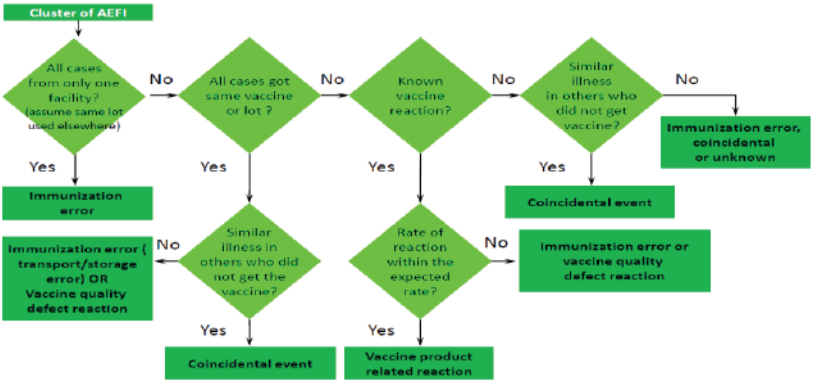
A cluster of AEFI is defined as two or more cases of the same adverse event related in time, place or vaccine administration. Exact nature of the relationship between the adverse events (e.g. duration of time, proximity of place); will differ by nature of events and the circumstances in which they occur.
Investigation of a cluster follows the same principles as indicated above with following steps;

- Establishment of a case definition, if there is no case definition laid down previously
- Identification of all immunized and unimmunized population who meet the case definition
- Obtaining immunization history (when, where and which vaccines were given)

Identification of any other common exposures of the cases

- If all cases received vaccines from the same health worker/ immunization clinic and there are no other cases – **Immunization related error is likely**
- If all cases received the same vaccine or lot from the different clinics and there are no similar cases in the general community - a problem with the **vaccine reaction is likely**
- If the event is a known vaccine reaction but occurring at an increased rate – **an immunization related error or a vaccine reactions are likely causes.**
- If cases include people in the same area in the same age group who were not immunized – event was probably **coincidental**.

Figure 4: Identifying cause of AEFI cluster



Source: WHO Aide Memore

4.6 Hypothesis to be tested in AEFI Investigation

The possible hypothesis of AEFI investigation is to test and identify whether the;

- Adverse event is not related to the vaccine and vaccination
- Adverse event is related to the vaccination; operational aspect of the programme
- Adverse Event is related to the vaccine

Results of the investigation should be entered in AEFI Investigation Form (Annexure11) by MOH and forwarded to the Epidemiology Unit with a copy to the RE as soon as possible.

There are many background factors / reasons involved in deciding whether an adverse event is actually caused by the vaccine. Vaccinations are carried out at an age when many underlying diseases become evident among children. The fact that the vaccine was administered within a reasonable time period of occurrence of signs and symptoms of a disease does not automatically suggest that the vaccine is the cause or aggravating or contributing factor. Systematic assessment of the patient and the relevant factors will determine the cause and effect relationship of the event.

4.6.1 Adverse events not related to the vaccine or vaccination

Some of the events may just coincide with the vaccine/vaccination; for instance, the event might have occurred even if the person had not received the vaccine. Occurrence of the event on a coincidental basis could be demonstrated if the same event also occurred among the unimmunized group in the population.

4.6.2 Adverse events related to vaccination

The following condition(s) can lead to adverse events related to vaccination, but not due to the inherent property of the vaccine.

- Inadequate dosage /over dosage
- Inadequate quantity of diluents
- Improper preparation of vaccines; reconstitution of the vaccines, using the wrong diluents, Substitution of vaccines or diluents with other medicinal drugs or other substances
- Incorrect method (route/site) of vaccine administration.
- Contamination of the vaccine or diluents
- Use of reconstituted vaccine at a subsequent session without discarding at the end of an immunization session or use beyond 6 hrs after reconstitution.
- Improper storage of vaccines following preparation
- Use of vaccine and diluents after their date of expiry
- Use of vaccine in contraindicated instances
- Misidentification of the vaccine recipient
- Unsafe use of needles and disposable syringes; improper handling and/or storage of needles and syringes and used after their date of expiry

The factors which need to be considered

- Whether reported cases are correctly classified, to ensure no error reports and no misclassification
- Whether several cases occurred in the same clinic or from different clinics
- Whether the unimmunized population of the same age group presented with the same symptoms/events
- Whether other recipients vaccinated with the same batch of vaccine presented with the same symptoms/events or not
- Whether vaccinator is the same person in all reported possible clustering cases

In any of the incidents mentioned, corrective measures should be initiated immediately in areas of logistics, training and supervision

4.6.3 Adverse events related to the vaccine

These are due to the inherent properties of the vaccine antigen or excipients (Adjuvant, preservatives, stabilizer, antibiotics or any other component). Minor events usually settle with treatment and have no long term consequences. Although serious events are very rare, it is important to investigate each case where the quality of vaccine is suspected to be the cause.

The factors to be considered during investigation of such cases;

- Frequency of occurrence (common/rare/not previously reported) - whether the events occur within the expected frequency range
- Known reaction to the vaccine
- Similar events reported among un-immunized population
- Event caused by the plausible mechanism due to biological properties of the vaccine
- Significant temporal relationship of the event and the vaccination
- Past history of similar events; related or independent of vaccination
- History of drug therapy; concomitant/previous
- Concomitant or preceding medical condition which could explain the event e.g. immunocompromised status of the recipient
- Any other factors that could explain the event; e.g. immunization related errors
- Laboratory results which would help in the investigation

If the event is serious, unexpected vaccine reaction or occurred with unexpected frequency;

- Contact RE / Epidemiology Unit immediately
- May temporarily suspend or withdraw the use of product at MOH level if recommended by Epidemiology Unit: the batch or lot of the suspected vaccine/ diluent/ syringe.

Vaccine suspension or withdrawal at district or national level would be done only on recommendation of national expert committee on AEFI/ Epidemiology Unit/NMRA

5. Analysis of AEFI Data

AEFI surveillance should include structured systematic data collection on the impact of vaccines used in the NIP. In addition, surveillance should include epidemiological analysis of data as well as dissemination of findings to advice Public health and hospital staff, NMRA, National Expert Committee and others who are interested or concerned on vaccine safety.

Analysis of data on AEFIs is contingent on the following components:

- Reporting source (reporting person, place, institute)
- Completeness of submitted AEFI forms.
- Verification and reassurance of data accuracy.
- Identifying health institutions where AEFIs are not reported. Determination of whether it is due to failure of reporting or whether there are no AEFIs to be reported. Checking on "Nil reporting".
- Assessing AEFI reports received during stipulated time period.
- Assessing number of events and rate for 100,000 doses of vaccine used.
- Categorization of the type of AEFI.
- Analysing each type of immunization errors by number and rates of relevant vaccines used in a specified time period.
- Comparison of the rates with available or expected known vaccine reactions and background rates.

5.1 Who should analyse the data?

Data analysis could be carried out at different levels in the AEFI surveillance system. MOH could carry out data analysis for the MOH area. District data is compiled and analyzed by RE while data analysis for the country is carried out by the Epidemiology Unit.

In analyzing data MOH plays an important part as it is the first and the best operational level where surveillance data can be used. All reports should be analyzed to identify the type of AEFI, particularly the immunization related errors. This is largely to carry out corrective action in a timely manner. Before the analysis, MOH needs to verify data and reassure its accuracy.

RE also needs to perform the same analysis for the district. Analysis by MOH area will help to identify issues and may focus on corrective action.

5.2 How should analyses the data?

The first step in analysis is to diagnose the case, which is done by the MOH at MOH level. Patient's signs and symptoms, the history of the event, patient's past medical history, data on suspected immunization and laboratory results all may contribute to the diagnosis. Standard case definitions should be used.(Annexure 1)

Secondly, all reported AEFI data need to be line listed and followed by tabulating by place (PHM divisions), person and time. Thirdly, analysis by antigens (e.g. PvV, MMR) and by type of reported adverse events (high fever, abscess) should be done. Number of doses administered for each antigen is the denominator for calculating reported AEFI rates for each antigen in a given time period (by month, quarter or year). Fourthly, analysis shall expand to the AEFI rates by first or second or third dose, when the antigen is administered more than once. For this, the number of doses administered of the given antigen as first, second or third dose need to be used as the denominator.

Table5 shows how to calculate adverse reaction rates by different antigens.

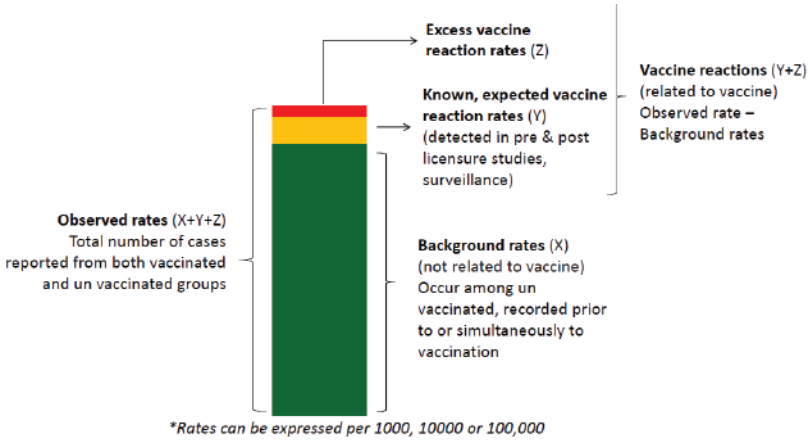
Table 5: Calculating adverse reaction rates by selected antigen in Sri Lanka –2014

Antigen	Number of doses administered	Fever (>39^{0}C)	Fever rates /100,000 doses Administered	Allergic reactions	Allergic reactions rates /100,000 doses administered
DPT	348,178	781	781/348,178 X100,000 =224.3	270	270/348,178 X100,000 =77.5
Penta	1,037,544	1326	1326/1,037,544 X100,000 =127.8	306	306/1,037,544 X100,000 = 29.5
MMR	702,850	110	110/702,850 X100,000 =15.7	231	231/702,850 X100,000 = 32.9

5.3 Interpretation of analyzed data

Interpretation of analyzed AEFI data is based on knowledge on expected rate, observed rate and background rates of given adverse reaction. (Figure 5)

Figure 5: Vaccine reaction rate, observed rate and background rate



Source: Global Manual on Surveillance of AEFI, WHO, 2014

Available expected rates for each type of AEFI for a given antigen will provide a guide to make decisions on corrective action to be taken on reported AEFIs. (Table 2)

It is also important to know about background rates of reported medical events in the country. Comparison of such background rates with reported rates of AEFI may provide a possibility of developing hypothesis of a coincidence. e.g Febrile seizures of varying aetiologies are common among young children and also may be possible following some vaccines (DTwP). Therefore it is important to know the rate of febrile seizures due to other reasons and expected rates following a given antigen. If the observed rated exceed the total of background and expected rates of given adverse reaction, this excessive vaccine reaction rate is a concern of 'real adverse vaccine reaction'. This comparison will essentially lead to describe the causality.

6. Follow -up Action

AEFI detection, investigation, analysis and causality assessment must lead to action if the credibility of immunization services is to remain high. These follow-up actions include diagnosis, treatment, reporting, communication and corrective actions..

6.1 Treatment

Treatment must be the first response to an AEFI. Mild symptoms such as mild fever and pain are likely to be of short duration and can be managed by assuring and educating parents during immunization. PHNS, PHM and PHI should also know how to identify serious AEFIs and when to refer to the MOH or hospital. It is very much important that all field health staff be aware with the General Circular on managing anaphylaxis on field setting (Annexure 2) and be prepared accordingly.

6.2 Corrective actions

When the investigation is completed and cause of AEFI is identified, it could be included into the relevant category and remedial action taken. Table 6 illustrates some follow up and corrective actions to be taken after investigating AEFI.

6.3 Training & awareness

AEFI is an opportunity for training and awareness for immunization team in both MOH and hospital settings. Irrespective of type or outcome of AEFI, it can use to update knowledge and develop skills and confidence on immunization safety among the staff and it is a responsibility of MOOH and also RE to carry out awareness and training on a regular basis.

Awareness can expand to involving all stakeholders link to the immunization programme such as: academia, school teachers/ students, volunteers, politicians and media.

Table 6: Follow up/ corrective actions to be taken after investigating AEFI

Vaccine quality defects	If a higher reaction rate than expected is being reported from a specific vaccine or batch then obtain information from the manufacturer and consider • Withdrawal/temporary suspension of the suspected batch of vaccine. • Arrange for return of implicated vaccine, if appropriate • Change manufacturing specifications or quality control • Replace the vaccine with a new stock of quality reassured vaccine
Immunization related errors	Correcting the cause of the error • Proper maintenance of cold chain • Intensify monitoring and supervision of health staff • Training of field health staff • Change procedure at the immunization clinics Whatever action is taken, it is important to review at a later date to check that the immunization errors have been corrected.
Coincidental	• Main task is to exclude other causes for AEFI • Communication with parents/community/field staff is crucial to impress that the cause and effect relationship is just coincidental • Patient should be referred to a clinician if the medical condition warrants treatment and medical care.
Injection Reaction	• This is due to the anxiety and fear of injection, which is usually common during school immunization programmes. • Effective communication with children to relieve their anxiety is important.
Unknown / undetermined	• Depending on the nature of the event, its extent and whether it is ongoing, further technical assistance from an expert may be needed to assist the investigation or causal assessment. • If necessary a special study needs to be conducted (to study possible signals).

