Lisa McGee's (VaxxChoice) Report on the 2022/2023 CDC Recommended Immunizations for Children

The CDC's 2022/2023 Recommended Childhood vaccines are each a significant component in a complex system of operational responsibilities, each with a very distinct presence and purpose. None of them are to protect against a disease and/or "virus". Each one is a military grade, government-controlled product. These "products" are all for sale; and all are sourced from a combined effort of biological and man-made "bacterium mutated strains". Many are sourced from aborted fetal cells from both human and non-human species. Examples of non-human being green monkey kidneys, ovaries of fall armyworm moth, to name a few. And almost all are soaked in extremely toxic formulas of bacterium yeast that are aggressive, hostile and destructive.

The ingredients are designed and crafted to detonate and cause destructive chaos to an already overly stressed biological environment (already evident in children). As mentioned above, the ingredients are the most harmful grade of mutated, hybrid strains of synthetic bacterium; sourced from both human and non-human sources, plants, molds, and fungus; samples of cowpie, smallpox, and plague, and much more. The bacterium are then infused with chemical compounds that are listed (globally) as environmental contaminants. These ingredients will be trafficked via the 'vaccine' as a gene, as a protein/enzyme, and in chemical compound formats. There is nothing "biological" once it reaches the end of the assembly line; and into the bodies of children, and adults.

1. COVID-19** Coronavirus disease 2019

The Novavax COVID-19 Vaccine, Adjuvanted is a suspension for intramuscular injection.
Dosage form: injection, suspension Drug class: Viral vaccines
Vaccination providers enrolled in the federal COVID-19 Vaccination Program must report all vaccine administration errors, all serious adverse events, cases of myocarditis, cases of pericarditis, cases of Multisystem Inflammatory Syndrome (MIS) in adults and children, and cases of COVID-19 that result in hospitalization or death following administration of the Novavax COVID-19 Vaccine, Adjuvanted.
See "MANDATORY REQUIREMENTS FOR THE NOVAVAX COVID-19 VACCINE, ADJUVANTED ADMINISTRATION UNDER EMERGENCY USE AUTHORIZATION" for reporting requirements.
https://www.drugs.com/pro/covid-19-vaccine-novavax.html

These protein-based nanoparticles work with our proprietary Matrix-M™ adjuvant, which helps to enhance immunogenicity, ie, the ability of the vaccine to provoke an immune response in the body. The recombinant DNA technology using a baculovirus expressions system in an insect cell line that is derived from *Sf9 cells of the Spodoptera frugiperda species. Sf9 cells, are derived from the immature ovaries of fall armyworm moth (Spodoptera frugiperda) pupae. Spodoptera frugiperda (fall armyworm) is a highly destructive invasive pest that feeds on numerous crops including maize and rice. It has developed sophisticated mechanisms to detoxify xenobiotics such as secondary plant metabolites as well as manmade insecticides.

6 steps to producing a Novavax investigational vaccine
1. After identifying an antigen that can be used to stimulate an immune response against the virus in question, the corresponding gene is modified and inserted into a baculovirus (a type of insect virus).
2. The baculovirus containing the recombinant antigen gene is used to infect cells from a certain type of moth (called Sf9 cells); the baculovirus multiplies (replicates) inside these cells.
3. As part of this replication process, the recombinant antigen gene from the baculovirus enters the Sf9 cell nucleus where it is transcribed into mRNA.
4. The natural machinery in the Sf9 cells translates the mRNA to produce large quantities of the recombinant antigen protein.
5. The recombinant antigen proteins are harvested from the surface of the Sf9 cells, purified, and arranged around a nanoparticle core.
6. The recombinant antigen protein nanoparticles are mixed with the Matrix-M adjuvant to create the investigational vaccine.
https://www.novavax.com/science-technology/recombinant-protein-based-nanoparticle-vaccine-technology

"The Sf9 insect cell line is a clonal isolate derived from the parental Spodoptera frugiperda cell line IPLB-Sf-21-AE, and it is a suitable host for expression of recombinant proteins from baculovirus expression systems (e.g., Invitrogen's Bac-

to-Bac® and Bac-N-Blue™ Expression Systems). Although insect cells have been historically cultured in stationary systems utilizing T-flasks and serum-supplemented basal medium, insect cells are generally not anchorage dependent and can easily be maintained in suspension culture."
https://www.thermofisher.com/us/en/home/references/gibco-cell-culture-basics/cell-morphology/morphology-of-sf9-cells.html

Product label Generic name: nvx-cov2373
NVX-CoV2373 vaccine (Novavax), a recombinant nanoparticle vaccine against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that contains the full-length spike glycoprotein of the prototype strain plus ***Matrix-M adjuvant**

***Matrix-M™**
Saponin-based adjuvants are widely used to enhance humoral and cellular immune responses towards vaccine antigens, although it is not yet completely known how they mediate their stimulatory effects. The aim of this study was to elucidate the mechanism of action of adjuvant Matrix-M™ without antigen and Alum was used as reference adjuvant. Adjuvant Matrix-M™ is comprised of 40 nm nanoparticles composed of Quillaja saponins, cholesterol and phospholipid. B cells and dendritic cells in ***dLNs** and spleen showed an increased expression of the co-stimulatory molecule ***CD86** and dendritic cells in dLNs expressed elevated levels of ***MHC class II**. The high-dose (30 µg) of Matrix-M™ induced detectable serum levels of IL-6 and MIP-1β 4 h post administration, most likely representing spillover of locally produced cytokines. A lesser increase of IL-6 in serum after administration of 12 µg Matrix-M™ was also observed. In conclusion, early immunostimulatory properties were demonstrated by Matrix-M™ alone, as therapeutic doses resulted in a local transient immune response with recruitment and activation of central immune cells to dLNs. These effects may play a role in enhancing uptake and presentation of vaccine antigens to elicit a competent immune response.
https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0041451

Definitions
*dLN is draining lymph nodes
molecule CD86 = CD86 (CD86 Molecule) is a Protein Coding gene. **Diseases associated with CD86 include Plague and Cowpox.

As a Gene The CD86 molecule represents as
P42081 *CD86_HUMAN - Protein T-lymphocyte activation antigen CD86. ***MHC class II -the major histocompatibility complex (MHC) is a large locus on vertebrate DNA containing a set of closely linked polymorphic genes that code for cell surface proteins essential for the adaptive immune system.

Some pathogens, such as Mycobacterium tuberculosis, Mycobacterium leprae, and Leishmania, are able to grow in the endocytic vesicles of macrophages without being killed by lysosomes. These macrophages can, however, become activated by T4-effector lymphocytes called TH1 cells and subsequently use intravehicular proteases to degrade the proteins from these pathogens into peptides for presentation to **MHC-II** molecules that pass through on their way to the cell surface.

Major Histocompatibility Complex (MHC) Molecules
https://bio.libretexts.org/Bookshelves/Microbiology/Microbiology_(Kaiser)/Unit_6%3A_Adaptive_Immunity/12%3A_Introduction_to_Adaptive_Immunity/12.3%3A_Major_Cells_and_Key_Cell_Surface_Molecules_Involved_in_Adaptive_Immune_Responses/12.3A%3A__Major_Histocompatibility_Complex__(MHC)_Molecules

***The Matrix-M™ adjuvant: A critical component of vaccines for the 21st century**
Matrix-M™ adjuvant is a key component of several novel vaccine candidates. The Matrix-M adjuvant consists of two distinct fractions of saponins purified from the *Quillaja saponaria Molina tree, combined with cholesterol and phospholipids to form 40-nm open cage-like nanoparticles, achieving potent adjuvanticity with a favorable safety profile. Matrix-M induces early activation of innate immune cells at the injection site and in the draining lymph nodes.
https://pubmed.ncbi.nlm.nih.gov/37113023/

***Quillaja saponaria Molina tree - Quillaia can increase the activity of the immune system.**

Quillaia (Quillaja saponaria) is a large evergreen tree found in Peru and Chile. Chemicals in the tree bark called **saponins** act as natural detergents. Quillaia is commonly consumed in foods. But it is possibly unsafe when used in larger amounts as medicine. Quillaia contains high amounts of tannins which can *causes stomach problems, as well as kidney and liver damage. Quillaia also contains chemicals called oxalates, which can ***cause kidney stones.

Natural and Synthetic Saponins as Vaccine Adjuvants
Saponin adjuvants have been extensively studied for their use in veterinary and human vaccines. Among them, QS-21 stands out owing to its unique profile of immunostimulant activity, inducing a balanced Th1/Th2 immunity, which is valuable to a broad scope of applications in combating various microbial pathogens, cancers, and other diseases. It has recently been approved for use in human vaccines as a key component of combination adjuvants. Despite its usefulness in research and clinic, the cellular and molecular mechanisms of QS-21 and other saponin adjuvants are poorly understood.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8001307/

Adverse effects
***Stomach and intestinal (gastrointestinal, GI) problems**:
Quillaia can irritate the GI tract. Don't use it if you have a stomach or intestinal disorder.

****Kidney disease**
The oxalate in quillaia can cause kidney stones. Don't use it if you have kidney disease or a history of kidney stones.

*****Pregnancy and breast-feeding: Quillaia is possibly unsafe when used as medicine while pregnant or breast-feeding. Avoid use.**

***Covid 19: COMIRNATY Original/Omicron BA.4-5 (15/15 mcg) - COVID-19 mRNA Vaccine**
Name of drug: Tozinameran/Famtozinameran
https://extranet.who.int/pqweb/vaccines/comirnaty-originalomicron-ba4-5

Pharmacology
BNT162b2 mRNA (V9) encodes the full-length of the SARS-CoV-2 Spike-glycoprotein with the modification of two nucleosides at residues 986 and 987 (replaced by proline; expressed protein named as P2 S).
Nonclinical Evaluation Report BNT162b2 %5BmRNA%5D COVID-19 vaccine (COMIRNATYTM)

Proline
Pseudomonas, Dithiobacter, Enterobacter and some species of Bacillus, which are able to use methylamine as a sole nitrogen source but not as a sole carbon source, were able to use (L)-proline as both a carbon and energy source(1). (L)-Proline was detected in smoke at 10.2% relative to major compound from the charring/burning of chitin present in the exoskeleton of crustaceans(1). It is present in cigarettes and mainstream and side stream tobacco smoke(2).
https://pubchem.ncbi.nlm.nih.gov/compound/proline

BNT162b2 [mRNA] COVID-19 vaccine - COMIRNATY
https://www.tga.gov.au/sites/default/files/foi-2389-06.pdf

Tozinameran
NUCLEOTIDE SUBSTITUTION 5'-TERMINUS m2-7,3'-OGppp(m1-2'-O)Ap mRNA CAP VNP8CZY34V
NUCLEOSIDE_SUBSTITUTION RESIDUE_SPECIFIC N1-METHYLPSEUDOURIDINE 09RAD4M6WF

N1-METHYLPSEUDOURIDINE
https://gsrs.ncats.nih.gov/ginas/app/beta/substances/6fefa717-6a4c-435f-a692-46189283764f

Tozinameran - 5085ZFP6SJ US approved 2021
https://drugs.ncats.io/substance/5085ZFP6SJ

N1-Methylpseudouridine 13860-38-3 | DTXSID50160724 - Searched by DTXSID50160724.

