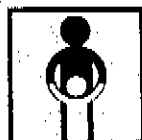

SURVEILLANCE OF

ADVERSE EVENTS

FOLLOWING IMMUNIZATION:

**FIELD GUIDE FOR MANAGERS OF
IMMUNIZATION PROGRAMMES**



Expanded Programme
on Immunization



World Health Organization
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INTRODUCTION

The goal of immunization is to protect the individual and the public from vaccine-preventable diseases. Although modern vaccines are safe, no vaccine is entirely without risk. Some people experience reactions after immunization ranging from mild side effects to life-threatening, but rare, illnesses. In some cases, these reactions are caused by the vaccine; in others, they are caused by an error in the administration of the vaccine; and in yet others, there is no relationship.

Whatever the cause, when an adverse event following an immunization (AEFI) upsets people to the extent that they refuse further immunizations for their children, the children are much more likely to get a vaccine-preventable disease, become seriously ill, disabled, and even die.

To increase immunization acceptance and improve the quality of services, the surveillance of severe AEFIs must become an integral part of immunization programmes. In response to a request by national programme managers in 1990, the Expanded Programme on Immunization (EPI) Global Advisory Group (GAG) of the World Health Organization (WHO) recommended that all immunization programmes monitor AEFIs and that WHO provide assistance in doing so. This guide was prepared in response.

The guide's purpose is to help managers at the central, regional, and district levels include AEFIs in disease surveillance. The guide begins with a chapter on planning such a system. Then, each step in AEFI surveillance is described:

- Detection and reporting
- Investigation
- Data analysis
- Corrective and other action
- Evaluation

The appendix includes recommended standard case definitions and examples of essential forms for documenting and monitoring AEFIs.

The benefits of immunizing against diseases like measles, neonatal tetanus, and polio far outweigh the risks of a medical incident caused by an immunization. Monitoring events related temporally to immunization will enable programme managers to reduce those risks even further.

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The first part of the report is a general introduction to the project. It describes the objectives of the study and the methods used to collect and analyze the data. The second part of the report is a detailed description of the results of the study. It includes a discussion of the findings and their implications for the field of research.

The third part of the report is a conclusion and a list of references. The conclusion summarizes the main findings of the study and provides a final assessment of the project. The references list the sources of information used in the study.

The fourth part of the report is an appendix containing additional information related to the study. This includes a list of the data sources used, a copy of the questionnaire used to collect the data, and a copy of the raw data. The appendix is intended to provide a complete record of the study for future reference.

The fifth part of the report is a list of the authors and their affiliations. This information is provided to acknowledge the contributions of the individuals involved in the study and to provide contact information for those interested in further research.

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1. PLANNING AEFI SURVEILLANCE

Programmes providing immunization services should include AEFI detection and reporting, investigation, data analysis, corrective and other actions, and evaluation. These are described in the next five chapters. Detection and reporting of severe AEFIs can be part of the disease surveillance system or other appropriate systems.

To establish a reporting system for severe AEFIs, e.g. through adaptation of the existing disease surveillance system, managers will have to address a number of issues and complete a number of tasks. The most important of these are summarized below. For details, see Chapters 2 through 6.

1. Obtain commitment from health policy makers to support an AEFI surveillance system. They should understand that AEFI detection followed by investigation and action increases public acceptance of immunization and improves the delivery of services. This raises immunization coverage which, in turn, leads to a reduction of disease.

2. At the central level, make decisions on the following issues:
 - Which AEFIs will be reported
 - How AEFIs will be reported - whether some should be reported immediately as well as in routine monthly reports
 - Which AEFIs will be investigated
 - How investigations will be carried out, and the period of time within which investigations should begin and be completed
 - How AEFI detection, investigation, and reporting will be incorporated into the country's other disease surveillance activities.

These issues are discussed in Chapters 2 and 3.

3. Assign responsibilities, such as:
 - Who has overall responsibility for AEFI surveillance
 - Who should receive immediate notice of events that are considered urgent

- Who should receive monthly reports of AEFIs
- Who should conduct case investigations of AEFIs (e.g. peripheral health workers, experienced clinicians)
- Who should review the findings, conclusions, and recommendations of the investigators (e.g. an expert medical panel)
- Who should direct corrective and other action.

These issues are discussed in Chapters 2, 3, 4 and 5.

4. Adapt and disseminate case definitions.

See Appendix A for WHO-recommended case definitions.

5. Revise or design and disseminate forms, e.g., monthly disease surveillance report forms, line lists, and AEFI case investigation forms.

These issues are discussed in Chapters 2 and 3 and Appendices B through E.

6. Train health workers, including managers and supervisors, for AEFI surveillance.

Health workers at the peripheral level must be able to:

- Recognize AEFIs, using official, standard case definitions.
- Take appropriate action when an AEFI is detected.
- Work with parents and other members of the public to encourage the reporting of AEFIs.

Health workers serving as investigators must learn case investigation skills, data analysis and the use of reporting forms.