6.4 Management of crisis situations

A crisis is a situation in which a real or potential loss of confidence in the vaccines or in the vaccination service occurs, precipitated by information about an adverse event. Usually, crisis can be avoided through foresight, care and training. Proper management of the crisis will strengthen the immunization programme and improve public confidence.

Steps on prevention of crisis

- Anticipate. Do not wait until a crisis occurs. Prepare for the unavoidable.
- Make available all the facts, those need for awareness/ communication.
- During district NIP related meetings/reviews, RDHS, Regional Epidemiologists and MOOH shall discuss and prepare a plan to react to a crisis when it occurs.
- Train vaccination personnel at all levels to respond adequately to the public; this should be done during MOOH monthly staff meetings or routine training.

6.5 Sharing AEFI information

Vaccine safety information needs to be shared with all MOOH and other stakeholders in order to ensure dissemination of correct information and thereby to ensure smooth functioning of NIP in the country. This may be done at two stages: sharing preliminary information at initial stage and final data/report after completion of investigation/causality assessment at a later stage.

- Ministry of Health (Higher officials: Secretary, Director General of Health Services, Deputy Director Generals)
- National Medicinal Regulatory Authority
- Medical Research Institute(National Control Laboratory)
- Professionals / Academia
- International agencies: WHO, UNICEF
- Manufacturers
- Other stakeholders

All AEFI data are available online on Epidemiology Unit website www.epid.gov.lk and published in WER and QEB of the Epidemiology Unit. It is the responsibility of MOOH and RE disseminate these published information with their respective staff and stakeholders.

6.6 Communication

Communication with parents, other members of the community and health staff need to be carried out under all circumstances. They should be kept informed about the investigation, results and action being taken or to be taken regarding the AEFI. It is crucial to highlight the benefits of immunization while communicating with the MOH staff/hospital staff/stake holders.

Key points to consider when communicating with parents/relations of the recipient, community and health staff:

- Listen to parents and their concerns empathetically
- Reassure and support the parent or recipient but do not make false promises
- Maintain frequent communication with the parents/guardian regarding the progress of the patient
- Inform parents about possible common adverse events and how to handle them
- Communicate continuously with parent, community and media during the investigation period to ensure their understanding of the risk-benefit balance of vaccination
- Avoid blaming health workers and focus on corrective action and quality of the NIP
- Communicate among all health authorities involved
- MOH staff also needs to be reassured and informed of the results of the investigation.
- Build up and maintain confidence among health staff

Be prepared to answer all questions relating to AEFI. Usual questions are;

- **WHO** is affected and what is responsible?
- **WHAT** has happened and what is being done about it?
- **WHERE** has it happened?
- **WHEN** did it happen?
- **WHY** did it happen?
- **WILL** it happen again?

Communication /Sharing AEFI information with Media

Media plays an important role in disseminating information and in developing public awareness. Use of media for the benefit of an immunization programme is necessary. Therefore, AEFI data may be shared with the media, when it is deemed necessary. However, sharing AEFI information with media is the responsibility of Ministry of Health and the Chief Epidemiologist may act on behalf of the Ministry of Health. In provinces and districts, respective Provincial Director of Health Services or Regional Director of Health Services too can communicate/share AEFI information. According to the ministerial/departmental instructions/regulations, sharing any information with media should be done only with prior approval from the Ministry. This does not

apply to heath awareness/public educational programmes carried out with media, because maintaining professional relationship with media is important.

Communication with the community:

In communicating with the community, it is useful to develop links with community leaders (local government members, religious leaders, Non-Governmental Organizations, particularly actively working in given areas), district staff (RDHS staff) and divisional staff (MOH staff) so that information can be disseminated as is necessary. MOH should support and provide appropriate information to his/her field staff to respond directly to community concerns. When there is a high level concern about a vaccine, known benefits of immunization in preventing serious vaccine preventable diseases compared to the uncertainty over vaccine adverse reactions (communication in risk-benefit of vaccines) can be emphasized through communication with the community.

7. Evaluation of the surveillance system of AEFI

The immunization safety surveillance system should be evaluated regularly to determine its effectiveness and should lead to remedial actions. Main indicators used for evaluation of effectiveness of the programme are given in Box 4:

Box 4: Indicators for evaluating AEFI surveillance system

At MOH Level:

- ***AEFI Reporting***
  - Comparing timeliness, completeness and accuracy of AEFI reporting with the Clinic and MOH AEFI registers
  - Comparing timeliness, completeness and accuracy of AEFI notifications with Hospital AEFI registers/BHTs/Admission & Discharge Registers
  - Comparing AEFI reporting rates by clinics / hospitals by quarterly/annually
  - Comparing timeliness, completeness and accuracy of AEFI monthly surveillance reports submitted to Epidemiology Unit and RE
  - Comparing proportion of "Nil Returns" of AEFI monthly surveillance reports submitted to Epidemiology Unit and RE

- ***AEFI investigations***
  - Comparing timeliness, completeness and accuracy of AEFI investigations to be done in a given time period

At District Level:

- ***AEFI Reporting***
  - Comparing timeliness, completeness and accuracy of notifications of AEFI by MOOH, Hospitals and private sector
  - Comparing timeliness, completeness and accuracy of AEFI monthly surveillance reports submitted by MOOH; Proportion of "Nil Returns"
  - Comparing 'AEFI Case Reporting Rates'* by MOOHs / hospitals (including private sector) in a given time period (quarterly/ annually) with national data
  - Comparing 'AEFI Reporting Rates'** by MOOHs / hospitals (including private sector) in a given time period (quarterly/ annually) with national data

- ***AEFI investigations***
  - Comparing timeliness, completeness and accuracy of AEFI investigations done by MOOH in a given time period
- **Audit of corrective action**
  - Proportion of corrective actions implemented from those were recommended to prevent future immunization related error by MOH

At National Level:

- ***AEFI Reporting***
  - Comparing timeliness, completeness and accuracy of AEFI notifications by MOOH, Hospitals and private sector
  - Comparing timeliness, completeness and accuracy of AEFI monthly surveillance reports AEFI submitted by MOOH
  - Comparing proportion of "Nil Returns" of AEFI monthly surveillance reports submitted by MOOH
  - Comparing timeliness, completeness and accuracy of RE monthly consolidated AEFI return submitted by Regional Epidemiologist
  - Comparing 'AEFI Case Reporting Rates'* by districts (including private sector) in a given time period (quarterly/ annually) with national data
  - Comparing 'AEFI Reporting Rates'** by districts (including private sector) in a given time period (quarterly/ annually) with national data

- ***AEFI investigations***
  - Comparing timeliness, completeness and accuracy of AEFI investigations done by MOOH/ RE in a given time period
  - Comparing number of serious AEFI completed with causality

- **Audit of corrective action**
  - Proportion of corrective actions are implemented from those were recommended, to prevent future immunization related error by MOH / districts

Note: * AEFI Case Reporting Rate

$$= \frac{\text{Total number of AEFI cases reported in a given time period}}{\text{Total number of children (persons) vaccinated during same period}} \times 1000$$

** AEFI Reporting Rate

$$= \frac{\text{Total number of AEFI reported in a given time period}}{\text{Total number of vaccine doses administered during same period}} \times 1000$$

Both 'AEFI Case Reporting Rate' and 'AEFI Reporting Rate' are indicators of AEFI surveillance system. Both show how different MOOH and different districts performance in AEFI surveillance. In 'AEFI Case Reporting Rate', *AEFI Case* defines here is a person, not an AEFI per se. Both these are is different from vaccine adverse Reaction rates, describes in Chapter 5 / Table 5, which indicates the performance of the given vaccine (antigen), but not the AEFI surveillance system.

The progress in immunization safety surveillance can also be monitored from the annual data reported to national level. Making the quarterly and annual reports available to MOH and hospital immunization staff encourage and provide positive feedback for their reporting. Publication of the data also allows international comparisons to be made.

Box 5: Indicators for vaccine safety performances

- Number of AEFI reports, categorized by type of reaction and vaccine(s) and causality assessment (with denominator data on number of doses of vaccine given)
- AEFI Reporting Rate by MOH and by districts
- AEFI Case Reporting Rate by MOH and by districts
- Rate of each adverse reaction by vaccine per 100,000 doses administered
- Proportions of serious AEFI reported by vaccines
- Summary of other important/unusual investigations

8. Roles and Responsibilities of Key Stakeholders

An effective AEFI surveillance system involves health workers at all levels in the NIP and other health service providers, such as hospital staff and private sector health care providers. This section identifies the key role players at different levels of the surveillance system and also outlines their roles and responsibilities in carrying out AEFI surveillance activities.

8.1 Responsibilities of MOH Office Staff

8.1.1 Role & Responsibilities of Public Health Midwife (PHM)

- Inquiries should be made from each recipient or parent/guardian of the recipient regarding any AEFIs experienced after previous vaccination at immunization clinics and record same in the CHDR (Annexure 7) and Clinic AEFI Register (Annexure 8).
- Inquiries should be made regarding any AEFIs in recipients during the PHMM field visit and if found they should be recorded in the pocket note book of the PHM. All information in the pocket note book should be entered in the Clinic AEFI Register.
- PHMM should bring the Clinic AEFI Register to MOH Office on monthly conference day or any other day selected by the MOH. All AEFI recorded in Clinic AEFI Register for that given period should be transferred into the MOH AEFI Register (Annexure 9)
- PHM also should enter summary number of AEFI reported by months in the Quarterly MCH Clinic Return (Form RH-MIS 527), which is submitted to MOH.
- PHM should inform SPHM, PHNS, and MOH immediately regarding serious adverse events, unusual AEFIs and deaths.
- If treatment is necessary for a particular condition the recipient having AEFIs should be referred to the MOH or to the nearest hospital.
- Whenever an opportunity is available, make aware and educate the community regarding AEFIs.

8.1.2 Role & Responsibilities of Supervisory Public Health Midwife (SPHM)

- Should inquire all vaccine recipients of any AEFIs experienced by them following previous vaccination during the screening for subsequent immunization at the clinic.

- Should monitor and supervise PHMM regarding immunization procedure, and detection and reporting of AEFIs. Any error in these should be identified and immediately corrected at the clinic session itself.
- Whenever an opportunity is available during the clinic session, parents/community should be educated and made aware on AEFIs.
- Should motivate PHMM to detect timely report AEFIs and conduct follow up.
- Should prepare the Monthly Surveillance report of AEFI timely and accurately and forward to the MOH for inspection and certification if this task has been delegated by the MOH.
- Should supervise or carry out transferring information from Clinic AEFI Register to MOH Office AEFI Register as delegated by the MOH.
- Should carry out transferring information from Quarterly MCH Clinic Return (Form RH-MIS 527) to MOH Office Maternal & Child Health Return (H-509, RH MIS – 2014) as delegated by the MOH.
- Should compare and monitor information on Clinic AEFI Register and Quarterly MCH Clinic Return (Form RH-MIS 527) for accuracy of AEFI information.
- Should compare and monitor information on MOH Office AEFI Register and Maternal & Child Health Return (H-509, RH MIS – 2014) for accuracy of AEFI information.
- Should train PHMM on quality and safe immunization practices.
- Should inform MOH immediately regarding serious adverse events, unusual AEFIs and deaths.

8.1.3 Role & Responsibilities of Public Health Inspector (PHI)

- Any AEFI identified during vaccination of students at schools during School Medical Inspection (SMI) or during field visits, should be recorded in the pocket note book and the data should be transferred into the "MOH Office AEFI Register" (Annexure 9) at the MOH Office.
- If there is a necessity, students with AEFI should be referred to the MOH or to the hospital.
- SPHI and MOH should be informed immediately regarding serious adverse events, unusual AEFIs and deaths.
- Area PHM and MOH should be informed any identified AEFI during his field visits.

8.1.4 Role &Responsibilities of Supervisory Public Health Inspector (SPHI)

- Whenever an opportunity is available during the SMI session parents/community/students should be educated and made aware on AEFIs.
- Should motivate PHII for timely reporting of AEFIs and conduct follow up.
- Should encourage the PHII to detect and report AEFIs.
- Should inform MOH immediately regarding serious adverse events, unusual AEFIs and deaths.