N1-Methylpseudouridine (abbreviated **m1Ψ**) is a natural archaeal tRNA component as well as a synthetic pyrimidine nucleoside used in biochemistry and molecular biology for in vitro transcription and is found in the SARS-CoV-2 mRNA vaccines tozinameran (Pfizer–BioNTech) and elasomeran (Moderna).[1]
https://comptox.epa.gov/dashboard/chemical/details/DTXSID50160724

N1-Methylpseudouridine
https://drugs.ncats.io/substance/09RAD4M6WF

Abdavomeran
https://drugs.ncats.io/substance/JV8KBX6XZG

SARS-COV2 B.1.1.7 VARIANT
https://gsrs.ncats.nih.gov/ginas/app/beta/substances/fcb6b16d-1cbf-4f60-bb59-4b2ef94a6452

Bacillus pumilus strain GB34 – SARS CoV2
https://ordspub.epa.gov/ords/pesticides/f?p=CHEMICALSEARCH:31::::1,3,31,7,12,25:P3_XCHEMICAL_ID:1304

Bacillus species; a potential source of anti-SARS-CoV-2 main protease inhibitors
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7814571/

Maintaining Safety with SARS-CoV-2 Vaccines
https://www.nejm.org/doi/full/10.1056/NEJMra2035343

2. HepB (Hepatitis B)

Hepatitis B Surface Antigen Vaccine - Patent US 6110706
Summary: HBV surface antigen particles, prepared by recombinant DNA technology are described, said particles being composed of epitopes from the group of surface peptides and/or core peptide of non-A, non-B hepatitis virus, hepatitis virus A and/or hepatitis virus B. Respective particles are especially characterized by a composition of different epitopes selected from pre-S and S peptides. There are also described DNA-sequences, plasmids and cell lines coding for respective HBV surface antigen particles as well as a new vaccine containing the same.
https://pubchem.ncbi.nlm.nih.gov/patent/US-6110706-A

Safety Datasheet: ENGERIX-B PRESERVATIVE FREE = * HEPATITIS B SURFACE ANTIGEN VACCINE HEPATITIS B (RECOMBINANT DNA) VACCINE (ADSORBED)
***DISODIUM HYDROGEN PHOSPHATE Composition/information on ingredients:**
Phosphate toxicity is likely due to the disturbance of other electrolytes when phosphate levels are high, producing symptoms including tetany, dehydration, hypotension, tachycardia, hyperpyrexia, cardiac arrest and coma. Risk of raising phosphate levels through use of sodium phosphate appears to be higher in smaller patients.
https://imgcdn.mckesson.com/CumulusWeb/Click_and_learn/SDS_SMKLPH_ENGERIXB_SYR_TIP_LOK_10MCG0.pdf

***Disodium hydrogen phosphate**
Corrosive and irritant. Ingestion of large amounts lowers urinary pH. If excessive phosphate salts are introduced intravenously or orally, they may prove toxic by reducing the concentration of Ca 2+ in the circulation and from the precipitation of calcium phosphate in soft tissues.
https://pubchem.ncbi.nlm.nih.gov/compound/Disodium-hydrogen-phosphate

Linked Proteins
P20910 ***Mycolysin (Streptomyces cacaoi)**
Like all peptidases in clan MA(E) mycolysin displays the *HEXXH motif (see below) in which the histidines (His202 and His206) are zinc ligands and the electrophilic Glu203 is a catalytic residue; Glu240 is the third zinc ligand and is found within the Glu-(Xaa)$_3$-Asp motif that is also found in thermolysin.
https://www.uniprot.org/uniprotkb/P20910/entry

***Mycolysin** *Mycolysin is a cloned metalloprotease

The structural chemistry and the biological aspects of mycolysin are critical. The gene encoding a protease of Streptomyces cacaoi was cloned and expressed in *Streptomyces lividans (S lividans). The protein secreted from this host was characterized as a new metalloprotease and was later named mycolysin. The gene cloned in S. lividans proved to be that for the precursor of mycolysin.
https://www.sciencedirect.com/science/article/abs/pii/B9780120796113501130

***Mycolysin - Toxicity**
Mucolysin Disease Interaction Major: hepatic encephalopathy Moderate: asthma, fluid overload, gastric hemorrhage

***Mycolysin Caution**
Mucolysin should be given in caution in asthma patients. Mucolysin seems to increase the effects of Nitroglycerin.

***Mycolysin side effects**
Effects such as nausea, headache, tinnitus, urticaria, stomatitis, rhinorrhoea, chills, fever, bronchospasm may be observed. Occasional cases of nausea and dyspepsia, rare cases of urticaria may be observed. Patients experiencing an overdose may present with vomiting, nausea, bronchospasm, periorbital angioedema, and hypotension. Treat patients with symptomatic and supportive measures. Hemodialysis may remove some acetylcysteine from circulation as it is somewhat protein bound.

***What is Mucolysin?**
Mucolysin (*Acetylcysteine) also known as *N-acetylcysteine (NAC), is a medication that is used to treat paracetamol (acetaminophen) overdose, and to loosen thick mucus in individuals with chronic bronchopulmonary disorders like pneumonia and bronchitis. It can be taken intravenously, by mouth, or inhaled as a mist. Mucolysin lightly decreased fertility was seen at doses above the maximum human dose. Limited case reports did not report any adverse fetal or neonatal outcomes. This drug crosses the placenta and was measurable in the serum of the infant.
https://www.medicinesfaq.com/brand/mucolysin - precaution

Synonyms/Aliases: *Acetylcysteine *N-acetylcysteine (NAC)
Patients experiencing an overdose may present with vomiting, nausea, bronchospasm, periorbital angioedema, and hypotension. Treat patients with symptomatic and supportive measures. Hemodialysis may remove some acetylcysteine from circulation as it is somewhat protein bound. Given its complicated regime, NAC has a high potential for iatrogenic errors, including overdose. A 23-year-old female developed hemolysis, thrombocytopenia, metabolic acidosis and acute renal failure after NAC overdose, and died after developing hemolytic uremic syndrome. Another case report describes a 20-year-old female, who developed hemolysis and elevated serum bilirubin. Massive accidental NAC administration in the order had resulted in cerebral edema, seizures, uncal herniation, and permanent brain injury in another patient with APAP overdose.
https://www.ncbi.nlm.nih.gov/books/NBK537183/

Peptidase family M5 (mycolysin family)
https://www.ebi.ac.uk/merops/cgi-bin/famsum?family=M5

****Streptomyces lividans**
(S lividans) chassis (engineered) strains delete endogenous gene clusters and introduce additional for site-specific integration of foreign DNA. Heterologous expression of secondary metabolite gene clusters is used to achieve increased production of desired compounds, activate cryptic gene clusters, manipulate clusters from genetically unamenable strains, obtain natural products from uncultivable species, create new unnatural pathways, etc. Several *Streptomyces* species are genetically engineered for use as hosts for heterologous expression of gene clusters.
https://microbialcellfactories.biomedcentral.com/articles/10.1186/s12934-020-1277-8

Streptomyces Associated with Humans and Animals
Members of Streptomyces may infect and cause disease to humans, including wound contamination and abscess formation. Only a few Streptomyces have been isolated from pathological material. Their role as agent of infectious disease cannot be ignored. Streptomyces are also reported to be respiratory allergens in humans. There is a report that indicates Streptomyces lanatus–mediated pneumonia in humans. Furthermore, there is also a rare case of lung coinfection by Streptomyces cinereoruber and Haemophilus influenzae. Besides, S. griseus is one of the most

frequently encountered *Actinomycetes in human specimens, according to the study performed by the Centers for Disease Control and Prevention.

The bacteria belonging to this genus are mainly found in soil but are also occasionally isolated from manure and other sources. Though the Streptomyces are eubacteria, they grow in the form of filaments or as mycelium and do not show the usual bacterial bacillary or coccoid forms. Streptomyces have a complex colony structure based on multinucleate, branching mycelia, with differentiation of the colony into vegetative and reproductive structures. This complex multicellular morphology demonstrates links between fungi and bacteria. However, it is now proved beyond doubt that Streptomycetes are prokaryotes. Their cell wall structure, genetic material and phages are similar to those of bacteria.
https://www.sciencedirect.com/topics/immunology-and-microbiology/streptomyces

***Actinomycetes**
Members of this family have evolved lifestyles differing to that of pathogens as demonstrated by Corynebacterium Mycobacterium, Nocardia, Tropheryma, and Propionibacterium. They are soil inhabitants (*Streptomyces*) and gastrointestinal commensals (*Bifidobacterium*). These bacteria resemble fungi in their morphology forming branching hyphae, asexual spores, and mycelium. This means that they have characteristics that are common to both fungi and bacteria; they are actually at the transition between bacteria and fungi. They are abundant and widely distributed in the soil leading to the claim that the characteristic smell of soil is actually due to the actinomycetes present. Some form mutualistic relationships with plants promoting their growth and protecting them from pathogens. In addition, they also form associations with green algae.
However, not all actinomycetes are beneficial microbes, some are plant pathogens causing diseases such as potato scab, wilt, and gall, as well as causing diseases in humans and animals.
https://www.sciencedirect.com/topics/immunology-and-microbiology/streptomyces

Synonym/alias: Actinomyces cacaoi
https://my.clevelandclinic.org/health/diseases/24981-actinomycosis

Enzyme: 3.4.24.31 (Streptomyces cacaoi)
https://www.genome.jp/dbget-bin/www_bget?ec:3.4.24.31

Streptomyces cacaoi - U.S. Fish & Wildlife Service
https://www.fws.gov/species/streptomyces-cacaoi-streptomyces-cacaoi

***HEXXH (His-Glu-X-X-His) = Metalloproteases**
Metalloproteases coordinate metal ions that facilitate cleavage of peptide bonds. The majority of metalloproteases use zinc, with a few using other metals such as cobalt. Metalloproteases use a triad composed of several different amino acids, such as histidine, aspartate, glutamate, arginine, and lysine, to bind the metal ion which, in turn, coordinates a water molecule as the ultimate nucleophile. One typically conserved motif, His-Glu-X-X-His (HEXXH), forms the active site of some metalloproteases, where the two His residues help coordinate the metal ion, which, together with the Glu, helps position the bound water molecule. The Glu residue activates the bound water, thus generating a nucleophilic hydroxyl (OH) that attacks the peptide bond. Cleavage of the peptide bond yields two fragments, neither of which is covalently linked to the enzyme.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8139524/

Synonym/alias: Actinomyces cacaoi
https://my.clevelandclinic.org/health/diseases/24981-actinomycosis

P0C781 **Protein X (Lactate dehydrogenase-elevating virus)**
Lactate dehydrogenase-elevating virus (LDV) is a mouse arterivirus, unusual in its extreme host specificity and its persistence in the circulation of the infected host that naturally infects wild mice. Although, probably not as frequent in laboratory mouse colonies as it used to be, LDV infection may affect experimental results, primarily through its effects on the host immune responses. On the other hand, because of its unique properties, LDV infections serve as a good animal model for viral persistence, virally induced immunomodulation, and pathogenic infection of neurons in the central nervous system.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7155438/

Additional information - Protein X (Lactate dehydrogenase-elevating virus)
https://www.criver.com/sites/default/files/resources/doc_a/LactateDehydrogenase-ElevatingVirusTechnicalSheet.pdf

P0C782 **Protein X (Lactate dehydrogenase elevating virus C)**
The apparently complete sequence of the RNA genome of the neurovirulent isolate of lactate dehydrogenase-elevating virus (LDV-C) has been determined. The LDV-C genome is at least 14,222 nucleotides in length and contains eight *open reading frames (ORFs). ORF 1a, which encodes a protein of 242.8 kDa and is located at the 5' end of the genome, contains at least two putative papain-like cysteine protease domains, and one putative chymotrypsin-like serine protease domain. Another domain of unknown function that is also conserved in coronaviruses and toroviruses is located at the C-terminus of the ORF 1b product. Three cleavage sites in the ORF 1a polyprotein and three in the ORF 1b polyprotein were predicted for the chymotrypsin-like protease and tentatively delimit the mature nonstructural proteins of LDV. Six small, overlapping 3' ORFs (ORFs 2 through 7) encode proteins with calculated sizes of 25.8, 21.6, 19.8, 23.9, 18.9, and 12.3 kDa. ORF 7 encodes the virion nucleocapsid protein *Vp-1, while ORF 6 encodes the nonglycosylated envelope protein Vp2. ORFs 5, 4, 3, and 2 each encode glycoproteins which may be virion envelope proteins. LDV is closely related to equine arteritis virus, Lelystad virus (LV), and simian hemorrhagic fever virus. These four viruses belong to a new group of positive-strand RNA viruses and are related to coronaviruses and toroviruses.
Lactate dehydrogenase elevating virus (strain C) (LDV)
https://www.uniprot.org/uniprotkb/P0C782/history

***Open Reading Frame (ORF)**
An open reading frame, as related to genomics, is a portion of a DNA sequence that does not include a stop codon (which functions as a stop signal). A codon is a DNA or RNA sequence of three nucleotides (a trinucleotide) that forms a unit of genomic information encoding a particular amino acid or signaling the termination of protein synthesis (stop codon). There are 64 different codons: 61 specify amino acids and 3 are used as stop codons. A long open reading frame is often part of a gene (that is, a sequence directly coding for a protein).
https://www.genome.gov/genetics-glossary/Open-Reading-Frame

