

VACCINE EXCIPIENT & MEDIA SUMMARY

<http://www.cdc.gov/nip/publications/pink/Appendices/A/Excipient.pdf>

Aluminum Hydroxide-Adjuvant-Anthrax (BioThrax), DTaP (Certiva, Infanrix, Acel-Imune), DT (Massachusetts), Td (Massachusetts), Hib (PedvaxHib), Hib-Hepatitis B (Comvax), Hepatitis A (Havrix, Vaqta), Hepatitis B (Engerix-B, Recombivax-HB), Lyme disease (LymeRix)

Synonyms: hydrated alumina, aluminum hydroxide

Stability: Stable. Incompatible with strong bases.

Toxicology: May act as a skin, respiratory or eye irritant.

Toxicity data: IPR (intraperitoneal) RAT LDLO (lowest published lethal dose) 150 mg kg⁻¹

Risk phrases: R36 (Irritating to eyes) R37 (Irritating to respiratory system) R38 (Irritating to skin)

Transport information: Non-hazardous for air, sea and road transport.

Personal protection: Safety glasses.

Safety phrases: S26 (In case of contact with eyes, rinse immediately with plenty of water and seek medical advice)

S36 (Wear suitable protective clothing) http://physchem.ox.ac.uk/MSDS/AL/aluminium_hydroxide.html

[Aluminum accumulation during treatment with aluminum hydroxide and dialysis in children and young adults with chronic renal disease](#) - The New England Journal of Medicine

[The Common Vaccine Adjuvant Aluminum Hydroxide Up-Regulates Accessory Properties of Human Monocytes via an Interleukin-4-Dependent Mechanism](#) - American Society for Microbiology Infection and Immunity

Aluminum Phosphate-Adjuvant-DTAP (Acel-Imune), DTWP (Massachusetts, BioPort), DT (Wyeth-Lederle), Td (Massachusetts, Wyeth-Lederle), Pneumococcal (Prevnar), Rabies (Bio- Rab)

Synonyms: Aluminophosphoric acid, Aluminum acid phosphate, Aluminum monophosphate, Aluminum phosphate

Potential Health Effects

Eye: Causes eye burns. May cause irreversible eye injury.

Skin: Causes skin irritation and burns, may lead to dermatitic reaction on long exposure.

Ingestion: Causes gastrointestinal tract burns. Causes severe pain, nausea, vomiting, diarrhoea, and shock.

Inhalation: Inhalation is not an expected hazard unless misted or heated to high temperatures. Mist or vapour inhalation can cause irritation and burns to the nose, throat, and upper respiratory tract. The result of spasm, inflammation and pulmonary edema may be fatal.

Chemical Stability: Stable under normal temperatures and pressures.

TOXICOLOGICAL INFORMATION: Oral Rabbit: LD50 (lethal dose 50 percent kill) 1530 mg/kg

Skin Rabbit: LD50 (lethal dose 50 percent kill) 2740 mg/kg

Chronic Effects: Damage to kidneys and liver http://www.panagri.co.uk/sds/SDS_Aluminium_phosphate.doc

Aluminum potassium sulfate-Adjuvant-DTAP (Tripedia), DTWP (Aventis Pasteur), DT (Aventis Pasteur), Td (Aventis Pasteur)

Emergency Overview: WARNING! HARMFUL IF SWALLOWED OR INHALED. CAUSES IRRITATION TO SKIN, EYES AND RESPIRATORY TRACT.

Synonyms: Sulfuric acid, aluminum potassium salt (2:1:1), dodecahydrate; potassium alum dodecahydrate; Alum

Potassium USP Powder TAC; Potassium alum; Potash alum; Alum; Kalinite

Potential Health Effects: This material hydrolyzes in water to form sulfuric acid, which is responsible for the irritating effects given below.

Inhalation: Causes irritation to the respiratory tract. Symptoms may include coughing, shortness of breath.

Ingestion: Causes irritation to the gastrointestinal tract. Symptoms may include nausea, vomiting and diarrhea. There have been two cases of fatal human poisonings from ingestion of 30 grams of alum.

Skin Contact: Causes irritation to skin. Symptoms include redness, itching, and pain.

Eye Contact: Causes irritation, redness, and pain.

Chronic Exposure: No information found.

Aggravation of Pre-existing Conditions: No information found.

First Aid Measures: Inhalation: Remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention.

Ingestion: If swallowed, DO NOT INDUCE VOMITING. Give large quantities of water. Never give anything by mouth to an unconscious person. Get medical attention immediately.

Skin Contact: Wipe off excess material from skin then immediately flush skin with plenty of water for at least 15 minutes. Remove contaminated clothing and shoes. Get medical attention. Wash clothing before reuse. Thoroughly clean shoes before reuse.

Critical Decisions Count

Eye Contact: Immediately flush eyes with plenty of water for at least 15 minutes, lifting upper and lower eyelids occasionally. Get medical attention.

Accidental Release Measures: Cover spill with sodium bicarbonate or soda ash and mix. Ventilate area of leak or spill. Keep unnecessary and unprotected people away from area of spill. Wear appropriate personal protective equipment as specified in Section 8. Spills: Pick up and place in a suitable container for reclamation or disposal, using a method that does not generate dust.

Skin Protection: Wear impervious protective clothing, including boots, gloves, lab coat, apron or coveralls, as appropriate, to prevent skin contact.

Eye Protection: Use chemical safety goggles and/or full face shield where dusting or splashing of solutions is possible. Maintain eye wash fountain and quick-drench facilities in work area. Label Hazard Warning: WARNING! HARMFUL IF SWALLOWED OR INHALED. CAUSES IRRITATION TO SKIN, EYES AND RESPIRATORY TRACT.

Label Precautions: Avoid breathing dust. Keep container closed. Use only with adequate ventilation. Wash thoroughly after handling. Avoid contact with eyes, skin and clothing.

Label First Aid:

If swallowed, DO NOT INDUCE VOMITING. Give large quantities of water. Never give anything by mouth to an unconscious person. If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. In case of contact, wipe off excess material from skin then immediately flush eyes or skin with plenty of water for at least 15 minutes. Remove contaminated clothing and shoes. Wash clothing before reuse. In all cases, get medical attention. <http://www.jtbaker.com/msds/englishhtml/a2856.htm>

Amino acids-Growth medium-Hepatitis A (Havrix), Typhoid oral (Vivotif)

Reference Guide for AMINO ACIDS <http://www.realtime.net/anr/aminoacd.html>

Ammonium sulfate-Protein fractionation-Hib (Act-HIB)

Stability: Stable. Contact with strong oxidizers may cause fire or explosion. Incompatible with strong bases.

Toxicology: Harmful if swallowed. Eye, skin and respiratory irritant.

Toxicity data : ORL (oral)-RAT LD50 (lethal dose 50 percent kill) 3000 mg kg⁻¹

IPR (intraperitoneal)-MUS (mouse) LD50 (lethal dose 50 percent kill) 610 mg kg⁻¹

IPR (intraperitoneal) -MUS (mouse) LD50 (lethal dose 50 percent kill) 610 mg kg⁻¹

Risk phrases: R20 (Harmful by inhalation) R36 (Irritating to eyes) R37 (Irritating to respiratory system) R38 (Irritating to skin)

Transport information: Non-hazardous for air, sea and road freight.

Personal protection: Safety glasses. Do not breathe dust.

Safety phrases: S26 (In case of contact with eyes, rinse immediately with plenty of water and seek medical advice)

S36 (Wear suitable protective clothing) http://physchem.ox.ac.uk/MSDS/AM/ammonium_sulfate.html

Amphotericin B-Anti-bacterial-Rabies (RabAvert)

Amphotericin B is a [polyene antifungal agent](#), first isolated by Gold et al from *Streptococcus nodosus* in 1955. It is an amphoteric compound composed of a hydrophilic polyhydroxyl chain along one side and a lipophilic polyene hydrocarbon chain on the other. Amphotericin B is poorly soluble in water. Amphotericin B is an antifungal agent that is used both topically and systemically for various fungal infections, especially invasive infections caused by **Candida**.

The drug acts by binding to steroidal alcohols in the cell membrane of susceptible fungi resulting in an increase of membrane permeability that allows leakage of the cellular contents. Common side effects include headache, fever, chills, irregular heartbeat, double vision, and occasionally convulsions and numbness.

<http://www.aegis.com/factshts/network/access/drugs/amph.html>

Ascorbic acid-Antioxidant-Typhoid oral (Vivotif)

Synonyms: Vitamin C, numerous trade names, L-ascorbic acid, L-(+)-ascorbic acid, L,3-ketothreohexuronic acid

Stability: Stable. May be light or air sensitive.

Toxicology: May be harmful if ingested in quantity. May act as an irritant.

Toxicity data: ORL (oral)-RAT LD50 (lethal dose 50 percent kill) 11900 mg kg⁻¹

ORL (oral)-MUS (mouse) LD50 (lethal dose 50 percent kill) 3367 mg kg⁻¹

Personal protection: None.

Safety phrases: S28 (After contact with skin, wash immediately with plenty of soap-suds) S37 (Wear suitable gloves)

S45 (In case of accident or if you feel unwell, seek medical advice immediately-show the label whenever possible)

http://physchem.ox.ac.uk/MSDS/AS/ascorbic_acid.html

Bactopeptone-Growth medium-Influenza (varies seasonally)

Critical Decisions Count

Beta-propiolactone-Viral inactivator-Influenza (Fluvirin), Rabies (Imovax, RabAvert)

Health Hazard Information

Acute Effects: Acute inhalation exposure *beta*-propiolactone causes severe irritation of the eyes, nose, throat, and respiratory tract in humans. Acute dermal exposure may cause irritation of the skin, blistering, or burns in humans. Contact with the eyes may cause permanent corneal opacification. Burns of the mouth and stomach may occur in humans following acute exposure via ingestion. Acute oral exposure has been observed to result in muscular spasms, respiratory difficulty, and convulsions at high levels in rats. In rats acutely exposed intravenously, liver and kidney tubular damage has been reported. Acute animal exposure tests in rats have demonstrated *beta*-propiolactone to have extreme acute toxicity by inhalation.

Cancer Risk: No information is available on the carcinogenic effects of *beta*-propiolactone in humans. Squamous cell carcinomas of the forestomach have been reported in orally exposed rats. In several studies of rats and mice exposed to *beta*-propiolactone via subcutaneous injection, local tumors have been observed at the site of injection.

Lymphomas and hepatomas have been reported in mice following intraperitoneal injection. In mice, hamsters, and guinea pigs dermally exposed, skin tumors have been observed. EPA has not classified *beta*-propiolactone for carcinogenicity. IARC has classified *beta*-propiolactone as a Group 2B, possible human carcinogen.

<http://www.epa.gov/ttn/atw/hlthef/propiola.html>

Benzethonium chloride-Preservative-Anthrax (BioThrax)

Synonyms: phemerol chloride, benzyldimethyl[2-[2-[4-(1,1,3,3-tetramethylbutyl)phenoxy]ethoxy]ethyl]ammonium chloride, salanine, BZT, diapp, quatrachlor, polymine d, phemithyn, benzethonium, antiseptol, disilyn, phermerol, various other trade names

Use: antiseptic, antiinfective, bacteriacide, detergent, preservative

Stability: Stable. Incompatible with strong oxidizing agents, soap, anionic detergents, nitrates, acids. Hygroscopic. Light sensitive.

Toxicology: Harmful if swallowed, inhaled or absorbed through the skin. Experimental neoplastigen.

Toxicity data: ORL (oral) -RAT LD50 (lethal dose 50 percent kill) 368 mg kg⁻¹

SCU (subcutaneous)-RAT LD50 (lethal dose 50 percent kill) 119 mg kg⁻¹

IPR (intraperitoneal)-RAT LD50 (lethal dose 50 percent kill) 16 mg kg⁻¹

ORL (oral)-MUS (mouse) LD50 (lethal dose 50 percent kill) 338 mg kg⁻¹

IVN (intravenous)-MUS (mouse) LD50 (lethal dose 50 percent kill) 30 mg kg⁻¹

IPR (intraperitoneal)-MUS (mouse) LD50 (lethal dose 50 percent kill) 15 mg kg⁻¹

Risk phrases: R20 (Harmful by inhalation) R21 (Harmful in contact with skin) R22 (Harmful if swallowed) R36 (Irritating to eyes) R37 (Irritating to respiratory system) R38 (Irritating to skin) R41 (Risk of serious damage to the eyes)

Transport information: UN No 8027. Hazard class 9. (Miscellaneous dangerous substances)

Personal protection: Safety glasses, adequate ventilation.

Safety phrases: S26 (In case of contact with eyes, rinse immediately with plenty of water and seek medical advice)

S36 (Wear suitable protective clothing) S37 (Wear suitable gloves) S39 (Wear eye / face protection)

http://physchem.ox.ac.uk/MSDS/BE/benzethonium_chloride.html

Bovine albumin or serum-Growth medium, protein stabilizer-Hepatitis A (Havrix, Vaqta), Poliovirus attenuated (Orimune), Rabies (Imovax, RabAvert), Vaccinia (DryVax), Varicella (Varivax)

Brilliant green-Dye-Vaccinia (DryVax)

Synonyms: diamond green, malachite green G, C.I. 42040, C.I. basic green 1

Stability: Stable. Incompatible with strong oxidizing agents.

Toxicology: May be harmful by inhalation, ingestion or through skin contact. May act as an irritant.

Irritation data: SKN (administration onto skin)-HMN (human) 2 mg/2D-I mld

Risk phrases: R20 (Harmful by inhalation) R21 (Harmful in contact with skin) R22 (Harmful if swallowed)

Personal protection: Safety glasses. Do not breathe dust.

