



...for Parents and Caregivers



Immunisation
Advisory
Centre

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Vaccine Ingredients

Vaccine manufacture and composition is complex and tightly regulated to maximise safety. The safety of the individual components, and of the whole of the vaccine, is carefully assessed before a vaccine can be licensed in New Zealand.

All vaccines contain an active component (the antigen) which generates the protective immune response. Vaccines may also contain additional components if required. A description of these, their function and safety is summarised in this fact sheet.

Types of vaccines and vaccine antigens

The components of the vaccine that generate an immune response are called antigens. These are, depending on the type of vaccine, either weakened forms or fragments of the disease-causing organism. The body responds to the shapes of these antigens which are very specific. Vaccines can be broadly classified as either live, inactivated or subunit. Ingredients vary depending on both the manufacturing process and the nature of the antigen.

Bacteria and viruses each have unique methods of infecting people and replicating themselves. A variety of techniques are used to manufacture vaccines because "one size does not fit" for all bacteria or viruses.

- **Live vaccines:**
the vaccines are live and can replicate in the body several times. The virus or bacteria has been weakened so it cannot cause the disease (e.g. measles, mumps and rubella).
- **Inactivated vaccines:**
made from killed bacteria or virus.
- **Subunit vaccines:**
use fragments such as proteins, toxoids or sugars (polysaccharides) derived from the disease-causing organism. Most vaccines on the current NZ schedule are subunit.

Vaccine additives

Vaccines may contain the following (if required):

- Adjuvant (Immune enhancer).
- Excipients - usually an inert substance other than the active ingredient included in the manufacturing process or contained in a finished pharmaceutical product.

Preservatives
Stabilisers
Buffers
Diluents
Residuals

Adjuvants

Inactivated and subunit vaccines usually require an immune enhancer called an adjuvant that helps promote a stronger immune response to the antigen.

Aluminium Salts

Aluminium salts have been used as adjuvants for over 70 years. Most commonly these are aluminium hydroxide, aluminium phosphate and potassium aluminium sulphate (alum). Aluminium adjuvants work by inducing a range of inflammatory factors to the local injection site and also appear to help retain the antigen at the injection site long enough for an immune response to be generated. Most of our current inactivated and subunit vaccines use aluminium salts and they have an impressive safety record. Additionally, the use of aluminium adjuvants in vaccines generally means that less antigen is required.

Some studies have found aluminium containing vaccines to be associated with local reactions and, less often, with the development of subcutaneous nodules at the injection site. This is particularly so if the injection is given too superficially. Other studies have reported fewer reactions with aluminium-containing vaccines than those without, and in some cases, fewer vaccine doses are needed.

An individual's exposure to aluminium from vaccines is far less than that received from a normal diet. Aluminium is the 8th most abundant element on earth and the most common metallic element. It is found in the blood of all animals, including humans, and we are constantly exposed to it. The average daily intake is 10-15mg. The Hep B vaccine has 0.235mg of aluminium; average water has about 0.2mg of aluminium per litre. Aluminium in vaccines is absorbed into the blood and excreted in urine via kidneys. 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.

MF59

MF59 is an oil in water emulsion. It is made with squalene (a hydrocarbon oil) which is common in foods as well as being produced in the body as precursor to cholesterol and steroid hormones. MF59 significantly enhances immune response to a variety of antigens. It is used in some influenza vaccines, pandemic vaccines and is being trialled in newer vaccines.

Preservatives

Preservatives stop unwanted microbial contamination of vaccines. They have been used in many vaccines for many years. There have been very few serious adverse events associated with the use of these preservatives.

Phenoxyethanol

The most commonly used preservative in vaccines is phenoxyethanol. It is also used in cosmetics, baby care products, eye and ear drops etc. Phenoxyethanol is absorbed through skin and excreted by being exhaled as well as being metabolised (broken down) and excreted via the urine and faeces. There is little toxicity in humans and some irritation with very high doses in animals. A volunteer once ingested 11mg of phenoxyethanol and excreted it in 2-3 days with no ill effects. (Toxicol Appl Pharmacol. 2002 Apr 15; 180(2):74-82. WHO FOOD ADDITIVES SERIES: 50)

Phenol

An aromatic alcohol used infrequently as a preservative in vaccines.

Thiomersal

A mercury derived compound that has been used in vaccines and other health care products internationally for many years. It is no longer present in the vaccines on the New Zealand childhood schedule. For more information about thiomersal see the IMAC thiomersal fact sheet and website. There is no evidence that thiomersal causes serious adverse events.