VP1, VP2, and VP3. Viral Genome
All polyomavirus family members form capsids, which are composed of three viral proteins, *VP1, VP2, and VP3. Viral genome, which is a double-stranded circular DNA complexed with cellular histones H2A, H2B, H3, and H4 in the form of chromatin, is surrounded by capsid proteins. It is estimated that the outer shell of the capsids is made up of VP1, organized into 72 pentamers (in the case of SV40), and each pentamer associates with a single VP2 and VP3. VP1 shows the ability to form pentamers when produced in either *Escherichia coli* or baculovirus systems
https://www.sciencedirect.com/topics/medicine-and-dentistry/protein-vp2

Synonyms/Aliases
1. Protein X - (gene X PRF: 1305266B) Organism - Woodchuck Hepatitis B Virus (isolate w64/pWS23) (WHV)
State: carcinoma; taxonomy: Virus.
KEYWORDS - Surface Antigen; cDNA Clone; Woodchuck Hepatitis Virus
http://www.recombinant-protein-dna.org/Virus-1733-Recombinant-Protein-cDNA-Protein-X.html

Protein X
RecName: Full=Large envelope protein; AltName: Full=L glycoprotein; AltName: Full=L-HBsAg; Short=LHB; AltName: Full=Large S protein; **AltName: Full=Large surface protein**; AltName: Full=Major surface antigen.
https://www.ncbi.nlm.nih.gov/protein/P11293

Protein X - alternative name - Full=Large S protein -
Phosphorylation of the Hepatitis B Virus Large Envelope Protein

***Attention**
2. Envelope E protein = SARS-CoV-2 viral particle
75 amino acids long, the envelope (E) protein is the smallest of the four structural proteins that make up the SARS-CoV-2 viral particle and is essential for the virus to infect cells. The human coronavirus SARS-CoV-2 encodes for at least two viroporins, a small 75 amino acid transmembrane protein known as the envelope (E) protein.

2a. Recombinant Envelope E - SARS CoV2 Products/Datasheets
Datasheet Envelope E - Recombinant SARS-CoV-2 K986P V987P Spike S2 His Protein, CF
SARS-CoV-2, which causes the global pandemic coronavirus disease 2019 (Covid-19), belongs to a family of viruses known as coronaviruses that also include MERS-CoV and SARS-CoV-1. Coronaviruses are commonly comprised of four structural proteins: Spike protein(S), Envelope protein (E), Membrane protein (M) and Nucleocapsid protein (N) (1).
Source: Human embryonic kidney cell, HEK293-derived sars-cov-2 Spike S2 Subunit protein
Ser686-Lys1211 (Lys986Pro, Val987Pro), with a C-terminal 6-His tag.
https://resources.rndsystems.com/pdfs/datasheets/10639-cv.pdf?v=20230712&_ga=2.128337484.1900435446.1689207634-461569935.1689207634

2b. Recombinant SARS-CoV-2 Surface glycoprotein
(Ser686-Lys1211) [His tag 002J) Source: Baculovirus, Baculovirus (CAT#: GP05-002J). The structural proteins of SARS-CoV-2 include the envelope protein (E).
https://www.creative-biolabs.com/glycoprotein/pdf/GP05-002J.pdf

3. VpX Viral protein = Simian immunodeficiency virus (SIV) and human immunodeficiency virus 2 (HIV-2)
Simian immunodeficiency virus (SIV) and human immunodeficiency virus 2 (HIV-2) display unique ability to infect nondividing target cells. Viral protein X (Vpx) of HIV-2/SIV is known to be involved in the nuclear import of viral genome in nondividing cells, but the mechanism remains poorly understood. The phosphorylation of Vpx plays a critical role in its interaction with human Nup153 and this interaction was found to be evolutionarily conserved in various SIV isolates and HIV-2.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7183765/

Mutants of HIV-1 Envelope Protein with Missing Hypervariable Domains (these connects to the linked proteins.)
https://pubchem.ncbi.nlm.nih.gov/patent/AT-112687-T

***Lactate dehydrogenase and C-reactive protein as predictors of respiratory failure in CoVID-19 patients**
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7282743/

***Lactate dehydrogenase**
(LDH or LD) is an enzyme found in nearly all living cells. LDH catalyzes the conversion of pyruvate to lactate and back, as it converts NAD^+ to NADH and back. A dehydrogenase is an enzyme that transfers a hydride from one molecule to another. LDH exists in four distinct enzyme classes. This article is specifically about the NAD(P)-dependent L-lactate dehydrogenase. Other LDHs act on D-lactate and/or are dependent on cytochrome c: D-lactate dehydrogenase (cytochrome) and L-lactate dehydrogenase (cytochrome). LDH is expressed extensively in body tissues, such as blood cells and heart muscle. Because it is released during tissue damage, it is a marker of common injuries and disease such as heart failure.
https://en.wikipedia.org/wiki/Lactate_dehydrogenase_elevating_virus
https://en.wikipedia.org/wiki/Lactate_dehydrogenase

Linked Genes
1041 CDSN - corneodesmosin (human)
386463 Cdsn - corneodesmosin (house mouse)
9735431 endA - deoxyribonuclease I (Dickeya dadantii 3937)

3. RV* Rotavirus
Two rotavirus vaccines are currently licensed for infants in the United States:
RotaTeq® (RV5) is given in 3 doses at ages 2 months, 4 months, and 6 months.

PRODUCT MONOGRAPH - RotaTeq® (RV5) - Rotarix® (RV1) is given in 2 doses at ages 2 months and 4 months
https://www.merck.ca/en/wp-content/uploads/sites/20/2021/04/ROTATEQ-PM_E.pdf

Rotavirus spike protein ΔVP8* as a novel carrier protein for conjugate vaccine platform with demonstrated antigenic potential for use as bivalent vaccine

Rotavirus spike protein ΔVP8* as a novel carrier protein for conjugate vaccine platform with demonstrated antigenic potential for use as bivalent vaccine - Conjugate vaccine platform is a promising strategy to overcome the poor immunogenicity of bacterial polysaccharide antigens in infants and children. A carrier protein in conjugate vaccines works not only as an immune stimulator to polysaccharide, but also as an immunogen; with the latter generally not considered as a measured outcome in real world. The potential of a conjugate vaccine platform to induce enhanced immunogenicity of a truncated rotavirus spike protein ΔVP8*. ΔVP8* was covalently conjugated to Vi capsular polysaccharide (Vi) of *Salmonella* Typhi to develop a bivalent vaccine, termed Vi-ΔVP8*. Results demonstrated that the Vi-ΔVP8* vaccine can induce specific immune responses against both antigens in immunized mice. The conjugate vaccine elicits high antibody titers and functional antibodies against *S*. Typhi and Rotavirus (RV) when compared to immunization with a single antigen. Together, these results indicate that Vi-ΔVP8* is a potent and immunogenic vaccine candidate, thus strengthening the potential of conjugate vaccine platform with enhanced immune responses to carrier protein, including ΔVP8*
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8586335/

Rotavirus spike protein VP4 mediates viroplasm assembly by association to actin filaments
Multiple studies have reported that a truncated rotavirus VP8* (ΔVP8*) subunit protein, from the proteolytic cleavage of the outer capsid spike protein VP4, is the target antigen due to its ability to induce highly potent neutralizing antibodies which confer strong protection against RV
https://www.biorxiv.org/content/biorxiv/early/2022/06/09/2022.06.08.495416.full.pdf

3a. RotaTeq®, Rotarix®, ROTAVAC®, and ROTASIIL®
At present, the most widely used live attenuated oral vaccines, demonstrating 80%-90% vaccine efficacy especially in developed countries. These vaccines are currently included in national immunization schedules in > 100 countries worldwide. However, the live attenuated oral vaccines showed impaired protection efficacy in developing countries where rotavirus vaccines are mostly needed. Poor nutrition, micronutrient deficiencies, and concurrent infection with other enteric pathogens may contribute to the diminished effectiveness of those attenuated vaccines. In addition, there is a small increased risk of intussusception in vaccinated infants.
https://www.sciencedirect.com/science/article/abs/pii/S0264410X21012822

***Patent: Truncated rotavirus vp8 protein and uses thereof (Rotavirus spike protein ΔVP8*)**
https://pubchem.ncbi.nlm.nih.gov/patent/WO-2015176586-A1

Linked Proteins: 142 total – (human and non -human)
P02248 Ubiquitin (human) (pig) - involved in endocytosis, DNA-damage responses. It also has distinct roles, such as in activation of protein kinases, and in signaling. Ribosomal protein L40 is essential for translation of a subset of cellular transcripts, and especially for cap-dependent translation of vesicular stomatitis virus mRNAs.
*Vesicular Stomatitis Virus –
https://www.aphis.usda.gov/publications/animal_health/fsc-vesicular-stomatitis.pdf

P08700 **Interleukin-3 (human)**
Receptor stimulation results in the rapid activation of JAK2 kinase activity leading to STAT5-mediated transcriptional program. *JAK2 kinase activity - The *Janus kinase 2 (JAK2)* gene directs cells to make the JAK2 protein, which stimulates cell growth and division. The JAK2 protein is particularly important for controlling blood cell production from hematopoietic blood-forming) stem cells. These stem cells are located in the bone marrow and have the ability to develop into new blood cells. The most common *JAK2* mutation found in blood disorders is known as *JAK2 V617F*, named for a mutation at a specific location in the *JAK2* gene. *JAK2* mutations are rare, they can cause various bone marrow disorders. These are known as myeloproliferative neoplasms (MPNs), where the bone marrow produces too many blood cells. Myeloproliferative neoplasms occur when blood stem cells produce too many of one or more types of blood cells, including red blood cells, white blood cells, and platelets. The effects of these neoplasms (abnormal growth of cells) slowly worsen as the number of extra blood cells increases.

P26678 **Cardiac phospholamban (human)**
Myocardial cells from failing human hearts are characterized by abnormal calcium handling, a negative force-frequency relationship, and decreased sarcoplasmic reticulum Ca^{2+} ATPase (SERCA2a) activity. In this study, we tested whether

contractile function can be improved by decreasing the inhibitory effects of phospholamban on SERCA2a with adenoviral gene transfer of antisense phospholamban (asPL).
https://www.ahajournals.org/doi/full/10.1161/hc0802.105564

P43155 **Carnitine O-acetyltransferase (human)**
Protein-Disease Associations: Acute diabetes complication and Ischemia - CRAT (Carnitine O-Acetyltransferase) is a Protein Coding gene. Diseases associated with CRAT include Neurodegeneration With Brain Iron Accumulation 8 and Neurodegeneration With Brain Iron Accumulation. Among its related pathways are Peroxisomal lipid metabolism and Metabolism. Gene Ontology (GO) annotations related to this gene include *signaling receptor binding* and *carnitine O-acetyltransferase activity*. An important paralog of this gene is CHAT.
https://www.genecards.org/cgi-bin/carddisp.pl?gene=CRAT

Bacterium Yeasts: (these are only a few)
P22782 Chloramphenicol acetyltransferase (Campylobacter coli)
Q4VR99 Spectinomycin 9-adenylyltransferase (Campylobacter jejuni)
P62579 Chloramphenicol acetyltransferase (Acinetobacter baumannii)
P0C1C1 Pectate lyase 2 (Pectobacterium carotovorum)
P62577 Chloramphenicol acetyltransferase (E. coli)
Q48454 Uncharacterized 42.6 kDa protein in cps region (Klebsiella pneumoniae)
P58777 Chloramphenicol acetyltransferase (Klebsiella sp.)
P07641 Chloramphenicol acetyltransferase (Proteus mirabilis)
P00485 Chloramphenicol acetyltransferase (Staphylococcus aureus)
P00486 Chloramphenicol acetyltransferase (Staphylococcus aureus)
P06135 Chloramphenicol acetyltransferase (Staphylococcus aureus)
P36882 Chloramphenicol acetyltransferase (Staphylococcus aureus)
P36883 Chloramphenicol acetyltransferase (Staphylococcus aureus)
Q8GAX4 Uncharacterized hydrolase in edin-B 3'region (Staphylococcus aureus)
P25309 Chloramphenicol acetyltransferase (Staphylococcus intermedius)

