



**Pan American Health Organization
Regional Office of the World Health Organization
Division of Vaccines and Immunization**

IMMUNIZATION SAFETY

**How to address events
allegedly attributable to
vaccination or immunization?**

Washington, DC, United States

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Division of Vaccines and Immunization.

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Contents

1. Purpose
2. Introduction
3. Vaccine Quality and Safety
4. Rates of Events Attributed to Vaccination or Immunization
 - a. Common mild events
 - b. Rare and severe events
 - c. Operational errors in the program
5. Investigation of Events Allegedly Attributable to Vaccination or Immunization
 - a. Stages of the investigation
 - b. Information and investigation
 - c. Steps to be taken
6. Event Reduction during Vaccination Campaigns
 - a. Measures to prevent ESAVI during the campaigns
7. Management of Crisis Situations
 - a. What is a crisis?
 - b. Why does a crisis arise?
 - c. Four steps for the management of ESAVI and prevention of crises
8. Communication and Information on Vaccination and Immunization Safety
 - a. Relations with the communications media
 - b. What is the perspective of the mass media?
 - c. How to give an interview or a press conference
 - d. Sixteen pieces of advice on style
 - f. Skills
9. Summary of Vaccines, Diseases They Prevent, and Disease Effects
10. Bibliographic References

01. Purpose

In order to maintain or improve confidence in national immunization programs, workers in the health sector, from the local level up to the central level of the Ministry of Health, should be familiarized with all aspects of vaccination; furthermore, they should be prepared to respond to any concerns of the population. Rapid response to public concern about vaccines, as well as immediate and clear communication of explanations and actions, will preserve the integrity of the immunization program.

The purpose of this document is to provide health workers with principles and procedures that should be followed in addressing concerns about vaccination risks. Proper implementation of this guide will aid in the acquisition of additional information on possible events allegedly attributable to vaccination or immunization (ESAVI). These data should be complemented with the information compiled in other analytic studies, such as clinical trials, thus maintaining confidence in the national immunization program.

It is hoped that this document will assist health workers in establishing adequate mechanisms for:

- determining the quality and safety of vaccines;
- knowing the rates of events that may be related to vaccines;
- reporting, investigating, and analyzing the events that are supposedly related to vaccines;
- taking steps to solve any problem identified in the investigation and to face any crisis;
- communicating efficiently and effectively with the community and with the communications media;
- reporting to parents on the events related to vaccines and on the diseases against which they provide protection.

02. Introduction

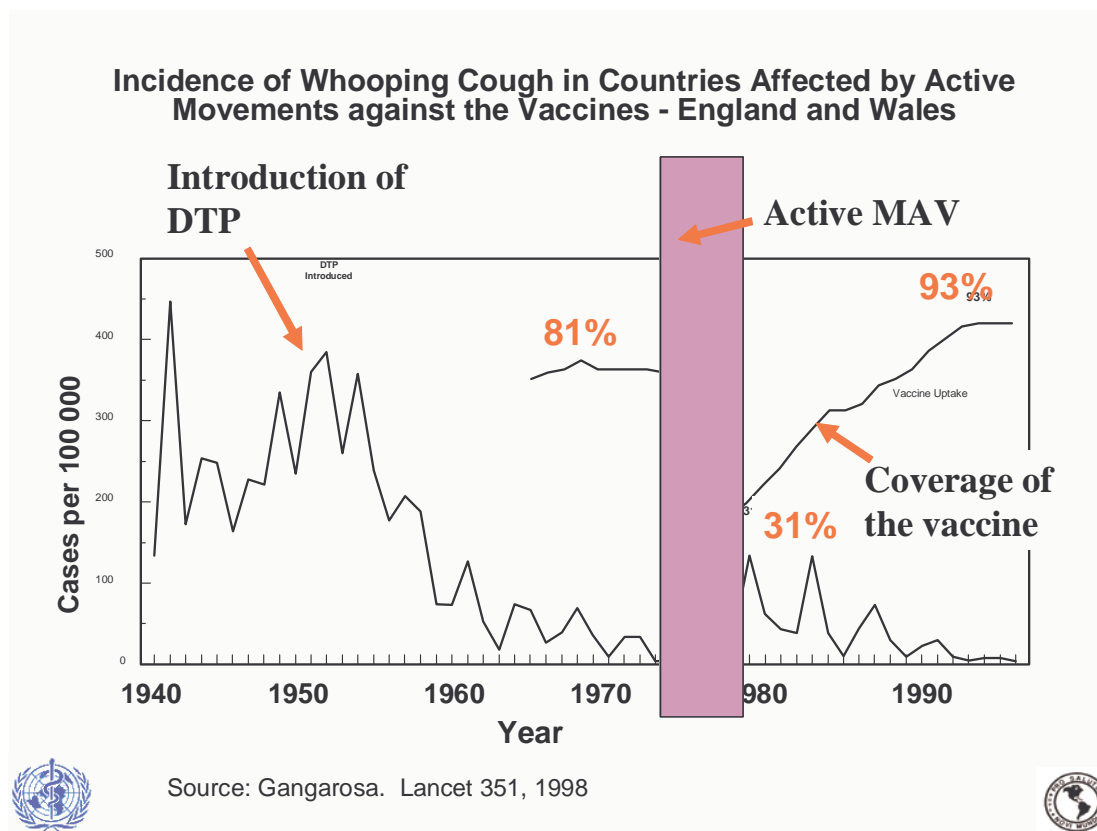
One of the greatest achievements in public health has been infectious disease prevention through immunization. Few interventions in this field that have prevented as many deaths and diseases as vaccinations administered through organized immunization programs. Although the discovery and introduction of vaccines occurred at the end of the 18th century, the surprising potential of vaccines was not truly recognized until 1977, when the eradication of smallpox was achieved.

Based on the lessons learned from the efforts to eradicate smallpox, other campaigns have been implemented in the Americas for the eradication of poliomyelitis and measles. As a result of the steadfast commitment to immunization on the part of health workers and parents, the last case of poliomyelitis in the Americas caused by the wild virus was recorded in Peru in August 1991. Furthermore, throughout the world the campaigns to eradicate it by 2005 continue. Measles transmission has been slowed after several years

of resurgence in Latin America. Campaigns are currently under way for its eradication, and there is also a strong commitment to measles control elsewhere in the world.