8.1.5 Role & Responsibilities of Public Health Nursing Sister (PHNS)

- Should inquire all vaccine recipients of any AEFIs experienced by them following previous vaccination during the screening for subsequent immunization at the clinic.
- Should monitor and supervise PHMM regarding immunization procedure, and detection and reporting of AEFIs. Any error in these should be identified and immediately corrected at the clinic session itself.
- Whenever an opportunity is available during the clinic session, parents/community should be educated and made aware on AEFIs.
- Should motivate PHMM to detect and timely reporting of AEFIs and conduct follow up.
- Should prepare the Monthly Surveillance report of AEFI timely and accurately and forward to the MOH for inspection and certification if this task has been delegated by the MOH.
- Should supervise transferring information from Clinic AEFI Register to MOH Office AEFI Register as delegated by the MOH.
- Should carry out transferring information from Quarterly MCH Clinic Return (Form RH-MIS 527) to MOH Office Maternal & Child Health Return (H-509, RH MIS – 2014) as delegated by the MOH.
- Should compare and monitor information on Clinic AEFI Register and Quarterly MCH Clinic Return (Form RH-MIS 527) for accuracy of AEFI information.
- Should compare and monitor information on MOH Office AEFI Register and Maternal & Child Health Return (H-509, RH MIS – 2014) for accuracy of AEFI information.
- Should train PHMM on quality and safe immunization practices.
- Should inform MOH immediately regarding serious adverse events, unusual AEFIs and deaths.

8.1.6 Role & Responsibilities of Medical Officer of Health (MOH)

- Inquiries should be made on any AEFIs experienced by the recipient following previous vaccination during the screening for subsequent immunization at the clinics.
- Should designate a responsible person for maintaining the MOH Office AEFI Register (Annexure 9) to include data from;
    - Information from clinic AEFI registers (on monthly conference day).
    - Notification from Medical Institutions
    - Notification from Private hospitals / General Practitioners (GP)
    - Information from any other source
- Should coordinate with hospitals and obtain information on AEFI from the wards and immunization clinics at government hospitals as well as from private hospitals/General Practitioners.
- Information in the MOH Office AEFI Register should be transferred to the Monthly Surveillance Report on AEFI (AEFI Form 2) to be sent to the Epidemiology Unit with a copy to RE on or before the 10th of the following month. This activity could be delegated to an officer (PHNS, SPHM). However, MOH should sign the form only after cross checking the details included in the forms with MOH office AEFI register. MOH is the responsible person for forwarding accurate and complete information in this AEFI Form 2 in a timely manner to the RE and Epidemiology Unit.
- Should motivate field health staff to detect and timely report AEFIs.
- Investigation of AEFIs is a responsibility of the MOH. Should immediately inform regarding unusual AEFIs, serious adverse events and deaths to the Regional Epidemiologist and to the Epidemiology Unit. Investigation of these cases should commence within 24 hours after receiving the information. May seek advices and assistance from RE or Epidemiology Unit, if necessary or event with a very serious /high public concern.
- Investigation reports should be sent to the Epidemiology Unit with a copy to RE with the monthly surveillance report on AEFI (AEFI Form 2). However, investigation reports of deaths and anaphylaxis, should submit to Epidemiology unit immediately after the investigation.
- If relevant, corrective action should be taken immediately following investigations
- Monitoring and supervision of the field health staff should be carried out regularly.

- Should provide guidance and adequate training to the field health staff on AEFI surveillance and good quality immunization practices. Whenever necessary staff should be re-trained.
- Should communicate with the staff and the community especially in an event of a serious AEFI: Public should be kept informed regarding what is being done during the investigation and once it is over, the conclusions and results should be shared with other members of the team and the community.

Note: All Additional Medical Officers of Health (AMOH) are also equally responsible to carry out above functions as directed by the MOH. If MOH is not available, then AMOH should take the complete responsibility of AEFI surveillance at MOH office.

8.2 Hospitals: Responsibilities of government /private hospital staff

- Inquiries should be made on any AEFIs experienced by the recipient following previous vaccination during the screening for subsequent immunization at the hospital immunization clinics.
- AEFI Reporting should be done immediately to MOH of the patient's residential area by the Medical Officer who is treating the patient on suspicion of AEFI using the Notification form for AEFI. This is applicable for both outdoor and indoor patients. For this purpose, it is recommended to provide a book of notification form for AEFI (Annexure 3) to both OPD and indoor settings. For reporting of anaphylaxis, special Anaphylaxis event record form to be used. (Annexure 4)
- Head of the institution is the final responsible officer regarding implementation of AEFI surveillance system in the hospital and need to delegate and designate a staff (Medical Officer or Nursing Officer) with a responsibility of the reporting of AEFI. The designated officer should maintain Hospital AEFI Register (Annexure 6)
- Serious adverse events, unusual AEFIs and deaths should be notified directly and immediately to the RE in addition to the Epidemiology Unit.
- Private medical institutions are also recommended to maintain and follow AEFI notification practices using notification form of AEFI, as it is done by government medical institutions.

8.3 District Level: Responsibilities of the Regional Epidemiologist

- Should undertake guiding and training the field staff on detection and timely reporting of AEFI and maintaining safe and quality immunization procedures.
- Should supervise data management; screening, compilation and analysis of AEFI data in the district.
- Should coordinate with the Epidemiology Unit and MOH staff.
- Should send district data from all MOH areas on AEFIs to the Epidemiology Unit before 20th of the following month, using Monthly Consolidated Return of AEFI (AEFI Form 4).(Annexure 10)
- District records on AEFI surveillance should be maintained.
- Regular supervisory visits should be undertaken for monitoring the routine immunization programme and detect problems in reporting or identify immunization related errors.
- Should keep up monitoring and supervision of field staff and ensure regular feedback to the staff regarding their AEFI activities.
- Review of MOH activities on AEFI should be carried out at least once in two months.
- Serious adverse events, unusual AEFIs and deaths should be immediately investigated with the MOH and immediately informed to the Epidemiology Unit. If necessary, Epidemiology Unit too will assist the team.

8.4 Roles & Responsibilities of National level institutions

8.4.1 Role & Responsibilities of the Epidemiology Unit

- Chief Epidemiologist will identify and assign a focal point within the unit to carry out all immunization safety activities.
- Should screen all Monthly Surveillance Reports on AEFI when received at the Epidemiology Unit and send for data entry.
- Should identify incomplete and erroneously filled forms and return for rectification.
- Should identify unusual and serious AEFIs.
- Should monitor investigation of AEFIs and send reminders for investigation of cases.
- Should assist investigations of deaths and unusual events conducted by district team.
- Should conduct investigation of any AEFI case which has a national significance.

- Should report deaths and unusual events to the team of experts in the AEFI expert committee.
- Analysis of AEFI data for completeness, timeliness, number of nil returns, rates of AEFIs, deaths and unusual events should be carried out monthly, quarterly and annually.
- Should present results at the Regional Epidemiologist's quarterly review and make arrangements to publish in the Quarterly Epidemiological Bulletin (QEB) and Weekly Epidemiological Report (WER).
- Should provide guidance and training to the district and MOH staff.
- Regular reviews in the districts should be conducted to identify weak areas /gaps and to support solve these problems.
- Should prepare detailed reports for the expert committee/ causality assessment committee meetings.

8.4.2 Role & Responsibilities of National Medicinal Regulatory Authority (NMRA)

In Sri Lanka, immunization safety surveillance is a joint responsibility of both Epidemiology Unit and the NMRA. The WHO has defined six functions to be carried out by National Regulatory Authority (NRA) as given below:

- Marketing authorization and licensing activities: with clear written instruction for registering vaccines
- Post marketing surveillance including AEFI: surveillance of vaccine field performance in safety and efficacy
- Lot release: system for vaccine Lot release
- Laboratory access: use of laboratory when needed to assure quality and safety of vaccines
- Regulatory inspection: Regular inspection of manufacturers for Good Manufacturing Practices compliance
- Regulatory oversight of vaccine clinical trials conducted in the country

Responsibility of NMRA

- Should carefully consider vaccine safety profile of all vaccines at registration and extension of registration: advice shall seek from Drug Evaluation Sub Committee (DESC), Epidemiology Unit and Medical Research Institute.(MRI)
- Should monitor all AEFIs reported by the Epidemiology Unit, Private institutions and registered vaccine suppliers and manufacturers.

- Should inform Epidemiology Unit any serious AEFI reported by private institutions, vaccine suppliers or vaccine manufacturers.
- Should assist investigations and causality assessment of any serious AEFI conducted by Epidemiology Unit.
- Should report AEFI deaths and serious AEFI to the AEFI expert committee.
- Should prepare reports for the expert committee/ causality assessment committee, when request is made by the committee.

8.4.3 Role & Responsibilities of Medical Research Institute (MRI)

Medical Research Institute (MRI) functions as the National Control Laboratory (NCL) in Sri Lanka

- Should carefully consider laboratory aspects of safety profile of aCll vaccines at registration and extension of registration: advicle shall seek from DESC /NMRA or/and, Epidemiology Unit.
- Should inform Epidemiology Unit and NMRA any serious AEFI reported by private institutions, vaccine suppliers or vaccine manufacturers on any EPI or non EPI vaccines.
- Should assist investigations and causality assessment of serious AEFI conducted by Epidemiology Unit or NMRA.
- Should prepare reports for the expert committee/ causality assessment committee, when request is made by the committee.

8.4.4 Role & Responsibilities of National Expert Committee on AEFI

- The committee shall review all reported serious AEFI/deaths presented for expert opinion by the Epidemiology Unit and conduct causality assessment to establish causality and to make necessary recommendations to rectify issues.
- Makes final decisions on causality assessment of unconcluded AEFI investigations; Shall advise Director General of Health Services (DGHS), Chief Epidemiologist (NIP Manager) and NMRA regarding AEFI related matters when request is made by any of them.
- The committee members will be appointed by the DGHS. The committee is chaired by an independent senior clinician and consists of Paediatricians (2-3), a Physician, a Neurologist, an Immunologist (MRI), a Virologist (MRI), a Microbiologist (MRI), a Pathologist, an Epidemiologist, a Judicial Medical Officer and a Pharmacologist. The committee could invite other clinical experts when necessary. Chief Epidemiologist will be the Secretary

and the convener to the committee. A committee member will serve for a period of two years but could be extended as long as the DGHS feels his/her service is necessary. All members require to submit a Declaration of Interests (for their given serving period) to Secretary to the committee and will agree to the Term of References as specified by the DGHS.

- The committee will meet at least twice a year and whenever necessary.

Websites on immunization safety

Epidemiology Unit, MoH, Sri Lanka ▪ All AEFI Forms ▪ Immunization Handbook ▪ Quarterly Epidemiological Bulletin ▪ Guidelines for paediatric autopsies on death following immunization ▪ Guidelines for initial management of anaphylaxis at field settings	www.epid.gov.lk
Brighton Collaboration	www.brightoncollaboration.org
Centre for Disease Control (CDC), USA Surveillance for adverse events following immunization using the vaccine adverse event reporting system (VAERS). In: Manual for the surveillance of vaccine-preventable diseases, second edition.Atlanta (GA): Centers for Disease Control and Prevention; 2011: Chapter 21	www.cdc.gov/nip/vacsafe www.cdc.gov/vaccinesafety/Activities/VSD.html www.cdc.gov/vaccines/recs/acip/default.htm www.cdc.gov/vaccines/pubs/surv-manual/chpt21-surv-adverse-events.html
Council for International Organizations of Medical Sciences (CIOMS)	www.cioms.ch/
Department of Health, UK	www.dh.gov.uk/en/Publicationsandstatistics/Publications/
Public Health Agency of Canada	www.phac-aspc.gc.ca/im/index-eng.php
WHO Aide memoire on investigation causality assessment	www.who.int/vaccine_safety/en/
WHO Global manual on surveillance of AEFI	www.who.int/vaccine_safety/publications/Global_Manual_on_Surveillance_of_AEFI.pdf
WHO E-learning course on Vaccine Safety Basics	www.who.int/entity/vaccine_safety/initiative/tech_support/en/index.html
WHO Injection safety	www.who.int/injection_safety/en/
WHO Manual on Causality assessment	www.who.int/vaccine_safety/publications/aevi_manual.pdf,
WHO position papers on vaccines	www.who.int/immunization/documents/positionpapers/en/index.html
WHO vaccine reaction rates information sheets	www.who.int/vaccine_safety/initiative/tools/vaccinfosheets/en/index.html

Annexure 1: List of working definitions to be used in AEFI surveillance

Local adverse events

- **Injection Site Abscess**

Occurrence of a fluctuant or draining fluid filled lesion at the site of injection with or without fever.

- **Bacterial:** Existence of purulence, inflammatory signs, fever, positive Gram stain, positive culture, or finding of neutrophil predominance of content will support a bacterial site abscess, but the absence of some of these signs will not rule it out.
- **Sterile:** there is no evidence of bacterial infection following investigation.

- **Lymphadenitis (includes supportive lymphadenitis)**

Occurrence of either:

- At least lymph node, 1.5cm in size (one adult finger width) or larger, or
- A draining sinus over a lymph node.

Almost exclusively caused by BCG and then occurring within 2 to 6 months after receipt of BCG vaccine on the same side as inoculation (mostly axillary)

- **Severe local reaction**

Redness and/ or swelling centred at the site of injection and one or more of the following:

- Swelling beyond the nearest joint
- Pain, redness and swelling of more than 3 days duration or
- Requires hospitalization

Local reactions of lesser intensity may occur commonly and are generally of little consequence. For monitoring purpose, priority should be given to severe local reactions as defined above.