Linked Genes: 29 total (human and non-human)
7295 TXN - thioredoxin (human)
25828 TXN2 - thioredoxin 2 (human)
100862683 ERVK-25 - endogenous retrovirus group K member 25 (human)
2541030 ubi4 - ubiquitin (fission yeast)
176718 ubq-2 - Ubiquitin (Caenorhabditis elegans)
858590 ECU02_0740i - ubiquitin (Encephalitozoon cuniculi GB-M1)
3874950 ubi - ubiquitin (Neurospora crassa OR74A)
850620 UBI4 - ubiquitin (Saccharomyces cerevisiae S288C)

4. DTaP Diphtheria, Pertussis, & Tetanus - BOOSTRIX (FDA recommended)
PRODUCT MONOGRAPH INCLUDING PATIENT MEDICATION INFORMATION
Combined diphtheria, tetanus, acellular pertussis (adsorbed) vaccine for booster vaccination
https://ca.gsk.com/media/6234/boostrix.pdf

***BOOSTRIX**
Is a Tdap vaccine that is given in a single booster shot. Boostrix is an immunization for teenagers and adults against tetanus, diphtheria, and pertussis. Boostrix contains tetanus and diphtheria toxoids, which are modified bacterial toxins that trigger the body to develop immunity, but they can't actually cause the disease. Boostrix also contains *acellular pertussis*, which is just one part of the bacteria that causes pertussis, and it can't cause the disease.
https://immunizationinfo.com/boostrix-vaccine/

Diphtheria toxoids
https://www.cdc.gov/vaccines/pubs/pinkbook/dip.html

Retaining the structural integrity of disulfide bonds in diphtheria toxoid carrier protein is crucial for the effectiveness of glycoconjugate vaccine candidates
Six proteins are currently used as carriers in licensed vaccines, including tetanus toxoid (TT), diphtheria toxoid (DT), Cross-Reactive Material 197 (CRM_{197}), the outer membrane protein complex of *Meningococcus* B (OMPC), protein D from *H. influenzae*, and the recombinant exotoxin A of *Pseudomonas aeruginosa*.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8864718/

Patent: Corynebacterium strain expressing high concentration of crm197
https://pubchem.ncbi.nlm.nih.gov/patent/WO-2020017832-A1

Cross-Reactive Material 197 (CRM_{197})
CRM197 Diphtheria toxin receptor a nontoxic mutation of diphtheria toxin (DT), can be taken up by BCECs via binding the receptor of the precursor of heparin-binding epidermal growth factor-like growth factor (HB-EGF), also known as the diphtheria toxin receptor (DTR) (Naglich et al., 1992). DTR is expressed on the BCECs, neurons, and glial cells. CRM197, coupled with PLGA. Nanoparticle could cross the Blood–brain barrier (BBB) and accumulate in CNS cells, such as glial cells, astrocytes. *In addition, CRM197-grafted PBCA NPs could carry the zidovudine (AZT) across the BBB

Patent: Crm197 Protein Carrier - WO-2022263574-A1
This invention relates to a Cross-Reactive Material (CRM) 197 polypeptide engineered to include a cysteine residue at a position corresponding to position 496 of SEQ ID NO: 1. The additional cysteine residue introduced into the CRM 197 polypeptide provides a free thiol group that can be used to conjugate a functional or cargo moiety (e.g., an immunogen or a drug). CRM197 polypeptides, CRM197 conjugates, methods of producing CRM197 conjugates, and therapeutic compositions, such as vaccines, comprising CRM 197 conjugates are provided.
https://pubchem.ncbi.nlm.nih.gov/patent/WO-2022263574-A1

Linked Proteins: (Mutated formats of Kinase products)
P15941 Mucin-1 (human) - The beta subunit contains a C-terminal domain which is involved in cell signaling, through phosphorylations and protein-protein interactions. Modulates signaling in *ERK, **SRC and **NF-kappa-B pathways. In activated T-cells, influences directly or indirectly the Ras/MAPK pathway. Promotes tumor progression. Regulates TP53-mediated transcription and determines cell fate in the genotoxic stress response. Binds, together with KLF4, the PE21 promoter element of TP53 and represses TP53 activity.
https://pubchem.ncbi.nlm.nih.gov/protein/P15941

Mucin 1 - Protein-Disease Associations
https://pubchem.ncbi.nlm.nih.gov/protein/P15941 - section=Diseases-and-Phenotypes

***ERK: The proteins extracellular signal-regulated kinase 1 (ERK1) ERK2**
Are the downstream components of a phosphor lay pathway that conveys growth and mitogenic signals largely channeled by the small RAS GTPases. By phosphorylating widely diverse substrates, ERK proteins govern a variety of evolutionarily conserved cellular processes in metazoans, the dysregulation of which contributes to the cause of distinct human diseases.

****SRC: Proto-oncogene tyrosine-protein kinase Src (human)**
Proto-oncogene tyrosine-protein kinase SRC also known as proto-oncogene c-Src, or simply c-Src (cellular Src; pronounced "sarc", as it is short for sarcoma), is a non-receptor tyrosine kinase protein that in humans is encoded by the *SRC* gene. It belongs to a family of Src family kinases and is similar to the v-Src (viral Src) gene of Rous sarcoma virus. Two transcript variants encoding the same protein have been found for this gene.
c-Src phosphorylates specific tyrosine residues in other tyrosine kinases. It plays a role in the regulation of embryonic development and cell growth. An elevated level of activity of c-Src is suggested to be linked to cancer progression by promoting other signals. Mutations in c-Src could be involved in the malignant progression of colon cancer

SRC - Pub Chem Protein summary
Proto-oncogene tyrosine-protein kinase Src (human) (Protein) – There are 32 associated diseases associated with this protein.

https://pubchem.ncbi.nlm.nih.gov/protein/P12931_-_section=Diseases-and-Phenotypes

*The proto-oncogene nonreceptor tyrosine-protein kinase *SRC* is a member of the *SRC* family of tyrosine kinases (SFKs), and its activation and overexpression have been shown to play a protumorigenic role in multiple solid cancers, including pancreatic ductal adenocarcinoma (PDAC). PDAC is currently the seventh-leading cause of cancer-related death worldwide, and, by 2030, it is predicted to become the second-leading cause of cancer-related death in the United States.
https://pubchem.ncbi.nlm.nih.gov/protein/P12931 - section=Protein-Protein-Interactions

*****NF-kappa-B pathways**
The transcription factor NF-κB regulates multiple aspects of innate and adaptive immune functions and serves as a pivotal mediator of inflammatory responses. NF-κB induces the expression of various pro-inflammatory genes, including those encoding cytokines and chemokines, and also participates in inflammasome regulation. In addition, NF-κB plays a critical role in regulating the survival, activation and differentiation of innate immune cells and inflammatory T cells. Consequently, deregulated NF-κB activation contributes to the pathogenic processes of various inflammatory diseases.

Pathways: (these are extremely toxic)
P98073 Enteropeptidase (human)
Q02496 Mucin-1 (house mouse)
Q5PY51 Diphtheria toxin (Corynebacterium diphtheriae)

Compound summary
Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine, Adsorbed - Not available because this is not a discrete structure.
https://pubchem.ncbi.nlm.nih.gov/compound/Tetanus-Toxoid_-Reduced-Diphtheria-Toxoid-and-Acellular-Pertussis-Vaccine_-Adsorbed

5. Hib* Haemophilus influenzae type b

Three monovalent Hib vaccines are available in the United States: PedvaxHIB (PRP-OMP, Merck), ActHIB (PRP-T, Sanofi) and Hiberix (PRP-T, GSK).
These vaccines are composed of Hib purified polyribosylribitol phosphate (PRP) capsular polysaccharide chemically bound (conjugated) to a protein to enhance the quality of the immune response to PRP. All three vaccines are approved for infants in a 3- or 4-dose series (depending on brand).

Two combination vaccines containing Hib are currently available in the United States: Pentacel (DTaP-IPV/Hib, Sanofi) and Vaxelis (DTaP-IPV-Hib-HepB, MSP Company). Pentacel is licensed for use in children younger than age 5 years and contains Hib conjugate, DTaP, and inactivated polio vaccines; it is approved as a 4-dose series for infants at age 2, 4, 6, and 15 through 18 months, but it is not approved for use as the DTaP/IPV booster dose recommended at age 4 to 6 years. Vaxelis (DTaP-IPV-Hib-HepB, MSP Company) is licensed for use in children younger than age 5 years and is FDA-approved and recommended by CDC as a 3-dose primary series of Hib for infants at age 2, 4, and 6 months. Vaxelis is not approved for use as a Hib booster (4th) dose. Vaxelis contains the same PRP-OMP Hib antigen as PedvaxHIB, but in a reduced amount.
https://www.drugs.com/pro/pedvaxhib.html

5a. Haemophilus influenzae Type b (Hib) Vaccine

Diphtheria toxoid (PRP-D), *Neisseria meningitidis outer membrane protein (PRP-OMP), **Tetanus toxoid (PRP-T) Diphtheria mutant carrier protein CRM197 (HbOC), PRP-D and HbOC vaccines are no longer available in the United States.
The following combination vaccines contain Hib conjugate vaccines:
- Diphtheria toxoid/Haemophilus influenzae type b conjugate vaccine/hepatitis B vaccine/inactivated poliovirus vaccine
- Diphtheria toxoid/Haemophilus influenzae type B conjugate vaccine/inactivated poliovirus vaccine
- Diphtheria/tetanus toxoids/pertussis vaccine/Haemophilus influenzae type b conjugate vaccine
- Meningococcal Haemophilus influenzae type b conjugate vaccine

https://www.merckmanuals.com/professional/infectious-diseases/immunization/haemophilus-influenzae-type-b-hib-vaccine

*Post marketing efficacy studies in the United States demonstrated variable efficacy (4,5). PRP vaccines were ineffective in children less than 18 months of age because of the T-cell-independent nature of the immune response to PRP polysaccharide (3).
https://www.cdc.gov/mmwr/preview/mmwrhtml/00023705.htm

Haemophilus influenzae type b (Hib)
Hib was the leading cause of bacterial meningitis and a common cause of other invasive diseases (such as epiglottitis, pneumonia, septic arthritis, cellulitis, purulent pericarditis, and bacteremia) among U.S. children younger than 5 years of age. An estimated 20,000 cases of invasive Hib disease occurred in this age group each year. Meningitis occurred in approximately two-thirds of children with invasive Hib disease; 15%–30% of survivors had hearing impairment or severe permanent neurologic sequelae. Approximately 4% of all cases were fatal.
https://www.immunize.org/askexperts/experts_hib.asp

5b. PedvaxHIB (PRP-OMP, Merck)
Synonym: NEISSERIA MENINGITIDIS SEROGROUP B (B-11 STRAIN) OUTER MEMBRANE PROTEIN COMPLEX THIOL MODIFIED FOR CONJUGATION

***NEISSERIA MENINGITIDIS SEROGROUP B (B-11 STRAIN) OUTER MEMBRANE PROTEIN COMPLEX THIOL MODIFIED FOR CONJUGATION**
FDA Global Substance Registration System (GSRS)
NEISSERIA MENINGITIDIS SEROGROUP B (STRAIN B-11) WHOLE
Fraction Name: OUTER MEMBRANE PROTEIN COMPLEX
https://gsrs.ncats.nih.gov/ginas/app/beta/substances/MC95ZF3C5A
https://gsrs.ncats.nih.gov/ginas/app/beta/substances/46KSF1PRP7

***Tetanus toxoid (PRP-T)**
- Severe allergic reaction (e.g., anaphylaxis) after a previous dose of this vaccine or any other containing diphtheria toxoid, tetanus toxoid, pertussis-containing vaccine, inactivated polio vaccine, Haemophilus b vaccine, or any ingredient in this vaccine
- Encephalopathy (e.g., coma, decreased level of consciousness, prolonged seizure) of unknown etiology within 7 days of a pertussis containing.
- Progressive neurologic disorder (including infantile spasms, uncontrolled epilepsy, progressive encephalopathy) after any pertussis-containing vaccine; do not administer until a treatment regimen has been established and the condition has stabilized.