Safety phrases: S36 (Wear suitable protective clothing) http://physchem.ox.ac.uk/MSDS/BR/brilliant_green.html

Chlortetracycline-Anti-bacterial-Rabies (RabAvert), Vaccinia (DryVax)

DNA-Manufacturing residue-Hepatitis A (Vaqta)

Ethylenediamine-tetraacetic acid sodium (EDTA)-Preservative-Rabies (RabAvert), Varicella (Varivax)

Routes of Exposure: Exposure to ethylenediamine can occur through inhalation, ingestion, and eye or skin contact, and absorption through the skin [Genium 1993]. Summary of toxicology: 1. Effects on Animals: Ethylenediamine is a corrosive liquid that is severely irritating to the skin and eyes. Systemic toxicity from exposure to high vapor

Critical Decisions Count

concentrations causes damage to the kidneys, liver, and lungs [Sittig 1991; Sax and Lewis 1989]. The LD(50) for acute oral exposure in rats has been reported variously as 500 mg/kg and 1160 mg/kg [ACGIH 1991; NIOSH 1991]. The dermal LD(50) in rabbits is 730 mg/kg [NIOSH 1991]. In rats fed 0.5 g/kg/day for two generations, some reduction in body weight and microscopic changes of the kidneys and liver were observed. Liver lesions were more prevalent among female than male rats [Hathaway et al. 1991]. An 8-hour exposure to 4,000 ppm ethylenediamine was uniformly fatal to rats; death was caused by kidney injury and lung damage. A similar exposure to 2,000 ppm was not lethal to rats. Thirty days of inhalation exposure to 484 ppm of ethylenediamine killed all exposed rats. Postmortem examination showed injury to the kidneys, liver, and lungs, and hair loss. No deaths and a lesser degree of injury were seen at 132 ppm, and no injury was noted at 125 ppm [Hathaway et al. 1991]. Undiluted liquid ethylenediamine painted on the shaved skin of rabbits caused severe skin irritation, blistering, and cell death. In rabbits, contact of the eye with solutions containing more than 5 percent ethylenediamine produced serious corneal damage, and contact of the eye with a 5-percent solution caused partial corneal opacity. Neutralized solutions of ethylenediamine were far less damaging to the eyes of rabbits than alkaline ones [Grant 1986; ACGIH 1991]. <http://www.osha-slc.gov/SLTC/healthguidelines/ethylenediamine/recognition.html#healthhazard>

Egg protein-Growth medium-Influenza (all brands), Yellow fever (YF-Vax)

Fetuin (a bovine serum protein)-Affinity ligand for chromatography-DTaP (Certiva)

Formaldehyde, formalin-Anti-microbial, preservative-Anthrax (BioThrax), DTaP (all brands), DTwP (all brands), DTwPHib (Tetramune), DT (all brands), Td (all brands), Hepatitis A (Havrix, Vaqta), Hib (ActHIB), Influenza (Fluogen, FluShield, Fluzone), Japanese encephalitis (JE -Vax), Poliovirus inactivated (Ipol)

Synonyms: bvf, FA, fannofom, formalith, formalin, formalin 40, formic aldehyde, formol, fyde, hoch, karsan, lysoform, methyl aldehyde, methylene glycol, methylene oxide, methanal, morbidic, oxomethane, oxymethylene, paraform, polyoxymethylene glycols, superlysoform

Stability: Stable. Strong reducing agent, especially in alkaline solution. Substances to be avoided include strong bases, strong acids, strong oxidising agents, aniline, phenol, isocyanates, anhydrides. Combustible. Light and air sensitive. Polymerizes spontaneously.

Toxicology: Causes burns. **Very toxic by inhalation, ingestion and through skin absorption. Readily absorbed through skin. Probable human carcinogen. Mutagen. May cause damage to kidneys. May cause allergic reactions. May cause sensitisation. May cause heritable genetic damage.** Lachrymator at levels from less than 20 ppm upwards. Very destructive of mucous membranes and upper respiratory tract, eyes and skin.

Toxicity data: IHL (inhalation)-TCLO (lowest published toxic concentration) HMN (human) 17 mg/m³/30m

ORL (oral)-WMN (woman) LDLO (lowest published lethal dose) 108 mg kg⁻¹

IPR (intraperitoneal)-MUS (mouse) LDLO (lowest published lethal dose) 16 mg kg⁻¹

ORL (oral)-RAT LD50 (lethal concentration 50 percent kill) 100 mg kg⁻¹

SKN (administration onto skin)-RBT (rabbit) LD50 (lethal concentration 50 percent kill) 270 mg kg⁻¹

Risk phrases: R10 (Flammable) R26 (Very toxic by inhalation) R27 (Very toxic in contact with skin) R28 (Very toxic if swallowed) R34 (Causes burns) R40 (Limited evidence of a carcinogenic effect) R41 (Risk of serious damage to the eyes) R43 (May cause sensitization by skin contact)

Transport information: UN No 1198. Packing group III. Hazard class 9 (Miscellaneous dangerous substances)

Personal protection: Safety glasses. Gloves. Good ventilation. <http://physchem.ox.ac.uk/MSDS/FO/formaldehyde.html>

Gelatin-Stabilizer in freeze-drying, solvent-DTaP (Acel-Imune, Tripedia), Influenza (Fluzone), Japanese encephalitis (JE-Vax), Measles (Attenuvax), Mumps (Mumpsvax), Rubella (Meruvax II), MMR (MMR-II), Rabies (RabAvert), Typhoid oral (Vivotif), Varicella (Varivax), Yellow fever (YFVax)

Gentamicin-Anti-bacterial-Influenza (FluShield) <http://www.vitacost.com/science/hn/Drug/Gentamicin.htm>

Glycerin-Solvent-Vaccinia (DryVax)

See glycerol Synonyms: glycerin, glycerine, 1,2,3-propanetriol, 1,2,3-trihydroxypropane

Use: Widely used as a food additive (emulsifier, thickener, stabilizer), cosmetic agent, lubricating agent, antifreeze etc.

Stability: Stable. Incompatible with perchloric acid, lead oxide, acetic anhydride, nitrobenzene, chlorine, peroxides.

Flammable.

Toxicology: Mist is a respiratory irritant at high concentrations. Repeated contact may cause dehydration of skin.

Typical TLV (Threshold Limit Value) 10 mg/m³ (nuisance).

Toxicity data: IPR (intraperitoneal)-RAT LD50 (lethal dose 50 percent kill) 8700 mg kg⁻¹

ORL (oral)-RAT LD50 (lethal dose 50 percent kill) 12600 mg kg⁻¹

Risk phrases: R36 (Irritating to eyes) R38 (Irritating to skin)

Critical Decisions Count

Personal protection: Minimize contact.

Safety phrases: S26 (In case of contact with eyes, rinse immediately with plenty of water and seek medical advice)

S36 (Wear suitable protective clothing) <http://ptcl.chem.ox.ac.uk/MSDS/GL/glycerol.html>

Glycine Protein-stabilizer-DTaP (Acel-Imune), DTwP-Hib (Tetramune), DT (most brands), Td (most brands)

Human serum albumin-Growth medium-Rabies (Imovax)

Hydrochloric acid-Adjust pH-DTaP (most brands), DT (most brands)

Concentrated: Synonyms: muriatic acid, chlorohydric acid

Stability

Stable. Avoid heat, flames. Incompatible with most common metals, amines, metal oxides, acetic anhydride, propiolactone, vinyl acetate, mercuric sulphate, calcium phosphide, formaldehyde, alkalies, carbonates, strong bases, sulphuric acid, chlorosulphonic acid.

Toxicology: Extremely corrosive. Inhalation of vapour can cause serious injury. Ingestion may be fatal. Liquid can cause severe damage to skin and eyes. TLV (Threshold Limit Value) 5 ppm (parts per million)

Toxicity data: ORL (oral) –RBT (rabbit) LD50 (lethal dose 50 percent kill) 900 mg kg⁻¹

IPR (intraperitoneal)-MUS (mouse) LD50 (lethal dose 50 percent kill) 40 mg kg⁻¹

IHL (inhalation)-RAT LC50 (lethal concentration 50 percent kill) 3124 ppm (parts per million) /1h.

IHL (inhalation)-HMN (human) LCLO (lowest published lethal concentration) 1300 ppm (parts per million) 30min

Risk phrases R23 (Toxic by inhalation) R24 (Toxic in contact with skin) R25 (Toxic if swallowed) R34 (Causes burns)

R36 (Irritating to eyes) R37 (Irritating to respiratory system) R38 (Irritating to skin)

Transport information UN No 1789 Packing group II Major hazard class 8.0 (Corrosive substances) Transport category 2

Environmental information: Lethal to fish from 25 mg/l up. Toxic for aquatic organisms due to pH shift.

Personal protection: Safety glasses or face mask, gloves. Effective ventilation.

Safety phrases: S26 (In case of contact with eyes, rinse immediately with plenty of water and seek medical advice)

S36 (Wear suitable protective clothing) S37 (Wear suitable gloves) S39 (Wear eye / face protection) S45 (In case of accident or if you feel unwell, seek medical advice immediately-show the label whenever possible)

http://ptcl.chem.ox.ac.uk/MSDS/HY/hydrochloric_acid.html

hydrochloric acid (1 molar) Synonyms: muriatic acid, chlorohydric acid, dilute hydrochloric acid, dilute HCL

Stability: Stable. Incompatible with most common metals, amines, metal oxides, acetic anhydride, propiolactone, vinyl acetate, mercuric sulphate, calcium phosphide, formaldehyde, alkalies, carbonates, strong bases, sulphuric acid, chlorosulphonic acid.

Toxicology: Corrosive. Inhalation of vapour is harmful. Ingestion may be fatal. Liquid can cause severe damage to skin and eyes. TLV (Threshold Limit Value) 5 ppm ()

Toxicity data (for the concentrated acid):ORL (oral)-RBT (rabbit) LD50 (lethal dose 50 percent kill) 900 mg kg⁻¹

IPR (intraperitoneal)-MUS (mouse) LD50 (lethal dose 50 percent kill) 40 mg kg⁻¹

IHL (inhalation)-RAT LC50 (lethal concentration 50 percent kill) 3124 ppm (parts per million)/1h.

IHL (inhalation)-HMN (human) LCLO (lowest published lethal concentration) 1300 ppm (parts per million) 30min

Risk phrases: R20 (Harmful by inhalation) R21 (Harmful in contact with skin) R22 (Harmful if swallowed) R36 (Irritating to eyes) R37 (Irritating to respiratory system) R38 (Irritating to skin)

Personal protection: Safety glasses. Effective ventilation.

Safety phrases: S26 (In case of contact with eyes, rinse immediately with plenty of water and seek medical advice)

S45 (In case of accident or if you feel unwell, seek medical advice immediately-show the label whenever possible)

http://ptcl.chem.ox.ac.uk/MSDS/HY/hydrochloric_acid_1M.html

Hydrogen peroxide-Toxin detoxifier-DTaP (Certiva)

30% solution: Synonyms: albione 30, albione 35, albione 50, albione 70, albione 35cg, albione 50cg, albione 70cg, interox, kastone, perone 30, perone 35, perone 50. Data also applies to solutions of similar strength.

Note: Typical concentrations lie in the range 3%-35%. **Solutions of much higher concentration (e.g. 60% and above) present significantly increased risks, and should not be used unless such strength is absolutely essential.**

Stability: Unstable - readily decomposes to water and oxygen. Light sensitive. May develop pressure in the bottle - take care when opening. Forms potentially explosive compounds with ketones, ethers, alcohols, hydrazine, glycerine, aniline, sodium borate, urea, sodium carbonate, triethylamine, sodium fluoride, sodium pyrophosphate and carboxylic acid anhydrides. Materials to avoid include combustibles, strong reducing agents, most common metals, organic materials, metallic salts, alkali, porous materials, especially wood, asbestos, soil, rust, strong oxidizing agents.

Critical Decisions Count

Toxicology: Toxic. Corrosive - can causes serious burns. Eye contact can cause serious injury, possibly blindness. Harmful by inhalation, ingestion and skin contact. Typical OEL 1 ppm (parts per million)
Toxicity data: ORL (oral)-MAN LDLO (lowest published lethal dose) 1429 mg kg-1
ORL (oral)-WMN (woman) LDLO (lowest published lethal dose) 1429 mg kg-1
ORL (oral)-RBT (rabbit) LD50 (lethal dose 50 percent kill) 820 mg kg-1
IVN (intravenous)-MUS (mouse) LD50 (lethal dose 50 percent kill) > 50 g kg-1
SKN (administration onto skin)-RAT LD50 (lethal dose 50 percent kill) 3000 mg kg-1
Risk phrases: R8 (Contact with combustible material may cause fire) R34 (Causes burns)
Transport information: UN Major hazard class 5.1. (Oxidizing agents) Packing group II. UN No 2014. EMS No 5.1-02.
Personal protection: Safety glasses are essential; acid-resistant gloves are suggested. Suitable ventilation.
Safety phrases: S3 (Keep in a cool place) S28 (After contact with skin, wash immediately with plenty of soap-suds)
S37 (Wear suitable gloves) S39 (Wear eye / face protection) S45 (In case of accident or if you feel unwell, seek medical advice immediately-show the label whenever possible.)
http://ptcl.chem.ox.ac.uk/MSDS/HY/hydrogen_peroxide_30pc.html

3% aqueous solution: Synonyms: dilute hydrogen peroxide (3 per cent)

Stability: Slightly unstable - will very slowly decompose. Decomposition is promoted by catalysts and heating, so store cool. Light sensitive, keep in the dark. May contain stabilizer. Reacts with rust, brass, zinc, nickel, finely powdered metals, copper and iron and their alloys.

Toxicology: May be harmful if swallowed or inhaled and in contact with the skin. Note that solutions of significantly higher concentration (30% is often used) present a much more pronounced risk, especially if splashed onto the skin or into the eyes. For data on 30% hydrogen peroxide, click here. Very concentrated solutions and pure hydrogen peroxide, as opposed to dilute solutions, are dangerous and should not be handled without expert instruction.

Personal protection: Safety glasses.