Despite significant progress in disease control, however, immunization is not free of controversy, and so the world has witnessed the dangers and effects of the interruption of vaccination. In the United Kingdom, public concern over the risks associated with whooping cough vaccines during the 1970s led to a reduction in vaccination coverage, which had been higher than 80% with 2,000-8,000 cases reported annually. When the coverage declined to 30%, the number of cases of whooping cough rose precipitously to over 100,000, resulting in deaths and hospitalizations that could have been avoided. After two major epidemics and a number of campaigns to educate the population about the disease and the vaccine, confidence in the vaccine and the immunization programs slowly recovered. Coverage rose to 95% by the middle of the decade and as a result, the lowest number of cases of whooping cough in the history of the United Kingdom was recorded (see Figure 1).

Figure 1



Every immunization program should endeavor to make vaccination risk-free. Furthermore, those in charge should address any cause for concern that arises in the population about the safety of immunization, for example the effects observed during clinical trials prior to the issuing of licenses or during the experimental stages of a vaccine's development.

The first years of a child's life constitute the period of greatest vulnerability to diseases and of the first manifestations of other problems (developmental disorders, hearing impairments, and others). It is precisely during that period that vaccines are administered and are interpreted as causal, although in many cases it is difficult to determine the true cause of the problem.

The technology continues to improve with time, as do the quality and effectiveness of the vaccines utilized. Although vaccines are now much safer than they were 40 years ago, every year new ones enter the market and information proliferates on the Internet, leading to the proliferation of the population's concerns about risks and benefits. Hence, immunization programs have a responsibility to address these concerns.

03. Vaccine Quality and Safety

All vaccines obtained through the World Health Organization (WHO) for national immunization programs have met the following requirements:

- examination of their characteristics
- adherence to the standards of good manufacturing practices, and
- approval by the national regulatory authority (NRA).

WHO certifies that a vaccine is of good quality if the NRA determines the quality of the vaccine, based on the six essential functions required of the producing laboratories; they must:

- Publish a set of clearly written licensing requirements (for products and manufacturers) and ensure compliance.
- Present an analysis of the results of the use of the vaccine in the field (safety and effectiveness).
- Have a system for lot release.
- Present laboratory test results, if necessary.
- Permit regular inspections to confirm adherence to the standards of good manufacturing practices.
- Evaluate clinical results through authorized clinical trials.

Before a license is granted, in order to meet the conditions required for registry, the safety and effectiveness of each vaccine must be demonstrated in clinical trials, conducted in different phases under controlled conditions.

The performance of the essential functions varies. In countries where the vaccines are produced, the NRA should require the performance of the six functions listed above. In countries that obtain vaccines through United Nations agencies (in the Region of the Americas vaccines are purchased through the PAHO/WHO Revolving Fund), the NRA are responsible for the following functions:

- Registration of vaccines.
- Postmarketing surveillance (follow-up study on effectiveness and postvaccination events).
- Release of lots of vaccines by:
 - document analysis (protocols and certificates of release from internal control that describe in detail the production process and the NRA in the producing country)
 - laboratory tests, or
 - both.

After the license is granted and the vaccine is administered to the population, follow-up studies of the vaccines are conducted (postmarketing surveillance). This monitoring provides information on the effectiveness of the vaccine, which, if properly communicated, can contribute valuable knowledge to the vaccination profile.

The existence of many events that are supposedly related to a given vaccine indicate that there may be a problem with its application (program operation errors), such as contamination, improper injection, problems in the cold chain, dosage errors, or dilution or administration of vaccines as though they were drugs. These problems can be corrected easily through the training and supervision of health workers and proper handling and storage techniques. It is imperative that each local health worker be aware of these potential problems and recognize them when they occur, so that they are corrected immediately.

In the following section mild and severe events are listed by type of vaccine. The events allegedly attributable to the vaccination or immunization vary with respect to their severity and frequency.

04. Rates of Events Attributed to Vaccination or Immunization

a. Common mild events

The purpose of a vaccine is to induce immunity (to form antibodies) through the reaction of the immune system of the vaccinated person. It is not surprising that vaccines generate certain mild side effects. A local reaction, fever, and general symptoms may be part of the normal immune response. Furthermore, some of the components of the vaccine (for example, the aluminum adjuvant, antibiotics, or preservatives) may produce reactions. An effective vaccine minimizes these reactions, while at the same time inducing maximum

immunity. The local reaction (at the injection site) is characterized by pain, swelling, or reddening. Presentation of symptomatic local reactions and fever is anticipated in nearly 10% of vaccinated individuals, except in the case of DTP or TT boosters, which produce fever in nearly half of those vaccinated.

BCG vaccination often causes a delayed local reaction that begins in the second week. It is a papule (light elevation in the skin) that becomes ulcerated and heals after several months. The keloid (rough enlarged scar) that BCG may leave is more common in Asian and African populations.

Summary of the rates of mild events attributed to vaccination or immunization

Vaccine	Local reaction (Pain, swelling and symptoms not reddening)	Fever	Irritability, discomfort and symptoms not
Hib (<i>Haemophilus influenzae</i> type b)	5-15%	2-10%	-
Hepatitis B	up to 30% in adults up to 5% in children	1-6%	-
Measles/MMR	up to 10%	up to 5%	up to 5%
Oral polio vaccine (OPV)	none	less than 1%	less than 1% a)
TT/DT	up to 10% b)	up to 10%	up to 25%
DTP c)	up to 50%	up to 50%	up to 60%
BCG d)	Common	-	-

(Note: The rates corresponding to the administration of the vaccines will be lower, because these symptoms occur normally in childhood, without vaccines).

- a) Diarrhea, headache, and muscle pain.
- b) It is probable that the rates of local reactions increase by 50 to 85% with the booster dose.
- c) For whole-cell whooping cough vaccine. The rates for acellular whooping cough vaccine are lower.
- d) Local reactogenicity varies from one vaccine to another, depending on the strain and the number of viable bacilli.

