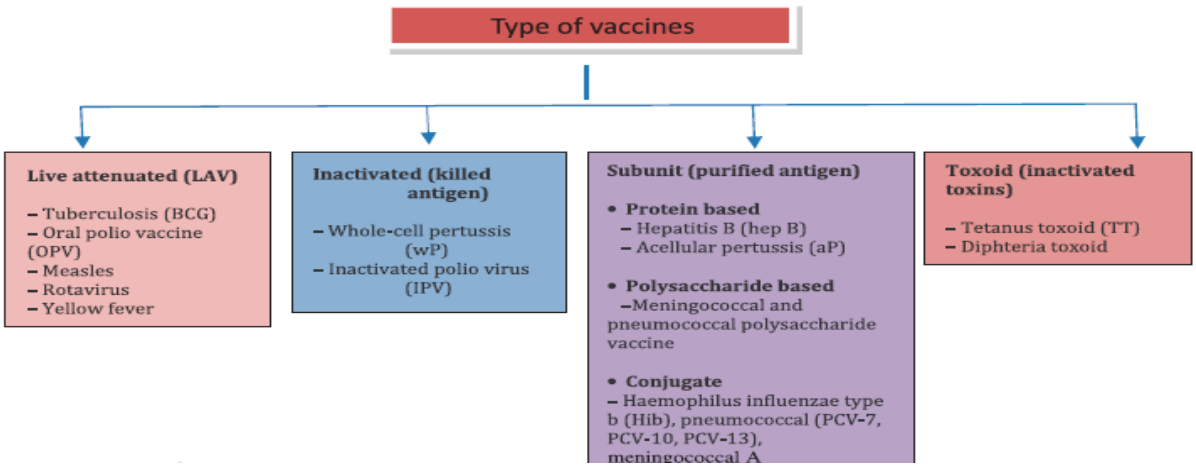
Revised AEFI Guidelines: Executive Summary

Introduction:

India's Universal Immunization Programme (UIP), targets around 27 million newborns and about 30 million pregnant women each year. The goal of immunization is to protect the individuals and the public from vaccine preventable diseases. India is the largest developing country manufacturer of vaccines and vaccines manufactured in India are used in all continents. Vaccines used in the country are safe and effective. However, like drugs and other pharmaceutical products, vaccines are not entirely without risk and adverse reactions may occur. Being a large consumer, leading manufacturer and exporter of vaccines, India is expected to have a well-developed AEFI Surveillance system. AEFI surveillance program demonstrates the country's intent of delivering quality immunization services with safe vaccines and ensure vaccine confidence. The AEFI surveillance system has been in place since 1988. The national AEFI guidelines were revised in 2005, 2010 and 2015. The guidelines provide information to health care providers and programme managers at national, state, district, block and primary health care levels for establishing a sensitive AEFI surveillance system. The national AEFI guidelines provide complete guidance and other details for reporting, investigating and conducting the causality assessment of cases reported as AEFIs.

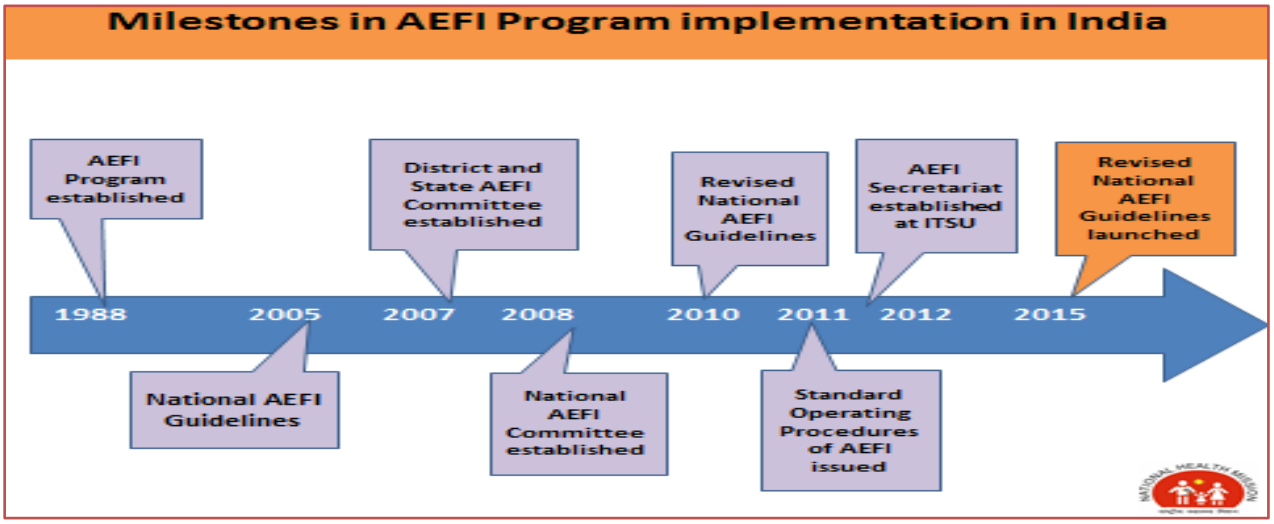
Principles of immunization and vaccines process