Safety phrases: S26 (In case of contact with eyes, rinse immediately with plenty of water and seek medical advice)
S36 (Wear suitable protective clothing) http://ptcl.chem.ox.ac.uk/MSDS/HY/hydrogen_peroxide_3pc.html

Kanamycin-Anti-bacterial-Lyme disease (LymeRix)

Drug description: Kanamycin is an anti-infective used for treatment of infections when penicillin or other less toxic drugs can't be used. Infections treated include bone, respiratory tract, skin, soft-tissue, and abdominal infections, complicated urinary tract infections, endocarditis, septicemia, and enterococcal infections. Treatment of enterococcal infections requires combination with penicillin.

Side effects: Hearing changes and reactions related to the ears, toxicity to kidneys, hypersensitivity reactions.

Dosage: Kanamycin is inactivated by penicillins when co-administered to people with kidney damage. Dosage is not to exceed 1.5 g/day. Blood levels should be monitored periodically during therapy. Monitor kidney functions throughout therapy. How long it may take to work: Effectiveness is indicated by resolution of signs and symptoms, usually within 3-5 days. Managing side effects: Report to your doctor any signs of hypersensitivity, ringing in ears, dizziness, or hearing loss. The most frequent sign of hypersensitivity to a drug is a stable, elevated rash called maculopapular rash (a skin rash that can have bumps). The reaction typically occurs eight to fourteen days after starting the drug. Most hypersensitivity reactions to a drug stop after discontinuing treatment. If the reaction is mild, sometimes you can continue the drug. <http://www.aegis.com/factshts/network/access/drugs/kana.html>

Lactose-Stabilizer in freeze-drying, filling-BCG (Tice), Hib (some packages), Meningococcal (Menomune), Typhoid oral (Vivotif)

Magnesium stearate-Lubricant for capsule filling-Typhoid oral (Vivotif)

Synonyms: octadecanoic acid magnesium salt, stearic acid magnesium salt, magnesium distearate

Use: food additive

Stability: Stable. Incompatible with strong oxidizing agents.

Toxicology: Generally regarded as safe.

Transport information: Non-hazardous for air, sea and road freight.

Personal protection: Minimize contact http://physchem.ox.ac.uk/MSDS/MA/magnesium_stearate.html

Monosodium glutamate (MSG)-Stabilizer-Varicella (Varivax)

Synonyms: sodium glutamate, DL-monosodium glutamate, MSG, sodium hydrogen glutamate, glutamic acid monosodium salt, monosodium DL-glutamate

Use: flavour enhancer, food additive approved for use in many countries

Stability: Stable. Incompatible with strong oxidizing agents

Toxicology: Not believed to present a significant risk to health.

Toxicity data: ORL (oral)-RAT LD50 (lethal dose 50 percent kill) 16600 mg kg-1

Critical Decisions Count

Transport information: Non-hazardous

Personal protection: Minimize contact http://physchem.ox.ac.uk/MSDS/MO/monosodium_glutamate.html

FDA comment on MSG-<http://www.cfsan.fda.gov/~lrd/msg.html>

Mouse serum protein-Growth medium-Japanese encephalitis (JE-Vax)

MRC-5 cellular protein-Growth medium-Hepatitis A (Havrix, Vaqta), Rabies (Imovax, RabAvert), Varicella (Varivax)
Lung, diploid, human

Derived from normal lung tissue of a 14-week-old male fetus by J. P. Jacobs in September 1966 (Nature 227: 168-170, 1970), the MRC-5 cell line was established in a growth medium consisting of Earle's Basal Medium in Earle's balanced salt solution supplemented with 10% calf serum. Following initial cultivation, subcultures were prepared twice weekly at a 1:2 ratio. When the cells reached approximately the 7th population doubling, the majority of the cultures were harvested to prepare a frozen cell stock. Subsequent observations revealed that the MRC-5 cells are capable of attaining 42-46 population doublings before onset of the decline in proliferation usually experienced with human fibroblast lines. The MRC-5 cell strain (like the WI-38 cell line) is susceptible to a wide range of human viruses.

Culture Medium: Minimum essential medium (Eagle), with 10% heat-inactivated fetal bovine serum.

Growth Characteristics: Cells seeded at a concentration of 4×10^4 cells/cm² in the above culture medium will be 100% confluent in 7 days.

Plating Efficiency: Less than 1%.

Morphology: Fibroblast-like.

Karyology: Chromosome Frequency Distribution is 46 Cells: $2n = 46$.

Species: Confirmed as human by cytotoxic-antibody dye exclusion test.

Common Utilization: Supports the growth of a broad range of viruses, including Adenoviruses; Coxsackie A; Cytomegalovirus; Echovirus; Herpes simplex Virus; Poliovirus; Rhinovirus; Respiratory Syncytial Virus; and Varicella Zoster Virus. Also used for in vitro cytotoxicity testing. <http://www.viomed.com/services/product/mrc5.htm>

Neomycin-Anti-bacterial-Influenza (Fluvirin), Measles (Attenuvax), Mumps (Mumpsvax), Rubella (Meruvax II), MMR (MMR-II), Polio virus attenuated (Orimune), Poliovirus inactivated (Ipol), Rabies (Imovax, RabAvert), Vaccinia (DryVax), Varicella (Varivax)

Neomycin is an antibacterial drug that is poorly absorbed when taken by mouth. It is combined with enteric coated erythromycin to suppress gastrointestinal (GI) bacteria before surgery to avoid infection. Neomycin is used to treat hepatic coma in cases of liver failure and is included in some antibiotic products used to treat infections of the eyes, ears, or skin

http://www.gnc.com/health_notes/Drug/Neomycin.htm#Introductory

Ovalbumin-Growth medium-Rabies (RabAvert)

Definition: [n] the white of an egg; the nutritive and protective gelatinous substance surrounding the yolk consisting mainly of albumin dissolved in water Synonyms: albumen, egg white See Also: egg, eggs, fixings, ingredient

<http://www.hyperdictionary.com/dictionary/ovalbumin>

Phenol-Preservative, anti-bacterial-Pneumococcal (Pneumovax-23), Typhoid inactivated (Typhim Vi), Vaccinia (DryVax)

Synonyms: benzenol, carboic acid, hydroxybenzene, monohydroxybenzene, monophenol, oxybenzene, phenic acid, phenylic acid, phenyl alcohol, phenylic alcohol

Stability: Stable. Substances to be avoided include strong oxidising agents, strong bases, strong acids, alkalies, calcium hypochlorite. Flammable. May discolour in light.

Toxicology: **This material is a systemic poison and constitutes a serious health hazard. The risks of using it in the laboratory must be fully assessed before work begins. Vesicant. TLV (Threshold Limit Value) 5 ppm. Acute poisoning by ingestion, inhalation or skin contact may lead to death. Phenol is readily absorbed through the skin.** Highly toxic by inhalation. Causes burns.

Toxicity data : ORL (oral)-HMN (human) LDLO (lowest published lethal dose) 140 mg kg-1

ORL (oral)-RAT LD50 (lethal dose 50 percent kill) 317 mg kg-1

IPR (intraperitoneal)-RAT LD50 (lethal dose 50 percent kill) 127 mg kg-1

ORL (oral)-RBT (rabbit) LDLO (lowest published lethal dose) 420 mg kg-1

Risk phrases: R24 (Toxic in contact with skin) R25 (Toxic if swallowed) R34 (Causes burns)

Personal protection: Safety glasses, gloves, good ventilation.

Safety phrases: S28 (After contact with skin, wash immediately with plenty of soap-suds) S45 (In case of accident or if you feel unwell, seek medical advice immediately-show the label whenever possible)

Critical Decisions Count

<http://physchem.ox.ac.uk/MSDS/PH/phenol.html>

Phenol red (phenolsulfonphthalein)-pH indicator, dye-Poliovirus attenuated (Orimune), Rabies (Imovax)

Stability: Stable. Incompatible with strong oxidizing agents.

Toxicology: May be harmful by ingestion, or through skin contact. May cause skin, eye or respiratory irritation.

Transport information: Non-hazardous for air, sea and road freight.

Personal protection: Generally regarded as presenting a low hazard. Handle with normal care.

http://physchem.ox.ac.uk/MSDS/PH/phenol_red.html

2-Phenoxyethanol-Preservative-DTaP (Infanrix), Hepatitis A (Havrix), Lyme disease (Lymerix), Poliovirus inactivated (Ipol)

Synonyms: arosol, dowanol EP, dowanol EPH, emery 6705, ethylene glycol phenyl ether, ethylene glycol monophenyl ether, phenoxetol, phenoxyethanol, rose ether, phenoxyethyl alcohol, 1-hydroxy-2-phenoxyethane, phenylmonoglycol ether, 2-phenoxyethanol, glycol monophenyl ether, beta-hydroxyethyl phenyl ether, various trade names

Uses: Used as a fixative for perfumes, a bactericide (in conjunction with quaternary ammonium compounds), an insect repellent, a topical antiseptic, a solvent for cellulose acetate, dyes, inks and resins, in organic synthesis of plasticizers, in germicides, in pharmaceuticals, in cosmetics and in preservatives.

Stability: Stable. Incompatible with strong oxidizing agents.

Toxicology: Harmful if swallowed, inhaled or absorbed through the skin. May cause reproductive defects. Severe eye and skin irritant.

Toxicity data: ORL (oral)-RAT LD50 (lethal dose 50 percent kill) 1260 mg kg-1

SKN (administration onto skin)-RAT LD50 (lethal dose 50 percent kill) 14422 mg kg-1

IPR (intraperitoneal)-RAT LD50 (lethal dose 50 percent kill) 554 mg kg-1

ORL (oral)-MUS (mouse) LD50 (lethal dose 50 percent kill) 933 mg kg-1

Irritation data: SKN (administration onto skin)-RBT (rabbit) 500 mg/24h mld (mild irritation effects)

EYE (administration into eye-irritant)-RBT (rabbit) 6 mg mod (moderate irritation effects)

EYE (administration into eye-irritant)-RBT (rabbit) 0.25 mg/24h sev (severe irritation effects)

Risk phrases: R20 (Harmful by inhalation) R21 (Harmful in contact with skin) R22 (Harmful if swallowed) R36 (Irritating to eyes)

Transport information: Non-hazardous for air, sea and road freight.

Personal protection: Safety glasses, adequate ventilation.

Safety phrases S2 (Keep out of the reach of children) S26 (In case of contact with eyes, rinse immediately with plenty of water and seek medical advice) <http://physchem.ox.ac.uk/MSDS/PH/2-phenoxyethanol.html>

Phosphate buffers (eg, disodium, monosodium, potassium, sodium dihydrogen phosphate)-Adjust pH-DTaP (all brands), DT (most brands), Hib (Act-Hib), Hepatitis A (Havrix), Hepatitis B (Engerix-B), Lyme disease (Lymerix), Poliovirus inactivated (Ipol), Rabies (BioRab), Typhoid inactivated (Typhim Vi), Varicella (Varivax)

Polydimethylsiloxane-Anti-foaming agent-Typhoid inactivated (Typhim Vi)

Polyethylene glycol p-isooctylphenyl ether (Triton X-100)-Nonionic surfactant (viral inactivation)- Influenza (Fluzone)

Synonyms: polyethylene glycol P-1,1,3,3-tetramethylbutylphenyl ether, octyl phenol ethoxylate, 4-octylphenol polyethoxylate, Mono 30

Stability: Stable. Incompatible with strong oxidizing agents. Viscosity increases as temperature falls and handling becomes difficult at temperatures below 20 C

Toxicology: Harmful if swallowed. Causes severe eye irritation. May be harmful if inhaled or in contact with skin.

Toxicology not fully investigated. The product may contain traces of ethylene oxide or dioxane, which are probable human carcinogens.

Toxicity data: ORL (oral)-RAT LD50 (lethal dose 50 percent kill) 1800 mg kg-1

IVN (intravenous)-MUS (mouse) LD50 (lethal dose 50 percent kill) 375 mg kg-1

Risk phrases: R22 (Harmful if swallowed) R41 (Harmful if swallowed)

Transport information: Non-hazardous for air, sea and road freight.

Personal protection: Safety glasses.

Safety phrases: S23 (Do not breathe vapour) S26 (In case of contact with eyes, rinse immediately with plenty of water and seek medical advice) S36 (Wear suitable protective clothing) http://physchem.ox.ac.uk/MSDS/TR/triton_X-100.html

Polymyxin B-Anti-bacterial-Influenza (Fluvirin), Poliovirus inactivated (Ipol), Vaccinia (DryVax)

Critical Decisions Count

Polymyxin B: Definition(s) from the Unified Medical Language System ® "A mixture of polymyxins B1 and B2, obtained from *Bacillus polymyxa* strains. They are basic polypeptides of about eight amino acids and have cationic detergent action on cell membranes. Polymyxin B is used for infections with gram-negative organisms, but may be neurotoxic and nephrotoxic." <http://www.diseasesdatabase.com/umlsdef.asp?gInqUserChoice=30930>
Purification, toxicity, and antiendotoxin activity of polymyxin B nonapeptide
<http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=172678>

Polyoxyethylene 9-10 nonylphenol (Triton N-101, octoxynol 9)-Nonionic surfactant (viral inactivation)-Influenza (Fluvirin)

Octoxynol-9: Nonionic surfactant mixtures varying in the number of repeating ethoxy (oxy-1,2-ethanediyl) groups. They are used as detergents, emulsifiers, wetting agents, defoaming agents, etc. Octoxynol-9, the compound with 9 repeating ethoxy groups, is a spermicide. <http://www.online-medical-dictionary.org/?q=Octoxynol-9>

Polysorbate 20-Surfactant-Hepatitis A (Havrix)

Synonyms: Polyoxyethylene sorbitan monolaurate; Polysorbate 20 NF

Potential Health Effects

Inhalation: Not expected to be a health hazard.

Ingestion: Large doses may produce abdominal spasms, diarrhea.

Skin Contact: May cause irritation or sensitization in sensitive individuals.

Eye Contact: May cause irritation.

Chronic Exposure: No information found.

Aggravation of Pre-existing Conditions: No information found.

First Aid Measures

Inhalation: Not expected to require first aid measures. Remove to fresh air. Get medical attention for any breathing difficulty.

