



**World Health
Organization**

REGIONAL OFFICE FOR **Europe**

Questions and Answers for health professionals on seasonal inactivated influenza vaccines*

Where to obtain more information on influenza?

The WHO Global Influenza Programme (GIP) provides Member States with strategic guidance, technical support and coordination of activities essential to make their health systems better prepared against seasonal, zoonotic and pandemic influenza threats to populations and individuals. Its web pages provide access to relevant documents and updates and can be accessed at: <http://www.who.int/influenza/en/>

The WHO Regional Office for Europe provides information pertinent to the Member States in its Region at:

<http://www.euro.who.int/en/what-we-do/health-topics/communicable-diseases/influenza>

Where to obtain more information on influenza vaccines?

In accordance with its mandate to provide guidance to Member States on health policy matters, WHO publishes vaccine position papers providing global vaccine and immunization recommendations for diseases that have an international public health impact. The papers summarize essential background information on the respective diseases and vaccines, and conclude with the current WHO position concerning their use in the global context. The WHO position paper on influenza vaccines is available at:

<http://www.who.int/wer/2005/wer8033.pdf>

Information on virus strain selection and regulatory issues are addressed at:

<http://www.who.int/influenza/vaccines/virus/en/>

<http://www.who.int/biologicals/publications/trs/areas/vaccines/influenza/en/index.html>

<http://www.who.int/biologicals/vaccines/influenza/en/index.html>

<http://www.who.int/influenza/vaccines/use/en/>

How long does it take to produce the seasonal influenza vaccine?

From the point of publication of recommended composition of influenza virus vaccines for use in the coming northern or southern hemisphere season, it takes approximately six months to produce the vaccine and release it for the use by the respective national regulatory authority.

What is the difference between pandemic and seasonal influenza vaccines?

The difference is in selection of the virus strain prompted by occurrence of a novel strain that is deemed to have pandemic potential and to which the population is naive. Pandemic vaccines tend to be monovalent, whereas the seasonal vaccines are trivalent and containing two A and one B influenza strain.

* Note: this document does not include questions and answers regarding *live attenuated* influenza vaccine

What is the composition of inactivated seasonal influenza vaccines?

The composition varies by product. In general, inactivated seasonal influenza vaccines contain: whole virion, split virion or virion subunits of the three selected strains. The virus is either propagated in fertilized chicken eggs or on a cell culture. Vaccines may include one or more of the following excipients include: buffers, residuals of growth medium (e.g. ovalbumin), residuals of antibiotics used on the growth medium (e.g. gentamycin, neomycin), inactivator residuals (e.g. formaldehyde, β -propiolactone), residuals of a splitting agent (e.g. octoxynol, polysorbate), stabilizers (e.g. gelatine), adjuvant (e.g. MF59), preservative (e.g. thiomersal).

Are seasonal influenza vaccines safe?

Seasonal influenza vaccines have been in use for more than 50 years and have a good safety record. National medicines regulatory authorities carefully examine the known and suspected risks and benefits of any vaccine prior to its licensing. Seasonal influenza vaccines are evaluated annually, given that their composition changes almost every year. The strengthening of post-marketing surveillance systems in recent years has enabled better recognition and reporting of adverse events following influenza immunization. Expansion of influenza immunization programmes to other priority groups or the general population has also allowed for better characterization of the products and expanded the understanding of the vaccine safety profile.

How should vaccine reactions be reported?

Countries have varying systems for drug or vaccine reaction reporting, which may be used by health care professionals only and/or by vaccine recipients, or their parents in the case of children. Reports are submitted to national vaccine- or pharmaco-vigilance centres using different methods, including using the Internet in some countries. Reports of serious events and those raising concerns should always be submitted to national authorities, as this is a prerequisite for safety evaluation.

What happens once an adverse event report following immunization is sent to the responsible national authority?

Individual reports are scrutinized for completeness of provided information and possible errors. In some instances, reports need to be validated, additional information requested and checked to see if provided information meets case definitions for certain conditions. Reports are stored in databases and analysed for any unexpected findings or unusual frequency of expected events. If the analysis outcomes indicate any potential problem, further studies and evaluation are conducted and all relevant national and international authorities informed. Once conclusions are reached, decisions are made on appropriate measures to ensure continuing use of the vaccine is safe.

Who should not have seasonal inactivated influenza vaccine?

Package inserts provide information on contraindications for specific vaccine product. As a general rule seasonal inactivated influenza vaccines should not be administered to:

- individuals with a history of anaphylaxis or other life-threatening allergic reactions to any of the constituents or trace residues of the vaccine;
- people with a history of a severe reaction to previous influenza vaccination;
- people who have previously developed Guillain-Barré syndrome (GBS) within six weeks of getting an influenza vaccine;

- children less than six months of age (inactivated influenza vaccine is not approved for this age group); and
- people who have a moderate-to-severe illness with a fever (they should wait until they recover to get vaccinated).