Central nervous system adverse events

- **Guillain barre Syndrome(GBS)**

Acute onset of rapidly progressive, ascending, symmetrical flaccid paralysis, without fever at onset of paralysis and with sensory loss. Cases are diagnosed by cerebrospinal fluid (CSF) investigation showing dissociation between

cellular count and protein content. GBS occurring with 30 days after immunization should be reported.

- **Encephalopathy**

Encephalopathy is an acute onset of major illness temporally linked with immunization and characterized by any two of the following three conditions.

- Seizures;
- Severe alternation in level of consciousness lasting for one day or more; and
- Distinct change in behavior lasting one day or more.

Cases occurring within 72 hours after vaccination should be reported.

- **Encephalitis**

Encephalitis is characterized by the above mentioned symptoms and signs of cerebral inflammation and, in many cases, CSF pleocytosis and /or virus isolation. Any encephalitis occurring within 1-4 weeks following immunization should be reported.

- **Meningitis**

Acute onset of major illness with fever, neck stiffness/positive meningeal signs (Kerning, Brudzinski). Symptoms may be subtle to similar to those of encephalitis. CSF examination is the most important diagnostic measure. CSF pleocytosis and/ or detection of microorganism (Gram stain or isolation}

- **Seizures**

Seizures lasting from several minutes to more than 15 minutes and not accompanied by focal neurological signs or symptoms.

- Febrile seizures or
- Afebrile seizures

- **Vaccine-Derived Paralytic Poliomyelitis**

Acute onset of flaccid paralysis within 4-30 days of receipt of oral polio virus vaccine (OPV), or within 4-75 days after contact with a vaccine recipient, with neurological deficits remaining 60 days after onset or death.

Other adverse events

- **Allergic reaction**

Characterized by one or more of the following (1) skin manifestations (e.g. hives, eczema); (2) wheezing; (3) facial or generalized oedema

- **Anaphylactic shock**

Circulatory failure (e.g. alteration of the level of consciousness, low arterial blood pressure, weakness or absence of peripheral pulses, cold extremities secondary to reduced peripheral circulation, flushed face and increased perspiration) with or without bronchospasm and / or laryngospasm/laryngeal oedema leading to respiratory distress occurring immediately after immunization.

- **Arthralgia**

Joint pain usually including the small peripheral joints.

- **Persistent:** Joint pain lasting longer than 10 days
- **Transient:** Joint pain lasting up to approximately 10 days.

- **High fever (>39 C^0 / 102^{0}F)**

The Endogenous elevation of at least one measured body temperature >39 ^{0}C/102 ^{0}F

- **Hypotensive-hyporesponsive episode (shock collapse)**

Sudden onset of pallor or cyanosis, decreased level or loss of responsiveness, decreased level of muscle tone (occurring within 48 hours of vaccination). The episode is transient and self limiting

- **Nodule at the injection site**

Presence of a discrete or well demarcated firm soft tissue mass or lump at the injection site that is sometimes referred to as a subcutaneous nodule, antigen cyst or granuloma, in the absence of abscess formation, erythema and warmth.

- **Osteitis / ostemyelitis**

Inflammation of the bone either due to BCG immunization (occurring within 8 to 16 months after immunization) or caused by other bacterial infection.

- ***Persistent screaming***

Inconsolable continuous crying lasting at least 3 hours accompanied by high-pitched screaming

- **Toxic- shock syndrome**

Abrupt onset of fever, vomiting and watery diarrhea within a few hours of immunization, often leading to death within 24-48 hours.

Annexure 2:Guidelines for initial management of Anaphylaxis at field settings

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சுகாதார அமைச்சு
Ministry of Health

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දිනය) 23/08/2011
திகதி
Date

General Circular No: 01-20/2001

Provincial/ Regional Directors of Health Services,
Medical Officers of Health,
All Heads of Medical Institutions

Guidelines for Initial Management of Anaphylaxis at Field Settings

Anaphylaxis is one of the most acute life-threatening hypersensitivity reactions that could occur following administration of a vaccine or any pharmacological agent. This could occur very rarely following vaccination, as an allergic reaction to the vaccine or its components. On average when a million is immunized one may develop anaphylaxis. Usually an anaphylactic reaction occurs within minutes of vaccination but in rare instances it could occur even after 12 hours of immunization.

Some people are more prone to develop anaphylaxis. e.g. persons who had developed an allergic reactions to a drug, vaccine or a food previously or those with a history of asthma or eczema. However some people without any such known risk factors could also develop anaphylaxis for the first time.

A person who develops anaphylaxis should be treated immediately to prevent life-threatening reactions and death. Hence it is very important to recognize the condition immediately in field clinic settings by the vaccinator, age appropriate first dose of adrenalin 1:1000 to be given immediately and the patient to be taken to the closest hospital for further management as soon as possible. To implement the contents of this guideline you are kindly requested to adhere to the following.

a) Ensure competency of the field health staff including Medical Officers, Nursing Officers, Public Health Inspectors and Public Health Midwives to recognize anaphylaxis early and administer the first dose of adrenaline, by thorough training of all field health staff as per national guidelines.

b) Estimate, procure and make available required quantities of Adrenaline 1: 1000 vials and 1 CC disposable syringes with 23 Gauge one inch needles.

c) Authorize field health staff in charge of field clinics to hire a vehicle in an emergency to transport the patient to the nearest hospital. The vehicle hire could be reimbursed to the field health staff subsequently.

Signs and symptoms of Anaphylaxis

Signs and symptoms of anaphylaxis are not distinctive to this condition alone. Signs and symptoms of anaphylaxis could be grouped according to the system of the body that is affected.

Skin and mucous membranes.

In over 80 % to 90 % of anaphylaxis reactions, skin and mucous membranes are affected. When only skin and mucous membranes are affected without involvement of other systems it could not be called anaphylaxis. However anaphylaxis could occur without the skin being affected.

- Tingling sensation around the lips
- Oedema of lips
- Itching of skin
    - specially in small children
        - scratching of forehead
        - scratching of hands
        - scratching of eyes & ears
- Generalized skin erythema
- Urticaria and oedematous patches
- Swelling in the throat (angio-oedema)
- Hoarseness of voice

Respiratory system

If a person prone to asthma develops an acute attack of asthma or difficulty in breathing after immunization it should be assumed that this could be a sign of an anaphylaxis reaction instead of assuming it as another attack of asthma and should mange accordingly.

• Cough • Wheezing • Difficulty in breathing	• Hoarseness • Rapid breathing • Stridor

Circulatory system

• Weak peripheral pulse • Lowered blood pressure	• Increased heart/pulse rate • Cold and clammy hands and feet

Nervous system

• Feeling of Anxiety and distress	• Loss of consciousness

Digestive system

• Stomachache (specially in small children) • Abdominal cramps	• Vomiting • Diarrhoea

Diagnosis of anaphylaxis

Following administration of a vaccine to a healthy recipient, if criteria mentioned below are met it could be suspected that the person is suffering from anaphylaxis.

1. with rapid onset of occurrence of signs and symptoms
2. when two or more of the above systems are affected

Treatment of anaphylaxis

The vaccine recipient with suspected anaphylaxis should never be left alone. Obtain help from those who are around and should ask to arrange transport the patient to the nearest hospital immediately. Vaccine recipient should be stretched out with the airway clear. If the vaccine recipient is conscious he/she should be kept supine with the feet raised higher than the head. If the patient is unconscious he/she should be kept in the left lateral position.

Adrenaline is the most important and effective drug in the treatment of anaphylaxis. Complications and death could be prevented by giving this drug as soon as possible (with the exception of infants).

Adrenaline 1:1000 solution should be given intra muscular (IM). **It should NEVER be given subcutaneous (SC) or intravenous (IV).**

It should be given on the middle 1/3 of the anterolateral aspect of the thigh.

In immunization field clinic settings **ONLY ONE DOSE** of adrenaline should be given.

Dosage of adrenaline 1:1000

Anaphylaxis among infants (less than 1 year of age) is very rare and **infants should not be given adrenaline in field clinic settings.**

Age	Dose of Adrenaline (1:1000)
12 months to 06 years	0.15 mg (**0.1ml**)
06 years to 12 years	0.2 mg (**0.2ml**)
12 years and over	0.3 mg (**0.3ml**)

Dose of adrenaline should not be changed even if the child is obese. A one inch 23 Gauge needle could be used to inject adrenaline to make sure it is delivered into the muscle. Before injecting the piston of the syringe should be drawn back to make sure that there is NO blood drawn into the syringe and hence the needle is not in a vein.

Immediately after administration of adrenaline patient should be taken to the closest hospital.

Management of a case of anaphylaxis

- Keep the patient in the supine position and ensure the airway is clear and keep the feet elevated higher than the head.
- If vaccine recipient is unconscious, keep in the left lateral position
- Give a single, age appropriate dose of adrenaline intra muscular (IM)
- Take the patient to the closest hospital immediately

Differentiation between anaphylaxis and a fainting attack.

Adults and adolescents could faint due to their fear of the anticipated pain or fear of the injection itself. In the case of infants and preschool children fainting is rare. Hence if an infant or preschool child becomes unconscious after immunization anaphylaxis should be suspected first.

Signs and symptoms that differentiate a case of anaphylaxis from a case of fainting

	Fainting attack	Anaphylaxis
Onset of signs and symptoms	Before immunization Or While immunizing Or Minutes after immunizing	Generally within minutes after immunization Could also occur a few hours after immunization
skin and mucous membranes	Generalized pallor Cold and clammy hands	Generalized skin erythema Itching of the skin (in children specially forehead, hands, eyes and ears) Tingling sensation around the lips Urticaria Swelling of lips (Angio-oedema) Cyanosis of finger tips and lips
Respiratory system	Rate of respiration normal Shallow breathing	Rapid respiratory rate Difficulty in breathing Cough Wheezing Stridor Hoarseness of voice Constrictive feeling of the chest In drawing of the chest

4

Circulatory system	Reduced heart rate Weak pulse Transient **absence** of peripheral pulse Carotid pulse is strong and easily felt Blood pressure could drop but when keeping the patient in supine position blood pressure soon returns to normal	Increased heart rate Weak pulse Pulse not felt sometimes Carotid pulse weak Hypotension. When keeping the patient in supine position blood pressure does not return to normal
Nervous system	Fiendishness or feeling faintish Light headedness Loss of consciousness. When keeping the patient in a supine position he soon becomes conscious	Patient is anxious and distressed Becomes unconscious and keeping the patient in supine position makes no difference
Digestive system	Vomiting	Vomiting Diarrhoea Stomachache (specially in small children) Abdominal cramps

Please be kind enough to bring the contents of this circular to the notice of all concerned in your institution.

Dr. Ajith Mendis
Director General of Health Services

cc : 01. DDG/PHS I
02. DDG/PHS II
03. Director MCH
04. Chief Epidemiologist
05. Director/ HEB
06. Director/ NIHS
07. Regional Epidemiologists
08. Medical Officers (MCH),
09. Medical Officers of Health

Annexure 3: Notification Form for Adverse Events Following Immunization (AEFI)

AEFI Form 1

Notification Form for Adverse Events Following Immunization (AEFI)

Patient Information						
Name:			MOH Division:			
Age: ☐☐ months/years		Sex: Male ☐	Female ☐	Telephone:		
Name & address of the Parent/Guardian:						
Information on the vaccine (primary suspected and other)						
Vaccine (Generic Name)	Vaccine (Trade name)*	Route	Dose (1st, 2nd, 3rd, 4th)	Batch/Lot Number	Expiry date	VVM Status (I, II, III, IV)
Diluent used: Yes ☐ No ☐	If "yes", Diluent batch/lot number			Expiry date of Diluent		
**Trade name is necessary only in private sector immunization*						
Place vaccine administered:					Date:	
Person vaccine administered: Doctor ☐ PHNS/Nurse ☐ PHM ☐ PHI ☐					Time: am/pm	

Adverse Events	
Local Adverse Events	Injection site abscess ☐ BCG Lymphadenitis ☐
Requiring investigation	Severe local reaction ☐
CNS Adverse Events	Vaccine associated paralytic poliomyelitis ☐ GBS ☐
Requiring Investigation	Encephalopathy ☐ Encephalitis ☐ Meningitis ☐
	Seizures Febrile ☐ Seizures Afebrile ☐
Other Adverse Events	Anaphylaxis ☐ Persistent screaming ☐ Osteitis / Osteomyelitis ☐
Requiring Investigation	Hypotonic Hyporesponsive Episode ☐ Toxic Shock Syndrome ☐
Adverse Events Not	Allergic reaction ☐ Arthralgia ☐
Requiring Investigation	High fever (>39ºC / 102ºF) ☐ Nodule at the injection site ☐
Other Adverse Events	a)
	b)

