

Vaccine components

Summary

Vaccines contain an active component (the antigen) which induces the immune response. They may also contain additional components such as preservatives, additives, adjuvants and traces of other components. This fact sheet provides information about vaccine components including why they are present, and what, if any, risks these components may pose to vaccine recipients.

The following commonly asked questions are answered below. More general information on the vaccine components is also available by following the links in 'Further reading'.

- What are the individual components in vaccines and why are they present?
 1. Active components
 2. Adjuvants
 3. Diluents
 4. Stabilisers
 5. Preservatives
 6. Trace components
- Do allergies to vaccines or vaccine components occur?
- Which vaccines contain animal-derived products and are there any alternatives?
- Which vaccines have used human tissue sources in their production?

What are the individual components in vaccines and why are they present?

1. Active components

The active component of a vaccine is known as the vaccine 'antigen'. This is a modified or partial form of the virus, bacteria or the toxin that causes the disease against which the vaccine protects. The vaccine antigen is altered from its original form so it no longer causes disease but it can produce an immune response. There are a number of ways this is achieved:

Attenuated live viruses

Natural or 'wild type' viruses cause disease by reproducing themselves many millions of times in the body's cells. In some vaccines where live virus is used, the virus has been treated and weakened (attenuated) in such a way that, when it is introduced to the body in the form of a vaccine, it induces an immune response without causing severe disease. The advantage of live, attenuated vaccines is that one or two doses usually provide lifelong immunity. Examples of attenuated live viral vaccines are the varicella, rotavirus and measles-mumps-rubella (MMR) vaccines.

Inactivated viruses

Some viruses or parts of viruses in vaccines are killed (inactivated) with a chemical such as formaldehyde. The killed virus cannot possibly reproduce itself or cause disease. The advantage of vaccines produced in this way is that the body still recognises the virus and produces an immune response. Because no viral replication occurs, these vaccines can be given to people with weakened immunity. The only disadvantage of these types of vaccines is that, generally, several doses must be given to achieve long-term immunity, but persons with weakened immunity may not respond to even multiple doses. Examples of inactivated vaccines are the inactivated poliomyelitis, influenza and hepatitis A vaccines.

Use part of the virus or bacterium

The hepatitis B, *Haemophilus influenzae* type b (Hib), and human papillomavirus (HPV) vaccines are examples of vaccines where only part of the virus or bacterium is used. The part of the virus or bacterium required to 'induce immunity' is identified and separated from the part which causes disease symptoms. In the case of hepatitis B, the vaccine is composed of a protein that resides on the surface of the virus. In the case of the *Haemophilus influenzae* type b (Hib) vaccine, only the outer coat, or polysaccharide, is used, joined on (conjugated) to a protein so that the immune system responds to it. These vaccines can be administered to people with weakened immunity, although, if the person's immune system is too weak, they may not develop a satisfactory immune response.

Use a toxin produced by the bacteria

Some vaccines are manufactured by chemically inactivating specific bacterial toxins. The inactivated toxin is then referred to as a toxoid and used to produce a vaccine, for example, diphtheria and tetanus-containing vaccines. In the case of tetanus infection, exposure to very little tetanus toxin is sufficient to cause disease, whereas only a small amount of the tetanus toxoid in the vaccine will induce a good immune response and cannot cause disease. Having tetanus infection does not induce a long-term immune response and non-immune individuals who contract tetanus must be fully vaccinated to protect against future exposure. The only way to be protected against tetanus and diphtheria is to be vaccinated using several doses of the appropriate vaccine.

2. Adjuvants

Adjuvants are used to enhance the immune response to a vaccine. They include various aluminium salts such as aluminium hydroxide, aluminium phosphate and potassium aluminium sulphate (alum). One way adjuvants are thought to improve the immune response is by keeping the antigen(s) near the injection site so that they can be readily accessed by cells of the immune system. The use of aluminium adjuvants in vaccines generally means that less antigen per dose of vaccine is required, and, in some cases, fewer vaccine doses are needed. The presence of adjuvants in vaccines can often be associated with the local reactions that occur at the injection site after vaccination.