Immunity is body's ability to protect against diseases. There are two basic mechanisms for acquiring immunity: active and passive. Active immunity can be natural, following an infection, can last a lifetime or through vaccination, which also lasts for a long period. Passive immunity also can be either natural or artificial both last for relatively shorter period. Vaccine is a biological product that improves immunity to a given disease. The vaccines could be a live attenuated, inactivated whole cell (killed), subunit and toxoid. The vaccines consist of excipients in the form of preservatives, adjuvants and other additives.



Basics of AEFI; recording and reporting of AEFIs in India

The new guidelines define Adverse Events Following Immunization (AEFI) as any **untoward medical occurrence** which **follows immunization** and which **does not necessarily have a causal relationship** with the usage of vaccines. These events may include one or more unfavorable or unintended sign, symptoms or laboratory findings which raises concern among immunization program managers, policy makers, family of beneficiary and the community. AEFIs can be common and minor (like fever, local pain and swelling), severe (like pain and swelling which spreads beyond the nearest joint or high grade fever) and serious AEFIs (conditions requiring hospitalization or leading to death or disability).



The AEFI Surveillance guidelines are an update to the AEFI Operational Guidelines, 2010 and are in line with the revised WHO/Council for International Organisations of Medical Sciences (CIOMS) guidelines. The key issues covered are:

- Strategies and systems for ensuring quality and safety of vaccines in the country
- Objectives of immunization safety and AEFI surveillance
- New classification of AEFI
- AEFI surveillance system - reporting, investigation, causality assessment and response processes
- Optimum use of vaccine surveillance safety data
- Communication strategy on immunization safety for public and media.

New classification:

In 2012, revised classification relevant to cause-specific categorization of AEFIs has been introduced (Table 1)

Table 1: Cause-specific categorization of AEFIs

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 due to one or more quality defects of the vaccine product, including its administration device as provided by the manufacturer
Immunization error-related reaction (formerly "programme error")	An AEFI that is caused by inappropriate vaccine handling, prescribing or administration and thus by its nature is preventable
Immunization anxiety-related reaction	An AEFI arising from anxiety about the immunization
Coincidental event	An AEFI that is caused by something other than the vaccine product, immunization error or immunization anxiety

Types of AEFIs by severity and frequency

1. Common minor AEFIs
2. Severe AEFIs
3. Serious AEFIs

Common minor AEFIs:
A vaccine induces immunity by causing the recipient's immune system to react to the vaccine. Therefore, local reaction, fever and systemic symptoms can result as part of the immune response. In addition, some of the vaccine's components (e.g. adjuvant, stabilizers or preservatives) can lead to reactions.

Severe AEFIs and serious AEFIs:
An AEFI will be considered serious if it results in death, requires hospitalization, results in persistent or significant disability/ incapacity or a cluster (two or more cases) of AEFIs occur in a geographical area.

AEFIs that are not minor but do not result in death, hospitalization or disability are categorized as severe. '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.

Reporting
The reporting of serious/severe AEFI is done using Case Reporting Format (CRF) (formerly First Information Report), which is prepared by the Medical Officer of the PHC or the reporter and then sent to the District Immunization Officer within 24 hours of getting the information of the case. In the next 24 hours, the DIO verifies the case details and sends it simultaneously to the

state and national level. The CRF gives only the most basic details of the affected person, vaccines and session details and status at the time of filling the format.