Contradictions
https://www.drugs.com/dosage/diphtheria-toxoid-haemophilus-b-conjugate-prp-t-vaccine-pertussis-acellular-poliovirus-vaccine-inactivated-tetanus-toxoid.html

***Diphtheria mutant carrier protein CRM197 (HbOC)**
Corynebacterium diphtheriae was shown to be the causative agent of diphtheria that an extracellular toxin, diphtheria toxin (DT) secreted by C. diphtheriae is responsible for toxicity (4). The formaldehyde-treated detoxified form of DT, diphtheria toxoid, has been successfully used for mass vaccination and is still widely used as a component of combination vaccines. A major contribution to the understanding of the mode of action of DT was the discovery of mutated forms in the early 1970s (7). Several phages encoding mutants of DT, named cross-reactive materials (CRMs), were isolated following nitrosoguanidine- based mutagenesis of the phage containing the gene encoding DT. Being naturally nontoxic, CRMs were immediately recognized as having great potential for vaccine development. The most important CRM identified was CRM197, an enzymatically inactive and nontoxic form of DT that contains a single amino acid substitution from Glycine to Glutamate in position 52 (8). Subsequently CRM197 was found to be an ideal carrier for con- jugate vaccines against encapsulated bacteria. Here, the carrier protein is covalently linked to poorly immunogenic and T-cell-in- dependent capsular polysaccharides, thus creating T-cell-dependent conjugate antigens that are highly immunogenic in infants
https://www.pnas.org/doi/pdf/10.1073/pnas.1201964109

Corynebacterium strain expressing high concentration of crm197

https://pubchem.ncbi.nlm.nih.gov/patent/WO-2020017832-A1

Molecular size characterization of Haemophilus influenzae type b polysaccharide-protein conjugate vaccines
Current vaccines against Haemophilus influenzae type b (Hib) consist of capsular polysaccharide, *polyribosylribitol phosphate (PRP), chemically conjugated to a carrier protein. The stability of the conjugate is essential for vaccine efficacy, as the target population for this vaccine includes infants, who do not mount an immune response to free polysaccharide vaccines. A method has been developed for determining structural stability and batch-to-batch consistency of Hib vaccines by the application of fast protein liquid chromatography (FPLC)
https://pubmed.ncbi.nlm.nih.gov/8735551/

6. PCV13, PCV15 (Pneumococcal disease)

Pneumococcal Polysaccharide Vaccine [Chemical/Ingredient] (Code N0000179488)
6a. VAXNEUVANCE (Pneumococcal 15-valent Conjugate Vaccine)
A sterile suspension of purified capsular polysaccharides from *S. pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F, and 33F individually conjugated to CRM197 (see above). Each pneumococcal capsular polysaccharide is activated via sodium metaperiodate oxidation and then individually conjugated to CRM197 carrier protein via reductive amination. CRM197 is a non-toxic variant of diphtheria toxin (originating from *Corynebacterium diphtheriae* C7) expressed recombinantly in *Pseudomonas fluorescens*. Each of the fifteen serotypes is manufactured independently using the same manufacturing steps with slight variations to accommodate for differences in strains, polysaccharides and process stream properties. Each *S. pneumoniae* serotype is grown in media containing yeast extract, dextrose, salts and soy peptone. Each polysaccharide is purified by a series of chemical and physical methods. Then each polysaccharide is chemically activated and conjugated to the carrier protein CRM197 to form each glycoconjugate. CRM197 is isolated from cultures grown in a glycerol-based, chemically defined, salt medium and purified by chromatography and ultrafiltration. The final vaccine is prepared by blending the fifteen glycoconjugates with aluminum phosphate adjuvant in a final buffer containing histidine, polysorbate 20 and sodium chloride.
https://www.ema.europa.eu/en/documents/product-information/vaxneuvance-epar-product-information_en.pdf

***Vaxneuvance (Merck) Pneumococcal 15-valent - suspension for injection in pre-filled syringe Pneumococcal polysaccharide conjugate vaccine (15-valent, adsorbed) -**
Abstract - The present disclosure relates to multivalent pneumococcal vaccine compositions comprising capsular pneumococcal polysaccharide serotypes each individually conjugated to carrier proteins. When conjugated, the combination of the capsular pneumococcal polysaccharide serotype and the carrier protein is referred to herein as a polysaccharide-protein conjugate. The pneumococcal vaccine compositions may further comprise one or more of the following; a pharmaceutically acceptable carrier, a pharmaceutically acceptable diluent, a buffer, a preservative, a stabilizer, an adjuvant, and/or a lyophilization excipient. Methods of making and administering the pneumococcal vaccine compositions described herein are also provided.
Patent summary: https://pubchem.ncbi.nlm.nih.gov/patent/WO-2018064444-A1

Linked Proteins

Q14764	Major vault protein (human)
Q9EQK5	Major vault protein (house mouse)
Q62667	Major vault protein (Norway rat)
P15926	C5a peptidase (Streptococcus pyogenes)
Q5PY51	Diphtheria toxin (Corynebacterium diphtheriae)
Q5EAJ7	Major vault protein (purple sea urchin)
Q6P3L0	Major vault protein (zebrafish)
Q9DGM7	Major vault protein (channel catfish)
Q6PF69	Major vault protein (African clawed frog)
Q5ZMI4	Major vault protein (chicken)
Q5R9N2	Major vault protein (Sumatran orangutan)
Q3SYU9	Major vault protein (cattle)
P00588	Diphtheria toxin (Corynephage beta)
P00587	Diphtheria toxin (Corynephage omega)
Q01268	Movement protein (Impatiens necrotic spot virus)
P36292	Movement protein (Tomato spotted wilt virus (strain Brazilian BR-01))

Q8NZ80 C5a peptidase (Streptococcus pyogenes MGAS8232)
P0DD35 C5a peptidase (Streptococcus pyogenes SSI-1)
P0DD34 C5a peptidase (Streptococcus pyogenes MGAS315)
Q57603 Hyperpolarization-activated voltage-gated potassium channel (Methanocaldococcus jannaschii DSM 2661)
Q5X9R0 C5a peptidase (Streptococcus pyogenes MGAS10394)
P58099 C5a peptidase (Streptococcus pyogenes serotype M1)

Two combination vaccines containing Hib are currently available in the United States: Pentacel (DTaP-IPV/Hib, Sanofi) and Vaxelis (DTaP-IPV-Hib-HepB, MSP Company). Pentacel is licensed for use in children younger than age 5 years and contains Hib conjugate, DTaP, and inactivated polio vaccines; it is approved as a 4-dose series for infants at age 2, 4, 6, and 15 through 18 months, but it is not approved for use as the DTaP/IPV booster dose recommended at age 4 to 6 years. Vaxelis (DTaP-IPV-Hib-HepB, MSP Company) is licensed for use in children younger than age 5 years and is FDA-approved and recommended by CDC as a 3-dose primary series of Hib for infants at age 2, 4, and 6 months. Vaxelis is not approved for use as a Hib booster (4th) dose. Vaxelis contains the same PRP-OMP Hib antigen as PedvaxHIB, but in a reduced amount.
https://www.drugs.com/pro/pedvaxhib.html

6b. Haemophilus influenzae Type b (Hib) Vaccine
Diphtheria toxoid (PRP-D), *Neisseria meningitidis outer membrane protein (PRP-OMP), **Tetanus toxoid (PRP-T) Diphtheria mutant carrier protein CRM197 (HbOC), PRP-D and HbOC vaccines are no longer available in the United States.
The following combination vaccines contain Hib conjugate vaccines:
- Diphtheria toxoid/Haemophilus influenzae type b conjugate vaccine/hepatitis B vaccine/inactivated poliovirus vaccine
- Diphtheria toxoid/Haemophilus influenzae type B conjugate vaccine/inactivated poliovirus vaccine
- Diphtheria/tetanus toxoids/pertussis vaccine/Haemophilus influenzae type b conjugate vaccine
- Meningococcal Haemophilus influenzae type b conjugate vaccine
https://www.merckmanuals.com/professional/infectious-diseases/immunization/haemophilus-influenzae-type-b-hib-vaccine

*Post marketing efficacy studies in the United States demonstrated variable efficacy (4,5). PRP vaccines were ineffective in children less than 18 months of age because of the T-cell-independent nature of the immune response to PRP polysaccharide (3).
https://www.cdc.gov/mmwr/preview/mmwrhtml/00023705.htm

Haemophilus influenzae type b (Hib)
https://www.immunize.org/askexperts/experts_hib.asp

6c. PedvaxHIB (PRP-OMP, Merck)
***NEISSERIA MENINGITIDIS SEROGROUP B (B-11 STRAIN) OUTER MEMBRANE PROTEIN COMPLEX THIOL MODIFIED FOR CONJUGATION**
FDA Global Substance Registration System (GSRS)
NEISSERIA MENINGITIDIS SEROGROUP B (STRAIN B-11) WHOLE
Fraction Name: OUTER MEMBRANE PROTEIN COMPLEX
https://gsrs.ncats.nih.gov/ginas/app/beta/substances/MC95ZF3C5A
https://gsrs.ncats.nih.gov/ginas/app/beta/substances/46KSF1PRP7

***Tetanus toxoid (PRP-T)**
- Severe allergic reaction (e.g., anaphylaxis) after a previous dose of this vaccine or any other containing diphtheria toxoid, tetanus toxoid, pertussis-containing vaccine, inactivated polio vaccine, Haemophilus b vaccine, or any ingredient in this vaccine
- Encephalopathy (e.g., coma, decreased level of consciousness, prolonged seizure) of unknown etiology within 7 days of a pertussis containing.

- Progressive neurologic disorder (including infantile spasms, uncontrolled epilepsy, progressive encephalopathy) after any pertussis-containing vaccine; do not administer until a treatment regimen has been established and the condition has stabilized.

Contradictions
https://www.drugs.com/dosage/diphtheria-toxoid-haemophilus-b-conjugate-prp-t-vaccine-pertussis-acellular-poliovirus-vaccine-inactivated-tetanus-toxoid.html

***Diphtheria mutant carrier protein CRM197 (HbOC)**
Corynebacterium diphtheriae was shown to be the causative agent of diphtheria that an extracellular toxin, diphtheria toxin (DT) secreted by C. diphtheriae is responsible for toxicity (4). The formaldehyde-treated detoxified form of DT, diphtheria toxoid, has been successfully used for mass vaccination and is still widely used as a component of combination vaccines. A major contribution to the understanding of the mode of action of DT was the discovery of mutated forms in the early 1970s (7). Several phages encoding mutants of DT, named cross-reactive materials (CRMs), were isolated following nitrosoguanidine- based mutagenesis of the phage containing the gene encoding DT. Being naturally nontoxic, CRMs were immediately recognized as having great potential for vaccine development. The most important CRM identified was CRM197, an enzymatically inactive and nontoxic form of DT that contains a single amino acid substitution from Glycine to Glutamate in position 52 (8). Subsequently CRM197 was found to be an ideal carrier for con- jugate vaccines against encapsulated bacteria. Here, the carrier protein is covalently linked to poorly immunogenic and T-cell-in- dependent capsular polysaccharides, thus creating T-cell-dependent conjugate antigens that are highly immunogenic in infants
https://www.pnas.org/doi/pdf/10.1073/pnas.1201964109

Corynebacterium strain expressing high concentration of crm197
https://pubchem.ncbi.nlm.nih.gov/patent/WO-2020017832-A1

Molecular size characterization of Haemophilus influenzae type b polysaccharide-protein conjugate vaccines
Current vaccines against Haemophilus influenzae type b (Hib) consist of capsular polysaccharide, *polyribosylribitol phosphate (PRP), chemically conjugated to a carrier protein. The stability of the conjugate is essential for vaccine efficacy, as the target population for this vaccine includes infants, who do not mount an immune response to free polysaccharide vaccines. A method has been developed for determining structural stability and batch-to-batch consistency of Hib vaccines by the application of fast protein liquid chromatography (FPLC)
https://pubmed.ncbi.nlm.nih.gov/8735551/