Supervisors must learn how to monitor AEFI reports for completeness, timeliness, and accuracy and how to recognize and correct programme errors *before* they lead to problems.

2. DETECTING AND REPORTING AEFIs

An adverse event following immunization is a medical incident that *takes place after* an immunization and is *believed to be caused by* the immunization. Although people often think that a medical incident after an immunization must be caused by the immunization, many such incidents are coincidental. Another belief - that vaccine is the most common cause of AEFIs - is also mistaken. Programme error, which can be prevented, is more often the cause.

To find the cause of an AEFI, the events must first be detected and reported. Countries may not have the resources to include *all* AEFIs in their surveillance systems, and it is not necessary to do so. Managers have choices in terms of which ones to report, how they are reported, what is reported, and when. In this chapter, these choices are discussed and recommended practices examined.

A. Which AEFIs should be included in AEFI surveillance?

All immunization programmes should monitor the following AEFIs (see Appendix A for case definitions):

1. All cases of BCG lymphadenitis.
2. All injection site abscesses.
3. All deaths that are thought by health workers, or the public, to be related to immunization.
4. All cases requiring hospitalization that are thought by health workers, or the public, to be related to immunization.
5. Other severe or unusual medical incidents that are thought by health workers, or the public, to be related to immunization.

With respect to the third, fourth, and fifth events, health workers may relate the event to immunization because it occurred within a month of an immunization, as its case definition indicates. However, some medical incidents can be related to immunization even if they have a delayed onset. The case definitions in Appendix A describe the most common of these incidents.

The above five categories of AEFIs are sometimes called "trigger" events because their presence stimulates or triggers a response.

Mature programmes may add to their lists of reportable diseases AEFIs which have medical or management interest but generate little public concern. For example, when the same vaccines from different manufacturers are being used, managers may wish to collect data on all reactions, including mild ones, to guide future purchasing.

It is important to recognize that even though an AEFI monitoring system will alert health workers to many problems, it may not detect very rare or delayed events. To confirm or disprove whether one or more of these AEFIs has occurred, specially designed studies must be used.

Adding the basic five AEFIs to an existing disease surveillance system represents a significant increase in responsibility for health workers and managers in most programmes. Balanced against this increase is the threat to children's health when adverse events are not recognized and no response is made. Including AEFIs in disease surveillance should bring most of the medical incidents that affect public acceptance of immunizations to the attention of health authorities who will respond.

B. Who should be involved in AEFI detection?

The detection of AEFIs should be the responsibility of:

- Health workers providing immunization services
- Health workers providing clinical treatment of AEFIs in health centres, hospitals, or special treatment facilities
- Parents who report AEFIs affecting their children
- Researchers conducting clinical studies or field trials.

Health workers. When parents bring a recently immunized, sick child for treatment, health workers should be able to detect an AEFI and to determine whether it is a trigger event requiring a report and further action. To do this, they must know what the trigger events are and be able to use the case definitions.

For mild problems, health workers should comfort and advise parents and treat the patient. It is not necessary to report these reactions, except for BCG lymphadenitis and injection site abscesses, unless parents' concerns are significant.

Parents and other members of the community should know what reactions to expect after each immunization and should be urged to bring a sick child about whom they are worried to a health centre or hospital. They should understand that some symptoms, like low fever or tenderness at the injection site, actually show that the vaccine is working. This knowledge will relieve anxiety about normal reactions and help people recognize more serious problems.

C. To whom should reports be submitted?

In many systems, peripheral and hospital health workers submit a routine surveillance report that includes AEFIs to their supervisors at the district level. The district supervisors then compile the data for reporting to higher levels. Managers should consider whether or not AEFIs, and which AEFIs, should be reported *directly* to the central level.

D. When should AEFIs be reported?

Deaths and hospitalizations should receive *immediate* attention and should be reported as soon as they are detected. Abscesses, lymphadenitis, and other AEFIs should also be reported immediately if they are causing community concern. Immediate reports may be made by telephone, which gives supervisors an opportunity to assess the validity of data without delay.

All AEFIs, including those reported immediately during the month, should be counted in routine, written, monthly surveillance reports.

E. How should AEFIs be reported?

In most situations, setting up a separate, parallel system for reporting AEFIs adds unnecessarily to health workers' reporting responsibilities. Incorporating AEFIs into the existing disease surveillance system makes good operational sense.

- a. **Which AEFIs should be added to the report form?** The trigger events (i.e. BCG lymphadenitis, abscess, death, hospitalization, and AEFIs causing community concern) should be reported. These five events may be added to an existing routine surveillance report form (see an example in Appendix B) or a new form may be designed that includes the names of the reportable AEFIs as well as the EPI target and other diseases.
- b. **What should be reported?** Only the monthly total of cases and, if there are no cases, zero must be reported. A good system will also describe any trends that the reporter has identified, actions taken in response, and recommendations.
- c. **How should supervisors monitor AEFI reports to identify problems?** Upon receiving a routine report, the supervisor should review it and log it in on a report receipt form (Appendix C).