Ingestion: Give several glasses of water to drink to dilute. If large amounts were swallowed, get medical advice.

Skin Contact: Immediately flush skin with plenty of soap and water for at least 15 minutes. Remove contaminated clothing and shoes. Wash clothing before reuse. Thoroughly clean shoes before reuse. Get medical attention if irritation develops.

Eye Contact: Immediately flush eyes with plenty of water for at least 15 minutes, lifting upper and lower eyelids occasionally. Get medical attention if irritation persists.

Stability: Stable under ordinary conditions of use and storage

Toxicological Information: Oral rat LD50 (lethal dose 50 percent kill) 36,700mg/kg. Investigated as a reproductive effector.

Label Hazard Warning: CAUTION! MAY CAUSE IRRITATION TO SKIN AND EYES.

Label Precautions: Avoid contact with eyes, skin and clothing. Keep container closed. Wash thoroughly after handling.

Label First Aid: In case of contact, immediately flush eyes or skin with plenty of water for at least 15 minutes. Get medical attention if irritation develops or persists.

Product Use: Laboratory Reagent. NOT INTENDED FOR INJECTABLE DRUG USE.

<http://www.herbalsoapsbyrj.com/ps20-msds.htm>

Did you know that the ingredient used to make some "tearless" or "Baby" shampoos is called Polysorbate 20, a derivative of Novocain, used by dentist and doctors as a numbing agent. Polysorbate 20 causes a numbing sensation to the eyes, preventing children from feeling the sting and burn from the strong detergents used.

<http://www.naturalhealthmarket.com/tearlessShamp.htm>

Polysorbate 80-Surfactant-DTaP (Acel-Imune, Infanrix, Tripedia), Influenza (Fluogen)

Polysorbate 80 is a nonionic surfactant used widely as an additive in foods, pharmaceutical preparations, and cosmetics as an emulsifier, dispersant, or stabilizer. Synonyms: Glycol; sorbitan mono-9-octadecenoate poly(oxy-1,2-ethanediyl) derivatives; polyoxyethylene (20) sorbitan mono-oleate; sorbitan mono-oleate; polyethylene oxide sorbitan mono-oleate <http://ntp-server.niehs.nih.gov/htdocs/LT-studies/tr415.html>

Polyoxyethylene (20) sorbitan monooleate; a mixture of polyoxyethylene ethers of mixed partial oleic esters of sorbitol anhydrides; used as an emulsifier, as in the preparation of pharmacologic products.

<http://www.books.md/P/dic/polysorbate80.php>

Potassium glutamate-Stabilizer-Rabies (RabAvert)

Silicon-Anti-foaming agent-Lyme disease (LymeRix)

Stability: Stable. Fine powder is highly flammable. Incompatible with oxidizing agents, bases, carbonates, alkali metals, lead and aluminium oxides, halogens, carbides, formic acid.

Critical Decisions Count

Toxicology: Generally regarded as safe. Typical TLV (Threshold Limit Value) TWA (time weighted average) 10 mg/m³.
Toxicity data: ORL (oral) -RAT LD50 (lethal dose 50 percent kill) 3160 mg kg⁻¹
Risk phrases: R11-powder (Highly flammable)
Transport information: Non-hazardous for air, sea and road freight.
Personal protection: Minimize contact.
Safety phrases: S16 (Keep away from sources of ignition) S43 (In case of fire use ...-there follows the type of fire-fighting equipment to be used) <http://physchem.ox.ac.uk/MSDS/SI/silicon.html>

Sodium acetate-Adjust pH-DT (some brands), Td (some brands)

Synonyms: sodium acetate anhydrous

Stability: Stable. Incompatible with strong oxidizing agents, halogens. Moisture sensitive.

Toxicology: May be harmful by ingestion, inhalation or through skin absorption. May act as an irritant.

Toxicity data ORL (oral)-RAT LD50 (lethal dose 50 percent kill) 3530 mg kg⁻¹

SCU (subcutaneous)-MUS (mouse) LD50 (lethal dose 50 percent kill) 3200 mg kg⁻¹

IHL (inhalation)-RAT LC50 (lethal concentration 50 percent kill) >30g m⁻³ / 1h

ORL (oral)-MUS (mouse) LD50 (lethal dose 50 percent kill) 6891 mg kg⁻¹

SKN (administration onto skin)-RBT (rabbit) LD50 (lethal dose 50 percent kill) >10000 mg kg⁻¹

Transport information: Non-hazardous for air, sea and road freight.

Personal protection: Safety glasses. Adequate ventilation

Safety phrases S22 (Do not breathe dust) S24 (Avoid contact with skin) S25 (Avoid contact with eyes)

http://physchem.ox.ac.uk/MSDS/SO/sodium_acetate.html

Sodium bisulfite-Preservative-Influenza (Fluogen)

Synonyms: sodium hydrogen sulfite, sodium acid sulfite, hydrogen sodium sulfite, sodium bisulphite, sodium hydrogen sulphite, sodium acid sulphite, hydrogen sodium sulphite, sulfurous acid sodium salt, hydrogen sulfite sodium

Stability: Stable. Incompatible with strong oxidizing agents, strong acids.

Toxicology: Harmful if swallowed or inhaled. **May cause allergic reaction in sensitive individuals, especially asthmatics.** Irritant. Typical TLV (Threshold Limit Value)/TWA (time weighted average) 5 mg/m³.

Toxicity data: ORL (oral)-RAT LD50 (lethal dose 50 percent kill) 2000 mg kg⁻¹

IPR (intraperitoneal)-RAT LD50 (lethal dose 50 percent kill) 650 mg kg⁻¹

IVN (intravenous)-RAT LD50 (lethal dose 50 percent kill) 115 mg kg⁻¹

Risk phrases: R20 (Harmful by inhalation) R22 (Harmful if swallowed) R36 (Irritating to eyes) R37 (Irritating to respiratory system) R38 (Irritating to skin)

Personal protection: Safety glasses, adequate ventilation.

Safety phrases: S26 (In case of contact with eyes, rinse immediately with plenty of water and seek medical advice)

S36 (Wear suitable protective clothing) http://physchem.ox.ac.uk/MSDS/SO/sodium_bisulfite.html

Sodium borate-Adjust pH-Hepatitis A (Vaqta), Hib-Hepatitis B (Comvax)

Sodium borate decahydrate; borax; sodium pyroborate

Hazards Identification-Emergency Overview: WARNING! HARMFUL IF SWALLOWED, INHALED OR ABSORBED THROUGH SKIN. CAUSES IRRITATION TO SKIN, EYES AND RESPIRATORY TRACT.

Potential Health Effects

Inhalation: Causes irritation to the respiratory tract. Symptoms may include coughing, shortness of breath.

Ingestion: May cause nausea, vomiting, diarrhea, muscular spasms, dullness, lethargy, circulatory depression, central nervous system depression, shock, kidney damage, coma, and death. Estimated lethal dose 15 to 20 grams.

Skin Contact: Causes irritation to skin. Symptoms include redness, itching, and pain. May be absorbed through the skin with possible systemic effects.

Eye Contact: Causes irritation, redness, and pain.

Chronic Exposure: Prolonged or repeated ingestion or skin absorption may cause anorexia, weight loss, vomiting, mild diarrhea, skin rash, convulsions, and anemia.

Aggravation of Pre-existing Conditions: No information found.

First Aid Measures

Inhalation: Remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention.

Ingestion: Induce vomiting immediately as directed by medical personnel. Never give anything by mouth to an unconscious person. Get medical attention.

Skin Contact: Immediately flush skin with plenty of water for at least 15 minutes while removing contaminated clothing and shoes. Get medical attention. Wash clothing before reuse. Thoroughly clean shoes before reuse.

Critical Decisions Count

Eye Contact: Immediately flush eyes with plenty of water for at least 15 minutes, lifting lower and upper eyelids occasionally. Get medical attention immediately.

Toxicological Information

Hydrate: Oral rat LD50 (lethal dose 50 percent kill): 2660 mg/kg. Investigated as a mutagen, reproductive effector.

Anhydrous: Investigated as a reproductive effector

Label Hazard Warning: WARNING! HARMFUL IF SWALLOWED, INHALED OR ABSORBED THROUGH SKIN. CAUSES IRRITATION TO SKIN, EYES AND RESPIRATORY TRACT.

Label Precautions: Avoid contact with eyes, skin and clothing. Avoid breathing dust. Keep container closed.

Use only with adequate ventilation. Wash thoroughly after handling.

Label First Aid: If swallowed, induce vomiting immediately as directed by medical personnel. Never give anything by mouth to an unconscious person. If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. In case of contact, immediately flush eyes or skin with plenty of water for at least 15 minutes while removing contaminated clothing and shoes. Wash clothing before reuse. In all cases, get medical attention.

Product Use: Laboratory Reagent. <http://www.sefsc.noaa.gov/HTMLdocs/SodiumBorate.htm>

Sodium chloride-Adjust tonicity-Most vaccines, including Anthrax, BCG, Cholera, DTaP, DTwP, DTwPHib, DT, Td, Hepatitis A, Hepatitis B, Hib, Influenza, Lyme disease, Pneumococcal, Polio inactivated, Rabies, Typhoid inactivated, Varicella, Yellow fever

Synonyms: extra fine 200 salt, extra fine 325 salt, H.G. blending, salt, sea salt, table salt, common salt, dendritis, rock salt, top flake, white crystal, saline, halite, purex, USP sodium chloride

Stability: Stable. Incompatible with strong oxidizing agents.

Toxicology: May cause skin, eye or respiratory irritation.

Toxicity data: ORL (oral)-RAT LD50 (lethal dose 50 percent kill) 3000 mg kg-1

ORL (oral)-MAN LDLO (lowest published lethal concentration) 1000 mg kg-1

ORL (oral)-MUS (mouse) LD50 (lethal dose 50 percent kill) 4000 mg kg-1

IPR (intraperitoneal)-MUS (mouse) LD50 (lethal dose 50 percent kill) 2602 mg kg-1

ICV (intracervical)-MUS (mouse) LD50 (lethal dose 50 percent kill) 131 mg kg-1

SKN (administration onto skin)-RBT (rabbit) LD50 (lethal dose 50 percent kill) >10000 mg kg-1

Irritation data: SKN (administration onto skin)-RBT (rabbit) 50 mg/24h mld (mild irritation effects)

Risk phrases: R36 (Irritating to eyes) R37 (Irritating to respiratory system) R38 (Irritating to skin)

Personal protection: Not believed to present a significant hazard to health.

Safety phrases: S26 (In case of contact with eyes, rinse immediately with plenty of water and seek medical advice)

S36 (Wear suitable protective clothing) http://physchem.ox.ac.uk/MSDS/SO/sodium_chloride.html

Sodium hydroxide-Adjust pH-DT (most brands), Td (most brands)

Synonyms: caustic soda, soda lye, lye, white caustic, sodium hydrate, fotofoil etchant, NAOH, STCC 4935235, sodium hydroxide pellets, Lewis red devil lye

Stability: Stable. Incompatible with a wide variety of materials including many metals, ammonium compounds, cyanides, acids, nitro compounds, phenols, combustible organics. Hygroscopic. Heat of solution is very high and may lead to a dangerously hot solution if small amounts of water are used.

Toxicology: Very corrosive. Causes severe burns. May cause serious permanent eye damage. Very harmful by ingestion. Harmful by skin contact or by inhalation of dust. Typical TLV (Threshold Limit Value) 2 mg m-1.

Toxicity data: IPR (intraperitoneal)-MUS (mouse) LD50 (lethal dose 50 percent kill) 40 mg kg-1

Irritation data: EYE (administration into eye-irritant)-MKY (monkey) 1%/24h sev (severe irritation effects)

SKN (administration onto skin)-RBT (rabbit) 500 mg/24h sev (severe irritation effects)

EYE (administration into eye-irritant)-RBT (rabbit) 1% sev (severe irritation effects)

Risk phrases: R35. (Causes severe burns)

Transport information: UN Major hazard class 8.0. (Corrosive substances) Packing group II. UN No 1823. EMS No 8.0-06.

Personal protection: Safety glasses, adequate ventilation, Neoprene or PVC gloves.

Safety phrases: S26 (In case of contact with eyes, rinse immediately with plenty of water and seek medical advice)

S37 (Wear suitable gloves) S39 (Wear eye / face protection) S45 (In case of accident or if you feel unwell, seek medical advice immediately-show the label whenever possible)

http://physchem.ox.ac.uk/MSDS/SO/sodium_hydroxide.html

Sorbitol-Stabilizer, solvent-Measles (Attenuvax), Mumps (Mumpsvox), Rubella (Meruvax II), MMR (MMR-II), Polio attenuated, Yellow fever (YF-Vax)

Synonyms: cholaxine, clucitol, diakarmon, gulitol, l-gulitol, karion, nivitin, sionit, sorbicolan, sorbite, d-sorbitol, sorbo, sorbol, sorbostyl, sorvilande

Critical Decisions Count

Stability: Stable. Avoid strong oxidizing agents. Protect from moisture.

Toxicology: No known hazards.

Toxicity data: ORL (oral)-RAT LD50 (lethal dose 50 percent kill) 16000 mg kg-1

SCU (subcutaneous)-RAT LD50 (lethal dose 50 percent kill) 29600 mg kg-1

IVN (intravenous)-RAT LD50 (lethal dose 50 percent kill) 7100 mg kg-1

Transport information: Non-hazardous for air, sea and road freight.

Personal protection: No special measures required.