7. PCV13, PCV15 (Pneumococcal disease)
Pneumococcal Polysaccharide Vaccine [Chemical/Ingredient] (Code N0000179488)

7a. VAXNEUVANCE (Pneumococcal 15-valent Conjugate Vaccine)
A sterile suspension of purified capsular polysaccharides from *S. pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F, and 33F individually conjugated to CRM197 (see above). Each pneumococcal capsular polysaccharide is activated via sodium metaperiodate oxidation and then individually conjugated to CRM197 carrier protein via reductive amination. CRM197 is a non-toxic variant of diphtheria toxin (originating from *Corynebacterium diphtheriae* C7) expressed recombinantly in *Pseudomonas fluorescens*. Each of the fifteen serotypes is manufactured independently using the same manufacturing steps with slight variations to accommodate for differences in strains, polysaccharides and process stream properties. Each *S. pneumoniae* serotype is grown in media containing yeast extract, dextrose, salts and soy peptone. Each polysaccharide is purified by a series of chemical and physical methods. Then each polysaccharide is chemically activated and conjugated to the carrier protein CRM197 to form each glycoconjugate. CRM197 is isolated from cultures grown in a glycerol-based, chemically defined, salt medium and purified by chromatography and ultrafiltration. The final vaccine is prepared by blending the fifteen glycoconjugates with aluminum phosphate adjuvant in a final buffer containing histidine, polysorbate 20 and sodium chloride.
https://www.ema.europa.eu/en/documents/product-information/vaxneuvance-epar-product-information_en.pdf

***Vaxneuvance (Merck) Pneumococcal 15-valent - suspension for injection in pre-filled syringe Pneumococcal polysaccharide conjugate vaccine (15-valent, adsorbed)**

Abstract - The present disclosure relates to multivalent pneumococcal vaccine compositions comprising capsular pneumococcal polysaccharide serotypes each individually conjugated to carrier proteins. When conjugated, the combination of the capsular pneumococcal polysaccharide serotype and the carrier protein is referred to herein as a polysaccharide-protein conjugate. The pneumococcal vaccine compositions may further comprise one or more of the following; a pharmaceutically acceptable carrier, a pharmaceutically acceptable diluent, a buffer, a preservative, a stabilizer, an adjuvant, and/or a lyophilization excipient. Methods of making and administering the pneumococcal vaccine compositions described herein are also provided.
Patent summary:
https://pubchem.ncbi.nlm.nih.gov/patent/WO-2018064444-A1

Linked Proteins

Q14764	Major vault protein (human)
Q9EQK5	Major vault protein (house mouse)
Q62667	Major vault protein (Norway rat)
P15926	C5a peptidase (Streptococcus pyogenes)
Q5PY51	Diphtheria toxin (Corynebacterium diphtheriae)
Q5EAJ7	Major vault protein (purple sea urchin)
Q6P3L0	Major vault protein (zebrafish)
Q9DGM7	Major vault protein (channel catfish)
Q6PF69	Major vault protein (African clawed frog)
Q5ZMI4	Major vault protein (chicken)
Q5R9N2	Major vault protein (Sumatran orangutan)
Q3SYU9	Major vault protein (cattle)
P00588	Diphtheria toxin (Corynephage beta)
P00587	Diphtheria toxin (Corynephage omega)
Q01268	Movement protein (Impatiens necrotic spot virus)
P36292	Movement protein (Tomato spotted wilt virus (strain Brazilian BR-01))
Q8NZ80	C5a peptidase (Streptococcus pyogenes MGAS8232)
P0DD35	C5a peptidase (Streptococcus pyogenes SSI-1)
P0DD34	C5a peptidase (Streptococcus pyogenes MGAS315)
Q57603	Hyperpolarization-activated voltage-gated potassium channel (Methanocaldococcus jannaschii DSM 2661)
Q5X9R0	C5a peptidase (Streptococcus pyogenes MGAS10394)
P58099	C5a peptidase (Streptococcus pyogenes serotype M1)

Linked Genes

10202	DHRS2 - dehydrogenase/reductase 2 (human)
105372315	ERVS71-1 - endogenous retrovirus group S71 member 1, envelope (human)
71412	Dhrs2 - dehydrogenase/reductase member 2 (house mouse)
691464	Dhrs2 - dehydrogenase/reductase 2 (Norway rat)
393539	dhrs4 - dehydrogenase/reductase (SDR family) member 4 (zebrafish)

Linked Taxonomies

9606	Homo sapiens (human)
1313	Streptococcus pneumoniae
1319	Streptococcus sp. 'group B'
1717	Corynebacterium diphtheriae
36470	Streptococcus sp. 'group A'
212258	Panda oleosa

***Vaxneuvance Pneumococcal 15-valent Conjugate Vaccine: COMPOUND SUMMARY**
FDA Pharmacological Classification
*Non-Proprietary Name: AMLODIPINE AND BENAZEPRIL HYDROCHLORIDE (Generic names) Aliases Norvasc

Amlodipine *Extremely Toxic

*Amlodipine is used for the treatment of hypertension, chronic stable angina and confirmed or suspected vasospastic angina. It has a role as an antihypertensive agent, a calcium channel blocker and a vasodilator agent. It is a dihydropyridine, a member of monochlorobenzenes, an ethyl ester, a methyl ester and a primary amino compound. Amlodipine has the ability to enhance the production of nitric oxide (NO), an important vasodilator that decreases blood pressure.

*GHS Hazard Statements (Amlodipine)
Toxic if swallowed - Danger Acute toxicity, oral corrosive, environmental contaminant. Causes serious eye damage [Danger Serious eye damage/eye irritation], Causes damage to organs through prolonged or repeated exposure [Warning Specific target organ toxicity, repeated exposure] Very toxic to aquatic life with long lasting effects
https://pubchem.ncbi.nlm.nih.gov/compound/amlodipine

7b. Pneumococcal 7-valent Conjugate Vaccine (Diphtheria CRM197 Protein) **Prevnar®**
***Attention:** This vaccine carries *Cross-Reactive Material 197 (CRM_{197}) - 9 Diphtheria toxin receptor Children will be getting a double dose of these in two separate vaccines – It is dangerously toxic. It is a vector that contains a plethora of toxins.

Conjugated to CRM197 carrier protein.
CRM197 is a nontoxic mutant of diphtheria toxin (originating from Corynebacterium diphtheriae C7) expressed recombinantly in Pseudomonas fluorescens. 2Adsorbed on aluminum phosphate adjuvant. 1 dose (0.5 mL) contains 125 micrograms aluminum (Al3+) and approximately 30 micrograms CRM197 carrier protein.
https://www.ema.europa.eu/en/documents/product-information/vaxneuvance-epar-product-information_en.pdf

***Diphtheria CRM197 Protein – *Extremely volatile compound/product**
Diphtheria toxin receptor, CRM197 - a nontoxic mutation of diphtheria toxin (DT), can be taken up by Primary brain capillary endothelial cells (BCECs) via binding the receptor of the precursor of heparin-binding epidermal growth factor-like growth factor (HB-EGF), also known as the diphtheria toxin receptor (DTR) However, the use of CRM197 is problematic as it has been used for vaccination against diphtheria, and the presence of antibodies may hinder the efficacy of this vector. In addition, it has been recently reported that CRM197 has a weak toxicity and specific care has to be taken in the use of CRM197 at high dose, although the toxicity of CRM197 is about 100 times less than that of the wild-type diphtheria. **Primary brain capillary endothelial cells (BCECs) are a promising tool to study the blood–brain barrier (BBB).

8. IPV - Poliovirus Vaccine, inactivated
***Components:** components, including 2-phenoxyethanol, formaldehyde, ***neomycin **streptomycin, and ***polymyxin B.** Inactivated poliovirus vaccine administration has been associated with Guillain-Barre syndrome. Inactivated poliovirus vaccine (IPV). Inactivated viral vaccines are produced from genetic material or surface proteins (antigens) from viruses grown in a lab and killed to eliminate their disease-causing ability. The concentrated vaccine is then purified, sterilized and diluted with a medium. Certain antibiotics are used in the production of inactivated poliovirus vaccine, and the vaccine also contains substances that preserve and stabilize it, and enhance immune response.
There are three types of wild poliovirus, WPV type 1, 2 and 3, which cause disease. Inactivated poliovirus vaccine contains antigens of all three WPV strains. Poliovirus vaccine stimulates the production of virus neutralizing antibodies by the immune system and protects a person from poliovirus infection and debilitating disease if exposed to the virus. The onset of protection is relatively slow, however, protection is long lasting.

***Neomycin:**
Neomycin may cause fetal harm and total irreversible bilateral congenital deafness when administered in pregnant women. It is used in veterinary medicine as a bactericidal drug. Prolonged administration could result in sufficient systemic drug levels to produce neurotoxicity, ototoxicity and/or nephrotoxicity. Delayed-onset irreversible deafness, renal failure and death due to neuromuscular blockade (regardless of the status of renal function).
GHS Hazard Statements
H302 (100%): Harmful if swallowed [Warning Acute toxicity, oral]
H317 (100%): May cause an allergic skin reaction [Warning Sensitization, Skin]
H334 (100%): May cause allergy or asthma symptoms or breathing difficulties if inhaled [Danger Sensitization, respiratory]

https://pubchem.ncbi.nlm.nih.gov/compound/neomycin

***Associated Disorders and Diseases (two examples)**
Pathological processes of the Vestibulocochlear Nerve, including the branches of Cochlear nerve and Vestibular nerve, Common examples are Vestibular neuritis, Cochlear neuritis, and Acoustic neuroma. Clinical signs are varying degree of HEARING LOSS; VERTIGO; and TINNITUS.

***Necrosis** - The death of cells in an organ or tissue due to disease, injury or failure of the blood supply.
Associated Disorders and Diseases - DNA Degradation, Necrotic - The random catabolism of DNA accompanying the irreversible damage to tissue which leads to the pathological death of one or more cells.
https://pubchem.ncbi.nlm.nih.gov/compound/neomycin - section=Associated-Disorders-and-Diseases

****Streptomycin** - The most common symptoms of streptomycin overdose are ototoxicity and vestibular impairment. Streptomycin is also associated with nephrotoxicity which presents as mild elevations in blood urea (Urea nitrogen is a waste product that your kidneys remove from your blood) mild proteinuria, and excess cellular excretion. While in severe cases, streptomycin may lead to permanent hearing loss and vestibular dysfunction, any associated nephrotoxicity is typically transient. In cases of toxicity, streptomycin serum concentrations may be lowered with dialysis.
ANIMAL STUDIES: Clinical signs of toxicity in mice included restlessness, respiratory depression, loss of balance, unconsciousness, motor paralysis and coma following all routes of administration. Coma was more often associated with subcutaneous dosing.
https://pubchem.ncbi.nlm.nih.gov/compound/19649 - section=Associated-Disorders-and-Diseases

*****Polymyxin B.** - Is contraindicated in those known to be hypersensitive to polymyxins and should be used with caution by patients with reduced renal function. Adverse Effects - The most common adverse effect associated with the systemic use of polymyxins is a dose-related. This related nephrotoxicity. is characterized by proteinuria, cylinduria, and cellular elements in the urine. Polymyxin-induced neurotoxicity includes a noncompetitive neuromuscular blockade causing reversible respiratory paralysis, parathesis that may be accompanied by dizziness, vertigo, ataxia, slurred speech, drowsiness or confusion. These effects are dose-related and reversible following discontinuation of the drug. Other adverse effects associated with the use of polymyxins include rash, endocrine/metabolic effects (hypocalcemia), and electrolyte abnormalities, such as hypochloremia, hyponatremia, and hypokalemia Scholar and Pratt (2000), Micromedex (2003), Kucers et al (1997).
https://www.sciencedirect.com/topics/agricultural-and-biological-sciences/polymyxin-b

*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 treatment of infections with gram-negative bacteria, but may be neurotoxic and nephrotoxic. Currently, polymyxin B and colistin (polymyxin E) have been developed for clinical use, where they are reserved as “last-line” therapies for multidrug-resistant (MDR) infections. Unfortunately, the incidences of strains resistant to polymyxins have been increasing globally, and polymyxin heteroresistance has been gaining appreciation as an important clinical challenge. These phenomena, along with bacterial tolerance to this antibiotic class, constitute important contributors to polymyxin treatment failure.
Causes of polymyxin treatment failure and new derivatives to fill the gap
https://www.nature.com/articles/s41429-022-00561-3

Polimixina B - Compound Summary
https://pubchem.ncbi.nlm.nih.gov/compound/Polimixina-B