Aluminium salts, in small amounts, have been added to certain vaccines for about 60 years and a recent review of all the available studies of aluminium-containing diphtheria, tetanus and pertussis vaccines (either alone or in combination) found that there was no evidence that aluminium salts in vaccines cause any serious or long-term adverse events. The exposure to aluminium from vaccines is far less than that received from diet or medications, such as some antacids. Although aluminium-containing vaccines have been associated with local reactions and, less often, with the development of subcutaneous nodules at the injection site, other studies have reported fewer reactions with aluminium-containing vaccines than those without aluminium.

3. Diluents

A diluent is a liquid provided separately and used to dilute a vaccine to the proper concentration prior to administration. This is usually sterile saline or sterile water.

4. Stabilisers

Additives are used as stabilisers and help maintain a vaccine's effectiveness by keeping the antigen and other vaccine components stable during storage. Stabilisers prevent the vaccine components adhering to the side of the vaccine vial. Examples of additives include lactose and sucrose (both sugars), glycine and monosodium glutamate (both of which are amino acids or salts of amino acids), and human or bovine (cow) serum albumin (both proteins). Gelatin, which is partially hydrolysed collagen, usually of bovine (cow) or porcine (pig) origin, is added to some vaccines as a stabiliser. Some members of the Islamic and Jewish faiths object to vaccination on the basis that some vaccines contain porcine-derived products. However, these concerns have been addressed by religious scholars (see 'Which vaccines contain animal-derived products and are there any alternatives?' below). An anaphylactic allergy to gelatin is a contraindication to vaccination with certain vaccines (see 'Do allergies to vaccines or vaccine components occur?' below).

5. Preservatives

Preservatives are used to prevent fungal and/or bacterial contamination of vaccines, and are present in some but not all vaccines. Originally, preservatives were introduced to prevent bacterial contamination of multi-dose vials. However, multi-dose vials are no longer used routinely in Australia. The preservatives used include thiomersal, phenoxyethanol and phenol. Thiomersal (also known as thimerosal) is a mercury-containing compound that is discussed in detail in the National Centre for Immunisation Research and Surveillance (NCIRS) [Thiomersal fact sheet](#).

Phenoxyethanol is an aromatic ether alcohol and is also used as a preservative in many cosmetics. There has been one case report suggesting that this preservative may be associated with eczema. However, this link has not been supported in other studies. Phenol is an aromatic alcohol used as a preservative in very few vaccines. Preservatives have been used in many vaccines and worldwide there have been very few serious adverse events associated with the use of these preservatives.

6. Trace components

Trace components are the remaining minute quantities of substances that have been used in the early stages of the production process of individual vaccines. Depending on the manufacturing process used this may include trace amounts of cell culture fluids, egg proteins, yeast,

antibiotics or inactivating agents. Usually, only minute traces of these substances are detected in the final vaccine product.

Antibiotics are sometimes used during the manufacturing process to ensure that bacterial contamination does not occur during the manufacturing process. Neomycin and/or polymyxin B are used in the manufacture of vaccines such as varicella (chickenpox) vaccines, some influenza vaccines, DTPa-combination vaccines and measles-mumps-rubella vaccine. Gentamicin is used in the manufacture of some influenza vaccines. No β -lactam or cephalosporin antibiotics are used in the manufacture of any vaccines currently used in Australia. Any individual with a severe allergy to any antibiotic or chemical who presents for vaccination should be appropriately assessed by the immunisation provider. The product information relating to each vaccine must be scrutinised for specific vaccine components before administering any vaccine to these individuals.

Inactivating agents are used during the manufacture of killed and toxoid vaccines. The bacteria, virus or toxin is inactivated during the manufacturing process but the antigenic components remain intact. The residual amount of these inactivating agents, for example formaldehyde or glutaraldehyde, in the final vaccine is very small.