<http://physchem.ox.ac.uk/MSDS/SO/sorbitol.html>

Streptomycin-Anti-bacterial-Influenza (Fluogen), Poliovirus attenuated (Orimune), Poliovirus inactivated (Ipol), Vaccinia (DryVax [dihydrostreptomycin])

Drug description: Streptomycin is an antibiotic used in combination with other drugs to treat tuberculosis (TB). TB is a chronic bacterial infection. TB causes more deaths worldwide than any other infectious disease. TB is spread through the air and usually affects the lungs, although other organs are sometimes involved. Some 1.7 billion people - one-third of the world's population - are infected with the predominant TB organism, Mycobacterium tuberculosis. Most people infected with M. tuberculosis never develop active TB. However, in persons with weakened immune systems, especially those infected with the HIV virus, TB may overcome the body's defenses, multiply and cause active disease. While streptomycin is no longer considered a first line treatment for TB, some strains of multi-drug resistant TB (MDRTB) are susceptible to treatment. Side effects: Severe nausea, vomiting, dizziness, rash and fever. Loss of hearing has been reported following long term use. Streptomycin should not be used in anyone with kidney impairment because it increases the risk of severe toxic reactions. Dosage: Streptomycin is given by intramuscular injection. Adults are given 1 g daily in combination with 5 g of PAS and 200-300 mg of isoniazid. Ultimately the streptomycin should be stopped or reduced to 1 g two to three times weekly. How long it may take to work: The total period of treatment for TB is a minimum of 1 year. Indication for stopping streptomycin may occur at any time earlier due to toxic symptoms, or if the infection becomes resistant to the drug. Managing side effects: Symptoms subside and recovery is usually complete after you stop taking the drug. Roaring noises, or ringing in the ears are signs that treatment with streptomycin should be stopped. <http://www.aegis.com/factsheets/network/access/drugs/stre.html>

Sucrose-Stabilizer in freeze-drying-Hib (Act-HIB), Typhoid oral (Vivotif), Varicella (Varivax)

Thimerosal-Preservative in some multidose containers (see package labeling for precise content)-DTaP (some containers), DTwP (most containers), DT (most brands), Td (most brands), Hepatitis B (some packages), Hib (some packages), Influenza (all brands), Japanese encephalitis (JEVax), Meningococcal (Menomune), Pneumococcal (Pnu-Imune 23), Rabies (BioRab)

Synonyms: ethyl-2-mercaptobenzoate(2-)-O,S--mercurate sodium, mercury((o-carboxyphenyl)thio)ethyl sodium salt, mercuriothiolate, merzonin sodium, SET, sodium ethylmercuric thiosalicylate, sodium merthiolate, thimerosalate, thiomersalate, merfamin, merthiolate, merthiolate sodium, merzonin, nosemack, merseptyl, 2-mercaptobenzoic acid mercury complex, elcide 75, thiomersal, ethylmercurithiosalicylic acid sodium salt, various other systematic and non-systematic names

Use: drug, anti-infective agent, preservative in cosmetics.

Stability: Stable. May degrade in sunlight. Incompatible with strong acids, strong bases, strong oxidizing agents, iodine, heavy metal salts.

Toxicology: Poison. Experimental neoplastigen and teratogen. Harmful by inhalation and ingestion. May cause reproductive damage. May be harmful through skin contact. Typical OEL 0.05 mg/m³.

Toxicity data: ORL (oral)-RAT LD50 (lethal dose 50 percent kill) 75 mg kg-1

SCU (subcutaneous)-RAT LD50 (lethal dose 50 percent kill) 98 mg kg-1

UNR (unreported)-RAT LD50 (lethal dose 50 percent kill) 40 mg kg-1

IVN (intravenous)-MUS (mouse) LD50 (lethal dose 50 percent kill) 30 mg kg-1

ORL (oral)-MUS (mouse) LD50 (lethal dose 50 percent kill) 91 mg kg-1

IPR (intraperitoneal)-MUS (mouse) LD50 (lethal dose 50 percent kill) 54 mg kg-1

IAL (intraaural)-CHD (child) LDLO (lowest published lethal dose) 60 mg kg-1/4w-i

Transport information: Hazard class 6.1. (Toxic substances) Packing group III. UN No 2025.

Personal protection: Safety glasses, adequate ventilation.

<http://physchem.ox.ac.uk/MSDS/TH/thimerosal.html>

Tri(n)butylphosphate-Viral inactivator-Influenza (FluShield)

Synonyms: phosphoric acid tri-n-butyl ester, tri-n-butyl phosphate

Stability: Stable. Combustible. Incompatible with strong oxidizing agents. May be water sensitive.

Toxicology: Irritant.

Critical Decisions Count

Toxicity data: ORL (oral)-RAT LD50 (lethal dose 50 percent kill) 3000 mg kg⁻¹

Transport information: Non-hazardous for air, sea and road freight.

Personal protection: Safety glasses.

http://physchem.ox.ac.uk/MSDS/TR/tributyl_phosphate.html

Vitamins unspecified-Growth medium-Rabies (Imovax)

Yeast protein-Growth medium-Hepatitis B (Engerix-B, Recombivax- HB), Hib (HibTiter), Hib-Hepatitis B (Comvax)

Glossary: <http://ptcl.chem.ox.ac.uk/MSDS/glossary/GLOSSARY.html>

Flash point -The Flash Point of a chemical is the lowest temperature at which a flame will propagate through the vapour of a combustible material to the liquid surface. It is determined by the vapour pressure of the liquid, since only when a sufficiently high vapour concentration is reached, can it support combustion. It should be noted that the source of ignition need not be an open flame, but could equally be, for example, the surface of a hot plate, or a steam pipe.

Intraperitoneal - Intraperitoneal is the term used when a chemical is contained within or administered through the peritoneum (the thin, transparent membrane that lines the walls of the abdomen). It may be abbreviated IP, IPN or IPR on safety data sheets.

Intravenous - Intravenous indicates the introduction of a material into or through a vein. This is frequently abbreviated IV or IVN in LD50 values quoted on Material Safety Data Sheets.

Irritant - An Irritant is a chemical which may cause reversible inflammation on contact.

LC50 - (Lethal Concentration 50) is the concentration of a chemical which kills 50% of a sample population. This measure is generally used when exposure to a chemical is through the animal breathing it in, while the LD50 is the measure generally used when exposure is by swallowing, through skin contact, or by injection.

LD50 - (Lethal Dose 50) is the dose of a chemical which kills 50% of a sample population. In full reporting, the dose, treatment and observation period should be given. Further, LD50, LC50, ED50 and similar figures are strictly only comparable when the age, sex and nutritional state of the animals is specified. Nevertheless, such values are widely reported and used as an effective measure of the potential toxicity of chemicals.

LDLO - LDLO is an abbreviation for Lethal Dose Low, the minimum amount of a chemical which tests have shown will be lethal to a specified type of animal. This is normally quoted in mg kg⁻¹ body weight.

OEL (Occupational Exposure Limit) - A (generally legally-enforceable) limit on the amount or concentration of a chemical to which workers may be exposed.

Oxidizing Agent - An Oxidizing Agent may be defined in various ways, depending upon the context in which the phrase is used. In broad terms it is often taken to mean a chemical which can act as an electron acceptor. Strong oxidizing agents are often very reactive chemicals, and, in contact with combustible material such as paper, sawdust, fabrics or powdered metals, may form unstable mixtures which constitute a risk of fire or explosion.

Reducing Agent - A Reducing Agent may be defined in various ways, depending upon the context in which the phrase is used. In broad terms it is often taken to mean a chemical which can act as an electron donor.

Subcutaneous - Subcutaneous means below the skin. The subcutaneous toxicity of a chemical is important if the chemical is injected (deliberately or accidentally) or is forced through the skin by injury.

Surfactant - A Surfactant lowers the surface tension of a liquid. Soaps and some components of detergents are typical surfactants.

TLV (Threshold Limit Value) - TLV is the maximum permissible concentration of a material, generally expressed in parts per million in air for some defined period of time (often 8 hours, but sometimes for 40 hours per week over an assumed working lifetime). These values, which may differ from country to country, are often backed up by regulation and therefore may be legally enforceable.

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TWA (Time Weighted Average) - This term is used in the specification of Occupational Exposure Limits (OELs) to define the average concentration of a chemical to which it is permissible to expose a worker over a period of time, typically 8 hours.

Merck & Co, Inc.
Whitehouse Station, NJ 08889

RECOMBIVAX HB® HEPATITIS B VACCINE (RECOMBINANT)

RECOMBIVAX HB* Hepatitis B Vaccine (Recombinant) is a non-infectious subunit viral vaccine derived from hepatitis B surface antigen (HBsAg) produced in yeast cells. A portion of the hepatitis B virus gene, coding for HBsAg, is cloned into yeast, and the vaccine for hepatitis B is produced from cultures of this recombinant yeast strain according to methods developed in the Merck Research Laboratories. The antigen is harvested and purified from fermentation cultures of a recombinant strain of the yeast *Saccharomyces cerevisiae* containing the gene for the *adw* subtype of HBsAg. The fermentation process involves growth of *Saccharomyces cerevisiae* on a complex fermentation medium which consists of an extract of yeast, soy peptone, dextrose, amino acids and mineral salts. The HBsAg protein is released from the yeast cells by cell disruption and purified by a series of physical and chemical methods. The purified protein is treated in phosphate buffer with formaldehyde and then coprecipitated with alum (potassium aluminum sulfate) to form bulk vaccine adjuvanted with amorphous aluminum hydroxyphosphate sulfate. The vaccine contains no detectable yeast DNA but may contain not more than 1% yeast protein. The vaccine produced by the Merck method has been shown to be comparable to the plasma-derived vaccine in terms of animal potency (mouse, monkey, and chimpanzee) and protective efficacy (chimpanzee and human). The vaccine against hepatitis B, prepared from recombinant yeast cultures, is free of association with human blood or blood products. Each lot of hepatitis B vaccine is tested for safety, in mice and guinea pigs, and for sterility. RECOMBIVAX HB is a sterile suspension for intramuscular injection. However, for persons at risk of hemorrhage following intramuscular injection, the vaccine may be administered subcutaneously. RECOMBIVAX HB Hepatitis B Vaccine (Recombinant) is supplied in three formulations. (See HOW SUPPLIED.) Pediatric/Adolescent Formulation (Without Preservative), 10 mcg/mL: each 0.5 mL dose contains 5 mcg of hepatitis B surface antigen. Adult Formulation (Without Preservative), 10 mcg/mL: each 1 mL dose contains 10 mcg of hepatitis B surface antigen. Dialysis Formulation (Without Preservative), 40 mcg/mL: each 1 mL dose contains 40 mcg of hepatitis B surface antigen. All formulations contain approximately 0.5 mg of aluminum (provided as amorphous aluminum hydroxyphosphate sulfate, previously referred to as aluminum hydroxide) per mL of vaccine. In each formulation, hepatitis B surface antigen is adsorbed onto approximately 0.5 mg of aluminum (provided as amorphous aluminum hydroxyphosphate sulfate) per mL of vaccine.

http://www.merck.com/product/usa/pi_circulars/r/recombivax_hb/recombivax_pi.pdf

VARIVAX® Varicella Virus Vaccine Live (Oka/Merck)

VARIVAX* [Varicella Virus Vaccine Live (Oka/Merck)] is a preparation of the Oka/Merck strain of live, attenuated varicella virus. The virus was initially obtained from a child with natural varicella, then introduced into human embryonic lung cell cultures, adapted to and propagated in embryonic guinea pig cell cultures and finally propagated in human diploid cell cultures (WI-38). Further passage of the virus for varicella vaccine was performed at Merck Research Laboratories (MRL) in human diploid cell cultures (MRC-5) that were free of adventitious agents. This live, attenuated varicella vaccine is a lyophilized preparation containing sucrose, phosphate, glutamate, and processed gelatin as stabilizers. VARIVAX, when reconstituted as directed, is a sterile preparation for subcutaneous administration. Each 0.5 mL dose contains the following: a minimum of 1350 PFU (plaque forming units) of Oka/Merck varicella virus when reconstituted and stored at room temperature for 30 minutes, approximately 25 mg of sucrose, 12.5 mg hydrolyzed gelatin, 3.2 mg sodium chloride, 0.5 mg monosodium L-glutamate, 0.45 mg of sodium phosphate dibasic, 0.08 mg of potassium phosphate monobasic, 0.08 mg of potassium chloride; residual components of MRC-5 cells including DNA and protein; and trace quantities of sodium phosphate monobasic, EDTA, neomycin, and fetal bovine serum. The product contains no preservative. http://www.merck.com/product/usa/pi_circulars/v/varivax/varivax_pi.pdf

M-M-R® II (MEASLES, MUMPS, and RUBELLA VIRUS VACCINE LIVE)

M-M-R* II (Measles, Mumps, and Rubella Virus Vaccine Live) is a live virus vaccine for vaccination against measles (rubeola), mumps and rubella (German measles). M-M-R II is a sterile lyophilized preparation of (1) ATTENUVAX* (Measles Virus Vaccine Live), a more attenuated line of measles virus, derived from Enders' attenuated Edmonston strain and propagated in chick embryo cell culture; (2) MUMPSVAX* (Mumps Virus Vaccine Live), the Jeryl Lynn** (B level) strain of mumps virus propagated in chick embryo cell culture; and (3) MERUVAX* II (Rubella Virus Vaccine Live), the Wistar RA 27/3 strain of live attenuated rubella virus propagated in WI-38 human diploid lung fibroblasts.1,2

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The growth medium for measles and mumps is Medium 199 (a buffered salt solution containing vitamins and amino acids and supplemented with fetal bovine serum) containing SPGA (sucrose, phosphate, glutamate, and human albumin) as stabilizer and neomycin. The growth medium for rubella is Minimum Essential Medium (MEM) [a buffered salt solution containing vitamins and amino acids and supplemented with fetal bovine serum] containing human serum albumin and neomycin. Sorbitol and hydrolyzed gelatin stabilizer are added to the individual virus harvests. The cells, virus pools, fetal bovine serum, and human albumin are all screened for the absence of adventitious agents. Human albumin is processed using the Cohn cold ethanol fractionation procedure. The reconstituted vaccine is for subcutaneous administration. Each 0.5 mL dose contains not less than 1,000 TCID₅₀ (tissue culture infectious doses) of measles virus; 20,000 TCID₅₀ of mumps virus; and 1,000 TCID₅₀ of rubella virus. Each dose of the vaccine is calculated to contain sorbitol (14.5 mg), sodium phosphate, sucrose (1.9 mg), sodium chloride, hydrolyzed gelatin (14.5 mg), human albumin (0.3 mg), fetal bovine serum (<1 ppm), other buffer and media ingredients and approximately 25 mcg of neomycin. The product contains no preservative.