GHS Classification in accordance with 29 CFR 1910 (OSHA HCS) - Acute toxicity, Oral (Category 4), H302
https://www.sigmaaldrich.com/US/en/sds/sigma/p4932

8a. *IPOL - Poliovirus Vaccine Inactivated (Monkey Kidney Cell) – FDA Approved Polio Vaccine
Poliovirus Vaccine Inactivated, Tradename: IPOL, Manufacturer: Sanofi Pasteur, SA
Indications: POL vaccine is indicated for active immunization of infants (as young as 6 weeks of age), children, and adults for the prevention of poliomyelitis caused by poliovirus Types 1, 2, and 3.
https://www.fda.gov/vaccines-blood-biologics/vaccines/ipol-poliovirus-vaccine-inactivated-monkey-kidney-cell

Poliovirus Vaccine Inactivated
IPOL®, Poliovirus Vaccine Inactivated, produced by Sanofi Pasteur SA, is a sterile suspension of three types of poliovirus: Type 1 (Mahoney), Type 2 (MEF-1), and Type 3 (Saukett). IPOL vaccine is a highly purified, inactivated poliovirus vaccine with enhanced potency. Each of the three strains of poliovirus is individually grown in *Vero cells, a continuous line of monkey kidney cells cultivated on microcarriers. (1) (2) The cells are grown in *Eagle MEM modified medium, supplemented with newborn calf bovine serum.
https://www.fda.gov/media/75695/download?attachment

WHO Vero Cells Vero CCL-81™ *These cells are present in the Dengue Virus Vaccine
The Vero cell line was initiated in 1962 from the kidney tissue derived from a normal, adult African green monkey. The cell line can be used in a variety of applications, including the detection of verotoxins, detection of virus in ground beef, efficacy testing, the study of malaria, media testing, and mycoplasma testing.
https://www.atcc.org/products/ccl-81

Vero Cells - Safety Datasheets
https://www.atcc.org/resources/safety-data-sheets

Patent: Attenuated viruses useful for vaccine
*This vaccine is made up entirely of extremely toxic chemical compounds
Summary: This invention provides an attenuated virus which comprises a modified viral genome containing nucleotide substitutions engineered in multiple locations in the genome, wherein the substitutions introduce synonymous deoptimized codons into the genome. The instant attenuated virus may be used in a vaccine composition for inducing a protective immune response in a subject. The invention also provides a method of synthesizing the instant attenuated virus. Further, this invention further provides a method for preventing a subject from becoming afflicted with a virus-associated disease comprising administering to the subject a prophylactically effective dose of a vaccine composition comprising the instant attenuated virus.
https://pubchem.ncbi.nlm.nih.gov/patent/US-9476032-B2_-_section=Full-Text

***MEM: Modified Eagle Medium** – ingredients: high glucose, non-essential amino acids, sodium pyruvate, and **__phenol red (salt),__ ethanolamine, glutathione, ascorbic acid, insulin, transferrin, ***AlbuMAX™ I lipid-rich bovine serum albumin for cell culture.
https://www.thermofisher.com/order/catalog/product/12491015

Phenol Red sodium salt - Hazards identification - Classification of the substance or mixture
PhH315 (100%): Causes skin irritation [Warning Skin corrosion/irritation]
H319 (98.18%): Causes serious eye irritation [Warning Serious eye damage/eye irritation]
H335 (100%): May cause respiratory irritation [Warning Specific target organ toxicity, single exposure; Respiratory tract irritation] https://pubchem.ncbi.nlm.nih.gov/compound/Phenol-Red-sodium-salt

Vendors - Phenol Red
https://www.sigmaaldrich.com/US/en/sds/sial/p4758

Phenolsulfonephthalein sodium salt (synonym)
https://www.chemicalbook.com/ProductMSDSDetailCB0426392_EN.htm_-_5

*EXTREMELY MPORTANT: AlbuMAX™ I lipid-rich bovine serum albumin - ALBUMAX I Lipid-Rich Bovine Serum was developed especially for use in cell culture media as a convenient, effective means to reduce or replace the requirement for serum supplementation. A proprietary chromatographic separations process is used by Invitrogen to isolate consistently high-quality product from New Zealand origin bovine plasma.
**For research use only. CAUTION: Not intended for human or animal diagnostic or therapeutic uses.
https://tools.thermofisher.com/content/sfs/manuals/3118.pdf

Bovine Serum Albumin (Lipid Fortified)
Bovogen Biologicals' BovoLep BSA product is a highly purified BSA product that has been fortified with a specially formulated 'cocktail' of non-animal synthetic lipids for the enhanced growth of fastidious organisms such as Leptospira.

https://bovogen.com/our-products/purified-proteins/bovine-serum-albumin-lipid-fortified/

***Leptospira**

Leptospirosis is an infectious disease caused by bacteria. It can lead to potentially fatal infections of the kidney, liver, brain, lung or heart. The bacteria that cause leptospirosis are spread through the urine of infected animals, which can get into water or soil and can survive there for weeks to months. Many different kinds of wild and domestic animals carry the bacterium. These can include, but are not limited to: cattle, pigs, horses, dogs, rodents, wild animals.
When these animals are infected, they may have no symptoms of the disease. Infected animals may continue to excrete the bacteria into the environment continuously or every once in a while, for a few months up to several years.
https://www.cdc.gov/leptospirosis/index.html

Leptospirosis: The "mysterious" mimic

Leptospirosis is a potentially fatal bacterial disease that can display a wide array of clinical presentations thus mimicking better-known illnesses. Although, leptospirosis is primarily a zoonotic disease, it frequently inflicts severe illness and death on communities around the globe Due to its nonspecific symptoms that mimic better-known diseases, leptospirosis has been frequently underdiagnosed and underreported. The pulmonary form of leptospirosis is characterized as a hemorrhagic pneumonia that can resemble pneumonic plague and hantavirus pulmonary syndrome.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2700559/

8. Influenza vaccines

The recommendations for egg-based and cell-based and recombinant flu vaccines are listed below:

Egg-based vaccine composition recommendations:
*an A/Victoria/2570/2019 (H1N1) pdm09-like virus;
*an A/Darwin/9/2021 (H3N2)-like virus (updated);
*a B/Austria/1359417/2021-like virus (B/Victoria lineage) (updated);
*a B/Phuket/3073/2013-like virus (B/Yamagata lineage)

Cell- or recombinant-based vaccine composition recommendations:
*an A/Wisconsin/588/2019 (H1N1) pdm09-like virus;
*an A/Darwin/6/2021 (H3N2)-like virus (updated);
*a B/Austria/1359417/2021-like virus (B/Victoria lineage) (updated);
*a B/Phuket/3073/2013-like virus (B/Yamagata lineage).
https://www.fda.gov/vaccines-blood-biologics/lot-release/influenza-vaccine-2022-2023-season

*Asthma is considered a precaution for use of quadrivalent live attenuated influenza vaccine (LAIV4) in persons aged ≥5 years because of concerns for wheezing events. We evaluated the safety of LAIV4 in children with asthma, comparing the proportion of children with asthma exacerbations after LAIV4 or quadrivalent inactivated influenza vaccine (IIV4).

8a. IIVA Influenza vaccine (inactivated)

FLUMIST QUADRIVALENT is contraindicated in persons who have had a severe allergic reaction (e.g., anaphylaxis) to any vaccine component, including egg protein, or after a previous dose of any influenza vaccine, and in children and adolescents receiving concomitant aspirin or aspirin-containing therapy. In clinical trials, the risks of hospitalization and wheezing were increased in children <24 months of age who received trivalent FluMist. Children <5 years of age with recurrent wheezing and persons of any age with asthma may be at increased risk of wheezing following FLUMIST QUADRIVALENT administration. FLUMIST QUADRIVALENT has not been studied in persons with severe asthma or active wheezing

*If Guillain-Barré syndrome has occurred within 6 weeks of any prior influenza vaccination, the decision to give FLUMIST QUADRIVALENT should be based on careful consideration of the potential benefits and risks FLUMIST QUADRIVALENT has not been studied in immunocompromised persons. The safety of FLUMIST QUADRIVALENT in individuals with underlying medical conditions predisposing them to wild-type influenza infection complications has not been established. Appropriate medical treatment and supervision must be available to manage possible anaphylactic reactions following administration of the vaccine.
https://www.fda.gov/media/160349/download?attachment

Flumist Quadrivalent is recommended as an option by the ACIP and AAP[1,2]
https://www.flumistquadrivalenthcp.com/vaccine-effectiveness-and-efficacy.html

Afluria Quadrivalent 2022-2023 (injection)
https://www.drugs.com/mtm/afluria-quadrivalent-2022-2023-injection.html

Quadrivalent Side Effects *Serious side effects
Influenza virus vaccine (inactivated) may cause adverse effects. Although not all of these side effects may occur, if they do occur, they may need medical attention. Check with your doctor or nurse immediately if any of the following side effects occur while taking influenza virus vaccine, inactivated: Black, tarry stools, bleeding gums, blood in the urine or stools, cough, difficulty swallowing, dizziness, fainting, fast heartbeat, hives, itching, rash, inability to move the arms and legs, large, hive-like swelling on the face, eyelids, lips, tongue, throat, hands, legs, feet, or sex organs, pinpoint red spots on the skin, puffiness or swelling of the eyelids or around the eyes, face, lips, or tongue, sudden numbness and weakness in the arms and legs, tightness in the chest, unusual bleeding or bruising, unusual tiredness or weakness. The most common adverse events were local reactions, myalgia, and headache, hemorrhage Cellulitis, (see description below) injection site inflammation, injection site sterile abscess.

Other: Chest tightness and Death
***Musculoskeletal**
Myalgia, chills/shivering, back pain, Muscle weakness, arthritis, arthralgia, myasthenia

***Nervous system**
Migraine, headache, drowsiness, lethargy
Neuralgia, paresthesia, convulsions (including febrile seizures), encephalopathy, neuritis or neuropathy, transverse myelitis, Guillain-Barre syndrome, abnormal gait, dizziness, hypoesthesia, hypokinesia, tremor, somnolence, syncope, facial or cranial nerve paralysis, encephalopathy, limb paralysis, confusion, paralysis (including Bell's Palsy), vertigo, exacerbation of symptoms of mitochondrial encephalomyopathy (Leigh syndrome), meningitis, eosinophilic meningitis, vaccine-associated encephalitis[Ref]

***Respiratory**
Very common (10% or more): Runny nose/nasal congestion (58%), cough (15%), upper respiratory tract infection (13%)
Common (1% to 10%): Sore throat, cough, oropharyngeal pain, rhinorrhea, wheezing, pharyngolaryngeal pain, nasopharyngitis, Rhinitis, laryngitis, dyspnea, dysphonia, bronchospasm, throat tightness, pharyngitis, epistaxis

***Gastrointestinal**
Vomiting, nausea, diarrhea, Dysphagia, abdominal pain, swelling of the mouth, throat, and/or tongue.

***Hypersensitivity**
Allergic reactions including anaphylactic shock, serum sickness, and death; Stevens-Johnson syndrome

***Immunologic - Infection, influenza-like illness**
***Cellulitis -** is a skin infection caused by bacteria. Cellulitis is common and can become severe. Cellulitis usually appears on the lower legs. It can also appear on the arms, face, and other areas. Cellulitis develops when bacteria enter a crack or break in your skin, such as a scratch, bite, or cut.
https://www.merckvaccines.com/mmr/

8b. LAIV4 (egg-based vaccine†)
***FluMist Quadrivalent (AstraZeneca**) in persons who have had a severe allergic reaction (eg, anaphylaxis) to any vaccine component, including egg protein, or after a previous dose of any influenza vaccine in children and adolescents receiving concomitant aspirin or aspirin-containing therapy.

*In clinical trials, the risks of hospitalization and wheezing were increased in children <24 months of age who received trivalent FluMist.

*Children <5 years of age with recurrent wheezing and persons of any age with asthma may be at increased risk of wheezing following FLUMIST QUADRIVALENT administration. FLUMIST QUADRIVALENT has not been studied in persons with severe asthma or active wheezing.

*If Guillain-Barré syndrome has occurred within 6 weeks of any prior influenza vaccination, the decision to give FLUMIST QUADRIVALENT should be based on careful consideration of the potential benefits and risks.