The other channel of reporting serious and minor AEFI from the level of occurrence of the AEFI up to the national level is through monthly progress reports. This is done using existing monthly immunization reporting formats such as the ones for National Rural Health Mission (NRHM), Health Management Information system (HMIS) etc. It is necessary for the peripheral health staff to submit a NIL monthly report in case no AEFI is detected from their area during the month. Minor AEFI that are brought to the notice of the health staff as a concern should be reported and documented in a linelist.

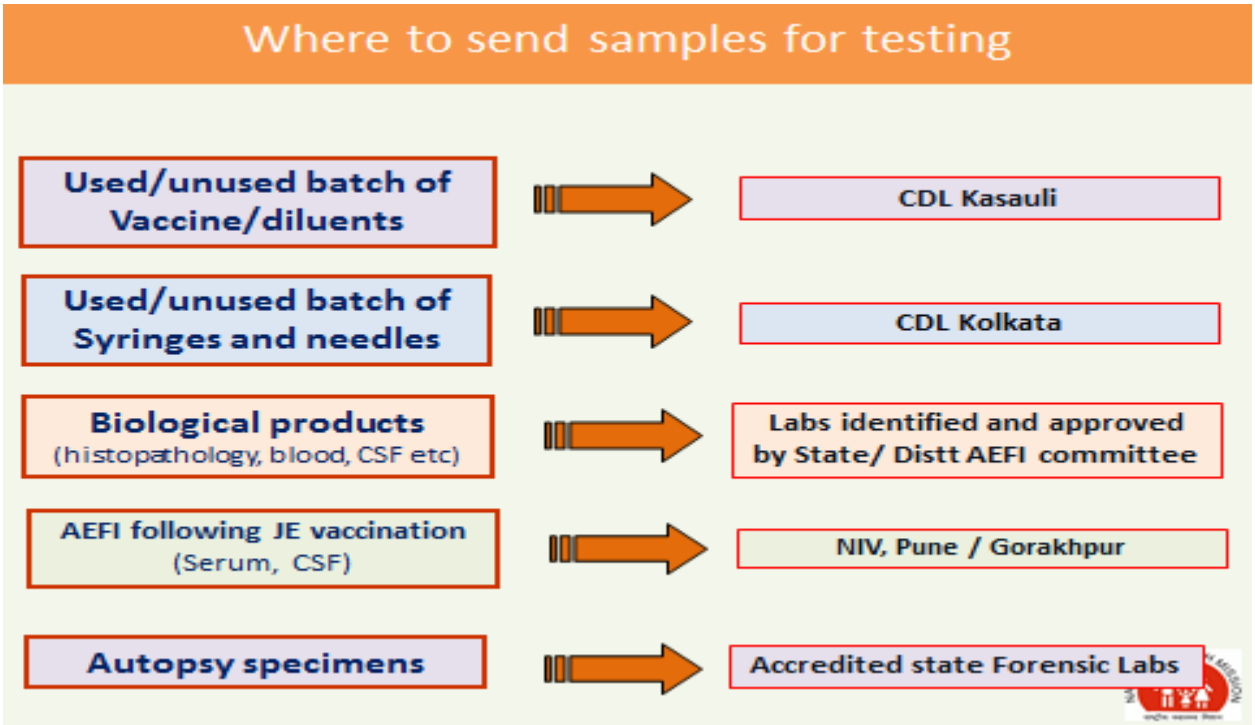
The guidelines provide directions to the State and District authorities that the key private health facilities, focal persons are identified and sensitized about the AEFI Surveillance and reporting system and encouraged to report AEFI. Involvement of ADR Monitoring centers in assisting the MO/DIO in reporting and investigation is also mentioned.

AEFI Investigation including lab sample collection

The ultimate goal of a case investigation is to make a clinical diagnosis based on the chronology of medical events, detailed medical history and other available evidence. The guidelines provide the directions to the State and district officials with regard to the steps to be followed while investigating the case. The DIO along with the members of the District AEFI Committee visits the immunization site, vaccine storage points, residence and locality of the patient and the treatment center to collect information regarding the pre-vaccination health status, treatment taken, hospitalization or postmortem reports, details of vaccination and cold chain. The epidemiological investigation is also an important aspect while investigating an AEFI. DIO ensures that the filled Preliminary Case Investigation Format (PCIF) is submitted to the state and the national level simultaneously within 10 days of notification.