Stabilisers

Stabilisers inhibit chemical reactions and prevent components separating or sticking to the vial during transport and storage. Examples of stabilisers include sugars such as lactose and sucrose, amino acids such as glycine and monosodiumglutamate (salts of amino acids), albumin which is a protein derived from 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.

Buffers

Buffers serve to resist changes in pH, adjust tonicity and maintain osmolarity. The most commonly used buffer is sodium chloride (table salt).

Diluents

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

Surfactants/emulsifiers

Surfactants or emulsifiers are wetting agents that alter the surface tension of a liquid and lower the tension between two liquids - like detergent. An example is Polysorbate 80 (Tween®) which is often used in foods such as ice cream. It is made from Sorbitol (sugar alcohol) and Oleic Acid (omega fatty acid).

Residuals

Residuals are the remaining minute quantities of substances that have been used during the manufacturing or production process of individual vaccines. Residuals will depend on the process used which may have involved cell culture fluids, egg proteins, yeast, antibiotics such as neomycin or streptomycin or inactivating agents such as formaldehyde (see IMAC fact sheet on formaldehyde for further information). These substances are only present as traces and often measured as parts per million and parts per billion in the final vaccine formulation.

Allergies to vaccine components

Very rarely, vaccines can provoke a serious allergic reaction called anaphylaxis. The risk of this occurring is about 1 per million doses of a vaccine. The components that are most likely to cause such a reaction are gelatin, egg proteins and antibiotics although theoretically an allergic reaction can be triggered by almost anything. For example there have been occasions where reactions have occurred as a result of the presence of latex in the stopper of the vial containing the vaccine.

Patients should always be assessed for their history of allergies prior to being immunised. There are very few occasions where vaccines should not be given. Only when there has been a history of anaphylaxis to a vaccine ingredient or previous dose of the same vaccine should consideration be given to avoiding the vaccine. Even when a person has had an anaphylactic reaction following exposure to egg they can usually be given MMR vaccine safely. The vaccine does not contain enough of the egg protein to pose a problem to people with egg allergy. Past reactions which have only involved the skin for example would not be considered a contraindication to receiving a vaccine.

Allergies to antibiotics also need careful evaluation.

Antibiotics in vaccines are only present in minute traces, usually insufficient to cause a problem. Also, an allergy to beta-lactam or cephalosporin antibiotics is not a contraindication for exposure to neomycin, polymyxin B or gentamycin which are the antibiotics found in vaccines.

Further advice about allergies and contraindications to vaccines should be sought from a medical practitioner with expertise in vaccines and vaccination or the 0800 IMMUNE advisory service.

Animal derived products

Some people have concerns about animal products in vaccines. This may be for either religious or faith-based reasons or concerns about the safety of animal derived products. Refer to the IMAC fact sheet on animal-derived products for further information.

All the vaccines in this fact sheet are prescription medicines. Talk to your doctor or nurse about the benefits and any risks. These vaccines are all fully funded on the immunisation schedule for certain age groups of children and adults. Check with your Doctor or Practice Nurse to find out more information on who is eligible for a funded vaccine. Or, you can view the immunisation schedule at <http://www.moh.govt.nz/moh.nsf/indexxmh/immunisation-schedule>.

Vaccines on the New Zealand Childhood Schedule from September 2008: Manufacture and Ingredients

Vaccine Contents - **Infanrix®-hexa**

Vaccine against diphtheria, tetanus, pertussis, polio, hepatitis B, *Haemophilus influenzae* type b (Hib) diseases.