Supervisors should monitor the number of cases of each trigger event that have been reported by each health centre each month. Keeping this information up to date will help them identify:

- whether the same kind of AEFI is occurring in the same health centre every month;

- whether different health centres are reporting the same kinds of AEFIs;
- how the AEFI incidents reported by different health centres compare.

In this way, supervisors can identify patterns, such as clusters, within or across health centres, and take appropriate action.

F. What happens next?

A case investigation is usually the first major action to be taken when an AEFI is reported and should begin without delay. Investigation may be initiated by the health worker who detects the AEFI, or by the supervisor who sees a pattern emerging among health centres in the district.

On the other hand, in some programmes for certain AEFIs no further action is taken after they are reported. Illnesses known to have no causal relation to immunizations, such as pneumonia after a DPT injection, are often treated this way. However, even in these cases, if parents or other members of the community are convinced that a medical event was caused by an immunization, they must be given the opportunity to discuss their concerns with health authorities.

3. INVESTIGATING AEFIs

The report of an AEFI will usually be followed by a case investigation or, when there is a cluster of AEFIs, by a series of case investigations.

A. Why should an adverse event case investigation be carried out?

The ultimate goal of a case investigation is to find the cause of an AEFI or cluster of AEFIs and correct it. If the cause is identified as programme error, remedial action can be taken promptly, and the public can be assured of the integrity of the immunization services. Even if the cause cannot be identified or the medical event was vaccine-induced, the fact that health workers investigated can in itself increase public confidence in immunizations.

B. What should an AEFI investigation accomplish?

The purposes of investigating AEFI cases are the following:

1. To confirm a reported diagnosis or propose other possible diagnoses, and clarify the outcome of the medical incident or incidents.
2. To identify the specifications of the vaccine used to immunize the patient or patients.
3. To examine the operational aspects of the programme. Even if an event seems to be vaccine-induced or coincidental, programme errors may have increased its severity.
4. To determine whether a reported event was a single incident or one of a cluster and, if a cluster, where the suspected immunizations were given and what vaccines were used.
5. To determine whether unimmunized people are experiencing the same medical incidents.

C. What should be investigated and when?

As discussed in Chapter 2, the following medical incidents, i.e. the trigger events, should be investigated:

- all cases of BCG lymphadenitis
- all injection site abscesses

- all deaths that occur within one month of an immunization
- all cases requiring hospitalization that occur within one month of an immunization
- all medical events that are believed to have been caused by an immunization and about which people are concerned.

Investigation should begin as soon as possible, ideally within 24 hours of detection by a health worker, to identify any programme errors that might be present, to correct them before other people are exposed to the same error, and to show members of the community that their health and concerns are taken seriously.

D. Who should be involved in AEFI investigations?

In most cases, a preliminary investigation can be made by the health worker who detected the case, i.e. a health centre staff member or a nurse or physician in a hospital. If no further investigation is made, the health worker will complete a case investigation form and report to a supervisor.

Serious AEFIs or clusters should be investigated by specially trained health workers from the district or central level.

E. What data should be collected?

For a case or cluster investigation to accomplish its purposes, the following data should be collected:

1. Data on each patient
 - demographic data about patient, including a unique case number;
 - history of patient's present illness - symptoms, when they appeared and their duration, treatment, outcome; diagnosis;
 - history of patient's past illnesses - reactions to previous doses, drug allergies, pre-existing neurological disorders, current medications;
 - immunization history - vaccine, dose number, date, and place of last immunization or immunizations, site of injection;
 - laboratory results about blood, stool, or other samples, if appropriate.

2. Data about the vaccine administered to the patient

- Lot number
- Expiry date
- Manufacturer
- When and from where vaccine was sent
- Laboratory results about vaccine, if appropriate.

3. Programme-related data. Common practices in storing and handling vaccines, giving immunizations, etc. in the health centre in which the suspected immunization (or immunizations) was/were given.

- Practices followed by health workers in:
 - storing vaccines, e.g. is DPT or TT frozen? are expired vaccines used?
 - handling vaccines during sessions, e.g. are DPT and TT properly shaken before use?
 - handling vaccines after sessions, e.g. are all open vials thrown away after sessions?
- Practices in reconstituting vaccines and giving immunizations:
 - Are the correct diluents used?
 - Are sterile diluents used?
 - Are the correct doses given?
 - Are vaccines injected by the right route and in the right place?
- Availability of needles and syringes
 - Are one sterile needle and one sterile syringe used for each injection?
- Practices in sterilizing equipment

4. Data on other people in the area

- Number of people who received immunizations with vaccine from the same lot or in the same immunization session, or both, and the number of these who fell ill and their symptoms. (Each such patient should have an AEFI case investigation form.)
- Number of unimmunized people or people immunized with other lots (from the same or a different manufacturer) who fell ill with similar symptoms.

5. Name of health worker who gave the immunization

All of these data should be recorded in an AEFI case investigation report, discussed in Part H below.