Instruction: Before reporting an AEFI, please refer to the definition for the relevant AEFI given in overleaf and make sure that reporting event agrees with the criteria stipulated in the definition
Date & Time onset of adverse event:
Date & Time referring to medical care :

Medical History/Other	**Outcome**
	Hospitalized: Yes No If "Yes": Hospital:
	BHT: Still in the hospital ☐ Discharged ☐
	Outcome: Recovered completely ☐ Partially recovered ☐ Death ☐

Reporting source		
Date of the notification:	Institution & Designation:	Telephone:
Name & Signature of the notifying officer/General Practitioner:		

(Medical Officers who attend any patient suffering from Adverse Effects Following Immunization shall notify in this form to the Medical Officer of Health the area of the patients residence)

Annexure 4: Anaphylaxis Event Record

Anaphylaxis Event Record

(To be completed by a Medical Officer)

Patient details											
Name:				MOH Area:			RDHS Area:				
Age	Date of birth		Sex	Ethnicity		Hospital:			BHT number:		
Past allergic history: Has patient had previous allergic reactions? ☐ Yes ☐ No If 'Yes', Allergen (Drug/Vaccine/Food/Other) - *specify*?											
Part I: Clinical features											
Date & time of clinical examination: Date(dd/mm/yy)									Time :		am/pm
Skin & Mucosa	☐ Urticaria ☐ Erythema ☐ Pruritus ☐ Prickle sensation						*Specify* the site of reaction:				
	Eye	☐ Red bilateral		☐ Red unilateral		☐ Itchy					
	Angioedema	☐ Tongue ☐ Throat ☐ Uvula ☐ Larynx ☐ Lip ☐ Face ☐ Limbs ☐ Other									
Respiratory system	☐ Sneezing ☐ Rhinorrhoea ☐ Sore throat	☐ Hoarse voice ☐ Stridor	☐ Sensation of throat closure ☐ Cough		☐ Tachypnoea ☐ Difficulty in swallowing ☐ Rhonchi		☐ Wheezing ☐ Indrawing / retractions ☐ Chest tightness		☐ Grunting ☐ Cyanosis ☐ Difficulty in breathing		
Circulatory system	BP (mmHg)	☐ Measured hypotension	☐ Decreased central venous pulse		☐ Capillary refill time >3secs		Heart rate (m)		☐ Tachycardia		
CNS	☐ Loss of consciousness		☐ Distress		☐ Other(*specify*):						
GIT	☐ Diarrhoea	☐ Nausea		☐ Abdominal pain/cramp			☐ Vomiting				
Diagnostic Criteria	☐ Rapid onset of occurrence of above sign & symptoms					☐ Two or more systems are affected					
Part 2: Suspected Product and exposure Information											
Date & Time of drug/vaccine administration: Date(dd/mm/yy)									Time :		am/pm
Drug ☐ Oral ☐ Parenteral			☐ Vaccine		☐ Serum		☐ Other (*specify*).				
Generic name :					Trade name :						
Batch number :		Expiry date :			*For vaccine*: VVM status ☐ I ☐ II ☐ III ☐ IV ☐ 1st dose ☐ 2nd dose ☐ 3rd dose ☐ 4th dose						
If diluent used, specify batch number & expiry date:											
If parenteral medicine/vaccine: ☐ Single dose ☐ Multi dose							☐ Liquid ☐ Lyophilised				
Route of administration: ☐ Oral ☐ IV ☐ IM ☐ SC ☐ ID ☐ Other(*specify*)											
Site of Administration: ☐ Deltoid ☐ Thigh ☐ Buttock ☐ Other (*specify*)											
Person who administered: ☐ Doctor ☐ Nurse ☐ PHI ☐ PHM ☐ Other (*specify*)											
Place of administration/reaction: ☐ Hospital ☐ MOH ☐ Clinic ☐ Private Hospital ☐ GP ☐ Other(specify)											

Part 3: Management

Was Adrenaline administered? ☐ Yes ☐ No

If 'Yes', Route : ☐ IM ☐ SC ☐ IV ☐ Other (*specify*) Dose:……ml

Place: ☐ Clinic ☐ MOH ☐ Hospital ☐ Other (*specify*) Time (*of 1st dose*):……am/pm

Person who administered adrenaline: ☐ Doctor ☐ Sister/Nurse ☐ PHI/PHM ☐ Other

Was a repeat dose of adrenaline given? ☐ Yes ☐ No	If 'Yes', describe (*including the time*)
What other medicines were administered? ☐ Yes ☐ No	If 'Yes', describe (*including the time*)

Any other details concerning medicines/management (*including CPR*)?

Investigation	Blood taken for mast cell Tryptase: ☐Yes ☐ No If 'Yes' specify the time interval after event: (*Note: Serum Tryptase levels peak 60-90 min after the onset of anaphylaxis and persist to 6 h. Therefore It is recommended that blood should be taken between 1 and 2 h after the initiation of symptoms.*)

Part 4: Outcome

Onset of first symptom: Date (dd/mm/yy) Time: …….. am/pm

Outcome: ☐ Full recovery ☐ Not fully recovered ☐ Recovered with sequelae ☐ Death

Specify details:

Time at outcome (recovery/death) Date (dd/mm/yy) Time: am/pm ☐ Unknown

Highest impact of Adverse drug event/Adverse Event Following Immunization:

☐ Did not interfere with daily activities ☐ Interfered, but did not prevent daily activities ☐ Prevented daily activities

Part 4: Any other comment

Details of Reporting Source

Name: Designation: Institute:

Signature Date: Telephone:

Definition: Anaphylaxis is defined as a severe, life-threatening, generalized or systemic hypersensitivity reaction, characterised by rapidly developing life-threatening airway and/or breathing and/or circulation and or gastrointestinal problems usually (not always) associated with skin and mucosal changes.

Annexure 5: Monthly Surveillance Report on Adverse Events Following Immunization

AEFI Form 2

Monthly surveillance report on Adverse Effects Following Immunization (AEFI)

RDHS Division : ..... MOH area : .....Month :..... Year: 201...

Adverse Events		BCG	OPV	Penta/DPT (Mark "P" for Penta or "T" for DTP in the row below against the dose) 1	2	3	4	Hep B	Measles	MMR	MR	DT	aTd	JE 1	2	Influenza			
1. Local Adverse Events																			
a. Injection site abscess																			
b. BCG lymphadenitis																			
c. Severe local reaction																			
2. Central Nervous System Adverse Events																			
a. Vaccine associated paralytic poliomyelitis																			
b. Guillen-Barre syndrome																			
c. Encephalopathy																			
d. Encephalitis																			
e. Seizures	Febrile																		
	Afebrile																		
3. Other Adverse Events																			
a. Death																			
b. Anaphylactic shock																			
c. Persistent screaming																			
d. HHE																			
e. Osteitis/Osteomyelitis																			
f. Toxic shock syndrome																			
g. Allergic reaction																			
h. Arthralgia																			
i. High fever (>39 C^0 / 102^{0}F)																			
4. Others (specify)																			
a.																			
b.																			
c.																			

Instructions:

1. Before reporting an AEFI, please refer to the definition for the relevant AEFI given overleaf and make sure that reporting event agrees with the criteria stipulated in the definition
2. Please correctly identify and enumerate the adverse events by correct antigen.
3. If a child/person has developed more than one adverse event, indicate only the most serious/important event here. (in this report under each adverse event reported will represent single individual)
4. **All deaths, anaphylaxis, hospitalizations and any event(s) with public concerns attributed to the immunization need to be investigated and investigation form (AEFI Form 3) should be sent to the Epidemiology Unit**. There are separate special investigation forms for deaths and anaphylaxis. It is recommended to send all investigated forms with this monthly surveillance report.
5. If any important observation is noted, please provide your comment (eg; Adverse events under category 4 here or, if any clustering is observed)

Comments: .....
.....
.....
.....

Name : ..... Designation: .....

Signature : ..... Date : .....

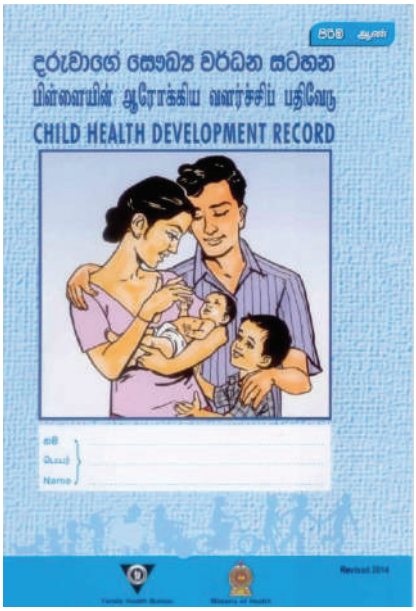
(This form should be completed by MOH and sent to the Epidemiology Unit before the 10th of the following month with a copy to the Regional Epidemiologist of the area)

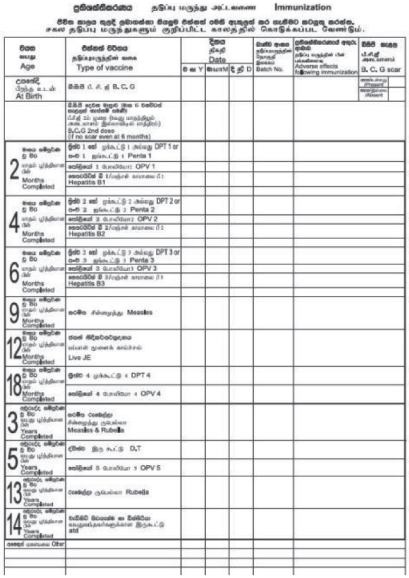
Annexure 6: Hospital AEFI Register

Hospital AEFI Register

Aerial Numbe [1]	Date of entry [2] (DD/MM/YY)	Adverse Event [3] (Specify)	Related Vaccine [4]		Date o Immunization [5] (DD/MM/YY)	Place of Immunization [6]	Name of the child/patient [7]	Age & Sex [8]	Address [9]	MOH area [10]	Date onset of AEFI [11] (DD/MM/YY)	Date notified to the MOH [12] (DD/MM/YY)	Remarks [13]
			Antigen	Dose									

Annexure 7: Child Health Development Record

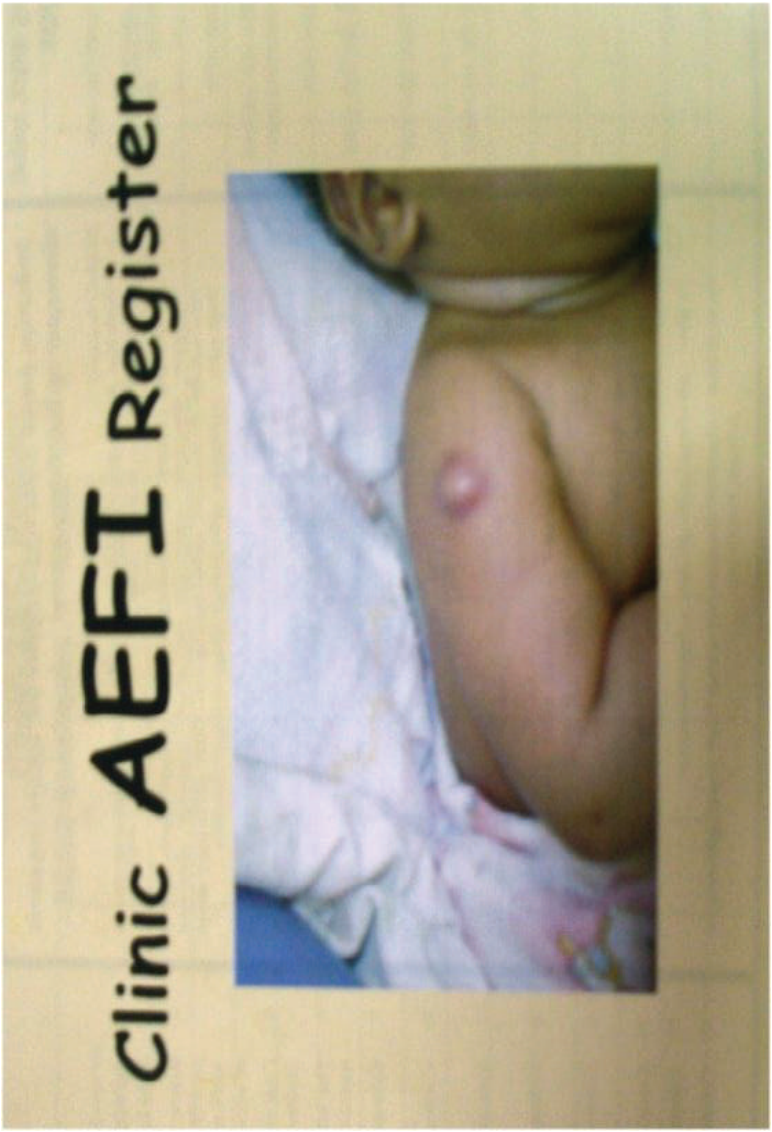




Immunization

Age	Type of vaccine	Date			Batch No.	Adverse effects following immunization	B. C. G scar
		B w Y	Month	දින D			
At Birth							
2 Months Completed							
4 Months Completed							
6 Months Completed							
9 Months Completed							
12 Months Completed							
18 Months Completed							
3 Years Completed							
5 Years Completed							
13 Years Completed							
14 Years Completed							