Vaccine type: Multivalent subunit

| Ingredients | Quantity/dose (0.5ml) | Function |
|---|--------------------------------|-----------------|
| Active substances | | |
| 1. Diphtheria toxoid, adsorbed (D) | not less than 30 IU | Immunogen |
| 2. Tetanus toxoid, adsorbed (T) | not less than 40 IU | Immunogen |
| 3. Pertussis toxoid, adsorbed (PT) | 25 µg | Immunogen |
| 4. Filamentous haemagglutinin, adsorbed (FHA) | 25 µg | Immunogen |
| 5. Pertactin (69kDa OMP - PRN adsorbed) | 8 µg | Immunogen |
| 6. r-DNA Hepatitis B surface antigen, adsorbed (HB-sAg) | 10 µg | Immunogen |
| 7. Inactivated Polio Virus (IPV) Type 1 | 40 DU | Immunogen |
| 8. Inactivated Polio Virus (IPV) Type 2 | 8 DU | Immunogen |
| 9. Inactivated Polio Virus (IPV) Type 3 | 32 DU | Immunogen |
| 10. Conjugate of <i>Haemophilus influenzae</i> type b capsular polysaccharide (PRP) and Tetanus toxoid (T), adsorbed (PRP-T) | 10 µg of PRP and 20-40 µg of T | Immunogen |
| Adjuvants | | |
| Aluminium | 0.82 mg | Adjuvant |
| 0.5 mg as aluminium hydroxide (Al(OH) ₃) | | |
| 0.32 mg as aluminium phosphate (AlPO ₄) | | |
| Excipients | | |
| 2-phenoxyethanol | 2.5 mg | Preservative |
| Sodium chloride (NaCl) | 4.5 mg | For isotonicity |
| Medium 199 (M199) (including aminoacids) | 1.15 mg (0.09 mg) | IPV stabiliser |
| Lactose | 12.6 mg | Hib stabiliser |
| Water (H ₂ O) for injections | 0.5 ml | Solvent |
| Potassium chloride (KCl), disodium phosphate, monopotassium phosphate, polysorbate 20 and 80, glycine, formaldehyde, neomycin sulphate, polymyxin B sulfate are also present as residuals from the manufacturing process. | | |

Vaccine Contents – Prevenar®

Vaccine against pneumococcal disease.
Vaccine type: Conjugate subunit (7 valent)

| Ingredients | Quantity/dose (0.5ml) | Function |
|---|---|---|
| Active substances Pneumococcal polysaccharide Serotype 4 Pneumococcal polysaccharide Serotype 6B Pneumococcal polysaccharide Serotype 9V Pneumococcal polysaccharide Serotype 14 Pneumococcal polysaccharide Serotype 18C Pneumococcal polysaccharide Serotype 19F Pneumococcal polysaccharide Serotype 23F All conjugated to CRM197 carrier protein | 2µg 4µg 2µg 2µg 2µg 2µg 2µg | Immunogen Immunogen Immunogen Immunogen Immunogen Immunogen Immunogen |
| Adjuvants Aluminium Phosphate | 0.5 mg | Adjuvant |
| Excipients Sodium chloride (NaCl) Water (H2O) for injections | | For isotonicity Solvent |

Vaccine Contents - Infanrix™-IPV

Vaccine against diphtheria, tetanus, pertussis and polio diseases.
Vaccine type: Multivalent subunit

| Ingredients | Quantity/dose (0.5ml) | Function |
|--|--|--|
| Active substances 1. Diphtheria toxoid, adsorbed (D) 2. Tetanus toxoid, adsorbed (T) 3. Pertussis toxoid, adsorbed (PT) 4. Filamentous haemagglutinin, adsorbed (FHA) 5. Pertactin (69kDa OMP - PRN adsorbed) 6. Inactivated Polio Virus (IPV) Type 1 7. Inactivated Polio Virus (IPV) Type 2 8. Inactivated Polio Virus (IPV) Type 3 | not less than 30 IU not less than 40 IU 25 µg 25 µg 8 µg 40 DU 8 DU 32 DU | Immunogen Immunogen Immunogen Immunogen Immunogen Immunogen Immunogen Immunogen |
| Adjuvants Aluminium hydroxide (Al(OH) ₃) | 0.5mg | Adjuvant |
| Excipients Sodium chloride Potassium chloride Disodium phosphate Monopotassium phosphate 2-phenoxyethanol Polysorbate 80 Glycine Process residual Formaldehyde M 199 Neomycin sulfate Polymyxin sulfate Water | 4.5mg Process Residual Process Residual Process Residual 2.5mg Process Residual Process Residual <10mcg 1.15mg Process Residual Process Residual | For isotonicity Preservative Surfactant Stabiliser Virus inactivation IPV stabiliser Antimicrobial Antimicrobial Solvent |

Vaccine Contents - Boostrix®

Booster vaccine against diphtheria, tetanus and pertussis diseases.
Vaccine type: Multivalent subunit

| Ingredients | Quantity/dose (0.5ml) | Function |
|---|---|--|
| Active substances 1. Diphtheria toxoid, adsorbed (D) 2. Tetanus toxoid, adsorbed (T) 3. Pertussis toxoid, adsorbed (PT) 4. Filamentous haemagglutinin, adsorbed (FHA) 5. Pertactin (69kDa OMP - PRN adsorbed) | not less than 2 IU not less than 20 IU 8 µg 8 µg 2.5 µg | Immunogen Immunogen Immunogen Immunogen Immunogen |
| Adjuvants Aluminium 0.5 mg as aluminium hydroxide (Al(OH) ₃) and Aluminium phosphate | 0.5 mg (<0.39 Al by assay) | Adjuvant |
| Excipients 2-phenoxyethanol Sodium chloride (NaCl) Process residual Formaldehyde Polysorbate 80 (Tween 80) Glycine | 2.5 mg 4.5 mg <1 mcg <100mcg Residual Residual | Preservative For isotonicity Toxoid inactivation Emulsifier Protein stabiliser |

