Vaccine safety messages

This document is intended to support immunization programme managers and staff in their efforts to secure sustainable funding for immunization.

HOW TO USE THIS DOCUMENT

Many people are concerned about the safety of vaccines and fear side effects, and decision-makers and partners may ask questions about this.

This document presents key messages concerning vaccine safety and adverse events following immunization (AEFI). Some supporting facts and data are also provided.

The document was developed based on the *WHO Global Manual on Surveillance of Adverse Events Following Immunization, 2014, and the WHO Vaccine Safety Basics Learning Manual, 2013*. You can refer to these materials for more information.

You can use the messages when asked about the safety of vaccines. With the background tables you can also use it to prepare for a meeting and know the facts about vaccine safety.

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Vaccine safety messages

What kind of events can happen after vaccination?

There are five categories of Adverse Events Following Immunization (AEFI):

1. Reactions caused by the inherent properties of the vaccine product.
2. Reactions caused by a quality defect in the vaccine.

→ EVENTS CAUSED BY REACTIONS TO THE **VACCINE CONSTITUENTS**

3. Inappropriate vaccine handling, prescribing or administration of the vaccine.

→ EVENTS CAUSED BY AN **ERROR**

4. Anxiety-related reaction.
5. Coincidental event.

→ EVENTS CAUSED BY **OTHER FACTORS**

Below you will find suggested messages related to each of these kinds of AEFIs. Some supporting facts and data are also provided in tables.

TIP

If you would like to learn more about AEFIs, refer to

- WHO Global Manual on Surveillance of Adverse Events Following Immunization, 2014: http://www.who.int/vaccine_safety/publications/aefi_surveillance/en/.
- WHO Vaccine Safety Basics Learning Manual, 2013:
  English: http://www.who.int/vaccine_safety/initiative/tech_support/ebasic/en/
  Russian: http://ru.vaccine-safety-training.org.

TIP

To know more about potential reactions caused by the vaccine product, refer to the WHO vaccine information sheets posted here: http://www.who.int/vaccine_safety/initiative/tools/vaccinfosheets/en/.

The info sheets provide a summary of the vaccine products in common use, and the rates of mild and severe adverse events (local and systemic) following immunization.

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Messages concerning events caused by reactions to the vaccine constituents

Vaccine reactions

- Most vaccine reactions are minor and temporary, such as a sore arm or mild fever.
- Any serious injury or death caused by a vaccine is a tragedy. Fortunately, such events are extremely rare. **(Table 1)**
- The dangers of vaccine-preventable diseases are far greater than any risks associated with vaccines. **(Table 2)**

Vaccine regulations

- Vaccines are safe, no matter which country they are produced in.
- Some vaccines are slightly more reactogenic than others. But vaccines are highly regulated and considered safe.
- Vaccine regulation includes a range of functions that cover the entire process from vaccine development through licensure to use.
  - Before licensure, vaccines undergo extensive testing and review for safety, immunogenicity and efficacy in the laboratory, in animals and in three phases of clinical trials in human subjects.
  - Monitoring adverse vaccine reactions is a major safety component of pre-licensure clinical trials. **(Table 3)**
  - Even after the vaccine has been approved, safety monitoring continues. **(Table 4)**
  - In addition, WHO's Global Advisory Committee on Vaccine Safety (GACVS) regularly reviews the safety of vaccines.

Messages concerning events caused by an error

Error-related events

- Error-related events are by nature preventable.
- Some error-related events are serious, some are minor and temporaly. **(Table 5)**

Avoiding errors

- In our country, great effort is invested in ensuring that error-related reactions do not happen.
- Most error-related reactions can be avoided by proper planning and preparedness of programme managers and vaccinators.
- Actions taken to avoid errors include the following.
  - Vaccinators are trained and closely supervised – so that they are equipped to store, handle, reconstitute and administer vaccines correctly.
  - The cold chain is maintained at all levels.
  - Only diluents supplied by the manufacturer are used.
  - Vaccines are not stored together with other medicines or substances (other than diluents).
  - Vaccinators make sure that the vacinee is fit to be vaccinated (i.e. no contraindications).
  - Proper syringes must be used. The use of syringes that can only be used once (auto-disable syringes) minimizes the risk of infection.
  - Any serious or unexpectedly severe AEFI is immediately and meticulously investigated to identify the cause and to correct practices accordingly.