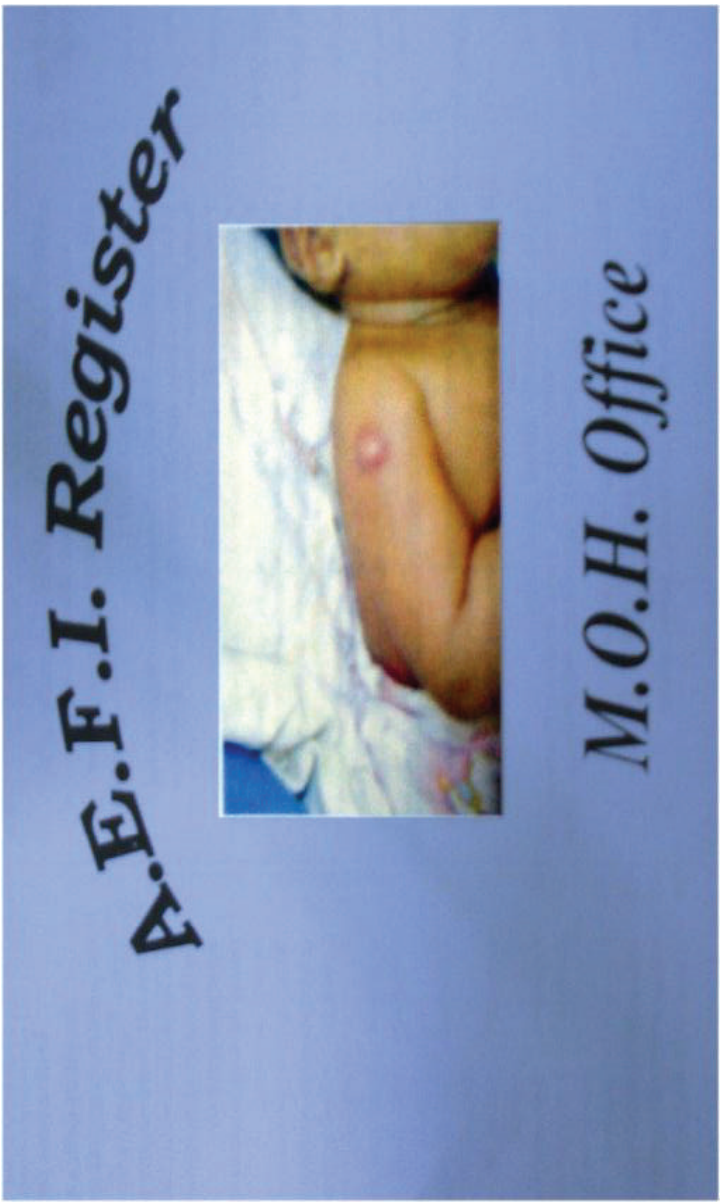
Annexure 8: Clinic AEFI Register



Clinic AEFI Register

`Serial No(1)	Registration Number of the CHDR (2)	Date of Report/Detection (3) (DD/MM/YY)	Adverse Event (4) (PL Specify)	Related Vaccine (5)		Batch No/ Lot No (6)	Date of Immunization (7) (DD/MM/YY)	Name of Child (8)	Address (9)	Remarks (10)
				Antigen	Dose					

Annexure 9: MOH Office AEFI Register



MOH Office AEFI Register

`Serial No(1)	Date of Entry (dd/mm/yy) (2)	Adverse Event (3) (PL Specify)	Related Vaccine (4)		Batch No/ Lot No (5)	Date of Immunization (6) (DD/MM/YY)	Place of Immunization (7)	Source of Notification (8) (CAR/MI/ GP/OS)	Name of Child (9)	Address (10)	Date of Investigation (11) (DD/MM/YY)	Remarks (12)
			Antigen	Dose								

Annex 10: Regional Epidemiologist Monthly Consolidate Return of AEFI

Regional Epidemiologist Monthly Consolidate Return of AEFI

RDHS Division:..... Month:.....

Serial No.	MOH Area	Adverse Events Requiring Investigation																			Adverse Events Not Requiring Investigation		
		Local Adverse Events			CNS Adverse Events									Other Adverse Events Requiring Investigation									
		Injection site abscess	BCG lymphadenitis	Severe local reaction	V.D. paralytic poliomyelitis	Guillen -Barre syndrome	Encepha lopathy	Encephalitis	Meningitis	Seizures				Anaphylactic	Persistent screaming	Hypotonic Hyporesponsive Episode	Osteitis/Osteomyelitis	Toxic shock syndrome	Allergic reaction	Arthralgia	High fever (>39 C/102 F)	Nodule at the injection site	Others	
										Febrile	Afebrile												
1																							
2																							
3																							
4																							
5																							
6																							
7																							
8																							
9																							
10																							
11																							
12																							
13																							
14																							
15																							
Total																							

(This form should be completed and sent to the epidemiology Unit on or before the 20th of the following month)

Date:..... .....

Regional Epidemiologist Signature.

Annexure 11: AEFI Case Investigation Form

AEFI Form 3

ADVERSE EVENTS FOLLOWING IMMUNIZATION (AEFI) CASE INVESTIGATION FORM

EPIDEMIOLOGY UNIT, MINISTRY OF HEALTH

The MOH should do the investigation personally. Necessary data should be obtained from the parents / patient / hospital by reference to the BHT / physician or from the diagnosis card. Early investigation and return is essential.

A. PARTICULARS OF PATIENT (Please (✓) appropriate box where applicable)

1. Name of patient (IN BLOCK LETTERS) :

2. Residential Address :

3. Date of Birth : ☐☐ / ☐☐ / ☐☐

4. Age	5. Sex	6. Ethnic group	7. RDHS Division	8. MOH area
☐☐/☐☐ y y / m m	☐ 1. Male ☐ 2. Female ☐ 3. Unknown	☐ 1. Sinhalese ☐ 2. Tamil ☐ 3. Moor ☐ 4. Others ☐ 5. Unknown	..... ☐☐	..... ☐☐

B. PRESENT ILLNESS / OUTCOME

09. What is the AEFI reported?	12. Was patient admitted to hospital ?	17. Outcome of the case
..... 10. Date of onset : ☐☐/☐☐/☐☐ d d m m y y 11. Where was the patient treated? ☐ 1. Govt. hospital ☐ 2. Pvt. hosp/practitioner ☐ 3. Other (specify)	1. Yes ☐ 2. No ☐ 3. Unknown ☐ 13. If yes, date of admission : ☐☐/☐☐/☐☐ d d m m y y 14. Name of hospital ..... 15. Ward : ..... 16. BHT No:	1. Cured ☐ 2. Died ☐ 3. Unknown ☐ 18. Date of discharge, transfer or death ☐☐/☐☐/☐☐ d d m m y y 19. If transferred name of hospital .....

C. CLINICAL DATA

(Case definition: An adverse event following immunization is any untoward medical occurrence which follows immunization and which does not necessarily have a causal relationship with the usage of the vaccine)

20. Symptoms and signs	21. Date of onset	22. Laboratory investigations	23. Treatment
☐ 1. Fever ☐ 2. Inconsolable cry ☐ 3. Painful swelling at the injection site ☐ 4. Enlarged tender axillary lymph nodes ☐ 5. Convulsions ☐ 6. Altered sensorium Any other symptoms and signs	☐☐/☐☐/☐☐☐☐ ☐☐/☐☐/☐☐☐☐ ☐☐/☐☐/☐☐☐☐ ☐☐/☐☐/☐☐☐☐ ☐☐/☐☐/☐☐☐☐ ☐☐/☐☐/☐☐☐☐ d d m m y y y y	....	....

D. PAST MEDICAL AND FAMILY HISTORY

		Yes	No	Unknown	If yes (specify) No. and place
24.	Existing congenital disorders	☐	☐	☐	.....
25.	Persisting underlying disease	☐	☐	☐	.....
26.	Previous history of significant illnesses	☐	☐	☐	.....
27.	Family history of similar event	☐	☐	☐	.....
28.	Previous history of similar event	☐	☐	☐	.....

E. OTHER RELEVANT HISTORY

		Yes	No	Specify
(i)	Delays in taking the patient to the hospital	☐	☐	.....
(ii)	Delays in transferring patient to another hospital for specialized treatment	☐	☐	.....
(iii)	Delays in receiving treatment	☐	☐	.....

F. IMMUNIZATION HISTORY

29. Date and time of immunization ☐☐/☐☐/☐☐☐☐ (dd/mm/yy) Time: ☐☐.☐☐

30. Place of immunization MOH clinic ☐ Government Hospital ☐
School ☐ Private Clinic ☐ Any other.....

31. Designation of the vaccinator
MOH ☐ PHNS ☐ PHM ☐
RMO ☐ PHI ☐ MO ☐ Others .....

32. Type of vaccine (Pleas ✓ appropriate box)	33. Dose	34. Expiry Date Please indicate the Vaccine No. on the dotted line from the Question 32	34. Batch No.	35. Manufacture	36 Diluents Batch No & Expiry date
☐ BCG ☐ OPV ☐ Penta ☐ MMR ☐ MR ☐ DPT ☐ DT ☐ aTd ☐ TT ☐ Hep B ☐ JE ☐ Influenza ☐ Others (specify)	☐ 1st ☐ 2nd ☐ 3rd ☐ 4th ☐ 5th	Vaccine ..... ☐☐/☐☐/☐☐ Vaccine ..... ☐☐/☐☐/☐☐ Vaccine ..... ☐☐/☐☐/☐☐ Vaccine ..... ☐☐/☐☐/☐☐ Vaccine ..... ☐☐/☐☐/☐☐ dd /mm /yy	....	....	

G. INFORMATION ON COLD CHAIN / STORAGE / VACCINATION TECHNIQUE

37. Vaccine and diluents stored in the	38. Vaccines transported in a	39. Status of the data lodger for 1 month period prior to the date of immunization.	40. Failure to maintain cold chain as indicated in the
☐1. MOH office ☐2. Clinic ☐3. Others ☐Specify	☐ 1. Vaccine flask or vaccine carrier ☐ 2. Cold box ☐ 3. Others (Specify)	Maximum temperature ..... Minimum temperature	40.1 VVM; Stage..... ☐. 40.2 Thermometer at the Main Compartment of refrigerator ☐

At the time of observation of the immunization	Satisfactory	Unsatisfactory	Not observed
41. Maintenance of Cold Chain			
1. Packing of vaccine	☐	☐	☐
2. Maintenance of cold chain in unopened/opened vials during immunization	☐	☐	☐
42. Vaccination procedure			
1. Reconstitution	☐	☐	☐
2. Drawing of vaccine	☐	☐	☐
3. Injection technique	☐	☐	☐
43. Please ✓ the appropriate box Reusable ☐ Disposable ☐	AD syringes ☐		

H. AEFI IN THE CLINIC CENTRE / FIELD

Any history of similar events reported among those vaccinated

44.	At the same clinic session	☐	☐	☐
45.	Using same vaccine at previous clinic sessions at the same clinic centre	☐	☐	☐
46.	Using same vaccine at the other clinic centers	☐	☐	☐
47.	History of similar events reported among those unimmunized (in the Field/Community)	☐	☐	☐

I. CONCLUSION AS TO THE CAUSE OF AEFI

Immunization errors related reaction Event caused by an error in vaccine preparation handling or administration	**Vaccine product related reaction** Event caused by the inherent properties of the vaccine	**Vaccine quality defect related reaction** Event caused due to quality defects of the vaccine product	**Immunization anxiety related reaction** Event from anxiety about or pain from the injection itself rather than the vaccine	**Coincidental events** Event that happens after immunization but not caused by the vaccine – a chance association	**Unknown**
If possible, describe the cause in below given area					

Corrective action taken:.....

.....

Remarks:.....

.....

Signature : ..... Name : .....Date : ..... Designation : .....

Please return to: Epidemiology Unit, 231, De Seram Place, Colombo 10. email: epidunit@sltnet.lk Tel : 011-2695112 / 2681548 Fax : 011-2696583

Annex 11a: Guidelines on Case Investigation

Record about the suspected vaccine

- Name and number of doses of all vaccines given on that day e.g. Penta-2
- Lot or batch number, manufacturer's name and expiry date.
- For vaccines which are reconstituted, the same information is required about diluents.
- Length of time the lot has been used
- List of vaccination centers receiving this lot
- Reports of other centers supplied with the lot and reporting of AEFI
- The conditions under which the vaccine was shipped, its present storage condition, state of vaccine vial monitor, and temperature record of refrigerator
- Storage of vaccine before it arrived at health facility, from where it was received from higher up the cold chain, vaccine monitor card.