F. From whom should data be collected?

1. **AEFI Patients.** Patients should be examined.
2. **Health workers and supervisors.** Health workers who gave immunizations during any suspect session or sessions should be interviewed. Supervisors of those health workers should be asked about immunization practice problems in the past.

Because the immunization session that preceded the AEFI under investigation is past, health workers may not remember, or even be aware of, errors in procedure. However, observation of sessions in the same facility with the same health workers might reveal the cause, since the bad practice may be repeated. The practices listed in Section E, 3, above should be included in such observations.

3. **Community members.** Investigators should talk to parents and others who were present during the immunization session or sessions in question about what they might have seen.

The public should be asked to report incidents of the same symptoms as those under investigation.

During the investigation, investigators should explain to health workers, parents, and others that, although every effort is being made to track down the cause, the reason for the event may never be found. This can help prepare them for a not-infrequent outcome of AEFI investigations - "cause unknown".

G. How should data be collected?

Methods to track down the cause should include: clinical examinations; interviews; review of patient registers; observation of immunization administration, vaccine handling, and storage; examination of health centre records and laboratory reports.

H. How should data be recorded?

Three kinds of records are useful: the AEFI case investigation report, the line list and the event description report.

The **AEFI case investigation report** provides a record of all available data about a patient. The health worker who detects and reports an AEFI should begin recording data on this form as soon as learning about the AEFI. During the case investigation, the same form will be used to record additional information about the case.

The case investigation report form should include all of the information listed in Section E above. (See Appendix D for an example.)

A **line list** is a roster of AEFIs investigated during a reporting period, usually one month. At the district level, the manager who is responsible for AEFI reporting prepares the line listing, basing it on investigation reports about cases in the district.

One line of information is written for each case. It includes: the case number; the patient's name and address; date and place of immunization; the vaccine (or vaccines) used; dose number (for multi-dose vaccines), manufacturer, and lot number; the patient's symptoms and date of onset of the event. This information is useful in identifying clusters or other patterns for further investigation and follow-up action. A line list form is shown in Appendix E.

The **event description report**, which provides a historical record of the AEFI and summarizes the findings and conclusions about a single AEFI or a cluster, is described in Chapter 4. It consists of a narrative describing and interpreting the event.

I. What happens next?

After an AEFI or cluster of AEFIs has been investigated and the community searched for other cases, data are compiled and reviewed, a diagnosis made, and a probable cause designated. These steps are described in Chapter 4.

4. ANALYSING AEFI DATA

Analysis of data on AEFIs consists of reviewing the case investigation report for each patient, reviewing other data about the event and the community in which it took place, making a final diagnosis, and identifying the probable cause. This is not an exact science: it might not be possible to make a diagnosis, the cause might not be evident, or there might be more than one cause. However, managers should try to get as much information as they can from the data.

A. Who should participate in data analysis?

Data analysis can be carried out initially by the health worker who detects the AEFI and conducts the case investigation. Other health workers, such as epidemiologists or other specialists who have taken part in the case investigation, should also participate in analysis.

In addition, a regional or national AEFI review committee can be convened to assist in the analysis and to review reports. They can play a major role in determining the cause and in classifying the event.

The central-level manager responsible for AEFIs should direct and monitor the process.

B. How should the case be diagnosed?

The first step in analysis is to diagnose the case, which can be done by the health worker who detects the AEFI or by a specially trained investigator. The patient's signs and symptoms, the history of the medical incident that precipitated the inquiry, the patient's past medical history, data on the suspected immunization, and laboratory results, contribute to the diagnosis. Standard case definitions should be used.

C. How should a cause be determined?

Causes of AEFIs are classified in four ways: programme-related, vaccine-induced, coincidental, or unknown. For a few medical events, the diagnosis itself will tell the analyst that the cause is programme-related or vaccine-induced or coincidental. In others, external evidence may be needed to identify the cause.

1. **Programme-related AEFIs.** Because at this point in most immunization programmes, more AEFIs will be related to programme errors than any other cause, the analyst's first step should be to examine the data for evidence of any errors in the storage, handling, or administration of vaccines.

For example, cases of toxic shock syndrome after a measles immunization followed by sepsis have been found to be caused by programme errors. Therefore, as soon as the case is diagnosed, the cause can be suspected to be programme-related. Attention can then be turned to finding out what the particular error was so that corrective action can be taken.

If the cause of an AEFI is not initially clear, evidence of the following errors may help in identification:

- Too much vaccine given in one dose
- Immunization injected in wrong place
- Syringes and needles improperly sterilized
- Used needles handled carelessly
- Vaccine reconstituted with incorrect diluent
- Wrong amount of diluent used
- Vaccine prepared incorrectly
- Drugs substituted for vaccine or diluent
- Vaccine or diluent contaminated
- Vaccine stored incorrectly
- Contraindications ignored, e.g. when a child who has had a severe reaction after a previous dose of DPT is immunized with the same vaccine
- Vaccine not thrown out at the end of an immunization session and used at a subsequent one.