The District AEFI Committee meets and discusses the case and summarizes the findings of the investigation in the Final CIF (FCIF) and gives its opinion on the probable diagnosis. The FCIF is sent within 70 days of notification to the State AEFI Committee and the Immunization Division along with all the relevant documents of the case. The guidelines mention that the investigation of reported AEFI death and cluster (two or more cases of the same adverse event related in time, place or vaccine administration) should be conducted without any delay. It is recommended that an autopsy in a death suspected to be due to an AEFI be performed as soon as possible (within 72 hours) to avoid tissue damage, development of postmortem artifacts and lysis of the adrenal glands, which can alter diagnosis. Use of Verbal Autopsy form in case of unexplained death/home death/inadequate information/insufficient medical records is a new addition in the guidelines. The format collects information regarding history, circumstances of death, medical examination, feeding history, etc. to rule out causes of death. Emphasis on timely, comprehensive and methodical investigation is given.

Guideline gives direction regarding the specimen collection and handling of implicated vaccine. The appropriate specimen in the correct quantity required for investigation should be collected and sent to the respective laboratory. ***Specimen collection is NOT needed for all cases. Only if appropriate****, the implicated vaccine, logistic samples, CSF, Serum (or other biological products) should be collected and dispatched to appropriate laboratories with LRF.*



<u>Investigation of reported sudden unexplained deaths following vaccination:</u>

Investigation of unexplained deaths following immunization is an issue of great importance with regard to the immunization programme. Proper causality assessment would enable differentiation of vaccine related deaths from deaths due to other causes. A special document has been developed to improve investigation of unexplained AEFI deaths. The verbal autopsy form has been designed based on the WHO and Centers for Disease Control and Prevention (CDC) sudden infant death investigation (SUIDI) form, whereas the guidance on conducting autopsy has been developed by a committee of leading experts in the field of immunology. The format should be filled by the investigating team while investigating the reports of AEFI deaths where information regarding the event is inadequate, such as

- brought dead to health facility,
- home death,
- insufficient medical records regarding the event,
- death in case that was not hospitalized or
- if clinical diagnosis is not possible based on available evidence.

The guidelines gives the guidance for conducting autopsy in cases of reported deaths. An autopsy must ideally be performed in every case of an AEFI death within 72 hours of death by forensic specialist or medical officer.

Causality Assessment:

Causality Assessment is the systematic evaluation of the information obtained about an AEFI to determine the likelihood of the event having been caused by the vaccine/s received. It is a critical part of AEFI monitoring and enhances confidence in the national immunization programme. The revised guidelines use the new revised WHO/CIOMS Causality (2014). The Guidelines encourages the state to conduct Causality Assessment for reported AEFI cases. The AEFI report must have investigation formats, relevant documents and a diagnosis for being eligible for Causality Assessment. The Causality Assessment process has four steps:

1. ***Eligibility***: To determine if the reported AEFI case satisfies the minimum criteria for Causality Assessment as mentioned above.
2. ***Checklist***: To systematically review the relevant and available information to address possible causal aspects of the AEFI
3. ***Algorithm***: To obtain a direction as to the Causality with the information gathered in the checklist.
4. ***Classification***: To categorize the AEFI's association to the vaccine/vaccination based on direction determined in the algorithm.

All the cases being investigated by the district should be assessed by the causality assessment experts of the state AEFI committee after discussing all the investigation formats and reports available. It is recommended to disseminate the results so that others can learn from the experience. Immunization errors will need to be corrected and for coincidental incidents, communication to maintain confidence is necessary.

AEFI Committees

The revised guidelines also give the detailed information on the AEFI Committees (district/state/ national) along with the terms of reference of the committee members. AEFI Committees provide technical inputs to review the factors leading to the adverse event and provide inputs to improve the system to provide safe and effective immunization. The committee should include members from various departments like pediatrician, microbiologist, pathologist, epidemiologist, neurologist, forensic expert, cold chain officer, representatives from IDSP, drug authority, and municipal corporation and partner agencies.