These common reactions appear one or two days after the administration of the vaccine, except for the fever and general symptoms produced by measles/MMR vaccine 5 to 12 days after vaccination. Although some 5% to 15% of those receiving measles/MMR vaccine present fever and exanthema during this time, only around 3% of the cases are attributable to the vaccine; the rest correspond to normal reactions in infancy, that is, to ordinary events.

b. Rare and severe events

Almost all rare vaccinal reactions (for example, convulsions, thrombocytopenia, episodes of hypotonia and hyporeactivity, and inconsolable persistent crying) are characterized by spontaneous remission and do not lead to subsequent problems or sequelae. Although

anaphylaxis can be fatal, it leaves no aftereffects if treated in a timely manner, and while encephalopathy is cited as a rare reaction to measles and DTP vaccines, in reality a causal relationship has not been demonstrated. Uncommon mild events are detailed in the following table:

**Summary of Severe Events Attributed to the Vaccination or Immunization.
Time They Take to Appear and Rates.**

Vaccine	Event	Time they take to appear	Rates per 1,000,000 doses
BCG	Suppurative lymphadenitis	2-6 months	100-1,000
	Osteitis from BCG (“BCGitis”)	1-12 months	1-700
	“BCGitis” spread by the BCG vaccine	1-12 months	2
Hib	Unknown	-	-
Hepatitis B	Anaphylaxis	0-1 Hour	1-2
	Guillain-Barré syndrome (vaccine obtained in plasma) *	0-6 weeks	5
Measles /MMR^{a)}	Febrile convulsions	5-12 days	333
	Thrombocytopenia (low platelet count)	15-35 days	33
	Anaphylaxis	0-1 hour	1-50
Oral polio vaccine (OPV)	Vaccine-associated paralytic poliomyelitis (VAPP)	4-30 days	1,4-3,4 ^{b)}
TT/DT	Neuritis of the brachial plexus	2-28 days	5-10
	Anaphylaxis	0-1 hour	1-6
	Sterile abscess	1-6 weeks	6-10
DTP	Persistent crying that lasts more than 3 hours	0-24 hours	1,000-60,000
	Convulsions	0-2 days	570 ^{c)}
	Episode of hypotonia and hyporeactivity (EHH)	0-24 hours	570
	Anaphylaxis	0-1 hour	20
	Encephalopathy	0-3 days (to level)	0-1
Yellow fever	Encephalitis subsequent to vaccination	7-21 days	500-4,000 in less than 6 m
	Allergic/anaphylaxis reaction	0-1 hour	5-20

a) There is no reaction (except for anaphylaxis) when there is immunity (~90% of those who receive a second dose); febrile convulsions are unlikely in children older than 6 years.

b) The risk of VAPP is higher with the first dose (1 in 1,400,000–3,400,000 doses) than with subsequent doses and contacts, 1 per 5,900,000 and 1 per 6,700,000 doses, respectively.

c) The convulsions are chiefly febrile in origin, and the rate depends on the personal and family history and the age, with a lower risk in infants under 4 months.

d) The isolated cases without a denominator hinder evaluation of the rate in older children and adults but are very rare (less than 1 case per 8,000,000 doses).

* The vaccine used in Peru is recombinant.

c. Program operation errors

Most reactions that are cited, whether “common and mild” or “rare and severe”, are difficult or impossible for the vaccinator to prevent. Nevertheless, there is one type of event that the vaccinator can prevent to a large extent. It concerns the “program operation error.” This error is more frequently human than caused by the vaccine or the technology.

It can usually be prevented through training for personnel, supervision, and an adequate supply of equipment for safe injection.

A program operation error may lead to a cluster of events, especially if a vaccinator does not follow what he was taught during training. Improper vaccination practices can give rise to abscesses or other blood-borne infections. The most serious result is toxic shock caused by improper handling of the vaccine vial after reconstitution. Several infants vaccinated from the same vial could die shortly after injection.

Operational Program Errors and their Consequences

Operational Program Error	Anticipated Event
<p><i>Non-sterile injection:</i></p> <ul style="list-style-type: none"> • Recycling of a syringe or disposable needle. • Use of syringes that do not ensure adequate sterility. • Contaminated vaccine or dilutant. • Utilization of lyophilized vaccines longer than indicated time of use. 	<ul style="list-style-type: none"> • Infection, as a localized abscess at the injection site, sepsis, toxic shock syndrome, or death. Blood-borne infection, such as hepatitis or HIV.
<p><i>Reconstitution error:</i></p> <ul style="list-style-type: none"> • Reconstitution with the wrong dilutant. • Replacement of the vaccine or dilutant with a drug. 	<ul style="list-style-type: none"> • Local abscess due to insufficient agitation. • Adverse effect of a drug--for example, insulin. • Death. • Ineffective vaccine.
<p><i>Injection in the wrong place:</i></p> <ul style="list-style-type: none"> • BCG administered subcutaneously. • DTP/DT/TT administered too superficially. • Injection in the buttock. 	<ul style="list-style-type: none"> • Reaction or local abscess. • Reaction or local abscess. • Injury to the sciatic nerve.
<p><i>Improper transport/storage of vaccines.</i></p>	<ul style="list-style-type: none"> • Local reaction due to frozen vaccine. • Ineffective vaccine* .
<p><i>Ignoring of contraindications.</i></p>	<ul style="list-style-type: none"> • Serious reaction foreseeable.

The information in this section serves for:

- Anticipating events for specific biologicals (type and number).
- Detecting events unrelated to vaccines (for example, unanticipated events).
- Comparing reported rates with expected rates (efficiency of the reporting).
- Launching an investigation if the reported rate exceeds the expected rate.

05. Investigation of Events Supposedly Attributable to Vaccination or Immunization (ESAVI)

It is difficult to determine if an event allegedly attributable to vaccination or immunization (ESAVI) is really the result of the administration of the vaccine and the subsequent immunization, especially in small children. On the one hand, in this age group many events that are attributed to vaccines occur with a certain frequency, and it is

difficult to distinguish between an event related to the administration of the vaccine and the natural occurrence of the incident.

Every event that the public, parents, the patient, or health workers consider related to a vaccine should be investigated at the local level. If the suspicion is justified (that is, the timing and the symptoms indicate the possibility of a connection to the vaccine), a more formal, standardized investigation should be initiated immediately, with regional and/or national support.

The purpose of the investigation is to confirm or rule out the vaccine as the cause of the reported event, to determine whether there are other possible causes, to confirm whether this is an isolated event, and to inform the parties involved.

a. Stages of the investigation

Initial evaluation: As soon as any ESAVI is recognized, the health worker should inform the parents or guardians that immunization is safe, give them confidence, and explain to them that there can be simultaneous events that are not necessarily due to the vaccine.