<http://www.ctvia.org/docs/Vaccine%20Pkg%20Insert%20-%20MMR%20-%20M-R%20II%20-%20Merck.pdf>

COMVAX® HAEMOPHILUS b CONJUGATE (MENINGOCOCCAL PROTEIN CONJUGATE) and HEPATITIS B (RECOMBINANT) VACCINE

COMVAX* [Haemophilus b Conjugate (Meningococcal Protein Conjugate) and Hepatitis B (Recombinant) Vaccine] is a sterile bivalent vaccine made of the antigenic components used in producing PedvaxHIB* [Haemophilus b Conjugate Vaccine (Meningococcal Protein Conjugate)] and RECOMBIVAX HB* [Hepatitis B Vaccine (Recombinant)]. These components are the *Haemophilus influenzae* type b capsular polysaccharide [polyribosylribitol phosphate (PRP)] that is covalently bound to an outer membrane protein complex (OMPC) of *Neisseria meningitidis* and hepatitis B surface antigen (HBsAg) from recombinant yeast cultures. *Haemophilus influenzae* type b and *Neisseria meningitidis* serogroup B are grown in complex fermentation media. The primary ingredients of the phenol-inactivated fermentation medium for *Haemophilus influenzae* include an extract of yeast, nicotinamide adenine dinucleotide, hemin chloride, soy peptone, dextrose, and mineral salts and for *Neisseria meningitidis* include an extract of yeast, amino acids and mineral salts. The PRP is purified from the culture broth by purification procedures which include ethanol fractionation, enzyme digestion, phenol extraction and diafiltration. The OMPC from *Neisseria meningitidis* is purified by detergent extraction, ultracentrifugation, diafiltration and sterile filtration. The PRP-OMPC conjugate is prepared by the chemical coupling of the highly purified PRP (polyribosylribitol phosphate) of *Haemophilus influenzae* type b (Haemophilus b, Ross strain) to an OMPC of the B11 strain of *Neisseria meningitidis* serogroup B. The coupling of the PRP to the OMPC is necessary for enhanced immunogenicity of the PRP. This coupling is confirmed by analysis of the components of the conjugate following chemical treatment which yields a unique amino acid. After conjugation, the aqueous bulk is then adsorbed onto an amorphous aluminum hydroxyphosphate sulfate adjuvant (previously referred to as aluminum hydroxide). HBsAg is produced in recombinant yeast cells. A portion of the hepatitis B virus gene, coding for HBsAg, is cloned into yeast, and the vaccine for hepatitis B is produced from cultures of this recombinant yeast strain according to methods developed in the Merck Research Laboratories. The antigen is harvested and purified from fermentation cultures of a recombinant strain of the yeast *Saccharomyces cerevisiae* containing the gene for the *adw* subtype of HBsAg. The fermentation process involves growth of *Saccharomyces cerevisiae* on a complex fermentation medium which consists of an extract of yeast, soy peptone, dextrose, amino acids and mineral salts. The HBsAg protein is released from the yeast cells by mechanical cell disruption and detergent extraction, and purified by a series of physical and chemical methods, which includes ion and hydrophobic chromatography, and diafiltration. The purified protein is treated in phosphate buffer with formaldehyde and then coprecipitated with alum (potassium aluminum sulfate) to form bulk vaccine adjuvanted with amorphous aluminum hydroxyphosphate sulfate. The vaccine contains no detectable yeast DNA, and 1% or less of the protein is of yeast origin. The individual PRP-OMPC and HBsAg adjuvanted bulks are combined to produce COMVAX. Each 0.5 mL dose of COMVAX is formulated to contain 7.5 mcg PRP conjugated to approximately 125 mcg OMPC, 5 mcg HBsAg, approximately 225 mcg aluminum as amorphous aluminum hydroxyphosphate sulfate, and 35 mcg sodium borate (decahydrate) as a pH stabilizer, in 0.9% sodium chloride. The vaccine contains not more than 0.0004% (w/v) residual formaldehyde. The potency of the PRP-OMPC component is measured by quantitating the polysaccharide concentration by an HPLC method. The potency of the HBsAg component is measured relative to a standard by an *in vitro* immunoassay. The product contains no preservative. COMVAX is a sterile suspension for intramuscular injection.

http://www.merck.com/product/usa/pi_circulars/c/comvax/comvax_pi.pdf

GlaxoSmithKline
Research Triangle Park, NC 27709

ENGERIX-B® Hepatitis B Vaccine (Recombinant)

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ENGERIX-B [Hepatitis B Vaccine (Recombinant)] is a noninfectious recombinant DNA hepatitis B vaccine developed and manufactured by GlaxoSmithKline Biologicals. It contains purified surface antigen of the virus obtained by culturing genetically engineered *Saccharomyces cerevisiae* cells, which carry the surface antigen gene of the hepatitis B virus. The surface antigen expressed in *Saccharomyces cerevisiae* cells is purified by several physicochemical steps and formulated as a suspension of the antigen adsorbed on aluminum hydroxide. The procedures used to manufacture ENGERIX-B result in a product that contains no more than 5% yeast protein. No substances of human origin are used in its manufacture. ENGERIX-B is supplied as a sterile suspension for intramuscular administration. The vaccine is ready for use without reconstitution; it must be shaken before administration since a fine white deposit with a clear colorless supernatant may form on storage. Pediatric/Adolescent: Each 0.5-mL dose contains 10 mcg of hepatitis B surface antigen adsorbed on 0.25 mg aluminum as aluminum hydroxide. The pediatric/adolescent vaccine is formulated without preservatives. The pediatric formulation contains a trace amount of thimerosal (<0.5 mcg mercury) from the manufacturing process, sodium chloride (9 mg/mL), and phosphate buffers (disodium phosphate dihydrate, 0.98 mg/mL; sodium dihydrogen phosphate dihydrate, 0.71 mg/mL). Adult: Each 1-mL adult dose contains 20 mcg of hepatitis B surface antigen adsorbed on 0.5 mg aluminum as aluminum hydroxide. The adult vaccine is formulated without preservatives. The adult formulation contains a trace amount of thimerosal (<1.0 mcg mercury) from the manufacturing process, sodium chloride (9 mg/mL), and phosphate buffers (disodium phosphate dihydrate, 0.98 mg/mL; sodium dihydrogen phosphate dihydrate, 0.71 mg/mL).

http://us.gsk.com/products/assets/us_engerixb.pdf

INFANRIX® Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed

INFANRIX (Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed) is a noninfectious, sterile combination of diphtheria and tetanus toxoids and 3 pertussis antigens [inactivated pertussis toxin (PT), filamentous hemagglutinin (FHA), and pertactin (69 kiloDalton outer membrane protein)] adsorbed onto aluminum hydroxide. INFANRIX is intended for intramuscular injection only. The diphtheria toxin is produced by growing *Corynebacterium diphtheriae* in Fenton medium containing a bovine extract. Tetanus toxin is produced by growing *Clostridium tetani* in a modified Latham medium derived from bovine casein. The bovine materials used in these extracts are sourced from countries which the United States Department of Agriculture (USDA) has determined neither have nor are at risk of bovine spongiform encephalopathy (BSE). Both toxins are detoxified with formaldehyde, concentrated by ultrafiltration, and purified by precipitation, dialysis, and sterile filtration. The 3 acellular pertussis antigens (PT, FHA, and pertactin) are isolated from *Bordetella pertussis* culture grown in modified Stainer-Scholte liquid medium. PT and FHA are isolated from the fermentation broth; pertactin is extracted from the cells by heat treatment and flocculation. The antigens are purified in successive chromatographic and precipitation steps. PT is detoxified using glutaraldehyde and formaldehyde. FHA and pertactin are treated with formaldehyde. Each antigen is individually adsorbed onto aluminum hydroxide. Each 0.5-mL dose is formulated to contain 25 Lf of diphtheria toxoid, 10 Lf of tetanus toxoid, 25 mcg of inactivated PT, 25 mcg of FHA, and 8 mcg of pertactin. Diphtheria and tetanus toxoid potency is determined by measuring the amount of neutralizing antitoxin in previously immunized guinea pigs. The potency of the acellular pertussis components (PT, FHA, and pertactin) is determined by enzyme-linked immunosorbent assay (ELISA) on sera from previously immunized mice. Each 0.5-mL dose also contains 2.5 mg of 2-phenoxyethanol as a preservative, 4.5 mg of NaCl, and aluminum adjuvant (not more than 0.625 mg aluminum by assay). Each dose also contains =100 mcg of residual formaldehyde and =100 mcg of polysorbate 80 (Tween 80). INFANRIX does not contain thimerosal.

http://us.gsk.com/products/assets/us_infanrix.pdf

BOOSTRIX Combined Diphtheria-Tetanus-acellular Pertussis (dTpa) Vaccine

The active ingredients of BOOSTRIX are non-infectious substances from tetanus, diphtheria bacteria and purified proteins of pertussis bacteria. **The vaccine cannot cause these diseases.** Each 0.5mL dose contains: 2 IU (2.5 Lf U) of diphtheria toxoid 20 IU (5 Lf U) of tetanus toxoid 8 mcg of pertussis toxoid, 8 mcg of filamentous haemagglutinin and 2.5 mcg of pertactin The inactive ingredients in the vaccine are: aluminium hydroxide, aluminium phosphate, formaldehyde, phenoxyethanol, polysorbate 80, sodium chloride (salt), glycine and water. The manufacture of this product includes exposure to bovine derived materials. No evidence exists that any case of vCJD (considered to be the human form of bovine spongiform encephalopathy) has resulted from the administration of any vaccine product.

[http://www.gsk.com.au/gskinternet/publishing.nsf/4a0f132842ea4d354a25685d0011fa04/90f909e883e5623dca256bf20018184a/\\$FILE/Boostrix.pdf](http://www.gsk.com.au/gskinternet/publishing.nsf/4a0f132842ea4d354a25685d0011fa04/90f909e883e5623dca256bf20018184a/$FILE/Boostrix.pdf)

**Aventis Pasteur Inc.
Swiftwater PA 18370 USA**

Critical Decisions Count

Tripedia® Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed

Tripedia®, Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed (DTaP), for intramuscular use, is a sterile preparation of diphtheria and tetanus toxoids adsorbed, with acellular pertussis vaccine in an isotonic sodium chloride solution containing thimerosal as a preservative and sodium phosphate to control pH. After shaking, the vaccine is a homogeneous white suspension. Tripedia® vaccine is distributed by Aventis Pasteur Inc. (AvP). *Corynebacterium diphtheriae* cultures are grown in a modified Mueller and Miller medium.² *Clostridium tetani* cultures are grown in a peptone-based medium containing a bovine extract. The meat used in this medium is US sourced. Both toxins are detoxified with formaldehyde. The detoxified materials are then separately purified by serial ammonium sulfate fractionation and diafiltration. The acellular pertussis vaccine components are isolated from culture fluids of Phase 1 *Bordetella pertussis* grown in a modified Stainer-Scholte medium.¹ After purification by salt precipitation, ultracentrifugation, and ultrafiltration, preparations containing varying amounts of both pertussis toxin (PT) and filamentous hemagglutinin (FHA) are combined to obtain a 1:1 ratio and treated with formaldehyde to inactivate PT. The diphtheria and tetanus toxoids are adsorbed using aluminum potassium sulfate (alum). The adsorbed toxoids are combined with acellular pertussis concentrate, and diluted to a final volume using sterile phosphate-buffered physiological saline. The 1 dose vial of vaccine is formulated without preservatives but contains a trace amount of thimerosal [(mercury derivative), (=0.3 µg mercury/dose)] from the manufacturing process. The multidose (7.5 mL) vial of vaccine contains the preservative thimerosal [(mercury derivative), 25 µg mercury/dose]. Each 0.5 mL dose contains, by assay, not more than 0.170 mg of aluminum and not more than 100 µg (0.02%) of residual formaldehyde. The vaccine contains gelatin and polysorbate 80 (Tween-80), which are used in the production of the pertussis concentrate. Each 0.5 mL dose is formulated to contain 6.7 Lf of diphtheria toxoid and 5 Lf of tetanus toxoid (both toxoids induce at least 2 units of antitoxin per mL in the guinea pig potency test), and 46.8 µg of pertussis antigens. This is represented in the final vaccine as approximately 23.4 µg of inactivated PT (also referred to as lymphocytosis promoting factor or LPF) and 23.4 µg of FHA. The inactivated acellular pertussis component contributes not more than 50 endotoxin units (EU) to the endotoxin content of 1 mL of DTaP. The potency of the pertussis components is evaluated by measuring the antibody response to PT and FHA in immunized mice using an ELISA system. When Tripedia® vaccine is used to reconstitute ActHIB® the combination vaccine is TriHIBit®. Each single 0.5 mL dose of TriHIBit®, **for the fourth dose only**, is formulated to contain 6.7 Lf of diphtheria toxoid, 5 Lf of tetanus toxoid (both toxoids induce at least 2 units of antitoxin per mL in the guinea pig potency test), 46.8 µg of pertussis antigens (approximately 23.4 µg of inactivated PT and 23.4 µg of FHA), 10 µg of purified *Haemophilus influenzae* type b capsular polysaccharide conjugated to 24 µg of inactivated tetanus toxoid, and 8.5% sucrose. **(Refer to ActHIB® package insert.)** http://www.vaccineshoppe.com/US_PDF/298-10_4043_4058.pdf

ActHIB® Haemophilus b Conjugate Vaccine (Tetanus Toxoid Conjugate)

ActHIB®, Haemophilus b Conjugate Vaccine (Tetanus Toxoid Conjugate), produced by Aventis Pasteur SA, is a sterile, lyophilized powder which is reconstituted at the time of use with either saline diluent (0.4% Sodium Chloride) or Aventis Pasteur Inc. (AvP) Diphtheria and Tetanus Toxoids and Pertussis Vaccine Adsorbed (whole-cell pertussis vaccine DTP) or Tripedia®, AvP Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed (DTaP) (when reconstituted known as TriHIBit®) for intramuscular use only. The vaccine consists of the Haemophilus b capsular polysaccharide (polyribosyl-ribitol-phosphate, PRP), a high molecular weight polymer prepared from the *Haemophilus influenzae* type b strain 1482 grown in a semi-synthetic medium, covalently bound to tetanus toxoid.¹ The lyophilized ActHIB® powder and saline diluent contain no preservative. The tetanus toxoid is prepared by extraction, ammonium sulfate purification, and formalin inactivation of the toxin from cultures of *Clostridium tetani* (Harvard strain) grown in a modified Mueller and Miller medium.² The toxoid is filter sterilized prior to the conjugation process. Potency of ActHIB® is specified on each lot by limits on the content of PRP polysaccharide and protein in each dose and the proportion of polysaccharide and protein in the vaccine which is characterized as high molecular weight conjugate.