Analysts should look for the errors listed above in every situation. In addition, if there is a cluster of events, analysts should study the line list and case investigation reports to see whether they show one or more of the following:

- The same health worker gave all of the suspect immunizations - an indication of programme error.
- Unimmunized people in the same age group in the same geographical area had the same symptoms - programme error would not be the cause, nor would these be vaccine-induced reactions.
- Others immunized with the same lot of vaccine in the same facility on the same day did not have the same symptoms - programme error might be the cause, but it is more probable that the events were vaccine-induced or coincidental.

If programme error can be ruled out as the cause or one of the causes of an AEFI or AEFIs under investigation, the analyst should look for evidence that it (or they) were vaccine-induced or coincidental.

2. **Vaccine-induced AEFIs** are caused by the reaction of a particular individual to a particular vaccine. Because this is a "personal" medical incident, it is highly unusual for more than one person to have a vaccine-induced reaction to the same vaccine in the same session.

Also within the vaccine-induced category are the very rare *vaccine-precipitated events*, which are medical incidents that would have occurred in the individual at some time but occurred sooner because of an immunization, e.g. a simple febrile seizure in a child with a family history of the same.

Most vaccine-induced AEFIs are mild and of short duration. Such AEFIs include mild systemic reactions like fever and rash or local reactions with redness, tenderness, and pain at the injection site. Injection site reactions occur in less than 10% of the children and women immunized.

BCG lymphadenitis, usually of limited duration, has been reported in 0.1 to 4.3% of immunized children under 2 years of age. Death after an immunization, whether vaccine-induced or caused by programme error, occurs in less than 0.2 of 100,000 DPT immunizations and in 0.02 to 0.3 of 100,000 measles immunizations.

As with many AEFIs, investigations of possible vaccine-induced events can be inconclusive. Researchers expect that, with increased AEFI reporting, investigation, and analysis, classifications will become more certain and the low incidence of vaccine-induced AEFIs will be confirmed.

3. **Coincidental AEFIs** are caused by something other than programme errors and individual reactions to vaccine. When the cause of an AEFI is coincidental, it means that the medical incident would have occurred even if the individual had not been immunized. Coincidental events are unrelated to immunizations or vaccines in any way except for the time that they occur.

The best evidence to support a conclusion that a medical incident is coincidental is that the *same event has been diagnosed in people who have not been immunized.*

4. **Unknown.** One other classification is helpful: "unknown" - for events with an unknown cause.

As time goes by, more research on the causes of specific AEFIs will be published, showing that they are either programme-related, vaccine-induced, or coincidental. This will further help analysts to identify causes and may reduce the "unknown" category.

D. When can a laboratory assist in the analysis?

The most important role of laboratories is to diagnose or to confirm a diagnosis of a medical event. Usually, testing for this purpose takes place when a patient is hospitalized.

Another function for laboratories is to analyse vaccines, but in this role they can only:

1. identify whether the vaccine in the vial is what the label says it is;
2. identify whether the vaccine being tested has been mishandled, e.g. by being frozen;
3. identify whether the vaccine being tested has been contaminated.

Laboratory tests of vaccine are of limited value when the vaccine being tested is from a different vial than the one used for the suspect immunization. In fact, the vial used on the day that the immunization was given *should not* be available for testing, since good practice requires that all open vials be thrown out at the end of the day. A vial from the same lot may be substituted, but the value of the findings will be weakened.

Under no circumstances should vaccine be sent for testing before the case investigation has been carried out. When an investigator does send vaccine, he or she must send a copy of the case investigation report with the sample and give clear instructions on what the vaccine should be tested for. For example:

- In the case of an injection site abscess, a test must be performed to determine the sterility of the vaccine.
- In the case of a local, long-lasting reaction, a test must be performed to measure the amount of aluminium in the vaccine.
- In the case of a suspected cluster of reactions to a reconstituted vaccine, a test must be performed to identify the diluent.

E. How should the results of the investigation be reported?

After data have been analysed, the analyst should prepare an event description report on the findings. In the case of a single AEFI, the analyst will give the reasons for the diagnosis and describe the cause or possible causes of the AEFI.

In the case of a cluster, the report will also describe:

- the number of people identified with the same AEFI;
- the antigen suspected;
- symptoms common among all patients;
- the number of people immunized with the same vaccine lot;
- the name of the health facility or facilities where the affected people were immunized;
- whether all facilities involved used the same vaccine lot;
- how many unimmunized people in the same age group in the same community or health centre catchment area had the same symptoms;
- the average time period between the immunization and onset of symptoms;
- immunization practices in the health facility or facilities involved, including their handling, storing, and administration of vaccines;
- laboratory findings, if appropriate.

The event description report should also provide a brief history of the event, including, but not limited to:

- who reported the AEFI and when, if it was a single event; who reported each AEFI in a cluster and when;
- who conducted the investigation;
- when the investigation began;
- how the investigation was conducted;
- which laboratory was used.

Supporting data, such as the AEFI case investigation and laboratory reports, should be appended to the report.