There should be an investigation of any serious event (one that endangers life or causes disability, hospitalization, or death), rumors, or events which occur in groups of people.

Until the investigation is completed, it is impossible to determine the causes of the event. These may be related to operational aspects of the program or to the vaccine, unrelated to the vaccine, or of unknown etiology. In some situations, external tests may be necessary to identify the cause.

b. Information and investigation

1. The investigation should begin within the first 24 hours.
2. The first step in the investigation is to make a detailed examination of the following
 - program refrigerator
 - work table
 - vaccination room
 - place where syringes are stored
 - list of drugs that are received and delivered to the health services (to review the flow of drugs).
3. The general data to be collected in the investigation are indicated below:

- Basic information that should be gathered:
 - ✓ Demographic data: age, sex, place of residence.
 - ✓ Family history.
 - ✓ Recent clinical summary (symptoms and signs, when they appeared, duration, clinical examination, auxiliary diagnostic tests, treatment, course).
 - ✓ Type of event, date of appearance, duration, and treatment of the clinical event.
 - ✓ Pathological and clinical history of the patient (at birth, previous reactions to vaccines, allergies to certain pharmaceutical preparations, preexisting neurological disorders, sleep apnea, drugs currently taken, etc.).
 - ✓ Vaccination history: type of vaccine utilized and date of the last dose, type of previous reaction (if any).
 - ✓ Housing and socioeconomic conditions, shelter, type of bed, and sleeping habits.
 - ✓ In the event of death, a description of how the body was found, position, temperature, type of secretion (if any) from the mouth or nostrils.
 - ✓ Full autopsy report, toxicological screening, and pathological anatomy.

- Identification of the vaccine and syringe utilized:
 - ✓ Lot number.
 - ✓ Dates of manufacture and expiration.
 - ✓ Manufacturing laboratory.
 - ✓ Origin of the vaccine/syringe, date of shipment and data of transport.
 - ✓ Physical appearance of the vaccine/syringe.
 - ✓ Results of the procedures to control vaccine quality.
 - ✓ Review of the production protocol of the implicated vaccine.

- Review of operational aspects of the program:
 - ✓ Vaccine storage.
 - ✓ Handling and transport of vaccines.
 - ✓ Use of dilutants, reconstitution of vaccines, and forms of administration.
 - ✓ Proper dosages.
 - ✓ Availability of needles and syringes, and appropriate practices.
 - ✓ Circumstances and the way vaccination is administered.
 - ✓ Health care practices in the health services.
 - ✓ Person who administered the vaccine.
 - ✓ Technique for administration.
 - ✓ Order of administration of the dose from the vial.
 - ✓ Cold chain.

- Monitoring of other children vaccinated with the same vial and/or lot.

- Determination of whether the reported event is an isolated incident or the same or similar symptoms occurred in one or more of the following:
 - ✓ Population vaccinated with the same lot of vaccine in the same period.
 - ✓ Unvaccinated population.

- ✓ Population vaccinated with a different vaccine lot (from the same manufacturer or another one).

4. For investigation of severe events, such as deaths allegedly attributable to the vaccination or immunization, it is recommended that the autopsy be performed within the first 72 hours, following the procedure below:

- If the child dies at home with no evident cause, upon its arrival at the health facility the physician should undertake a detailed verbal autopsy with the mother, take a clinical history, and examine the body externally in search of signs of disease, such as jaundice (yellow staining of skin and sclerae), petechiae, cyanosis, or pallor.
 - If possible, x-ray the body.
 - Coordinate with the autopsy department of each jurisdiction for:
 - a. Perform of the autopsy as soon as possible to avoid tissue lysis (in the adrenal glands, for example), which can hinder diagnosis. During this process the autopsy form is filled out, which will aid the forensic expert by providing the patient's history.
 - b. Sampling for toxicological screening, providing 80 to 100 g of liver, 80 to 100 g of brain, and the stomach contents. If there are no gastric contents, a section of stomach should be sent. All the samples will be sent together in a wide-mouthed bottle with no additives (without formalin or other additional substance). For preservation use only cold packs.
 - c. Sampling for pathological anatomical examination, providing 3 to 4 cm of each organ: for example, a fragment of the brain with meninges, a fragment of each of the 5 lobes of the lung, fragments from both adrenal glands (located on the kidneys), as well as from any other organ in which pathologies are suspected. In each case, the sample will be representative of the suspicious area. The specimens are to be sent together in a wide-mouthed bottle, with sufficient formalin to cover all the pieces.
 - d. Both sets of samples should be sent to the reference laboratory for thanatological and auxiliary examinations. All the samples should be labeled with the name and autopsy form number and be accompanied by the documents requesting the examination and investigation, and the conclusions from the autopsy, which should list the cause of death, utilizing ICD 10, and, if possible, the causative agents. The epicrisis of the CH should be added.
 - The reference laboratory for thanatological and auxiliary examinations will send the results to the immunization program of the Ministry of Health.
5. When ESAVI occur unexpectedly or at unexpected rates, samples will be collected from the compromised vaccine lots for reevaluation of the quality control of each of them.

After the investigation, the information should be analyzed to determine the cause, confirm the diagnosis, or suggest other possible diagnoses.

c. Steps to be taken

The steps to be taken will be based on the conclusions of the investigation, which will have one of the following results:

- 1) The event is definitively not related to the vaccination.
- 2) The event is related to the vaccination.
 - It is related to the operational aspects of the program.
 - It is related to the vaccine.
- 3) The investigation is not conclusive.

When the investigation is finished and the results obtained, they should be reported to the interested parties. To this end, clear communication will be necessary, and the information should be disseminated to the parents, the community, and the Region, and, at the center, to the health authorities, professional associations, or the entire country, including the mass media, when appropriate.

Conclusions from the investigation

1.-The event is definitively not related to the vaccination.

Some clinical cases simply coincide with the vaccination; that is, the event might have occurred even if the person had not received the vaccine. The best way of sustaining the argument that the event is simply coincidental to the vaccination is to demonstrate that the same event also occurred in a population group that was not immunized.

Although the ESAVI has not been linked to the vaccination, it may require adequate medical monitoring, and thus a mechanism for referral to the necessary health services should be established.

2.-The event is related to the vaccination.