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Messages concerning events caused by other factors

Being vaccinated can cause an anxiety-related reaction

- In anticipation of or as a result of **any** injection, individuals can experience fear or anxiety-related reactions. These can include symptoms such as fainting, hyperventilation, vomiting, convulsions, dizziness and headache.

- These are common and well-known reactions to **fear** of the injection and are not related to the vaccine itself.

A reaction can be strictly coincidental

- Vaccinations are often scheduled in infancy and childhood, when other illnesses are common, or to protect the fragile health of older adults.

- Taking into account normal incidence of disease and death in these age groups, such unfortunate events will sometimes happen shortly after vaccination. **(Table 6)** This becomes especially evident during a mass campaign when many people are vaccinated.

- At first sight, the public and media, and maybe even health care workers, may see a causal link between the vaccine and the event, even when such a link does not exist.

- In our country, any serious or unexpectedly severe adverse event following immunization is immediately and meticulously investigated to determine whether it was caused by the vaccine or simply an unfortunate coincidental event.

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Message: Very serious events following immunization are extremely rare

Table 1: Frequency of vaccine adverse reactions of commonly used vaccines

BCG VACCINE SUMMARY	
VACCINE ADVERSE REACTIONS	**FREQUENCY CATEGORY**
• Injection site reaction (Papule, mild ulceration orscar)	Very common
• Suppurative lymphadenitis	Uncommon to Rare
• BCG osteitis	Uncommon to Very rare
• Disseminated BCG disease or systemic BCG-itis	Very Rare
• Immunine Reconstitution Inflammatory Syndrome (IRIS)	Very Rare

MEASLES VACCINES SUMMARY	
VACCINE ADVERSE REACTIONS	**FREQUENCY CATEGORY**
• Fever	Common to Very common
• Rash	Common
• Injection site reaction	Very common
• Febrile seizures	Rare
• Encephalomyelitis	Very rare
• Thrombocytopenia	Very rare
• Anaphylaxis	Very rare

RUBELLA VACCINES SUMMARY	
VACCINE ADVERSE REACTIONS	**FREQUENCY CATEGORY**
• Fever	Common
• Injection site reaction	Very common
• Acute Arthralgia (adults)	Very common
• Acute Arthritis (adults)	Very common

MUMPS VACCINES SUMMARY	
VACCINE ADVERSE REACTIONS	**FREQUENCY CATEGORY**
• Injection site reaction	Very common
• Parotid swelling	Common
• Aseptic meningitis	Very common

ROTAVIRUS VACCINES SUMMARY	
VACCINE ADVERSE REACTIONS	**FREQUENCY CATEGORY**
• Intussusception	Very rare

DTP VACCINES SUMMARY	
VACCINE ADVERSE REACTIONS	**FREQUENCY CATEGORY**
Whole cell Pertussis vaccines	
• Fever 37.8°C - 38.9°C	Very common
• Injection site Redness	Very common
• Swelling	Very common
• Pain (Severe-Moderate)	Very common
• Fussiness (Severe-Moderate)	Very common
• Drowsiness	Very common
• Anorexia	Very common
• Vomiting	Common
• Persistent screaming	Uncommon to Rare
• Hypotonic-hyporesponsive episode (HHE)	Very rare
• Seizures	Very rare
• Encephalopathy	Very rare
• Anaphylaxis	
A cellullar Pertussis vaccines	
• Fever 37.8°C - 38.9°C	Common
• Injection site Redness	Common to Very common
• Injectionsite swelling	Common to Very common
• Pain (Severe-Moderate)	Uncommon to Common
• Fussiness (Severe-Moderate)	Common to Very common
• Drowsiness	Very Common
• Anorexia	Very Common
• Vomiting	Very Common
• Persistent screaming	Uncommon
• HHE	Rare
• Seizures	Very rare

HIB VACCINES SUMMARY	
VACCINE ADVERSE REACTIONS	**FREQUENCY CATEGORY**
• Fever	Common
• Injection site reaction	Very common

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Table 1 – continued

TETANUS VACCINES SUMMARY	
VACCINE ADVERSE REACTIONS	**FREQUENCY CATEGORY**
• Brachial neuritis	Very rare
• Anaphylaxis	Very rare

HEPATITIS B VACCINES SUMMARY	
VACCINE ADVERSE REACTIONS	**FREQUENCY CATEGORY**
• Fever	Common
• Headache	Common
• Injection site pain	Common to Very common
• Injection site redness	Common
• Injection site swelling	Common
• Anaphylaxis	Very rare