Certain vaccines, such as influenza vaccines, may contain traces of egg proteins as the virus to be used for the vaccine is grown in actual chicken eggs before it is inactivated. Measles and mumps (but not rubella or varicella) vaccine viruses are grown in chick embryo tissue cultures and it is now recognised that MMR (and MMRV) vaccines contain negligible amounts of egg protein and can be safely given to children with egg allergy, even anaphylactic egg allergy. Other vaccines, such as the hepatitis B vaccines, hepatitis B-combination vaccines and human papillomavirus (HPV) vaccines, are manufactured using yeast. Production steps such as filtering and centrifugation greatly reduce the amounts of all of these products in the final vaccine; however, trace amounts may still be present.

Do allergies to vaccines or vaccine components occur?

Vaccines rarely produce allergy or anaphylaxis (a rapid and serious form of allergic reaction). Overall, the total risk of anaphylaxis in children and adolescents after one vaccination has been reported as <1 case per one million doses. Antibiotics, gelatin and egg proteins are the components most often implicated in these allergic reactions. Yeast has only rarely been associated with

vaccine-related allergic reaction. In addition, people allergic to latex are potentially at risk, not from the vaccine itself but the presence of latex in the equipment used to hold the vaccine such as vaccine vial stoppers (bungs) and syringe plungers. Very few vaccine bungs contain natural latex. The product information sheet should be consulted to check for the presence of latex.

It is important that immunisation providers assess each individual for a history of allergies and previous reactions to vaccines prior to giving any dose of vaccine. However, depending on the allergy identified, there may often NOT be a contraindication to vaccination. For example, a history of an allergy to antibiotics most commonly relates to β -lactam or related antibiotics, and is not a contraindication to vaccines that contain neomycin, polymyxin B or gentamicin (see 'Trace components' above). Previous reactions to neomycin that just involved the skin are not considered a risk factor for anaphylaxis to vaccines manufactured with neomycin since there are only trace amounts of this antibiotic in the final product. Similarly, the measles and mumps components of MMR vaccine do not contain sufficient amounts of egg ovalbumin to contraindicate MMR vaccination of people with egg allergy (even anaphylaxis).

Where necessary, further advice should be sought from a medical practitioner with expertise in vaccination, the immunisation section within your State or Territory health authority, or your local Public Health Unit (see *The Australian Immunisation Handbook* Appendix 1, *Contact details for Australian, State and Territory Government health authorities and communicable disease control*). In addition, information about specialist immunisation clinics is available through state-based contacts listed in the most current edition of *The Australian Immunisation Handbook* or on the Immunise Australia Program website: <http://www.immunise.health.gov.au>. Information on how to access these clinics can be provided by your local health authority.

Immunisation providers are trained to provide treatment in the rare event that a severe allergic response occurs immediately following a vaccine dose.

Which vaccines contain animal-derived products and are there any alternatives?

Community concerns around animal products in vaccines generally fall into two categories:

1) religious or faith-based concerns about the use of animal-derived products, and 2) concern about the

possibility of animal diseases ‘crossing over’ to humans through use of vaccines.

1) Some vaccines utilise porcine (pork) products in the manufacturing process. This concern has been raised by some religious groups that have faith-based concerns about the consumption of pork. Scholars of these religions have various exceptions or rulings which allow the ‘ingestion’ of porcine or porcine-derived products in this context:

- For Muslims: Shariah law includes the principle of transformation in which unclean products can be made clean by extensive processing, thus making it permissible for observant Muslims to receive vaccines, even if the vaccines contain porcine gelatin (see ‘Stabilisers’ above).
- Judaism permits the use of non-edible forms of porcine products.
- Seventh-Day Adventists are not forbidden to use pork-derived medical products.

2) Bovine serum albumin or fetal calf serum is used in some vaccines and there were theoretical concerns that vaccines could be contaminated with variant Creutzfeldt-Jakob disease (vCJD). These theoretical concerns arose because the United Kingdom has documented rare cases of vCJD in humans following the ingestion of products from animals infected with bovine spongiform encephalopathy (BSE, also known as ‘mad cow disease’).