Record about local immunization services

- Vaccine storage and distribution
- Diluents distribution and storage
- Reconstitution (maximum period allowed after reconstitution)
- Storage of opened vials
- Disposal of used vials
- Use of AD syringes and waste disposal
- Name of vaccinator(s)
- Details of training in immunization practice
- Whether there is supervision

Observe the service in action

- What else is stored in the refrigerator
- What vaccine are stored with other drugs
- Whether any vials have lost their label
- Whether similar containers are stored next to vaccine vials which could be confused with them
- How reconstitution of vaccine is carried out
- How and where the diluents are stored.
- How the injections are administered
- How needles and syringes are re-sterilized or disposed of
- What happens to opened vials
- Whether any open vials were contaminated.

Ask about other people in the area

- Whether others received the same vaccine
- Whether others fell ill
- Name of health worker(s) who gave immunization which resulted in AEFI

Formulate a working hypothesis (so far) as to what was the probable cause of the

AEFI for example:

- Programme related
  - Vaccine transportation or storage error
  - Reconstitution error
  - Unsterile practice
  - Incorrect administration technique
- Vaccine induced
  - Vaccine manufacturer error
  - Vaccine associated (but not manufacturer error)
- Coincidental
- Other
- Unknown

Collection and dispatch of specimens

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

Record the following

- What specimens have been collected
- Date of collection
- Date of dispatch
- Destination laboratory

Result and conclusions

- Laboratory results
- Clinical findings
- Findings of in-site investigation
- Summary of finding

Notes on specimen taking

Only specimens which are absolutely necessary for the investigation should be collected and dispatched. Their selection depends on the working hypothesis related to the events:

From the patient

- Blood, urine, CSF, swab from wound /abscess site as appropriate
- Autopsy specimens (If death occurred) as above, plus tissue samples for histology.

The **vaccine** in use at the vaccination center:

- Collect the actual opened vials of vaccine and diluents used to inject the child (or children) who suffered AEFI. If the clinic systems is working properly, investigators should not be able to locate them. Nonetheless, a through search must be made to try to locate them.

- Collect some unopened vials, two from the health center and five from central stores, of the same vaccine and diluents from the same refrigerator where the implicated vaccines were stored.

  The vaccine may be tested for toxicity, sterility and adjuvant (e.g. aluminum content) and the diluents for sterility and chemical composition. The testing of vaccine should be requested on a clear suspension and not as a routine.

The syringes and needles

As with the vaccine, the needles and syringes may not be readily located and a thorough search must be made to try to locate them. Unless the AEFI occurred immediately after immunization, a properly functioning clinic will certainly have disposed of, or sterilized the used syringes and needles.

- If located all needles should be capped with extreme caution (beware of needle stick injury)
- If disposable or autodestruct syringes are used, collect a sample of unopened needles and stringers. They will usually be tested for bacterial contamination.

Notes on dispatch of specimens

- All specimens (whether of human origin, vaccines, diluents or equipment) should be **labeled** and **sealed** in containers or plastic bags.
- Specimens containing liquid should be kept **upright.**
- They should be transported in **ice** to the central laboratory for analysis.
- Be sure the transport time is less than the **cold life** of the ice.

- Attach in a separate envelope a copy of the **Case Investigation** Form to help the laboratory perform the correct tests as well as the model laboratory request form.
- **Send a copy** directly to the laboratory, ahead of the specimens. Once at the central laboratory, a decision will be made whether to send specimens to international laboratories for toxicology etc.

Annexure 12: Investigation of Deaths Following Immunization

Format for Investigation of Deaths Following Immunization

Part A	Background information
Part B	Investigation of the sequelae leading to death/Past History of the child
Part C	Investigation of the Hospital Management of the death
Part D	Investigation of the vaccine management and cold chain monitoring of the MOOH
Part E	Autopsy findings
Part F	Causal assessment of the death

Part A	**Background Information**

1. Name of the child:----------

2. Date of Death: ----------

3. Details of source of information

	Date	Informant/source
First notification to MOOH		
First notification to RE		
First notification to Epid Unit		

4. Information regarding the death investigators/investigation

Name & Designation Contact No.	Name & Designation Contact No.	Date(s) of investigation

Part B	**Investigation of the sequelae leading to death/Past History of the child**

1. Identification and Related Basic Information

Name, address and contact no. of parent or guardian			
Date of Birth			
Age on the date of immunization			
Sex:			
Ethnic Group			
Gestational Age			
Birth Weight			
Weight at the time of immunization			
RDHS Division			
MOH Area			
Incriminated Vaccines			
Date of immunization		Time	
Time interval between immunization and death			

2. Clinical description/sequelae of the event as described by the mother

2.1 Assessment of the child prior to immunization

2.1.1 Feeding:----------

2.1.2 Activity:----------

2.1.3 Features suggestive of any acute illness (please specify)

2.2 Any Medication within 24 hours prior to immunization: Y/N If yes, please specify.

Drug	Dose/frequency	Last dose given at (time)_

.3 Assessment of the child during immunization

.3.1 Details of the immunization procedure

i. Incriminated vaccine/s:----------

ii. Place and time of immunization:----------

iii. Medication simultaneous with immunization: Y/N

If yes please specify

2.3.2 Post immunization observation (Any adverse events noted)

2.3.3 . Assessment of the child during post immunization period

i. Feeding:----------

ii. Activity:----------

iii. Urine output;----------

2.3.4 Description of significant adverse events noted by the mother following immunization

i----------

ii.----------

2.3.5 Measures taken by the mother/guardian to overcome the above adverse event:

i. Traditional medication: Y/N(if yes please specify)

---

ii. Treatment at GP/ Govt. Hospital OPD/ Other : Y/N
if yes, please specify

- When was medical advise seek:----------
- medical advise provided/tentative diagnosis:----------

- medication prescribed/dose/frequency/how many doses given/when was last dosage

---

---

iii. Any other measures? (Please specify)----------

2.3.6. Out come of the above measures on observed adverse event (please specify)

2.4 Was the child hospitalized? YES /NO
If yes please specify details according to mother/guardian

2.5 Description of the final event according to the mother/guardian

---

	Date	Time	Person
When the child was last seen alive?			
When was child first seen unresponsive?			
When was child pronounced dead?			

2.5.1 Details of death confirmation:

2.5.2 If child had been asleep during death, please inquire following details

i. Sleeping place:----------

ii. Sleeping position-general:----------

iii. Position child found dead/position during last sleep:----------

---

iv. Other people who slept in the same place with the child:----------

---

3. Antenatal, and birth History

3.1. Antenatal Complications:----------

3.2. Natal period

Place of delivery: ----------

Period of gestation:----------

Mode of delivery:----------

(if mode is other than normal vaginal delivery please mention the indication)

Birth weight:----------

Apgar at birth:----------

Any significant finding detected by neonatal examination

Any PBU admissions: Y/N

If yes, please specify details (Indication for admission, duration, management and Follow up visits, outcome of the child) & annex a copy of diagnosis/follow up notes

---

---

4. Dietary History

4.1. Duration of exclusive breast feeding:----------

4.2 Details of introduction to weaning foods:----------

4.3 Current diet (brief description):----------

4.4 Any identified food allergies:----------

5. Development History

Highest milestone developed at the time of death:

Gross motor	
Fine motor	
Hearing, Vision	
Social development	

6. Past medical problems of the child

6.1 Hospitalizations

Disease/disorder/Diagnosis	Duration of illness	Institution/Medical Personnel involved

(Please annex copies of diagnosis cards)

6.2. Underlying congenital /acquired diseases or disorders for which child was currently on treatment/follow up

Disease/disorder	Duration of illness	Institution/medical Personnel involved	Management

6.3. Past history of evidence of abuse/ harm/ neglect/ accidental injury/ previous need for child protection.

Injury	Period	Institution/medical Personnel involved	Management

7. Previous immunizations

Vaccine	Date of administration	Batch No.	Adverse events

8. Family History / Social History

8.1. Details of parents

	Mother	Father
Name		
Age		
Educational Level		
Occupation		
Income		
Smoking/alcohol use		

8.2. Details of other siblings

			Number	Age
Number of siblings	Elder	M		
		F		
	Younger	M		
		F		

8.2.1. Any neonatal deaths in the family :(YES/ NO)
If yes please mention details and cause of death

8.2.2. Any infant deaths in the family: (YES/NO)
If yes please mention details and cause of death

8.2.3. Deaths or any other medical problems/hospitalizations among other children:

---

e. Similar deaths among close genetic relatives: (YES/NO)

Part C	Details of the management of the case at medical institution

1. Identification and Related Basic Information

Name of the Institution	
Date & time of admission	
Name & Designation of the admitting officer	
Name & Designation of the medical officer in charge of the subsequent follow-up	

2. Clinical description and examination findings as per medical records/by admitting officer and immediate management

---

---

3. Details of examination findings and subsequent management as per medical records

---

3.1. Examination findings

General Examination	
Cardiovascular system	
Respiratory system	
Abdomen	
Central Nervous system	
Pulse Oximeter reading	

3.2. Investigations:

	Investigation	Interpretation
Radiological		
Haematological		
Bio chemical		

3.3 Management

3.3.1 Pharmacological

3.3.2. Non-Pharmacological

3.3.3. Tentative diagnosis/identified problems

3.3.4 Details pertinent to resuscitation of the child

Part D	Investigation of vaccine management and cold chain at MOH office

1. Information on vaccine/cold chain and vaccination technique

1. Details of the vaccine

Vaccine	Batch No.	Expiry date	Manufacturer

2 Details of vaccine administration

Anatomical site of immunization	
Needle length and gauge	
Route of Administration, dose	
number of children immunized at same clinic on same day	
number of children immunized with same vaccine at same clinic on same day	
Similar events with other children	

3 Details of cold chain monitoring

Was there a break down in cold chain since the receipt of incriminated stocks of vaccine at the MOH office according to the daily temperature record	
Was there a break down in cold chain since the receipt of incriminated stocks of vaccine at the MOH office according to the temperature data lodger	
Status of the VVM on the stocks of incriminated vaccines	

Part E	Autopsy findings

1. Description of the autopsy

1.1 Autopsy performed: Y/N
1.2 Autopsy protocol used: Y/N
1.3 Offices involved in autopsy:

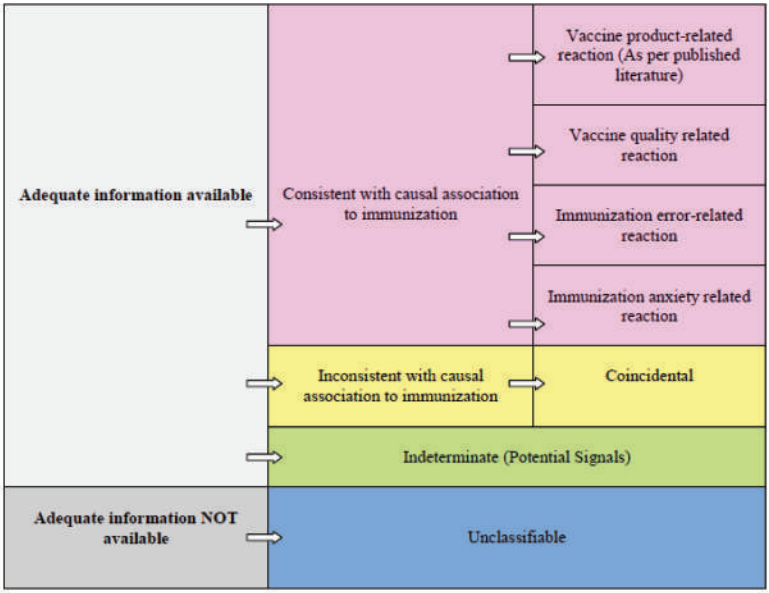
	Name/s	Designation	Institution
Medical officer conducted the autopsy			
Medical officer who conducted the histopathology Examination			
Other officers involved in death investigation(specify)			

1.4. Detailed description of autopsy findings

	Detailed description of autopsy findings
Gross pathology	
Histology	
Toxicology	
Microbiology	
Radiology	
Metabolic screening	
Biochemistry	
Other	

Part F	Causality assessment by Expert Committee

Date of causality assessment by expert committee:----------



Conclusion:

Annexure 13: Guidelines for Paediatric Autopsies on Death Following Immunization

General Circular No: 01-25/2012
16 May 2012

Guidelines for paediatric autopsies on deaths following Immunization

Surveillance of Adverse Events Following Immunization (AEFI) is an important part of the National Immunization Programme (NIP) to ensure vaccine safety. It is of utmost importance to identify and establish causes of all serious AEFI including deaths to carry out timely follow-up and corrective action to safeguard the vaccine recipients and also to maintain public trust on the NIP.

On a recommendation by the national expert committee on vaccine safety and AEFI, it is advised to carry out a comprehensive autopsy for the establishment of cause of death whenever the cause of death is suspected with a vaccination. Investigation of suspected infant deaths following immunization is an issue of great national importance with regard to the Immunization programme, as the proper causality assessment would enable to differentiate vaccine related deaths from deaths due to other causes. The assistance that could be provided by a comprehensive autopsy in the establishment of the cause of death is immense, and adherence to a standard protocol would enable obtaining that assistance to the optimum. The College of Forensic Pathologists in Sri Lanka has drafted a detailed protocol on paediatric autopsy and this guideline will function as an interim guideline based on the detailed protocol and until it is available for implementation.