Managers should use these reports, not only to determine what actions to take, but to evaluate the effectiveness and efficiency of the system in responding to AEFIs. (See Chapter 6.)

F. What happens next?

Recommendations will have been made by the analyst based on his or her findings and conclusions. These recommendations should include the actions that should be taken to remedy the problem. A senior manager must then decide which actions should and can be implemented. The kinds of actions that might be planned are described in Chapter 5.

5. TAKING ACTION

AEFI detection, investigation, and analysis must lead to action for the credibility of immunization services to remain high. These actions include: treatment, communication, correction of programme error, and research.

A. Treatment

Treatment must be the first response to an AEFI. Mild symptoms, such as fever, can be treated by parents or health workers and eventually should go away by themselves. Health workers must also know how to treat, and when to refer, serious AEFIs. Treatment suggestions for mild symptoms are given in *Immunization in Practice*, EPI/WHO, and other publications.

Some programmes, which would otherwise charge for treatment, will provide it without charge to people who have an adverse event following immunization, especially when it appears to be caused by programme error or is vaccine-induced.

B. Communication with parents and other members of the community

Communication with parents, health workers not involved in the investigation, other people in the community, and the press must take place no matter what the circumstances of the event. This is particularly important when public anxiety is high.

The district manager or another knowledgeable person in authority should set up means for continuous communication between health workers (investigators, peripheral health workers, supervisors, and managers) and the community, directly and through the press. The public should be frequently informed about what is being done during the investigation. When it is over, conclusions and recommendations should be shared and the public told what is being done to remedy any problems found.

The key to maintaining confidence in health services is to be honest. If the cause of the AEFI has not been identified, people should be told. If the cause has been insufficient sterilization of needles and syringes or some other programme error, the actions being taken to remedy the problem should be explained.

When death occurs because of a programme error, special precautions may have to be taken to protect health workers from harm by the community. Health workers who are implicated in the error might have to be removed from the scene before the findings are communicated.

Vaccine-induced AEFIs can be a sensitive communication problem because prevention is so difficult. The public needs to be assured that severe vaccine-induced events are rare,

even though this will not comfort the patient's family. In some cases, managers may find it appropriate to provide technical information on the low incidence of these events. In many situations, however, statistics will be meaningless and the best that can be done is to show sympathy and concern.

C. Improving Service Delivery

If an AEFI was caused by programme error, such as improper handling of vaccines or faulty immunization technique, the actions to be taken will probably include one or more of the following.

1. **Logistics.** Improving logistics will be the appropriate response if programme errors can be traced to the lack of supplies or equipment or to a failure in the cold chain.

Managers should investigate suspected breaks in the cold chain to find the cause and take appropriate measures. These might include training or supervision or the problem might be solved by providing more or better supplies or equipment (needles, syringes, sterilizers, vaccine carriers, cold packs) or by providing more vaccine or diluent.

2. **Training.** Solving operational problems through training will deal with lack of skills and knowledge and with poor attitude.

Effective immunization services call for health workers who can detect AEFIs and provide immunization services safely and who care about doing so. When an AEFI has been caused, or made worse, by service delivery errors and the investigator identifies the specific error, training can focus on correcting that error.

If the investigator tracks an error to one health worker, that health worker's immunization activities should be terminated immediately, at least until he or she masters the missing skill. (As noted above, it may also be necessary to remove the worker from the area in which the incident took place.)

Training must be designed so that the health worker can practise the relevant skills until mastery. Materials for training in immunization skills are available from WHO/EPI Geneva. See *Immunization in Practice*, WHO/EPI, Geneva.

3. **Supervision.** Supervisors should give immediate feedback to health workers on their AEFI activities and on their routine surveillance, case investigation and other reports.

Wherever AEFIs are reported, supervision should be intensified. Supervisors throughout the country should watch for any problem (e.g. in sterilization of equipment or vaccine storage) that has caused a cluster of AEFIs. If past training or supervision in the relevant skill has been weak, the problem could be widespread.

See *Training for Mid-level Managers: Help to Make it Work*, WHO/EPI Geneva, for materials on how to plan and schedule supervisory visits.

D. Learning more about AEFIs

Many gaps exist in our knowledge about AEFIs. Research is often inconclusive because case definitions are not available, are used inconsistently, or the information is biased. Some AEFIs are seen so rarely that it is difficult to come to firm conclusions about their causes.

Studies are being carried out in many countries to close the knowledge gap, for example examining the relationship between particular medical incidents such as encephalitis, and particular vaccines, such as DPT and measles. Routine surveillance of AEFIs will also lead eventually to a better understanding of the reasons for their occurrence and their rates of incidence.

6. EVALUATING AEFI SURVEILLANCE

AEFI surveillance should be evaluated regularly and should lead to remedial actions.