HUMAN PAPILOMA VACCINES (HPV) SUMMARY	
VACCINE ADVERSE REACTIONS	**FREQUENCY CATEGORY**
Bivalent HPV Vaccine	
• Fever	Common
• Headache	Very common
• Injection site pain	Very common
• Redness	Very common
• Swelling	Very common
• Rash	Uncommon
• Arthralgia	Very common
• Myalgia	Very common
• Fatigue	Very common
• Gastrointestinal disorders	Very common
Quadrivalent HPV Vaccine	
• Fever 37.8°C - 38.9°C	Very Common
• Injection site Redness	Common
• Injectionsite swelling	Common
• Pain (Severe-Moderate)	Common
• Fussiness (Severe-Moderate)	Common
• Drowsiness	Common
• Anorexia	Common
• Vomiting	Common
• Persistent screaming	Common
• HHE	Very common
• Seizures	Very rare

POLIO VACCINES SUMMARY	
VACCINE ADVERSE REACTIONS	**FREQUENCY CATEGORY**
Whole cell Pertussis vaccines	
• Vaccine – associated paralytic paralysis (VAPP) – Recipient VAPP – Total VAPP	 Very Rare Very Rare
Inactivated Polio Vaccine (IPV)	
• Injection site erythema	Uncommon to Common
• Injection site induration	Common to Very common
• Injection site tenderness	Very Common

PNEUMOCOCCAL VACCINES SUMMARY	
VACCINE ADVERSE REACTIONS	**FREQUENCY CATEGORY**
Unconjugated vaccine (PPSV)	
• Fever > 39°C	Uncommon
• Injection site reaction	Very common
Conjugated vaccine (PCV)	
• Fever > 39°C	Uncommon
• Injection site reaction	Very common

VARICELLA VACCINES SUMMARY	
VACCINE ADVERSE REACTIONS	**FREQUENCY CATEGORY**
• Febrile seizures	Rare
• Fever > 39°C	Very Common
• Injection site reaction	Common to Very Common
• Site rash (local/generalized	Common

YELLOW FEVER VACCINES SUMMARY	
VACCINE ADVERSE REACTIONS	**FREQUENCY CATEGORY**
• Vaccine-associated viscerotropic disease	Very rare

KEY		
Very common	> 1/10	> 10%
Common	> 1/100 and < 1/10	> 1% and < 10%
Uncommon	> 1/1000 and < 1/100	> 0.1% and < 1%
Rare	> 1/10 000 and < 1/1000	> 0.01% and < 0.1%
Very rare	< 1/10 000	< 0.01%

Source: WHO Global Manual on Adverse Events Following Immunization, 2014.

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Message: The dangers of vaccine-preventable diseases are far greater than any risks associated with vaccines.

Table 2: Serious health risks following infection vs following vaccination

	MEASLES INFECTION (A)	MEASLES VACCINE (B)
Death	0.1 – 1/1000 (up to 5 – 15%)	0
Post-infectious encephalomyelitis (inflammation of the brain and spinal cord)	0.5/1000	1/100 000–million
Subacute sclerosing panencephalitis (chronic brain inflammation)	1/100 000	0
Pneumonia	1 – 6%	0
Otitis (middle ear infection)	7 – 9%	0
Diarrhoea	6%	0
Anaphylaxis (serious allergic reaction)	0	1/100 000–million
Thrombocytopenia (deficiency of platelets in the blood)	Not properly quantified (c)	1/30 000 (d)

a. Risks after natural measles are calculated in terms of events per number of cases.
b. Risks after vaccination are calculated in terms of events per number of doses.
c. Although there have been several reports of thrombocytopenia occuring after measles including bleeding, the risk has not been property quantified.
d. This risk has been reported after measles – mumps – rubella (MMR) vaccination and cannot be only attributed to the measles component.
Source: WHO Vaccine Safety Basics Learning Manual, 2013, adopted from P. Duclos, BJ Ward. Measles Vaccines, A Review of Adverse Events, Drug Safety 1998; Dec 19 (6): 435-454.

Message: Vaccines undergo extensive testing and review before licensure

Table 3: The process of clinical trials and assessment of vaccine safety

	ACTIVITY	SAMPLE SIZE (ESTIMATES)
Clinical Trial Phase I	Test the safety and immunogenicity of a vaccine candidate in a few low-risk individuals (usually healthy adults) to determine tolerability.	10 – 100
Clinical Trial Phase II	Monitor safety, potential side effects, immune response, and determine optimum dosage and schedule.	100 – 1000
Clinical Trial Phase III	Address clinical efficacy in disease prevention and provide further safety information from more heterogeneous populations and longer times of observation.	1000 – 10 000
Submission	The vaccine application is submitted to regulatory authorities for approval to market.	—
Introduction	Involves making the vaccine available for use.	—

Source: WHO Vaccine Safety Basics Learning Manual, 2013.