When ActHIB® is reconstituted with saline diluent, each single dose of 0.5 mL is formulated to contain 10 µg of purified capsular polysaccharide conjugated to 24 µg of inactivated tetanus toxoid, and 8.5% of sucrose. When ActHIB® is combined with AvP DTP vaccine by reconstitution, each single dose (0.5 mL) is formulated to contain 10 µg of purified capsular polysaccharide conjugated to 24 µg of inactivated tetanus toxoid, 8.5% of sucrose, 6.7 Lf of diphtheria toxoid, 5 Lf of tetanus toxoid and an estimate of 4 protective units of pertussis vaccine. Thimerosal (mercury derivative) 1:10,000 is added as a preservative to AvP DTP vaccine. **(Refer to product insert for AvP whole-cell DTP.)**

When ActHIB® is combined with Tripedia® (TriHIBit®) by reconstitution **for booster dose**, each single dose (0.5 mL) is formulated to contain 10 µg of purified capsular polysaccharide conjugated to 24 µg of inactivated tetanus toxoid, 8.5% of sucrose, 6.7 Lf of diphtheria toxoid, 5 Lf of tetanus toxoid and 46.8 µg of pertussis antigens. The 0.6 mL vial of Tripedia® is formulated without preservatives but contains a trace amount of thimerosal [(mercury derivative), (=0.3 µg mercury/dose)] from the manufacturing process. **(Refer to product insert for Tripedia®.)** http://www.vaccineshoppe.com/US_PDF/545_05_4045.pdf

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DAPTACEL. Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed

DAPTACEL™, Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed, for intramuscular use, manufactured by Aventis Pasteur Limited, is a sterile suspension of pertussis antigens and diphtheria and tetanus toxoids adsorbed on aluminum phosphate in a sterile isotonic sodium chloride solution. After shaking, the vaccine is a white homogeneous cloudy suspension. Each dose of DAPTACEL™ contains the following active ingredients: pertussis toxoid 10 µg, filamentous hemagglutinin (FHA) 5 µg, pertactin (PRN) 3 µg, fimbriae types 2 and 3 5 µg diphtheria toxoid 15 Lf, tetanus toxoid 5 Lf. Other ingredients per dose include 3.3 mg (0.6% v/v) 2-phenoxyethanol as the preservative, 0.33 mg of aluminum as the adjuvant, =0.1 mg residual formaldehyde and <50 ng residual glutaraldehyde. The acellular pertussis vaccine components are produced from *Bordetella pertussis* cultures grown in Stainer-Scholte medium¹ modified by the addition of casamino acids and dimethyl-beta-cyclodextrin. The fimbriae types 2 and 3 are extracted from the bacterial cells and the pertussis toxin, FHA and PRN are prepared from the supernatant. These proteins are purified by sequential filtration, saltprecipitation, ultrafiltration and chromatography. Pertussis toxin is inactivated with glutaraldehyde and FHA is treated with formaldehyde. The individual antigens are adsorbed separately onto aluminum phosphate. *Corynebacterium diphtheriae* is grown in modified Mueller's growth medium.² After ammonium sulfate fractionation, the diphtheria toxin is detoxified with formalin and diafiltered. *Clostridium tetani* is grown in modified Mueller-Miller casamino acid medium without beef heart infusion.³ Tetanus toxin is detoxified with formalin and purified by ammonium sulfate fractionation and diafiltration. Diphtheria and tetanus toxoids are individually adsorbed onto aluminum phosphate. The adsorbed diphtheria, tetanus and acellular pertussis components are combined in a sterile isotonic sodium chloride solution containing 2-phenoxyethanol as preservative. Both diphtheria and tetanus toxoids induce at least 2 units of antitoxin per mL in the guinea pig potency test. The potency of the acellular pertussis vaccine components is evaluated by the antibody response of immunized mice to pertussis toxin, FHA, PRN and fimbriae types 2 and 3 measured by enzyme-linked immunosorbent assay (ELISA).
http://www.vaccineshoppe.com/US_PDF/DAPTACEL_3973_6.02.pdf

Fluzone® Influenza Virus Vaccine 2002 – 2003 Formula

Fluzone®, Influenza Virus Vaccine, (Zonal Purified, Subvirion) for intramuscular use, is a sterile suspension prepared from influenza viruses propagated in chicken embryos. The virus-containing fluids are harvested and inactivated with formaldehyde. Influenza virus is concentrated and purified in a linear sucrose density gradient solution using a continuous flow centrifuge. The virus is then chemically disrupted using Polyethylene Glycol p-Isooctylphenyl Ether (Triton® X-100 – A registered trademark of Rohm and Haas, Co.) producing a “split-antigen.” The split-antigen is then further purified by chemical means and suspended in sodium phosphate-buffered isotonic sodium chloride solution. Fluzone has been standardized according to USPHS requirements for the 2002-2003 influenza season and is formulated to contain 45 micrograms (µg) hemagglutinin (HA) per 0.5 mL dose, in the recommended ratio of 15 µg HA each, representative of the following three prototype strains: A/New Caledonia/20/99 (H1N1), A/Panama/2007/99 (H3N2) (an A/Moscow/10/99-like strain) and B/Hong Kong/1434/2002 (a B/Hong Kong/330/2001-like strain).¹ Gelatin 0.05% is added as a stabilizer. Fluzone is supplied in two unit dose preservative-free presentations distinguished by a pink syringe plunger rod: a 0.25 mL prefilled syringe (for pediatric use) and a 0.5 mL prefilled syringe; both are formulated without preservatives but contain a trace amount of thimerosal [(contains 49.6% mercury), (=0.5 µg Hg/0.25 mL dose) (=1.0 µg Hg/0.5 mL dose)] from the manufacturing process. Fluzone is also supplied in two other presentations: a 0.5 mL prefilled syringe and 5 mL vial of vaccine, of which both contain the preservative thimerosal [(mercury containing compound), 25 µg mercury/0.5 mL dose]. Fluzone, after shaking syringe/vial well, is essentially clear and slightly opalescent in color. ANTIBIOTICS ARE NOT USED IN THE MANUFACTURE OF FLUZONE.
https://www.vaccineshoppe.com/US_PDF/Fluzone_P-free_2002.2003_4675.4681.pdf

Fluzone® Influenza Virus Vaccine 2003 – 2004 Formula

Fluzone®, Influenza Virus Vaccine, (Zonal Purified, Subvirion) for intramuscular use, is a sterile suspension prepared from influenza viruses propagated in fertilized chicken eggs. The virus-containing fluids are harvested and inactivated with formaldehyde. Influenza virus is concentrated and purified in a linear sucrose density gradient solution using a continuous flow centrifuge. The virus is then chemically disrupted using a nonionic surfactant (Triton® X-100 – A registered trademark of Union Carbide, Co.) producing a “split-virus.” The split-virus is then further purified by chemical means and suspended in sodium phosphate-buffered isotonic sodium chloride solution. Fluzone has been standardized according to USPHS requirements for the 2003–2004 influenza season and is formulated to contain 45 micrograms (µg) hemagglutinin (HA) per 0.5 mL dose, in the recommended ratio of 15 µg HA each, representative of the following three prototype strains: A/New Caledonia/20/99 (H1N1), A/Panama/2007/99 (H3N2) (an A/Moscow/10/99-like strain) and B/Hong Kong/1434/2002 (a B/Hong Kong/330/2001-like strain).¹ Gelatin 0.05% is added as a stabilizer. Fluzone is supplied in a unit dose preservative-free presentation distinguished by a pink syringe plunger rod in a 0.25 mL prefilled syringe (for pediatric use), formulated without preservatives but containing a trace amount of thimerosal [(contains 49.6% mercury), (=0.5 µg Hg/0.25 mL dose) (=1.0 µg Hg/0.5 mL dose)] from the manufacturing process. Fluzone is also supplied in two other presentations: a 0.5 mL prefilled syringe and 5 mL

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vial of vaccine, both of which contain the preservative thimerosal [(mercury containing compound), 25 µg mercury/0.5 mL dose]. Fluzone, after shaking syringe/vial well, is essentially clear and slightly opalescent in color. ANTIBIOTICS ARE NOT USED IN THE MANUFACTURE OF FLUZONE.

https://www.vaccineshoppe.com/US_PDF/Fluzone_2003.2004.pdf

IPOL Poliovirus Vaccine Inactivated

IPOL Poliovirus Vaccine Inactivated, produced by Aventis Pasteur SA, is a sterile suspension of three types of poliovirus: Type 1 (Mahoney), Type 2 (MEF-1), and Type 3 (Saukett). IPOL™ is a highly purified, inactivated poliovirus vaccine produced by microcarrier culture. This culture technique and improvements in purification, concentration and standardization of poliovirus antigen produce a more potent and consistent immunogenic vaccine than the IPV available in the US prior to 1988. The viruses are grown in cultures of VERO cells, a continuous line of monkey kidney cells, by the microcarrier technique. The cells are grown in Eagle MEM modified medium, supplemented with newborn calf serum tested for adventitious agents prior to use, originated from countries free of bovine spongiform encephalopathy. For viral growth the culture medium is replaced by M-199, without calf serum. After clarification and filtration, viral suspensions are concentrated by ultrafiltration, and purified by three liquid chromatography steps; one column of anion exchanger, one column of gel filtration and again one column of anion exchanger. After re-equilibration of the purified viral suspension, with Medium M-199 and adjustment of the antigen titer, the monovalent viral suspensions are inactivated at + 37°C for at least 12 days with 1:4000 formalin. Each sterile immunizing dose (0.5 mL) of trivalent vaccine is formulated to contain 40 D antigen units of Type 1, 8 D antigen units of Type 2, and 32 D antigen units of Type 3 poliovirus. For each lot of IPOL™, D-antigen content is determined *in vitro* using the D-antigen ELISA assay and immunogenicity is determined by *in vivo* testing in animals. IPOL™ is produced from vaccine concentrates diluted with M-199 medium. Also present are 0.5% of 2-phenoxyethanol and a maximum of 0.02% of formaldehyde per dose as preservatives. Neomycin, streptomycin and polymyxin B are used in vaccine production, and although purification procedures eliminate measurable amounts, less than 5 ng neomycin, 200 ng streptomycin and 25 ng polymyxin B per dose may still be present. The residual calf serum protein is less than 1 ppm in the final vaccine. The vaccine is clear and colorless and should be administered intramuscularly or subcutaneously.

http://www.vaccineshoppe.com/US_PDF/860-10_4305_4308.pdf

Tubersol® Tuberculin Purified Protein Derivative (Mantoux) Diagnostic Antigen

Tuberculin Purified Protein Derivative¹ (Mantoux) - TUBERSOL® for intradermal (Mantoux) tuberculin testing is available in a stabilized solution bio-equivalent to 5 U.S. units (TU) PPD-S per test dose (0.1 mL). TUBERSOL® is prepared by Aventis Pasteur Limited from a large Master Batch, Connaught Tuberculin (CT68) and is a cell-free purified protein fraction obtained from a human strain of Mycobacterium tuberculosis grown on a protein-free synthetic medium, and inactivated.² TUBERSOL® is a sterile isotonic solution of Tuberculin in phosphate buffered saline containing Tween 80 (0.0005%) as a stabilizer. Phenol 0.28% is added as a preservative.^{3,4,5} Prior to release, each successive lot is tested for potency in sensitized guinea pigs in comparison with the U.S. Standard Tuberculin PPD-S.

http://www.vaccineshoppe.com/US_PDF/752-21_4611.pdf

SmithKline Beecham Pharmaceuticals
Philadelphia, PA 19101

PEDIARIX. Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed, Hepatitis B (Recombinant) and Inactivated Poliovirus Vaccine Combined

PEDIARIX™ [Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed, Hepatitis B (Recombinant) and Inactivated Poliovirus Vaccine Combined] is a noninfectious, sterile, multivalent vaccine for intramuscular administration manufactured by SmithKline Beecham Biologicals. It contains diphtheria and tetanus toxoids, 3 pertussis antigens (inactivated pertussis toxin [PT], filamentous hemagglutinin [FHA], and pertactin [69 kiloDalton outer membrane protein]), hepatitis B surface antigen, plus poliovirus Type 1 (Mahoney), Type 2 (MEF-1), and Type 3 (Saukett). The diphtheria toxoid, tetanus toxoid, and pertussis antigens are the same as those in INFANRIX® (Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed). The hepatitis B surface antigen is the same as that in ENGERIX-B® [Hepatitis B Vaccine (Recombinant)]. The diphtheria toxin is produced by growing *Corynebacterium diphtheriae* in Fenton medium containing a bovine extract. Tetanus toxin is produced by growing *Clostridium tetani* in a modified Latham medium derived from bovine casein. The bovine materials used in these extracts are sourced from countries which the United States Department of Agriculture (USDA) has determined neither have nor are at risk of bovine spongiform encephalopathy (BSE). Both toxins are detoxified with formaldehyde, concentrated by ultrafiltration, and purified by precipitation, dialysis, and sterile filtration. The 3 acellular pertussis antigens (PT, FHA, and pertactin) are isolated from *Bordetella pertussis* culture grown in modified Stainer-Scholte