A. What indicators should be used?

The indicators for evaluating AEFI surveillance are similar to those used to measure the performance of the disease surveillance system in general, as described in other materials. (See WHO/EPI's *Improving Routine Systems for Surveillance of Infectious Diseases including EPI Target Diseases: Guidelines for National Programme Managers*.) The indicators include:

- timeliness, completeness, and accuracy of routine AEFI surveillance reports;
- swiftness with which case investigation begins after a trigger event is reported;
- appropriateness of actions taken to avoid further programme errors;
- increase in immunization programme participation.

B. How should the system be evaluated?

1. **Completeness, timeliness, and accuracy of reporting.** Every month supervisors should check monthly surveillance reports as they are received in the district office and, in turn, in the central office. A report receipt form (Appendix C) is useful for monitoring the dates on which routine reports are received and the completeness of reporting.

On visits to health facilities, supervisors should periodically check the accuracy of routine disease surveillance reports by comparing them to the facility's patient register. They should talk to health workers and observe their work to make sure that recommended improvements have become a part of daily practice.

Methods for monitoring reporting are described in WHO/EPI's manual on *Training for Mid-level Managers: Disease Surveillance*.

2. **Swiftness with which case investigation begins after a trigger event is reported.** At the end of each AEFI investigation, the senior manager should evaluate the speed of response to the reported event. From case

investigation and event description reports managers can learn:

- whether the AEFI was reported within 24 hours of detection, if it was one of those that is supposed to be reported immediately;
 - whether an investigation was begun within 48 hours after the report was received.
3. **Appropriateness of actions taken to avoid further programme errors.** Managers should review case investigation and event description reports to assure themselves that the actions proposed for the elimination of programme errors are adequate.

Supervisory visits should focus on whether the actions were actually taken and what their effects were. Health workers should monitor their own activities by observing the ways in which vaccines are stored, handled and administered in their facilities and by correcting problems on their own.

4. **Increase in immunization programme participation.** Over time, AEFI surveillance should result in an increase in immunization coverage. The extent to which this is achieved is a good sign of the impact of the surveillance system and should be measured every three to five years. Monthly AEFI surveillance reports, yearly AEFI reports (see below), and coverage data can be used for these measurements.

C. How should progress in AEFI surveillance be reported?

In addition to the immediate feedback they receive on their case investigation and event description reports, health workers should be given the results of monitoring and evaluation as soon as they are determined. If deficiencies are revealed at a certain level, health workers at that level should be involved in planning for corrective action.

After AEFI surveillance has become fully operational, the senior manager should submit annual reports of AEFI activity to the programme manager. Such reports might include:

- Number of AEFI reports received annually
- Number of AEFIs by type (i.e. each of the five trigger events)
- Number of AEFIs by antigen
- Classification of events by cause: programme error, vaccine-induced, coincidental, or unknown
- Unusually severe AEFIs
- Unusual events.

A final note:

Although this guide focusses on adverse events following immunization, we should remember that, for diseases such as measles, tetanus, polio and pertussis, the benefits of immunization far outweigh the risks of a medical incident. **Children are much more likely to get one of these diseases if they are not protected than they are to get a severe AEFI.**

APPENDICES

- Appendix A: Case Definitions for Monitoring Adverse Events Following Immunization
- Appendix B: Monthly Disease Surveillance Report Form, adapted for the reporting of AEFIs
- Appendix C: Surveillance Report Receipt Form
- Appendix D: AEFI Case Investigation Form
- Appendix E: Line List Form

APPENDIX A

List of Definitions for Monitoring of Adverse Events Following Immunization

from the Proceedings of a Workshop on Standardization of Definitions for
Post-Marketing Surveillance of Adverse Vaccine Reactions

Co-sponsored by the Laboratory Centre for Disease Control,
Health and Welfare, Canada
and
the World Health Organization

30-31 October, 1991

List of Definitions for Monitoring of Adverse Events Following Immunization

All of the following adverse events should be reported if temporally related to immunization. Unless otherwise specified this includes all such events occurring within four weeks of a vaccine administration.

1. Local Adverse Events

Injection-Site Abscess

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

<u>Bacterial</u>	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.
<u>Sterile</u>	There is no evidence of bacterial infection following investigation.

Lymphadenitis (Includes Suppurative Lymphadenitis)

Occurrence of either:

- (1) at least on lymph node, 1.5 cm in size (one adult finger width) or larger; or
- (2) 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:

- (1) swelling beyond the nearest joint;
- (2) pain, redness and swelling of more than 3 days duration; or
- (3) requires hospitalization.

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

2. Central Nervous System Adverse Events

Acute Paralysis

A. Vaccine-Associated Paralytic Poliomyelitis

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

B. Guillain-Barré 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:

- (1) Seizures;
- (2) Severe alteration in level of consciousness lasting for one day or more; and
- (3) Distinct change in behaviour 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 (Kernig, 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.

A. Febrile Seizures; or

B. Afebrile Seizures.

3. 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 edema.

Anaphylactoid Reaction (acute hypersensitivity reaction)

Exaggerated acute reaction, occurring within 2 hours after immunization, characterized by one or more of the following: 1) wheezing and shortness of breath due to bronchospasm; 2) laryngospasm/laryngeal edema; 3) one or more skin manifestations, e.g. hives, facial edema, or generalized edema.