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Message: After the vaccine has been approved, monitoring continues

Table 4: Surveillance used to monitor the safety of vaccines after licensing

Reporting from health care workers and patients	Spontaneous reporting from health care workers is the cornerstone of most post-licensure safety monitoring systems because of its ability to capture unexpected events.
Clinical trials	Vaccines may undergo clinical trials after licensure to assess the effects of changes in vaccine formulation, vaccine strain, age at vaccination, number and timing of vaccine doses, simultaneous administration and interchangeability of vaccines from different manufacturers on vaccine safety and immunogenicity.
Surveillance studies	To improve the ability to detect adverse events that are not detected during pre-licensure trials, some recently licensed vaccines in developed countries have undergone formal surveillance studies, involving cohorts as large as 100 000 and lasting four to six years.
Linked databases	Large linked databases (LLDBs) are large administrative databases from defined populations that are linked to enable the sharing of data across platforms. These databases have become useful to vaccine safety surveillance: covering populations numbering from thousands to millions, they can detect very rare adverse events.
Clinical centres	Several clinics work to monitor immunization safety; address the gaps in scientific knowledge about rare and serious events following immunization; and conduct research e.g. on immunization-associated health risks; immunization-associated health risks and vaccine adverse events and the role of individual variation.

Source: WHO Vaccine Safety Basics Learning Manual, 2013.

Message: Some error-related events are serious, some are mild and temporary

Table 5: Examples of immunization errors and possible AEFIs

IMMUNIZATION ERROR	POSSIBLE AEFI
NON-STERILE INJECTION • **Reuse of disposable syringe or needle leading to contamination of the vial, especially in multi-dose vials** • **Improperly sterilized syringe or needle** • **Contaminated vaccine or diluent**	• Local injection site reactions (e.g., abscess, swelling, cellulitis, induration) • Sepsis • Toxic shock syndrome • Blood-borne transmission of disease, e.g., hepatitis B, HIV • Death
RECONSTITUTION ERROR • **Inadequate shaking of vaccine** • **Reconstitution with incorrect diluent** • **Drug substituted for vaccine or diluent** • **Reuse of reconstituted vaccine at subsequent session**	• Local abcess • Vaccine ineffective (not strictly an AEFI, but a vaccine failure) • Effect of drug, e.g., insulin, oxytocin, muscle relaxants • Toxic shock syndrome • Death
INJECTION AT INCORRECT SITE • **BCG given subcutaneously** • **DTP/DT/TT too superficial** • **Injection into buttocks**	• Local reaction or abscess or other local reaction • Local reaction or abscess or other local reaction • Sciatic nerve damage
Vaccine transported/stored incorrectly	• Increased local reaction from frozen vaccine • Ineffective vaccine (vaccine failure)
Contraindication ignored	• Avoidable severe reaction

Source: WHO Vaccine Safety Basics Learning Manual, 2013.

Message: Taking into account normal incidence of disease and death in the relevant age groups, coincidental events are inevitable when vaccinating

Table 6: Example of expected coincidental deaths following DTP vaccination (selected countries)

COUNTRY	INFANT MORTALITY RATE PER 1000 LIVE BIRTHS (IMR)	NUMBER OF BIRTHS PER YEAR (N)	NUMBER OF INFANT DEATH DURING YEAR IN		
			Month after immunization	Week after immunization	Day after immunization
			=(IMRxN/12)×nv×ppv	=(IMR×N/52)×nv×ppv	=(IMR×N/365)×nv×ppv
Australia	5	267 000	300	69	10
Cambodia	69	361 000	5605	1293	185
China	18	18 134 000	73 443	16 948	2421
Japan	3	1 034 000	698	161	23
Laos	48	170 000	1836	424	61
New Zealand	5	58 000	65	15	2
Philippines	26	2 236 000	13 081	3019	431

Note: Assumes uniform distribution of deaths and children who are near to death will still be immunized.
nv = number of immunization doses: assumed here to be three dose schedule; 3.
ppv= proportion of population vaccinated: assumed here to be 90% for each dose; 0.9.
Source: Infant mortality and births from 2008 Immunization summary, WHO/UNICEF (The 2010 edition).