Critical Decisions Count

liquid medium. PT and FHA are isolated from the fermentation broth; pertactin is extracted from the cells by heat treatment and flocculation. The antigens are purified in successive chromatographic and precipitation steps. PT is detoxified using glutaraldehyde and formaldehyde. FHA and pertactin are treated with formaldehyde. The hepatitis B surface antigen (HBsAg) is obtained by culturing genetically engineered *Saccharomyces cerevisiae* cells, which carry the surface antigen gene of the hepatitis B virus, in synthetic medium. The surface antigen expressed in the *S. cerevisiae* cells is purified by several physicochemical steps, which include precipitation, ion exchange chromatography, and ultrafiltration. The purified HBsAg undergoes dialysis with cysteine to remove residual thimerosal. The inactivated poliovirus component of PEDIARIX is an enhanced potency component. Each of the 3 strains of poliovirus is individually grown in VERO cells, a continuous line of monkey kidney cells, cultivated on microcarriers. Calf serum and lactalbumin hydrolysate are used during VERO cell culture and/or virus culture. Calf serum is sourced from countries the USDA has determined neither have nor are at risk of BSE. After clarification, each viral suspension is purified by ultrafiltration, diafiltration, and successive chromatographic steps, and inactivated with formaldehyde. The 3 purified viral strains are then pooled to form a trivalent concentrate. The diphtheria, tetanus, and pertussis antigens are individually adsorbed onto aluminum hydroxide; hepatitis B component is adsorbed onto aluminum phosphate. All antigens are then diluted and combined to produce the final formulated vaccine. Each 0.5-mL dose is formulated to contain 25 Lf of diphtheria toxoid, 10 Lf of tetanus toxoid, 25 mcg of inactivated PT, 25 mcg of FHA, 8 mcg of pertactin, 10 mcg of HBsAg, 40 D-antigen Units (DU) of Type 1 poliovirus, 8 DU of Type 2 poliovirus, and 32 DU of Type 3 poliovirus. Diphtheria and tetanus toxoid potency is determined by measuring the amount of neutralizing antitoxin in previously immunized guinea pigs. The potency of the acellular pertussis components (PT, FHA, and pertactin) is determined by enzyme-linked immunosorbent assay (ELISA) on sera from previously immunized mice. Potency of the hepatitis B component is established by HBsAg ELISA. The potency of the inactivated poliovirus component is determined by using the D-antigen ELISA and by a poliovirus neutralizing cell culture assay on sera from previously immunized rats. Each 0.5-mL dose also contains 2.5 mg of 2-phenoxyethanol as a preservative, 4.5 mg of NaCl, and aluminum adjuvant (not more than 0.85 mg aluminum by assay). Each dose also contains <100 mcg of residual formaldehyde and <100 mcg of polysorbate 80 (Tween 80). Thimerosal is used at the early stages of manufacture and is removed by subsequent purification steps to below the analytical limit of detection (<25 ng of mercury/20 mcg HBsAg) which upon calculation is <12.5 ng mercury per dose. Neomycin sulfate and polymyxin B are used in the polio vaccine manufacturing process and may be present in the final vaccine at <0.05 ng neomycin and <0.01 ng polymyxin B per dose. The procedures used to manufacture the HBsAg antigen result in a product that contains <5% yeast protein.

<http://www.fda.gov/cber/label/dtapsmi121302LB.pdf>

Wyeth-Ayerst Laboratories Philadelphia, PA 19101

Pevnar Pneumococcal 7-valent Conjugate Vaccine (Diphtheria CRM197 Protein)

Pneumococcal 7-valent Conjugate Vaccine (Diphtheria CRM197 Protein), Pevnar[®], is a sterile solution of saccharides of the capsular antigens of *Streptococcus pneumoniae* serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F individually conjugated to diphtheria CRM197 protein. Each serotype is grown in soy peptone broth. The individual polysaccharides are purified through centrifugation, precipitation, ultrafiltration, and column chromatography. The polysaccharides are chemically activated to make saccharides which are directly conjugated to the protein carrier CRM197 to form the glycoconjugate. This is effected by reductive amination. CRM197 is a nontoxic variant of diphtheria toxin isolated from cultures of *Corynebacterium diphtheriae* strain C7 (β197) grown in a casamino acids and yeast extract-based medium. CRM197 is purified through ultrafiltration, ammonium sulfate precipitation, and ion-exchange chromatography. The individual glycoconjugates are purified by ultrafiltration and column chromatography and are analyzed for saccharide to protein ratios, molecular size, free saccharide, and free protein. The individual glycoconjugates are compounded to formulate the vaccine, Pevnar[®]. Potency of the formulated vaccine is determined by quantification of each of the saccharide antigens, and by the saccharide to protein ratios in the individual glycoconjugates. Pevnar[®] is manufactured as a liquid preparation. Each 0.5 mL dose is formulated to 35 contain: 2 µg of each saccharide for serotypes 4, 9V, 14, 18C, 19F, and 23F, and 4 µg of serotype 6B per dose (16 µg total saccharide); approximately 20 µg of CRM197 carrier protein; and 0.125 mg of aluminum per 0.5 mL dose as aluminum phosphate adjuvant. <http://www.fda.gov/cber/label/pneuled100102LB.pdf>

MedImmune Vaccines, Inc. Gaithersburg, MD 20878

Critical Decisions Count

FluMist™ Influenza Virus Vaccine Live, Intranasal 2003-2004 Formula

Influenza Virus Vaccine Live, Intranasal (FluMist™) is a live trivalent nasally administered vaccine intended for active immunization for the prevention of influenza. Each 0.5 mL dose is formulated to contain 106.5-7.5 TCID₅₀ (median tissue culture infectious dose) of live attenuated influenza virus reassortants of the strains recommended by the U.S. Public

Health Service (USPHS) for the 2003-2004 season: A/New Caledonia/20/99 (H1N1), A/Panama/2007/99 (H3N2) (A/Moscow/10/99-like), and B/Hong Kong/330/2001 [1]. These strains are (a) *antigenically representative* of influenza viruses that may circulate in humans during the 2003-2004 influenza season; (b) *cold-adapted (ca)* (i.e., they replicate efficiently at 25°C, a temperature that is restrictive for replication of many wild-type viruses); (c) *temperature-sensitive (ts)* (i.e., they are restricted in replication at 37°C (Type B strains) or 39°C (Type A strains), temperatures at which many wild-type influenza viruses grow efficiently); and (d) *attenuated (att)* so as not to produce classic influenza-like illness in the ferret model of human influenza infection. The cumulative effect of the antigenic properties and the *ca*, *ts*, and *att* phenotype is that the vaccine viruses replicate in the nasopharynx to produce protective immunity. Each of the three influenza virus strains contained in FluMist is a genetic reassortant of a Master Donor Virus (MDV) and a wild-type influenza virus. The MDVs (A/Ann Arbor/6/60 and B/Ann Arbor/1/66) were developed by serial passage at sequentially lower temperatures in specific pathogen-free (SPF) primary chick kidney cells [2]. During this process, the MDVs acquired the *ca*, *ts* and *att* phenotype and multiple mutations in the gene segments that encode viral proteins other than the surface glycoproteins. The individual contribution of the genetic sequences of the six non-glycoprotein MDV genes (“internal gene segments”) to the *ca*, *ts*, and *att* phenotype is not completely understood. However, at least five genetic loci in three different internal gene segments of the Type A MDV and at least three genetic loci in two different internal gene segments of the Type B MDV contribute to the *ts* property [3, 4]. For each of the three strains in FluMist, the six internal gene segments responsible for *ca*, *ts*, and *att* phenotypes are derived from the MDV, and the two segments that encode the two surface glycoproteins, hemagglutinin (HA) and neuraminidase (NA), are derived from the corresponding antigenically relevant wild-type influenza viruses that have been recommended by the USPHS for inclusion in the annual vaccine formulation. Thus, the three viruses contained in FluMist maintain the replication characteristics and phenotypic properties of the MDV and express the HA and NA of wild-type viruses that are related to strains expected to circulate during the 2003-2004 influenza season. Viral harvests used in the production of FluMist are produced by inoculating each of the three reassortant viruses into specific pathogen-free (SPF) eggs that are incubated to allow for vaccine virus replication. The allantoic fluid of these eggs is harvested, clarified by centrifugation, and stabilized with buffer containing sucrose, potassium phosphate, and monosodium glutamate (0.47 mg/dose). Viral harvests from the three strains (H1N1, H3N2, and B) are subsequently blended and diluted to desired potency with allantoic fluid derived from uninfected SPF eggs to produce trivalent bulk vaccine. Each lot of viral harvest is tested for *ca*, *ts*, and *att* and is also tested extensively by *in vitro* and *in vivo* methods to detect adventitious agents. The bulk vaccine is then filled directly into individual sprayers for nasal administration. These sprayers are labeled and stored at 2-8°C. Gentamicin sulfate is added early in the manufacturing process during preparation of reassortant viruses at a calculated concentration of approximately 1 µg/mL. Later steps of the manufacturing process do not use gentamicin, resulting in a diluted residual concentration in the final product of <0.015 µg/mL (limit of detection of the assay). FluMist does not contain any preservatives.

<http://www.fda.gov/cber/label/inflmed061703LB.pdf>

Lederle Laboratories

Acel-Immune DTaP Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed
produced using formaldehyde, thimerosal, aluminum hydroxide, aluminum phosphate, polysorbate 80, gelatin

HibTiter Haemophilus Influenzae Type B (Hib)
produced using polyribosylribitol, ammonium sulfate, thimerosal
medium: chemically defined, yeast based

Orimune Poliovirus Vaccine Live Oral Trivalent
produced using 3 types of attenuated polioviruses, streptomycin, neomycin, calf serum, sorbitol
medium: monkey kidney cell culture

Connaught Laboratories

Act HIB Haemophilus Influenzae Type B (Hib) Tetanus Toxoid Conjugate
produced using ammonium sulfate, formalin, sucrose, thimerosal
medium: semi-synthetic

Critical Decisions Count

IPOL Inactivated Polio Vaccine

produced using 3 types of polio virus, formaldehyde, phenoxyethanol (antifreeze), neomycin, streptomycin, polymyxin B

medium: VERO cells, a continuous line of monkey kidney cells

Menomune Meningococcal Polysaccharide Vaccine

produced using thimerosal, lactose

medium: freeze dried polysaccharide antigens from Neisseria Meningitidis

Imovax Rabies Vaccine Adsorbed

produced using human albumin, neomycin sulfate, phenol red indicator

medium: human diploid cells (originating from human aborted fetal tissue)

Merck & Co, Inc.

Attenuvax Measles Virus Vaccine Live

produced using neomycin, sorbitol, hydrolyzed gelatin

medium: chick embryo

Biavax Rubella and Mumps Virus Vaccine Live

produced using neomycin, sorbitol, hydrolyzed gelatin

medium: human diploid cells (originating from human aborted fetal tissue)

MMR Measles Mumps Rubella Live Virus Vaccine

produced using sorbitol, neomycin, hydrolyzed gelatin

mediums: M&M - chick embryo

Rubella - human diploid cells (originating from human aborted fetal tissue)

M-R-Vax Measles and Rubella Virus Vaccine Live

produced using neomycin, sorbitol, hydrolyzed gelatin

mediums: M - chick embryo R - human diploid cells (originating from human aborted fetal tissue)

Meruvax II Rubella Virus Vaccine Live

produced using neomycin, sorbitol, hydrolyzed gelatin

medium: human diploid cells (originating from human aborted fetal tissue)

MumpsVax Mumps Virus Vaccine Live

produced using neomycin, sorbitol, hydrolyzed gelatin

medium: human diploid cells (originating from human aborted fetal tissue)

Pneumovax Pneumococcal Vaccine Polyvalent

produced using phenol and capsular polysaccharides from the 23 most prevalent pneumococcal types

Recombivax Hepatitis B Vaccine Recombinant

produced using thimerosal, aluminum hydroxide

medium: yeast (residual < 1% yeast protein)

Varivax Varicella Virus Vaccine Live

produced using sucrose, phosphate, glutamate, processed gelatin

medium: human diploid cells (originating from human aborted fetal tissue)

SmithKline Beecham Pharmaceuticals

DPT Diphtheria and Tetanus Toxoids and Pertussis Vaccine Adsorbed

produced using aluminum phosphate, formaldehyde, ammonium sulfate, washed sheep red blood cells, glycerol, sodium chloride, thimerosal

Critical Decisions Count

medium: porcine (pig) pancreatic hydrolysate of casein

Energix-B Hepatitis B

produced using aluminum hydroxide, thimerosal

medium: yeast (possibly 5% residual)

Havrix Hepatitis A

produced using formalin, aluminum hydroxide, phenoxyethanol (antifreeze), polysorbate 20, residual MRC5 proteins (from medium)

medium: human diploid cells (originating from human aborted fetal tissue)

Rabies Vaccine Adsorbed

produced using betapropiolactone, aluminum phosphate, sodium ethylmercurithiosalicylate (thimerosal), phenol red

medium: fetal rhesus monkey lung cells

Medeva Pharmaceuticals

Fluvirin Influenza Virus Vaccine

produced using embryonic fluid (chicken egg), neomycin, polymyxin, thimerosal, betapropiolactone

medium: embryonic fluid (chicken egg)

Wyeth-Ayerst

FluShield Influenza Virus Vaccine, Trivalent, Types A&B

produced using gentamicin sulfate, formaldehyde, polysorbate 80, tri(n)butylphosphate, thimerosal

medium: chick embryos

RotaShield Rotavirus Vaccine, Live, Oral, Tetravalent

produced using 1 rhesus monkey rotavirus, 3 rhesus-human reassortant viruses, sucrose, monosodium glutamate (MSG), potassium monophosphate, potassium diphosphate, fetal bovine serum, neomycin sulfate, amphotericin B

medium: fetal rhesus diploid cell line