### AIDE MEMOIRE

An adverse event following immunization (AEFIs) is a medical incident that takes place after an immunization, causes concern and is believed to be caused by the immunization. Programmes providing immunization services should include a system for AEFI detection and reporting, investigation and management, data analysis, corrective action, relevant communication and evaluation of the system.

The ultimate goal of an investigation is to determine whether the vaccine or immunization process is responsible for the reported event(s) or to find another and correct it if possible, and reassure the public.

There are 4 possible causes of AEFI:
- **Vaccine reaction**: event caused by some component of the vaccine – the active component of the vaccine itself, the preservative, the stabilizer or other. The majority of vaccine reactions are “common” and expected, mild, settle without treatment and have no long-term consequences. More serious reactions are very rare – usually of a fairly predictable (albeit extremely low) frequency;
- **Programme error**: event caused by error in vaccine preparation, handling or administration;
- **Coincidence**: event where something happens after the immunization but is not caused by the vaccine or the programme; and
- **Injection reaction**: event arising from anxiety about the injection (needle).

The purposes of investigating AEFI cases are:
1. to confirm a reported diagnosis of AEFI and clarify the details and outcome;
2. to determine whether unimmunized persons are experiencing the same medical event(s);
3. to investigate the link between the vaccine given and the AEFI;
4. to determine the contribution of operational aspects of the programme to the reported AEFI;
5. to determine whether a reported event was isolated or part of a cluster;
6. to determine the cause of the AEFI so as to provide the best intervention/medical care and take any further action deemed necessary.

In most cases, a preliminary investigation of an AEFI can be made by the health worker who detected the case, e.g., a health centre staff member or a nurse or physician in a hospital.

**Serious AEFI cases** or **AEFI clusters** should be investigated immediately with involvement from central levels including epidemiological and/or clinical expertise. A cluster of AEFIs can be defined as two or more cases of the same adverse event related in time, place or vaccine administered.

**Inadequate planning or response** may lead to a crisis with loss of confidence in the vaccination service. It is essential that programme managers:
1. ** anticipate** the crisis and be prepared to deal with it when it occurs;
2. ** verify** the facts of any event before making any public statement;
3. ** are familiar with a plan** for reacting to any crisis should it happen;
4. ** be well informed** so that appropriate national and regional managers can be rapidly briefed to take charge and deal with political and media enquiries.

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### Checklist

1. **Be prepared**
   - Read the resource documents on reporting, management and investigation of AEFIs.
   - Develop standards: case definitions for reportable AEFIs, use of reporting forms and investigation procedures.
   - Designate and train staff to conduct an AEFI investigation using the investigation form.
   - Train staff on how to collect specimens.
   - Establish procedure, criteria and designated person for notifying WHO and UNICEF (if UN-supplied vaccine) or other relevant party depending on procurement mechanism.
   - Establish a National Technical Advisory Committee with representation from major medical organizations.
   - Identify a spokesperson for public communications.

2. **Receiving a report**
   - Ensure immediate reporting of most serious events and rapid attention to reports received.
   - Verify the information in the report and classify and assess the AEFI using established case definitions. Decide whether it needs further investigating.
   - If investigation is warranted, travel to the location of the AEFI, or delegate responsibility to another trained person.

3. **Investigate and collect data**
   - Ask about the patient.
   - Ask about the vaccine and other drugs potentially received.
   - Ask about other vaccinees.
   - Ask about immunization services.
   - Observe the service in action.
   - Ask about cases in unvaccinated persons.
   - Establish a more specific case definition if needed.
   - Formulate a hypothesis as to what caused the AEFI.

   Collect specimens if appropriate:
   - from the patient.
   - the vaccine (and diluent if applicable).
   - the syringes and needles.

4. **Dispatch specimens** to appropriate testing facility (laboratory, regulatory authority, etc.).

5. **Analyze the data**
   - Review epidemiological, clinical, and laboratory findings.
   - Summarize and report findings.

6. **Take action**
   - Communicate with health staff.
   - Communicate findings and action to the parents and public.
   - Correct problem (based on the cause) by improving training, supervision, and/or distribution of vaccines/injection equipment.
   - Replace vaccines if indicated.

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### Vaccination Reaction:

There are 4 possible causes of AEFI:

- **Injection reaction**: event arising from anxiety about the injection (needle).
- **Vaccine reaction**: event caused by some component of the vaccine – the active component of the vaccine itself, the preservative, the stabilizer or other. The majority of vaccine reactions are “common” and expected, mild, settle without treatment and have no long-term consequences. More serious reactions are very rare – usually of a fairly predictable (albeit extremely low) frequency;
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Did the vaccine or its delivery cause the reactions?

It will be necessary to determine if there is a causal association between the vaccine and the adverse event. In each case the following should be considered:

- **Consistency of findings** – are all reported AEFIs the same?
- **Temporal sequence** – confirm that the symptoms of AEFI occurred only after, not before, the vaccine was given and if the vaccine-event interval is compatible with a vaccine reaction
- **Biological plausibility** – does the medical event seem plausibly due to an effect of the vaccine or other concomitant or preceding conditions?
- **Previously known reaction** – check if this type of reaction is known to be related to the vaccine and with which frequency
- **Specificity and strength of association** – establish if the same events are being reported in unvaccinated persons and if so, how often and if the cluster is limited to one health center or not

### Concomitant or preceding conditions

AEFI evaluation requires a 2 by 2 table of exposures and outcomes and data should be collected in order to more fully complete the table and calculate a risk of event from receipt of the vaccine i.e. (a/a+c)/(b/b+d). Cell a represents case reports only

<table>
<thead>
<tr>
<th>Possible Adverse Event</th>
<th>No Adverse Event</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vaccinated</strong></td>
<td>a</td>
</tr>
<tr>
<td><strong>Unvaccinated</strong></td>
<td>b</td>
</tr>
</tbody>
</table>

#### Suggested steps for the identification of the most likely cause of a cluster of AEFIs

- **Cluster of AEFIs**
  - All cases from only one facility (same for used at same time)?
  - Known vaccine reaction? Yes No
  - Programme error or batch problem or programme error?
  - Known illness in others who didn’t get vaccine? Yes No
  - Vaccine reaction?
  - Known vaccine reaction?
  - Coincidental event
  - Programme error or previously “unknown” vaccine reaction

#### Words of advice

- The investigation should start within 24 hours of notification
- There is seldom need to test the vaccine unless clearly indicated by the epidemiologic investigation, but cold chain should be maintained
- A national committee can be very helpful in reviewing the outcome of the investigation and communication of findings
- Access medical files
- Rule out alternative aetiologies than the vaccination. The fact that an adverse event of the same nature has been previously related to a particular vaccine does not always mean that the case under investigation is also related to the vaccine
- Have direct discussions with the patients or parents if possible

Additional information on the definitions, monitoring, management and investigation of AEFIs can be found on the World-Wide Web at [www.who.int/immunization_safety/en](http://www.who.int/immunization_safety/en).