• Related to the operational aspects of the program

That is, when the events are caused by one or more of the following errors:

- ✓ Inadequate dosage.
- ✓ Incorrect method of administration.
- ✓ Unsafe use of needle and disposable syringe.
- ✓ Failure to verify the condition of the packaging that guarantees the sterility of needles and syringes.
- ✓ Improper handling of needles and syringes.
- ✓ Reconstitution of the vaccines with the wrong dilutant.
- ✓ Improper quantity of dilutant.
- ✓ Improper preparation of vaccines.

- ✓ Substitution of vaccines or dilutants with drugs or other substances.
- ✓ Contamination of the vaccine or the dilutant.
- ✓ Improper storage of the vaccines and syringes.
- ✓ Vaccines and syringes used after their expiration date.
- ✓ The errors cited thus far are program operation errors.

What should be checked?

- ✓ Whether several cases occur and whether the same health worker administered the vaccines.
- ✓ Whether the unimmunized population in the same age group and the same geographical area presents the same symptoms.
- ✓ Whether the other people immunized with the same lot of vaccine in the same geographical area present the same symptoms.
- ✓ Whether the other people immunized with the same lot of vaccine in the same establishments on the same day do not present the same symptoms.

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

▪ **Related to the vaccine**

This type of event implies a personal effect and is very rare (see Section 4). It is very important to investigate each case, and while one expects the confirmation of a minimal incidence of cases related to the vaccine the following can occur:

- a) The event occurred within the expected frequency range (see Section 4).
- b) The event was unexpected or occurred with unexpected frequency. In this case, the following steps should be taken immediately:
 - ✓ Temporarily suspend the use of the product: the type or lot of vaccine/syringe that is suspected.
 - ✓ Coordinate a reevaluation of the quality of the vaccine with the NRA and communicate with the manufacturer, if necessary.
 - ✓ Arrange for the return of the vaccine, if appropriate.
 - ✓ Report the findings of the investigation to the Pan American Health Organization so that the information is disseminated internationally.

3.- The investigation is in conclusive.

When causality cannot be determined, in addition to reporting the findings of the investigation to the interested parties, the reason that no conclusion was drawn should be indicated, along with whatever progress was made.

06. Event Reduction during Vaccination Campaigns

The number of observed events is directly related to the number of administered doses; in other words, if a vaccination campaign is being carried out with the application of a high number of doses, it is to be expected that the number of events will also increase, but the ratio (number of events/number of doses) should remain the same.

During a campaign, the following may occur:

-Apparent increase in ESAVI for one or more of the following reasons:

- Application of a large number of doses of the vaccine over a short period, which means that a greater number of ESAVI than expected may be registered. This can cause concern among the people even though the adverse event rate remains the same.
- Both the health workers and the public tend to be more aware of ESAVI during the campaigns, especially when injectable vaccines are used.
- During a campaign there is a greater circulation of rumors, which can have a negative impact on its later stages. Unlike what occurs with ESAVI registered during normal vaccination programs, the campaign can be affected before there has been sufficient time to counteract the rumors.
- Campaigns can generate a lack of acceptance in given areas. ESAVI that occur during a campaign can worsen an already negative situation and be utilized to justify criticisms.
- Vaccines are sometimes administered to broader age groups (usually to older people) than during routine vaccination, and program personnel may have less experience in treating the types of reactions or adverse events that these groups may experience.

Real increase in ESAVI:

- Personnel may feel pressured by the number of children to be vaccinated in a short period and may try to simplify their work by not observing the customary safety practices for the injections. This would increase the risk of adverse events through program errors.
- It is also possible that additional personnel, unfamiliar with a given vaccine, are used, thus increasing the program operation errors.

a. Measures to prevent ESAVI during campaigns

Strategies to reduce program errors

- Use only quality vaccines approved by the United Nations or NRA and disposable syringes for injectable vaccines.
- Ensure adequate distribution of the dilutant and of the material injectable together with the vaccine.
- Reconstitute the vaccine only with the dilutant provided with the vaccine.
- Utilize a disposable needle and a syringe of the size recommended for each type of vaccine and for each vaccination.
- Train health workers in the proper procedures for reconstituting lyophilized vaccines and in appropriate techniques for administration.
- Discard yellow fever vaccine one hour after reconstitution and measles vaccine at the time recommended. For opened bottles, follow the policy recommended by PAHO/WHO.
- Plan the disposal of the injectable material so that it is risk-free.
- DO NOT store drugs and other substances in the EPI refrigerator; it is to be used exclusively for vaccines.
- Specify the contraindications to the administration of the vaccine and the precautions that the personnel in charge of its application in the field should take.
- Train and supervise workers appropriately so that they observe safe injection practices.
- Investigate any program operation error so that it is not repeated.

Implementation of a fast and flexible surveillance system for ESAVI

In mass campaigns it is essential to perform some type of monitoring of ESAVI. If this is not done, it is probable that word of these events will reach the ears of the public before Ministry of Health personnel hear about them. If this occurs, the situation is very difficult to control. The surveillance system should be simple, flexible, and fast. The planning includes the following measures:

- Deciding **who** will have general responsibility, who should be the coordinator, and who the spokesperson.
- Deciding **what** to report, how to report it, and what to investigate. Decide who should receive the reports and who should participate in the investigation, if one is needed.

It is necessary to make sure that the list of events is not complicated. It should include:

- all abscesses produced at the application site;
- all deaths attributed to the vaccination;
- all hospitalizations registered as a result of the vaccination;

- any serious or atypical fact attributable to the vaccination (or that, in opinion of the personnel or the parents, are so attributable).
- **Training** personnel in the events that can be expected and how handle them.
- Developing **speedy mechanisms for sending information** on happenings in the field to the person responsible for monitoring ESAVI (telephone or fax).
- **Analyzing** the data promptly (this it does not necessarily imply a complex analysis) and quickly taking the appropriate steps. A critical report should not end up abandoned on some desk.
- Providing weekly **feedback** to assure the personnel and the community that no problem has occurred.
- Considering the possibility of creating a **committee** that reviews ESAVI, analyzes the cause of the reported events (it could include, for example, a neurologist, a pediatrician, an immunologist, and a pathologist) and that can be convened as needed. It is advisable that its members be official representatives of the most important professional associations.
- **Monitoring** the lots of all vaccines and the places where they were distributed in the regional and national areas.

07. Management of Crisis Situations

a. What is a crisis?