This question about vaccines and the use of bovine serum albumin has been addressed by the Australian Therapeutic Goods Administration (TGA), which requires that vaccine manufacturers adhere to strict standards and provide detailed information on the source of all materials used in the manufacturing process. These requirements include control on the source country of the animals used, the nature of the tissue used, and details of the manufacturing processes. In Australia, no case of vCJD from vaccines has been demonstrated and the TGA (after reports to the NHMRC Special Expert Committee on Transmissible Spongiform Encephalopathies) concluded that the vaccines used in Australia meet high safety standards and that any risk of transmission is theoretical only. Internationally, advisory bodies also consistently state that the potential risk to vaccine recipients is essentially non-existent.

Which vaccines have used human tissue sources in their production?

Certain viruses grown for use in vaccines require the use of ‘cell lines’. These cell lines (called human diploid cell lines – WI-38 and MRC-5) were originally derived from human fetal tissue. The vaccines manufactured using cell lines originally derived from fetal tissue include: rubella vaccine and MMR vaccine, hepatitis A vaccines, varicella vaccines, rabies vaccine, and oral polio (Sabin) vaccine (no longer available in Australia).

A fact sheet discussing the use of vaccines prepared using human cell lines is being developed by NCIRS.

Further reading

Aickin R, Hill D, Kemp A. Measles immunisation in children with allergy to egg. *BMJ* 1994; 309: 223–225.

Bohlke K, Davis RL, Marcy SM, et al. Risk of anaphylaxis after vaccination of children and adolescents. *Pediatrics* 2003; 112: 815–820.

Eldred BE, Dean AJ, McGuire TM, Nash AL. Vaccine components and constituents: responding to consumer concerns. *Medical Journal of Australia* 2006; 184: 170–175.

Jefferson T, Rudin M, Di Pietrantonj C. Adverse events after immunization with aluminium-containing DTP vaccines: systematic review of the evidence. *The Lancet Infectious Diseases* 2004; 4: 84–90.

Myths and realities: responding to arguments against immunisation. 4th edition. Canberra: Australian Government Department of Health and Ageing, 2008. Available at:

<http://immunise.health.gov.au/internet/immunise/publishing.nsf/Content/uci-myths-guideprov>

National Health and Medical Research Council (NHMRC). *The Australian Immunisation Handbook*. 9th edition. Canberra: Australian Government Department of Health and Ageing, 2008. Available at:

<http://immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook-home>

Offit PA, Jew RK. Addressing concerns: do vaccines contain harmful preservatives, adjuvants, additives, or residuals? *Pediatrics* 2003; 112: 1394–1401.

O’Hagan DT, Rappuoli R. The safety of vaccines. *Drug Discovery Today* 2004; 19: 846–854.

Thompson WW, Price C, Goodson B, et al. Early thimerosal exposure and neuropsychological outcomes at

7 to 10 years. *New England Journal of Medicine* 2007; 357: 1281–1292.

Additional web-based information (accessed December 2009)

Australian Government Department of Health and Ageing, Therapeutic Goods Administration. BSE risk associated with the use of materials of bovine origin during the manufacture of vaccines: questions and answers. 2007. Available at:

<http://www.tga.gov.au/docs/html/bsefaq.htm>

Department of Health and Children, Ireland. Possible questions regarding oral polio vaccine and human serum albumin/vCJD issue. 2000. Available at:

<http://www.dohc.ie/press/releases/2000/20001219b.html>

Johns Hopkins Bloomberg School of Public Health. Religious leaders approval of use of vaccines containing porcine gelatin. 2003. Available at:

<http://www.vaccinesafety.edu/Porcinevaccineapproval.htm>

National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases (NCIRS). Homeopathy and vaccination fact sheet. 2007. Available at: <http://ncirs.edu.au/immunisation/fact-sheets/homeopathy-fact-sheet.pdf>

National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases (NCIRS). Thiomersal fact sheet. 2009. Available at: <http://ncirs.edu.au/immunisation/fact-sheets/thiomersal-fact-sheet.pdf>

World Health Organization (WHO), Regional Office for the Eastern Mediterranean. Statement arising from a seminar held by the Islamic Organization for Medical Sciences on 'The judicially prohibited and impure substances in foodstuff and drugs'. 2001. Available at: <http://www.immunize.org/concerns/porcine.pdf>