Vaccine Contents – Hiberix™

Vaccine against *Haemophilus influenzae* type b (Hib) disease.
Vaccine type: Conjugate subunit

| Ingredients | Quantity/dose (0.5ml) | Function |
|--|-----------------------|--|
| Active substances <i>Haemophilus influenzae</i> type b polysaccharide Conjugated to tetanus toxoid as carrier protein | 10µg 30µg | Immunogen |
| Adjuvants Nil. The protein carrier acts as an adjuvant. | | |
| Excipients Lactose Sodium Chloride Water for injection (separate from Hib pellet) | 4.5mg 0.5mL | Stabiliser For isotonicity Diluent |

Vaccine Contents: M-M-R® II

Vaccine against measles, mumps and rubella diseases.

Vaccine type: Live attenuated viral

| Ingredients | Quantity/dose (0.5ml) | Function |
|---|--|---------------------------|
| Active substances | | |
| Measles virus | >1,000 CCID50 (50% cell culture infectious dose) | Immunogen |
| Mumps virus | >12,500 CCID50 | Immunogen |
| Rubella virus | >1,000 CCID50 | Immunogen |
| Adjuvants | | |
| Nil. | | |
| Excipients | | |
| Sorbitol | 14.5 mg | Stabiliser/solvent |
| Sucrose | 1.9 mg | Stabiliser |
| Sodium phosphate | | Adjust tonicity |
| Sodium chloride | | Stabiliser |
| Hydrolysed gelatin | 14.5 mg | Component of growth media |
| Human albumin | 0.3 mg | Component of growth media |
| Fetal bovine serum | <1 ppm | antibacterial |
| Neomycin. | 25 mcg | |
| Other residuals from manufacture: Dibasic Potassium Phosphate, Eagle Minimum Essential medium, Medium 199, Monobasic potassium phosphate, Monosodium glutamate, Phenolsulfonphthalein, Sodium Bicarbonate | | |

Vaccine Contents - Gardasil®

Vaccine against human papillomavirus disease.

Vaccine type: Subunit

| Ingredients | Quantity/dose (0.5ml) | Function |
|---|-----------------------|------------------------|
| HPV 6 L1 protein | 20 µg | Antigen |
| HPV 11 L1 protein | 40 µg | Antigen |
| HPV 16 L1 protein | 40 µg | Antigen |
| HPV 18 L1 protein | 20 µg | Antigen |
| Aluminium (as aluminium hydroxyphosphate sulphate) | 225 µg | Adjuvant |
| Sodium chloride | 9.56mg | Control osmolarity |
| L-histidine | 0.78mg | Buffer |
| Polysorbate 80 | 50 µg | Stability |
| Sodium borate | 35 µg | Residual from adjuvant |
| Water | | For injection |

References and Additional Information

Medsafe New Zealand: consumer information sheets and vaccine data sheets, <http://www.medsafe.govt.nz>

National network for immunisation Information, Vaccine components web page http://www.immunizationinfo.org/vaccine_components.cfm

Offit, PA and RK Jew 2003. Addressing Parents Concerns: Do Vaccines contain Harmful Preservatives, Adjuvants, Additives , or Residuals? *Paediatrics*. 112(6 Pt 1): 1394-7.

Centers for Disease Control and Prevention. *Epidemiology and Prevention of Vaccine-Preventable Diseases*. Atkinson W, Hamborsky J, McIntyre L, Wolfe S, eds. 10th ed. Washington DC: Public Health Foundation, 2008.

All the vaccines in this fact sheet are prescription medicines. Talk to your doctor or nurse about the benefits and any risks. These vaccines are all fully funded on the immunisation schedule for certain age groups of children and adults. Check with you Doctor or Practice Nurse to find out more information on who is eligible for a funded vaccine. Or, you can view the immunisation schedule at <http://www.moh.govt.nz/moh.nsf/indexmh/immunisation-schedule>.