In the context of ESAVI, 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 (real or supposed). Often, crises can be avoided through foresight, care, and training. If managed properly, the crisis will strengthen the program and boost public confidence.

ESAVI are unavoidable, but when the immunization program is well-organized they can be minimized. Accordingly, it is necessary to draft plans to deal with each of them.

One ESAVI might be the death of three infants after routine measles vaccination, administered by the same vaccinator in a single morning. Another might be the result of the publication of medical research that involved proving how detrimental a given vaccine is.

For some years there has been a continuous undercurrent of concern about the use of vaccines, especially in infants. There are several reasons for this, including the high educational level of parents in all countries who are better informed and have access to material that presents arguments for and against vaccination. As the incidence of preventable diseases is reduced through vaccination, parents may perceive that the risk incurred in vaccinating their children is greater than the risk of contracting the disease. Program operation errors are more likely and their occurrence leads to a decline in public confidence in the EPI.

b. Why does a crisis arise?

A crisis can arise for reasons that are outside the direct control of the program (for example, the publication of an article in the press). Or perhaps the information on a program operation error has been poorly handled by a health worker or a political spokesman. It can also be the result of lack of planning, of inadequate management of relations with the media, of lack of public support, or of deficiencies in communication of vaccination policies. Suddenly, the communications media develops a great interest in this issue, and the health authorities find themselves having to respond to difficult questions, before a country that listens and observes very carefully.

c. Four steps for the management of ESAVI and prevention of crises

What can a health authority do in the face of a crisis? Certain steps should be taken in advance, notably:

1. Anticipate. Do not wait until a crisis occurs. Prepare for the unavoidable.
2. Train vaccination personnel at all levels to respond adequately.
3. Confirm all the facts before making any public statements.
4. Prepare a plan to react to a crisis when it occurs.

Anticipate

- Determine who will be responsible for answering questions. This function should be assigned to someone with authority so that people see clearly that high-level personnel are taking charge.
- Develop relationships with the media, especially with journalists specializing in health issues. This should be done by supplying the media with information on health in general. It is useful to provide concrete informative summaries on anticipated events and the frequency with which they occur under normal conditions. Thus, when in a report a specific event is announced along with its frequency, the journalists will already have background material on it. Pay special attention to relationships with well-disposed journalists, whose support can be requested in a crisis.
- Prepare pertinent questions and answers and informative summaries about ESAVI.
- Before a mass campaign begins, make list of the problems that can arise. Distribute press releases before beginning the campaign; thus the press will know the levels of ESAVI to be expected.
- Establish accredited information channels by issuing public awareness messages on health over the radio or in a health journal.

- Seek technical assistance from a local public relations specialist or someone similar, to learn how to manage ESAVI.
- Make sure that there is a budget allotment for training, planning, and reacting to crises.

Training

Train yourself and the other senior managers. Include staff members at the local levels to acquaint them with the media. Attention should be paid to preparation of written material and training for newspaper, radio, and television interviews. Raise awareness among the staff about aspects of the target population and the importance of body language.

Verify the facts

- As soon as information on an adverse incident is received, it is necessary to determine what actually happened. This should be done by going to the source of the information by the fastest means--by telephone, for example. Be careful with second-hand reports; investigate to determine whether the source is credible.
- Next, decide if the ESAVI is indeed that. Some events are the result of a longer-term process and to single one out may not be appropriate. For example, if a woman complains that the hepatitis B vaccine has given her multiple sclerosis, it is not a crisis, but requires a longer-term response. On the other hand, a call to temporarily interrupt the use of the vaccine can indeed be a crisis.
- One should also wonder whether the ESAVI has a simple scientific explanation, if additional studies are needed, or if a similar event occurred in another country.

Plan the responses

- Create a crisis working group in which representatives of the population participate, if appropriate. Examine the legal, technical, and communication aspects.
- Issue a preliminary statement within a few hours. Communicate with receptive journalists with whom a relationship already exists.
- Establish a mechanism for communicating with journalists.
- Launch a serious technical investigation and keep the press informed about the progress made.
- Designate the person who will be responsible.
- If the incident is of great magnitude, call a press conference daily. Try to meet the expectations of the media in every way possible.
- Review your knowledge of relationships with the public information media if an appreciable amount of time has passed since the last training.
- Organize and herald support measures for the people affected--i.e., covering expenditures or setting up a telephone consultation service, without acknowledging any blame.

- Consider the possibility of eliciting the support of celebrities, a noted athlete, or other well-known individuals who are willing to support vaccination publicly.
- Conduct a rapid opinion poll.
- Evaluate the event and assimilate the lessons it offers about how things could be handled better the next time.

08. Communication and Information on the Safety of Vaccination and Immunization

The immunization program should make an effort to improve the channels of communication with the community and health workers, providing with all frankness and accuracy essential and complete information on the investigations under way on the risks of the vaccination. The messages should be disseminated quickly and address the concerns of the population.

Educational materials that promote vaccination and point out its benefits and risks should be available. Furthermore, workers in the health sector should be informed of events caused by program operation errors and should receive training to avoid an increase in ESAVI. During critical periods, such as vaccination campaigns and investigations in progress, health workers should have easy access to data on the details of immunization and should accurately and truthfully disseminate the information provided by the health authority.

a. Relations with the communications media

The mass media play an important role in the public's perception of vaccination and can have a positive or negative influence. Mass media support for vaccination, especially after the announcement of an ESAVI, can depend to a large extent on the communication skills of the health authorities. Statements and press conferences are useful tools in orienting the interest of the media when an adverse event occurs. The basic principles that apply are honesty and trust.

It is important to communicate with professional organizations, health professionals, and local health workers, insofar as possible, before informing the communications media. It is necessary to teach health workers how to address people's concerns about a particular matter. If health professionals and health workers can calm the public with precise, up-to-date information, damage to the program will be minimized.

The objective of this section is to promote an understanding of the media's orientation and provide concrete information on how messages should be transmitted to help improve the public's perception of vaccination.

b. What is the perspective of the mass media?

Understanding what the media desire with respect to a news item can help the health authorities to provide information that meets their expectations, while presenting a clear, positive view of vaccination. The media are especially interested in news that captures the attention of the public and helps to sell more copies or to enlarge the radio or television audience. One of the techniques utilized is to dramatize and personalize the reporting. If the media are given inappropriate material, they may sometimes portray the health services or staff that administer the vaccinations as indifferent, impersonal, incompetent, and even dangerous.