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 edema leading to respiratory distress occurring immediately after immunization.

Arthralgia

Joint pain usually including the small peripheral joints.

A. Persistent

Joint pain lasting longer than 10 days.

B. Transient

Joint pain lasting up to approximately 10 days.

Disseminated BCG-itis

Disseminated infection occurring within 1 to 12 months after BCG vaccination and confirmed by isolation of *Mycobacterium bovis* BCG strain.

Fever

A. Fever, mild

Temperature 38°C - 38.9°C (rectal)

B. Fever, high

Temperature 39°C - 40.4°C (rectal)

C. Fever, extreme (hyperpyrexia)

Temperature higher than or equal to 40.5°C (rectal)

D. Fever, unspecified

Temperature presumed to be high but not measured.

Only high and extreme fever should be reported.

Hypotensive-Hyporesponsive Episode (shock collapse)

Sudden onset of paleness, decreased level or loss of responsiveness, decreased level or loss of muscle tone (occurring within 24 hours of vaccination). The episode is transient and self-limiting.

Osteitis/Osteomyelitis

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.

Sepsis

Acute onset of severe generalized illness due to bacterial infection and confirmed by positive blood culture.

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.

Appendix A

4. Other severe and unusual events occurring within 4 weeks after immunization and not covered under no. 1, 2, or 3.

Any death of a vaccine recipient temporally linked (within 4 weeks) to immunization, where no other clear cause of death can be established, should be reported.

In addition, any unusual events should be reported.

APPENDIX B

Monthly Surveillance Report

Health facility: _____ Dates: from _____ to _____

Disease	Tally cases of disease	Total number of cases
Poliomyelitis		
Neonatal Tetanus*		
Measles		
BCG Lymphadenitis		
Injection Site Abscess		
Hospitalization - Cause:		
Death - Cause:		
Other AEFIs - Specify:		

What are the possible explanations for increased/decreased number of cases, compared to last month?*

Actions taken and/or recommendations:**

Signature: _____ Date: _____

* Refers to children less than one month of age.

** Attach additional sheets if necessary.

APPENDIX C

DATES SURVEILLANCE REPORTS RECEIVED												
District: _____ Year: _____												
REPORTING UNITS	Date Report Received for the Month of:											
	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
Health Centre A												
Health Centre B												
Health Centre C												
Health Centre D												
Health Centre E												
Health Centre F												
Hospital A												
TOTAL												

Receipt of monthly surveillance forms.

APPENDIX D

AEFI Case Investigation Report

The health worker who detects an AEFI should begin filling in this form. The health worker (or workers) who conducts the investigation and analyses the data should then complete the report.

- I. Patient ID No. _____
1. Date of Birth (DD MM YY): _____ 2. Sex: _____
3. Family name: _____ 4. First Name: _____
5. Parents' names: _____
6. Address: _____
- _____

II. Immunization History

1. Date of immunization (DD MM YY): _____
2. Names and dose numbers of vaccines given that day to this patient:
- _____
- _____
3. Manufacturer and lot numbers of suspect vaccine or vaccines:
- _____
- _____
- Explain how these were identified: _____
- _____
4. Immunization facility: _____
5. Name of vaccinator: _____
6. Observations on storage and handling of other vaccines in stock:
- _____
- _____

Appendix D

III. Medical Incident

1. Symptoms, with date and time of onset of each: _____

2. Laboratory findings: _____

3. History of reactions to previous doses, drug allergies, etc.:

4. Treatment and outcome: _____

IV. Summary of Event

State whether this event was part of a cluster or was a single occurrence and explain why you think so.

Note: If this AEFI was part of a cluster, the Event Description Report will provide detailed information about the cluster. (See Chapter 4 of the Guide.)

Investigated by: _____

Date (DD MM YY): _____

Glossary

Definitions

Adverse Event Following Immunization (AEFI)

A medical incident that takes place after an immunization and is believed to be caused by the immunization.

Cluster

Two or more cases of the same adverse events following immunizations related in time, geography, or the vaccine administered.

Coincidental AEFI

A medical incident that would have occurred whether the individual had received an immunization prior to the incident or not.

Programme-related AEFI or Programme Error

A medical incident that was caused by some error in the transportation, storage, handling, or administration of vaccine.

Reactions: Serious

A reaction that results in death or hospitalization or that is treated with prescription drugs.

Mild

A reaction that is not "serious".

Trigger event

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

Vaccine-induced AEFI

A medical incident that is caused by the reaction of a particular individual to a particular vaccine. These events are due to the intrinsic characteristics of the vaccine and the individual responses of the person.

Abbreviations

AEFI
BCG
DPT
EPI
GAG
OPV
WHO

Adverse Event Following Immunization
Bacille Calmette Guerin vaccine against tuberculosis
Vaccine against Diphtheria, Pertussis, and Tetanus
Expanded Programme on Immunization
Global Advisory Group of the EPI
Oral Polio Vaccine
World Health Organization