Considering the importance of autopsy in the investigation of infant/child deaths following immunization, head of the institution needs to make arrangements for a death inquest and conducting an autopsy. In an event of infant/child death following immunization at home, conducting an autopsy is important and the respective authority shall be aware of this guideline and followed the same. Where possible, autopsies of all deaths following immunization should be carried out by a specialist in forensic medicine. Where a specialist is not available the autopsy should be performed by a medical officer qualified with Diploma in Legal Medicine, who is also trained in performing such post mortems. Where both are not available the hospital authorities should make arrangements with the closest specialist in forensic

medicine regarding conducting the post-mortem. It is the responsibility of the hospital authority to make transport arrangements.

This guideline provides measures to be followed and adhered to in a standard autopsy protocol which would enable conduct of a comprehensive causality assessment of a reported death following immunization.

In an event of all such deaths a detailed autopsy should be performed including the following;

- review of detailed preclinical and clinical history including laboratory and radiological findings,
- if necessary visit to the death scene for additional evidence,
- radiological, histopathological, toxicological and microbiological investigations.

Microbiologist and Histopathologist of the local institution will be the focal point for microbiology and histopathology examinations respectively. Where a specialist Microbiologist and/or Histopathologist is not available at the local level, or when virological / immunological investigations need to be carried out focal point for such examinations will be the MRI (Tel: 112693532-4).

Also, in situations where the cause of death is inconclusive or not straightforward, obtaining a second opinion on histopathological examinations from another pathologist is recommended. Department of Government Analyst (Tel: 2694786, 2694787, 2695881, 2699753) will be the focal point for toxicological examinations. It is advisable to contact the respective institutions on detailed information on collection, storage and transport of specimens.
Where possible samples of the organs should be preserved for further evaluation at the institution where the postmortem is conducted.
The epidemiology Unit should be informed (Tel: 112695112, Fax: 112696583) by the head of the institution and the Regional Epidemiologist of the district to be contacted to coordinate assistance. In situations where local facilities are insufficient to perform such examinations, assistance from the Epidemiology Unit could be obtained to seek external assistance. The Medical Officer of Health (MOH) or MOH staff who carried out the vaccination shall provide all necessary information to carry out the autopsy, but their presence during the autopsy is not mandatory.

1. Basic Information

Information about the identity of the deceased and the details of authorization should be obtained and included in the report.

2. Preliminaries

Antemortem samples should be taken over and investigated in cases such as alleged intoxications, allergy related incidents etc. Therefore, as soon as information is received the clinical staff should be advised to preserve the antemortem samples such as blood in a plain bottle, urine, CSF, vomitus, faeces, sputum, swabs etc that have already been obtained and hand them over to the forensic specialist at the earliest. In an anaphylactic reaction, ante-mortem samples collected between 30 min to preferably 3 hours after reaction (up to 6 hours) and 24 hour baseline samples (if available) are to sent for immunological investigations. If there is a delay in transport centrifuge the sample and refrigerate at 4^0 C.

Ward staff should be advised to document all therapeutic interventions. The area MOH, where child is vaccinated need to be informed by the head of the institution to preserve and handover empty vials, diluents, syringes, needles, with control samples of same batch. Regional Epidemiologist should coordinate this activity.

- Ensure maintenance of the chain of custody throughout the investigation (collected by, custody of, dispatched to).
- Record date and time of collection and type of preservative for each and every ante-mortem sample collected
- Document reports of clinical investigations and medical records related to the incident such as microbiology, biochemistry, immunology, histopathology, haematology, radiology etc.

3. Pre autopsy information

Obtain a detailed history which includes past medical history, drug history, immunization history, history of allergies and findings of medical records etc.

4. Pre autopsy preparation

Preserve autopsy blood – untreated and spun – in case required for later analysis. Make arrangements to take photographs at the autopsy. Be prepared to take X-rays if and when necessary while dissection (specially in cases of suspected air embolism). Be prepared to preserve the heart after careful dissection if the cause of death cannot be ascertained at the end of the autopsy.

5. External examination

In addition to routine external examination, record features of allergic reaction, anthropometric parameters when relevant (Weight, Height/Crown-heel length, Crown-rump length, Foot length, Occipito-frontal circumference, Chest circumference at nipple level, Abdominal circumference at umbilicus), Congenital abnormalities, nutritional and developmental state, features of neglect, therapeutic interventions , and paraphernalia, features of complications of therapy such as presence of subcutaneous emphysema etc. It is important to examine vaccination/ injection site regarding local reaction.

6. Internal examination

In addition to routine internal examination, record features of allergy and anaphylaxis such as laryngeal oedema, petechial haemorrhages, froth / secretions in upper airway, mucus plugging of the bronchi, effusions in body cavities, tissue oedma and the degree of local reaction at the vaccination/ injection site etc.

Look for complications of therapy such as pneumothorax, degree of haemorrhage in relation to puncture sites . Look for congenital abnormalities

Whenever possible record the weights of internal organs including thymus (children).

7. Post-mortem samples

Samples for microbiology, immunology, histopathology and virology, should be collected according to the instructions given by the relevant laboratories. (Details of instruction on sending samples to MRI is available on laboratory manual issued by the SLCM or could be obtained from the respective departments at the MRI by telephone 112693532-4). All samples should be clearly labelled and dated. The request form should have the patient's information, a short history including clinical presentation, duration of illness

and date of death. Indicate the necessary tests (if known) to be performed. In case special investigations are needed, contact the laboratory for instructions prior to sending samples. If possible mention the tentative /provisional diagnosis. MRI will accept the samples for special investigations 24 hours / day, 7 days of the week.

7.1 Histopathology

Samples for histopathology obtained from all major organs are as follows: any macroscopically visible lesions should be described in detail and sample extensively. Sample should be taken in 10% formal saline or in dry ice for frozen section. Specify the required special stains when necessary.

- *Central nervous system:* Brain (If the brain is to be examined after fixation suspend in 20% formal saline for two weeks). Sections from Middle frontal gyrus, hippocampus, basal ganglia (putamen+globus pallidus)+ insular cortex, mamillary bodies, thalamus, left cerebellum, dentate nucleus, mid brain, pons, and medulla should be obtained.
- *Cardio-vascular system*: Myocardium (LV, RV, RA, LA, septum , other areas where relevant), cardiac valves, coronary arteries, conduction system and others
- *Respiratory system* : Epiglottis, Tonsils, Larynx, Trachea, Bronchi and Lungs- (at least one sample from each lobe including hilum and periphery) Hilar lymph nodes
- *Digestive system*: liver, pancreas,
- *Genitourinary system:* Kidneys including cortex and medulla
- *Mononuclear Phagocyte system*: Spleen, thymus, bone marrow
- *Endocrine system*: Adrenal gland, pituitary, thyroid gland
- Other: eg. Injection sites, including control, injuries and others

7.2 Microbiology

7.2.1 Bacteriological Investigation

Type of specimens and tests: Blood for culture, CSF and body fluids for culture, pus for culture, tissues for culture and blood for serology
Collection and transport:

- Blood and Body- fluids for Culture after death should be collected as early as possible and preferably before the body is sent to the morgue.

- If the body is already at post-mortem, following guidelines should be followed: Blood, CSF and Body- fluids should be collected before the dissection is started. Follow Standard Precautions for collection of samples. Clean the over-lying skin with 70% alcohol. Draw the sample using a sterile disposable needle and syringe. For Blood –culture 3-5 ml blood (heart or venous) should be added into a blood-culture bottle with 30-40 ml BHI and mix carefully.
- CSF and other Body- fluids also should be sent in sterile screw-capped containers.

  (Send these samples as soon as possible at room- temperature).
- Tissue samples should be sent in sterile N. Saline in screw capped containers.
- Pus samples / swabs in sterile screw capped containers.
- Blood for serology and bacterial testing: Plain blood in sterile containers.

7.2.2 Immunology

A post mortem sample for serum tryptase should be taken from femoral vessels, and not heart blood. Serum should be separated and stored at 4^0C, or frozen if the assay is delayed.

The circumstances regarding the death are important, as tryptase levels are also increased after myocardial infarction, trauma, amniotic fluid embolism and sudden infant death. Serum tryptase rises in anaphylaxis, if shock is present, or after insect stings, or in circumstances where the allergen enters the body parenterally. Anaphylaxis following ingestion of an allergenic food does not usually lead to an increase in tryptase levels.

Information on allergy to foods (particularly beef, pork, milk, gelatine, previous vaccination) should be obtained. A blood sample should be sent to the Medical Research Institute for testing for allergen specific IgE.

7.2.3 Mycological (fungal) investigations

- Blood: 5-10 ml of venous blood should be collected under strict aseptic precautions. The lid should be wiped with 70% alcohol before inserting the needle to inoculate the blood into a culture bottle containing Brain Heart Infusion (BHI) broth. Mix well and keep at room temperature till dispatched. Smaller volumes of blood from neonates should be collected into paediatric BHI bottles (1-5 ml).(send as soon as possible to the laboratory)

- Bone marrow: 2-3 ml of bone marrow aspirate should be placed in a sterile screw capped container with 0.5 ml of 1:1000 heparin. (Send within 24 hours to the laboratory)
- CSF: 3-5 ml of CSF should be collected into a sterile screw capped bottle.
- Body fluids: Chest, abdominal fluid and any drain fluid should be collected aseptically in to a sterile screw capped bottle
- Respiratory tract: Tissues should be collected into a sterile screw capped bottle containing normal saline. Another sample should be sent in formal saline for histology.
- Blood for serology: 1-2 ml of blood should be collected into a plain bottle.

7.2.4. Virology Investigation

General Considerations: Most antigen / antibody detection assays in virology are compatible with serum / plasma. If the blood is haemolysed as it happens when blood is taken during the post mortem (PM) examination, these tests cannot be performed. Therefore it is recommended to the clinicians, to take a blood sample just before or immediately after death if possible. Similarly other samples like CSF, lung tissue etc, also are recommended to be collected just before or after death. If the facilities are available, serum should be separated before transport.

It is recommended to take multiple specimens including blood, CSF, respiratory secretions, stool, lung tissue etc.
Plural fluid, peritoneal fluid, pericardial fluid etc has limited value as antigen / antibody detection assays cannot be performed using these samples.
Tissue samples, swabs, respiratory secretions are collected into virus transport medium (VTM). VTM can be collected from the Department of Virology, MRI. It can be kept for few weeks at + 4^0 C (Do not use if the colour has changed from yellowish orange to pink)

All samples, especially the samples intended for virus isolation / molecular assays should be collected with sterile precautions to prevent contamination (If tissue samples are taken, use separate sterile instrument set for each site).

All samples should be transported early to the laboratory at + 4^0 C. Samples should be stored at + 4^0 C until transport is arranged. For the transport of specimens, ice packs are preferred than ice cubes, to maintain the temperature. If ice cubes are used, the samples should be packed in polythene bags separately so that there is no leaking once the ice gets melted.

- Blood: Ideally collected just before or just after death or during the autopsy and should be collected into dry, sterile bottle (for PCR collect into lysis buffer). Also blood sample can be collected from heart during the PM. Allowed to clot at room temperature. If facilities are available separate the serum.
- CSF: Ideally collected just before or just after death or during the autopsy, should be collected into dry, sterile bottle and to be sent to the laboratory early.Respiratory specimens (Nasopharyngeal swabs, tracheal swabs, bronchial aspirates or swabs): Ideally collected just before or just after death or during the autopsy and should be collected into virus transport medium (VTM). Use sterile throat swabs. Rub the surface with the swab to collect the epithelial cells. Insert the swab with the specimen into the container with VTM.
- Faeces: Collect during the autopsy into dry, bottle. Collect 5 -10 g of faeces (rectal swabs are not satisfactory) in to a leak proof container and sent to the laboratory early. However, anal swabs are not useful in viral diagnosis and not encouraged.
- Vesicular fluid / scrapings / swabs: Collect during the autopsy into virus transport medium (VTM).
- Tissue specimens (lung, spleen, lymph nodes, myocardium, brain): Collect during the autopsy. Use true cut biopsy needle & collect lung necropsy specimens just before or just after death in fatal case of suspected pneumonia. Take 3 specimens one into VTM, one into 70% alcohol, one into formalin. Should collect into container with virus transport medium (VTM). Collect tissue of 1cm x1cm x 1cm size from suspected areas.

7.2.5 Samples for electron microscopy

Mast cell degranulation is an important finding in allergy and anaphylaxis. Presence of this in myocardium specially around coronary arteries can be fatal and has to be differentiated from myocarditis. Therefore a section from the myocardium for this is essential and the sample should be 3mm thick tissue in gluteraldehyde.

Please bring the contents of this circular to the notice of all officers concerned in your Province/ District/ Institution/ Unit.

Dr. U. A. Mendis
Director General of Health Services

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