It is relatively easy for some news to generate panic and anger about an incident that is either not related to the vaccination (although it coincides with it) or is a program operation error without serious repercussions. Furthermore, the media tend to report several events, overlooking the fact that, in context, their frequency is very low. One incident linked to vaccination by the media even though its cause is unknown can arouse a great deal of fear. Given these circumstances, it is important to develop good communication skills to avoid this type of unfortunate situation.

c. How to give an interview or a press conference

When an ESAVI arouses a great deal of media interest, it is advisable to hold a press conference or to accede to a request for an interview. When all journalists have access to the same information and none are excluded, they cannot give as much emphasis to that news and it is more difficult for them to sensationalize it. A press conference is also more effective when there is great interest on the part of the media, since it makes it possible to transmit the message to many journalists all at once. It also gives the representatives of other organizations an opportunity to voice support for vaccination and for the approach used to investigate the problem. In some situations, obtaining support from certain professional organizations helps to generate more confidence.

Media interest is usually greater in the initial stages, when relatively little is really known about the events and their possible causes. In this context, rumors are very likely to spread and cause enormous damage. It is prudent, therefore, to call a press conference immediately, even though the available information may be very limited. This will improve relations with journalists and keep them from circulating rumors. At the end of the press conference, it is a good idea to inform journalists that in a few days, at most, another press conference will be held and that detailed information on the facts and on the investigation will be provided at that time. It is also advisable to maintain periodic contact with the media, reporting on the progress made in the investigation and concluding with a summary of the results and all the corrective action taken or anticipated.

How to prepare a press release:

All the information to be conveyed in a press conference should be prepared well in advance and included in a press release. It is necessary to include:

- A full account of the facts (in terms that can be understood by people unfamiliar with the health services or vaccination) set in the appropriate context (for example, an isolated event, a coincidental event) to prevent the incident from tainting the entire immunization program.
- Information on whether the incident is currently happening and if new cases are expected.
- A summary of the steps taken or anticipated (depending on the situation, these can range from a plan of action to a finished investigation).
- The causes of the incident (if they have been identified with reasonable certainty and are not just hypothetical) and the corrective action taken or planned.

How to prepare for a press conference

Before accepting an interview, find out what topics will be addressed at the press conference and how the information will be used. Anticipate the questions and prepare the answers. Preparation for a press conference includes:

- Identifying the key messages that one wishes to convey.
- Designating a spokesman.
- Preparing a file of informational material for all the journalists and other community leaders. This should consist of:
 - a concise press release containing all the essential information.
 - complementary background (for example, the advantages of vaccination).
 - a set of questions and answers that includes the questions that have already been formulated or that may be posed by a concerned public.

The **key messages** in favor of immunization can include:

- The effectiveness of vaccination in preventing disease has been well-demonstrated.
- It is more hazardous not to vaccinate, because of the potential serious complications of the disease. It is much safer to be vaccinated than to contract the disease. The idea that they are the same or practically the same, which many try to spread, is not correct.
- Vaccines can cause reactions, but they are usually mild and disappear spontaneously; very rarely do they lead to serious or long-term problems.
- Vaccine-preventable diseases have left the memory of millions of dead or disabled individuals before the introduction of vaccines, and without their ongoing use that situation would return.
- The safety of vaccines is of fundamental concern to the providers of vaccination services, and any anomaly in this regard is investigated and corrected (hence the advantages of establishing a solid mechanism to monitor the safety of vaccines).
- The ESAVI is being investigated, but it is presumed to be coincidental or due to a local problem (depending on the type of event); in the meantime, however, it is necessary to continue with the vaccination program to protect the population from the disease.

- Steps are being taken in this regard.

d. Sixteen pieces of advice on style

Some practical advice on style and techniques for dealing with the media is given below:

- Be **sincere**. Don't lie. If you don't know something, say so, but promise to look into the matter. Be frank and open. You might say, "This is what happened; we are dealing with it." An attitude of this type is important in establishing a lasting relationship with the media and is the basis for winning confidence about vaccination. A lie or an attempt to conceal the truth can become bigger news than the original event.
- Be understanding. Convey an image of solidity, humanitarianism, and competence with respect to yourself and the vaccination service.
- Be **responsible**. Don't be defensive. Say, for example: "We are going to find out whether the information is correct." Nevertheless, accept the responsibility that is yours and avoid blaming others.
- Be **sensitive**. Hold a press conference a day, if needed, to address the concerns of the public and the media. It can become an instrument for building a solid relationship with them.
- Remain **calm** in the face of uncertainty. You can say, "For the moment we don't, but we have taken the necessary steps to find the answer to your question."
- Be **aware** of body language. Expressions, looks, gestures, and body positioning have great significance.
- Be **positive**. Whenever possible, describe the situation in positive terms. Avoid negative, brusque, or contemptuous comments and use terms like vaccine safety (which has a positive connotation) instead of adverse event. Employ a positive turn of phrase. Just as the media can utilize a situation to present arguments against vaccination, with a little interest and reflection the information on the same situation can be used to promote a positive attitude toward vaccination. The most negative initial communication with a journalist can be turned into an advantage for the immunization program.
- Be **prepared**, so that you can communicate the essential concepts. Prepare beforehand. Know what you want to say and take the initiative in leading the interview to the chosen terrain. Transmit the ideas that you want to convey. Think beforehand about the difficult questions that might be posed and prepare your responses to them.
- Stay **serious**. Jokes can be disastrous. In any case, the subject is rarely amusing.
- Be **calm!** Avoid extemporaneous remarks. Don't give information that has not been requested and that can lead to awkward situations.
- Be **dynamic** and maintain control of the interview.
- Be **nice...** even when things get complicated! It will have an impact on the audience if, in the face of provocation, you manage to rise above the situation. Do not resort to sarcasm or something worse.
- Be aware of your greatest **vulnerabilities** and be prepared to respond when asked about them.

- Don't stray from the questions you feel **safe** in answering.
- **“Steer”** complicated subjects to firmer ground. If necessary, restate the question in your own words.
- Be **clear**. Avoid jargon. When talking about complex medical concepts, use simple sentences. Give examples that are easy to understand, if they can clarify your meaning.

e. Skills

Everyone who deals with the communications media should acquire the following skills:

- Ability to communicate the concept of risk adequately.
- Ability to convey complex concepts simply.
- Interpersonal skills, such as the ability to express empathy.
- Specific skills for the communications media, such as being able to handle television interviews.
- Ability to rapidly acquire and process pertinent information..