Monitoring of AEFI surveillance

The guideline emphasizes on monitoring performance of the AEFI Surveillance system. The key indicators defined are as follows:

For routine AEFI:

1. Percent of routine reports (zero reports) received on time
2. Percent of AEFI cases line listed
3. Percent of Serious AEFI cases

For serious AEFI:

1. Percent of Serious AEFI cases reported on time
2. Percent serious AEFI cases with Case Reporting Form (CRF) shared with the state and centre on time
3. Percent of Serious AEFI cases investigated on time
4. Percent of Serious AEFI cases with completed investigation
5. Percent of Serious AEFI cases classified for causality by the state AEFI Committee on time

Operational aspects of AEFI surveillance:

The overall goal of AEFI Surveillance is to reduce morbidity and mortality due to AEFI and minimize the negative impact of AEFI on public health. The revised guidelines describes the roles and responsibility of the key personnel involved in the AEFI Surveillance system. The importance of involvement of ASHA, anganwadi worker, Health supervisor at all the levels (community, sub-center) in the surveillance system is emphasized. The medical officer apart from detecting and reporting the event is responsible for management of the case as well. AEFI surveillance can be improved by involvement of professional organizations such as IAP and IMA. Use of online software (IDSurv) for reporting infectious disease is a provision for reporting AEFI. Role and responsibilities of the District Officials in the form of reporting, investigating, maintaining linelist of reported AEFI, coordinating with ADR monitoring center and private/government medical colleges is mentioned. At the State level, the State Immunization officer should maintain AEFI documentation, help in investigation of cases if required and involve State Drug controller and other partner agencies. The State should perform the Causality Assessment of reported cases. SEPIO should also review and analyze the AEFI reported through HMIS and other reporting channels.

AEFI is a vital functional component of the National Regulatory Authority (NRA). The NRA is essential not only for assurance of vaccine quality in the country but also for prequalification of vaccines.

AEFI Secretariat is established in 2012 within the Ministry of Health & Family Welfare to strengthen AEFI surveillance in the country. It is hosted at the Immunization Technical Support Unit (ITSU) set up by the MOHFW, Government of India. Four Zonal AEFI Consultants have been appointed to liaise with the immunization program managers and the other vaccine safety stakeholders at the state and district levels. The AEFI Secretariat receives constant guidance and support from the National AEFI Committee and has established collaboration with Lady

Hardinge Medical College, New Delhi which is designated as National AEFI Technical Collaborating Center (NATCC) to provide oversight and support to the AEFI Secretariat.

The guidelines also describes the need for liaison of the District Committee with the police in investigation of the reported AEFI.

Vaccine risk communication and handling of media:

Effective communication around vaccine safety including management of public reactions requires serious investment of resources and efforts towards strategic communication for Immunization.

The guidelines introduced the strategic communication plan to address the short term crisis (in cases of AEFI) and long term support that the immunization programme require at the national and local level. The plan focuses on regular communication with the community and local media on RI activities to encourage use of vaccines and thus help in improving the vaccine coverage levels.

An AEFI response protocol has standardized procedures for communication to help handle a crisis promptly and in the correct manner. It identifies the spokesperson who will respond in crisis situations at all the levels. The protocol recommends that in case of media interest in an AEFI crisis, a press release should be issued as early as possible (preferably within first 6 hours).

National Regulatory Authority and its affiliated institutions and convergence with AEFI Surveillance Program:

The guideline describes the role of National Drug Regulatory Authority and Pharmacovigilance Program of India PVPI and the importance of coordination between the CDSCO and the Immunization Division, MOHFW. The results of the causality assessment approved by the National AEFI Committee is shared with the CDSCO which analyses the results to take further necessary regulatory actions (such as inspections, amendments to product inserts, reporting by manufacturers, etc.). The IPC (Indian Pharmacopoeia Commission) has established a data sharing arrangement with the AEFI Secretariat for ensuring convergence in vaccine safety reports and their adequate investigations.

Reference:

1. Adverse Events Following Immunization - Surveillance and Response Operational Guidelines, MOHFW, 2015. http://itsu.org.in/repository-resources/AEFI-Surveillance-and-Response-Operational-Guidelines-2015.pdf