What are the expected side effects of influenza vaccines?

Different side effects can be associated with influenza vaccination. Their frequency depends on the type of vaccine, method of administration and age of vaccine recipient.

Inactivated vaccines commonly cause local reactions at injection site (soreness, swelling, redness) and may cause systemic reactions (fever, muscle or joint aches, headache). These symptoms are generally mild, self-limited and last 1-2 days. Systemic symptoms may occur more frequently in children compared to the elderly.

Rarely, influenza vaccines can cause allergic reactions such as hives, angioedema (rapid swelling of deeper skin layers, mucosa and submucosal tissues), asthma or anaphylaxis (severe multisystem allergic reaction) due to hypersensitivity to certain vaccine components.

What about safety for pregnant women?

Pregnant women are at increased risk for serious consequences from influenza. Immunizing pregnant women protects them against severe outcomes of the disease and also provides protection for the newborn. No specific risks have been identified with use of seasonal influenza vaccines during any of the pregnancy trimesters, and influenza vaccination is considered safe.

How do children react to influenza vaccine?

The most frequent vaccine reactions in children following influenza immunization are similar to those seen after other childhood immunizations (such as soreness at the injection site or fever). A child's health care provider or vaccinator can advise on the most appropriate methods for relief of the symptoms. If there are concerns about a child's safety from a reaction, consult a health care provider as soon as possible. Please note that a child may suffer from a condition not related to immunization, which coincidentally develops after vaccination.

Is there a risk of catching illness from the vaccine itself?

Inactivated vaccines contain killed virus or parts of virus, which cannot cause disease. The vaccines may cause some side-effects, which may also be seen with influenza disease, i.e. muscle ache or fever, but these symptoms, sometimes associated with vaccination, are generally less pronounced and of much shorter duration.

Why do some people who have been vaccinated still get influenza?

No vaccine provides 100% protection against disease, but they do greatly reduce the risk of disease. Furthermore influenza vaccines only become effective about 14 days after vaccination, therefore those infected shortly before (1-3 days) or shortly after immunization may still get the disease. Vaccinated individuals may also get influenza caused by a different strain of influenza virus for which the vaccine does not provide protection. It is not possible to predict exactly which strains of influenza virus will circulate in a given season (with an additional six-month time-lag between advice being given on a vaccine strain and first production of that vaccine). People who have received influenza vaccine may subsequently have an illness, caused by other common viruses, that is mistaken for influenza, and they falsely believe that the vaccine failed to protect them or that vaccine had caused the disease.

Do seasonal inactivated influenza vaccines contain thiomersal, which some believe is a risk to health?

Thiomersal is a commonly used vaccine preservative to prevent vaccine contamination by bacteria during use. Inactivated vaccines will contain thiomersal if they are supplied in multi-dose vials. Some products can have "traces" of thiomersal when the chemical is used during the production process as an antibacterial agent, which is later removed during the purification process.

Thiomersal does not contain methyl mercury, which is a naturally occurring compound whose toxic effects on humans have been well studied. Thiomersal contains a different form of mercury (i.e. ethyl mercury, which does not accumulate, is metabolized and removed from the body much faster than methyl mercury).

Scientific groups have rigorously reviewed the safety of thiomersal. There is no evidence of toxicity in infants, children or adults, including pregnant women, exposed to thiomersal in vaccines. More information is available at:

http://www.who.int/vaccine_safety/topics/thiomersal/en/index.html

Why do some seasonal inactivated influenza vaccines contain adjuvants and others don't?

Adjuvants are substances that enhance the immune response in vaccines and can make them more effective. They have been used for many years in some vaccines. Some seasonal influenza vaccines that are intended for people known to have poor immune responses to immunization contain an adjuvant. Manufacturers decide whether a product is formulated with or without an adjuvant. Adjuvants used with seasonal inactivated influenza vaccines are already licensed for use over two decades or are licensed with other vaccines (e.g. hepatitis B) and have a safe track record.

Can influenza vaccination cause chronic diseases?

Current evidence does not indicate that seasonal inactivated influenza vaccines either induce or aggravate the course of chronic diseases in vaccine recipients. Careful assessment is required to clarify whether adverse events that occur after vaccination are actually caused by an influenza vaccination.

Can influenza vaccination cause Guillain Barré syndrome?

Guillain Barré syndrome (GBS) is a rapidly developing, immune-mediated disorder of the peripheral nervous system that results in muscular weakness. Most people recover completely but some have chronic weakness. It can develop following a variety of infections, including influenza. In people who have been immunized with available vaccines, the frequency of GBS usually is the same as in unvaccinated people. Extensive studies and data analysis of influenza vaccines have only found a well-established causal association with the 1976 vaccine that contained an H1N1 swine-influenza-like virus. No other clear association has been found with either seasonal or pandemic influenza vaccines.