ESAVI can generally be avoided. Do everything possible, because they do not happen if training is adequate. If in spite of everything a crisis occurs, make sure that, through proper management, the problem evolves positively and results in the strengthening of public confidence in vaccines.

09. Summary of Vaccines, Diseases They Prevent, and Disease Effects

Vaccine	Disease	Effects of the disease
Sabin (oral polio vaccine)	Poliomyelitis Microorganism: Poliomyelitis virus	Mild symptoms (fever, nausea, vomiting) are presented in 4% to 8% of infections; 1% to 2% of the infections give rise to aseptic meningitis; less than 1% result in paralysis. The case-fatality rate for the cases of paralysis ranges from 2% to 10%.
DTP (diphtheria, tetanus, whooping cough)	Diphtheria Microorganism: <i>Corynebacterium diphtheriae</i>	The effects are related to the toxin. The case-fatality rate is 5% to 10% (mortality is higher in the young and the elderly). Myocardopathy and neuritis/neuropathy. There are also cutaneous and nasal forms of the disease.
	Whooping cough Microorganism: <i>Bordetella pertussis</i> .	Highly contagious disease of the respiratory tract (case rates of over 90% in contacts with unvaccinated people). The characteristic paroxysmal cough with inspiratory stridor gives the disease its name. It can also lead to pneumonia, convulsions, and encephalopathy. Approximately 1 in 200 patients under 6 months die. Approximately 200,000 to 300,000 deaths worldwide are attributed to whooping cough.
	Tetanus Microorganism: <i>Clostridium tetani</i> .	The infection causes painful muscle contractions, that begin in the neck and the jaw (trismus) and then progress to the trunk. For neonatal tetanus, the case-fatality rates are high (in cases with short incubation periods, over 80%). The tetanus case-fatality rates are specific to each country and range from less than 1% to 90%.
DT (diphtheria, tetanus)	See the previous sections on diphtheria and tetanus.	See the previous sections on diphtheria and tetanus.
TT (tetanus toxoid)	See the previous section on tetanus.	See the previous section on tetanus.
MMR (measles, mumps, rubella)	Measles Microorganism: Measles virus.	Highly contagious acute disease with fever, conjunctivitis, runny nose, cough, and Koplik spots. The characteristic exanthema appears 3 to 7 days later. Complications can arise through bacterial superinfection in 10% of the cases. The case-fatality rate in the developed countries is approximately 0.2%, and in the developing countries, 3% to 5%. Acute encephalitis occurs in 1 in 1,000 cases, and subacute sclerosing panencephalitis (SSPE) as a late complication (several years after the infection) in 1 in 100,000 cases.

	Mumps Microorganism: Mumps virus	Approximately 1 in every 200 children contracts encephalitis. Nearly 2/3 of those infected present edema of the salivary glands (parotid). Orchitis (inflammation of the testes) occurs in 1 in 5 postpubertal males. Sterility is an uncommon complication. Deafness can occur but is uncommon.
	Rubella Microorganism: Rubella virus.	Approximately 50% of the cases are subclinical. The infection causes a mild febrile disorder with exanthema and lymphadenopathy. Occasionally, arthritis and arthralgias occur. Encephalitis and thrombocytopenia are uncommon complications. Congenital rubella syndrome occurs in approximately 90% of infants infected during the first trimester of pregnancy. The children are born with congenital malformations, such as deafness, cataracts, microcephaly, mental retardation, heart defects, and bone diseases, and pregnant women run the risk of miscarriage.
<i>Haemophilus influenzae</i> type b (Hib)	<i>Haemophilus influenzae</i> infections Microorganism: <i>Haemophilus influenzae</i> type b (Hib)	Before the introduction of the vaccine, Hib was the most common bacterial cause of meningitis. The meningitis case-fatality rate is about 5%. Approximately 10% to 15% have neurological sequelae, and severe deafness occurs in 15% to 20% of cases. Before the vaccine, Hib was also the leading cause of epiglottitis, whose case-fatality rate is 1%. It also causes cellulitis and pneumonia.
Hepatitis B	Hepatitis B infection Microorganism: Hepatitis B virus	It causes a broad range of disease manifestations: fulminating fatal hepatitis, clinical hepatitis with jaundice, subacute disease with symptoms, and nonspecific asymptomatic seroconversion. Chronic hepatitis B infection occurs in up to 30% of children infected after birth and in 5% to 10% of older children /adolescents. The acute disease has a case-fatality rate of 1% to 2%. The chronic infection can lead to cirrhosis of the liver or to hepatocellular carcinoma.
Yellow fever	Yellow fever Microorganism: Yellow fever virus Vector: Mosquito	Around 15% of those infected contract a serious disease with several phases: acute, in remission, and toxic. With the onset of the toxic phase, the case-fatality rate approaches 50%. People immunized naturally or by vaccination seem to present a milder clinical disease. The case-fatality rates in unimmunized populations can exceed 50%.
BCG	Tuberculosis	It causes lung disease, meningitis,

(Bacillus of Calmette-Guérin vaccine)	Microorganism: <i>Mycobacterium tuberculosis</i> .	and disseminated infection. The infection is generally latent for long periods and is reactivated in later stages of life.
Pneumococcal vaccine (<i>Streptococcus pneumoniae</i>)	Pneumococcal disease Microorganism: <i>Streptococcus pneumoniae</i>	After the introduction of the vaccine against <i>H. influenzae</i> type b, pneumococci became one of the most common bacterial causes of meningitis. Pneumococcal meningitis case-fatality rates vary from 10 to 30%. This microorganism also causes acute otitis media, pneumonia, and other invasive diseases. Mortality from the invasive diseases is high in populations with chronic diseases and with compromised immune systems
Meningococcal vaccine (<i>Neisseria meningitidis</i>)	Meningococcal disease Microorganism: <i>Neisseria meningitidis</i>	Since the introduction of the vaccine against <i>H. influenzae</i> type b, this organism has become one of the most common causes of meningitis (together with pneumococci). Meningococemia is another invasive disorder caused by this bacterium. The fulminating cases can present purpura, disseminated intravascular coagulation, shock, coma, or even death.

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