9. (MMR) Measles, mumps, and rubella

9a. PRIORIX - A lyophilized mixed preparation of the attenuated Schwarz measles, RIT 4385 mumps (derived from Jeryl Lynn strain) and Wistar RA 27/3 rubella strains of viruses, separately obtained by propagation either in chick embryo tissue cultures (mumps and measles) or MRC5 human diploid cells (rubella). PRIORIX, was approved for use in the U.S. PRIORIX is made by GlaxoSmithKline Biologicals. So, this month, we thought it would be useful to discuss how these vaccines compare. PRIORIX vaccine also contains small quantities of sugars, lactose, and amino acids as well as bovine serum albumin, ovalbumin, and neomycin.

***Active ingredients - Both of the MMR vaccines contain live, weakened viruses that are similar, if not identical, and are delivered in much the same doses**

***Measles component**

MMR II contains the modified Enders' Edmonston strain (Moraten) and PRIORIX contains the Schwarz strain; however, these strains are identical at the level of nucleotide sequences.

***Mumps component**

MMR II contains the "Jeryl Lynn" strain of mumps virus, which is composed of two lineages of the virus (JL1 and JL2). PRIORIX contains the RIT4385 strain, which contains only JL1. The JL1 components in the two vaccines are identical at the protein level. ***MMR II** vaccine also contains small quantities of sugars as well as bovine-sourced products (gelatin and fetal bovine serum), human albumin, and neomycin.

***Rubella component**

Both vaccines (Mumps and Rubella) contain the Wistar RA 27/3 strain developed by Dr. Stanley Plotkin. They are identical at the nucleotide sequence level. *Because in both cases, the vaccines contain live, weakened viruses, neither contains preservatives. Likewise, the viruses are grown in the same types of cells during the vaccine production process. This means that the measles and mumps components are grown in chick embryo cells, and the rubella component is grown in human fetal fibroblast cells. However, the MMR II rubella component is grown in WI-38 cells, and the PRIORIX rubella component is grown in MRC-5 cells. These are the same two cell lines used for all other vaccines grown in fetal cells, except COVID-19 adenovirus-based vaccines, which use fetal retinal cells. (Note: For more information about the history of fetal fibroblast cell lines refer to the resources section of this article.)
https://www.chop.edu/news/news-views-what-should-i-know-about-new-mmr-vaccine-priorix

***Immunogenicity**

Antibody responses following receipt of PRIORIX were similar to those found following receipt of MMR II after both the first and second doses. Likewise, persistence of antibody levels measured two years after vaccination were similar.

***Safety**

Side effect profiles were similar for both vaccines, including the rates and average timing of febrile seizures. Overall, for any MMR vaccine, febrile seizures are estimated to develop at a rate of 3.3 to 8.7 per 10,000 doses, and they are most likely to occur 6 to 11 days after vaccination. A rare and temporary side effect of measles vaccine is thrombocytopenia, or decreased numbers of platelets. This condition results in decreased blood-clotting efficiency. Comparisons between the rates of thrombocytopenia following receipt of either MMR vaccine found no significant differences.
https://www.chop.edu/news/news-views-what-should-i-know-about-new-mmr-vaccine-priorix
https://ca.gsk.com/media/6254/priorix.pdf

9b. M-M-R®II

Is a vaccine indicated for active immunization for the prevention of measles, mumps, and rubella in individuals 12 months of age or older. The first dose of M-M-R®II is administered at 12 to 15 months of age and the second dose of M-M-R®II is administered at 4 to 6 years of age.

***M-M-R Safety concerns**
*M-M-R®II (Merck) is contraindicated in certain individuals, including those with: a history of hypersensitivity to any component of the vaccine, including gelatin; a history of anaphylactic reaction to neomycin; individuals who are immunodeficient or immunosuppressed due to disease or medical therapy; an active febrile illness; active untreated tuberculosis; or those who are pregnant or are planning to become pregnant within the next month. Caution should be employed in administration of M-M-R®IIto persons with: a history of febrile seizure or family history of febrile seizures; immediate-type hypersensitivity reactions to eggs; thrombocytopenia.

*Vaccination should be deferred in individuals with a family history of congenital or hereditary immunodeficiency until the individual's immune status has been evaluated and the individual has been found to be immunocompetent.

*Immune globulins (IG) and other blood products should not be given concurrently with M-M-R®II. The ACIP has specific recommendations for intervals between administration of antibody-containing products and live virus vaccines.

*The following adverse reactions have been identified during both the subcutaneous and intramuscular use of M-M-R®II or its components in clinical trials or reported during post-approval use: fever, rash, and injection-site reactions.

*The following adverse reactions have been identified during the subcutaneous use of M-M-R®II or its components in clinical trials or reported during post-approval use: headache, dizziness, febrile convulsions, anaphylaxis and anaphylactoid reactions, arthritis, thrombocytopenia, encephalitis and encephalopathy.
https://www.merckvaccines.com/mmr/
https://www.merck.com/product/usa/pi_circulars/m/mmr_ii/mmr_ii_pi.pdf

***Thrombocytopenia – Side effect present from both vaccines**
Transient thrombocytopenia has been reported within 4-6 weeks following vaccination with measles, mumps, and rubella vaccine. Carefully evaluate the potential risk and benefit of vaccination in children with thrombocytopenia or in those who experienced thrombocytopenia after vaccination with a previous dose of a measles, mumps, and rubella-containing vaccine.
https://www.businesswire.com/news/home/20230306005169/en/US-FDA-Approves-Intramuscular-Administration-for-Merck's-MMRV-Family-of-Vaccines-M-M-RII-Measles-Mumps-and-Rubella-Virus-Vaccine-Live-VARIVAX-Varicella-Virus-Vaccine-Live-and-ProQuad-Measles-Mumps-Rubella-and-Varicella-Virus-Vaccine-Live

10. Varivax (Varicella Virus Vaccine Live)
VARIVAX is a vaccine indicated for active immunization for the prevention of varicella in individuals 12 months of age or older.

Patent - Varicella vaccine and process for its preparation US-4000256-A MERCK & CO INC (1976)
Summary - Preparation of safe, live, attenuated varicella virus vaccine by serial propagation of varicella virus in tissue cell culture systems. https://pubchem.ncbi.nlm.nih.gov/patent/US-4000256-A

Linked Genes
213 **ALB - albumin (human)**
Enables several functions, including anion binding activity; identical protein binding activity; and toxic substance binding activity. Contributes to oxygen binding activity. Involved in cellular response to starvation; maintenance of mitochondrion location; and negative regulation of apoptotic process. Located in Golgi apparatus; endoplasmic reticulum; and extracellular exosome. Part of protein-containing complex. Implicated in several diseases, including blood protein disease; hepatobiliary system cancer (multiple); hyperthyroxinemia; middle cerebral artery infarction; and psoriasis. Biomarker of several diseases, including carcinoma (multiple); heart disease (multiple); hematologic cancer (multiple); liver disease (multiple); and lung disease (multiple).

85302 **FBF1 - Fas binding factor 1 (human) synonym: Fas (TNFRSF6) binding factor 1**

The protein encoded by this gene is a member of the TNF-receptor superfamily. This receptor contains a death domain. It has been shown to play a central role in the physiological regulation of programmed cell death, and has been implicated in the pathogenesis of various malignancies and diseases of the immune system. The interaction of this receptor with its ligand allows the formation of a death-inducing signaling complex that includes Fas-associated death domain protein (FADD), caspase 8, and caspase 10. The autoproteolytic processing of the caspases in the complex triggers a downstream caspase cascade, and leads to apoptosis.

11657 **Alb - albumin (house mouse)**
This gene encodes albumin, an abundant plasma protein essential for maintaining oncotic pressure that functions as a carrier protein for various molecules such as steroids and fatty acids in blood. This gene is primarily expressed in liver where the encoded protein undergoes proteolytic processing before secretion into the plasma. Predicted to enable several]toxic substance binding activity; and zinc ion binding activity. Predicted to contribute to oxygen binding activity. Predicted to be involved in several processes, including cellular response to starvation; maintenance of mitochondrion location; and positive regulation of circadian sleep/wake cycle, non-REM sleep. Located in cytoplasm and extracellular space. *Is expressed in several structures, including alimentary system; brain; genitourinary system; liver and biliary system; and trunk musculature. Human ortholog(s) of this gene implicated in several diseases, including blood protein disease; hepatobiliary system cancer (multiple); hyperthyroxinemia; middle cerebral artery infarction; and psoriasis. Orthologous to human ALB (albumin).

24186 **Alb - albumin (Norway rat)**
Enables several functions, including fatty acid binding activity; modified amino acid binding activity; and zinc ion binding activity. Involved in several processes, including positive regulation of circadian sleep/wake cycle, non-REM sleep; response to mercury ion; and response to platinum ion. Located in basement membrane and extracellular space. Used to study familial hyperlipidemia. Biomarker of Reye syndrome; obstructive jaundice; and protein-energy malnutrition. Human ortholog(s) of this gene implicated in several diseases, including blood protein disease; hepatobiliary system cancer (multiple); hyperthyroxinemia; middle cerebral artery infarction; and psoriasis. Orthologous to human ALB (albumin)

247744 **alb - alberich (fruit fly) Taxonomy: Drosophila melanogaster (fruit fly)**
GENE SUMMARY: Dredd - Death related ced-3/Nedd2-like caspase (fruit fly)
Enables cysteine-type endopeptidase activator activity involved in apoptotic process and endopeptidase activity. Involved in several processes, including peripheral nervous system neuron development; regulation of defense response; and sperm individualization. Located in cytoplasm. Is expressed in several structures, including adult Malpighian tubule; dorsal ridge; egg chamber; embryonic head segment; and presumptive embryonic/larval central nervous system. Human ortholog(s) of this gene implicated in autoimmune lymphoproliferative syndrome type 2A; non-Hodgkin lymphoma; and stomach cancer. Orthologous to human CASP10 (caspase 10).

558311 **slc45a2 - solute carrier family 45 member 2 (zebrafish)**
Synonym/aliases: albino, absent in melanoma 1, alb
Predicted to enable sucrose: proton symporter activity. Acts upstream of or within melanocyte differentiation and response to light stimulus. Predicted to be active in membrane. Is expressed in several structures, including melanoblast; optic vesicle; pigment cell; presumptive retinal pigmented epithelium; and retina. Used to study cataract. Human

397731 **alb.L - albumin L homeolog (African clawed frog) Synonym/aliases**
Binds water, Ca(2+), Na(+), K(+), fatty acids, hormones, bilirubin and drugs. Its main function is the regulation of the colloidal osmotic pressure of blood.

Synonym/aliases
ALB (albumin) [*Homo sapiens* (human)]
This gene encodes the most abundant protein in human blood. This protein functions in the regulation of blood plasma colloid osmotic pressure and acts as a carrier protein for a wide range of endogenous molecules including hormones, fatty acids, and metabolites, as well as exogenous drugs. Additionally, this protein exhibits an esterase-like activity with broad substrate specificity. The encoded preproprotein is proteolytically processed to generate the mature protein. A peptide derived from this protein, EPI-X4, is an endogenous inhibitor of the CXCR4 chemokine receptor.
Annotation information

Note: This gene has been reviewed for its involvement in coronavirus biology, and is relevant for COVID-19 prognosis.
https://pubchem.ncbi.nlm.nih.gov/gene/213

Albumin (human)
https://www.drugs.com/mtm/albumin-human.html

***68 kDa serum albumin**
protein is present in increasing amounts in the soluble fractions of fast, slow and cardiac muscles of the rabbit.

***Serum albumin**
Is the main protein that's found in our blood. It's made in our liver, but we need a very good diet with enough protein to make the right amount. Serum albumin has many important jobs. It acts like a magnet in the blood to keep fluid in the right place throughout your body. When it's too low, you may get swelling from the build up of fluid in your feet, ankles, hands, around your eyes, lower back, or other parts of your body. Albumin also carries important substances throughout the body, like hormones and drugs. So, when serum albumin is low, these important products can't get to where they are needed in your body.

100034206 **ALB - albumin (horse)**
Binds water, Ca(2+), Na(+), K(+), fatty acids, hormones, bilirubin and drugs. Its main function is the regulation of the colloidal osmotic pressure of blood. Major zinc transporter in plasma, typically binds about 80% of all plasma zinc (By similarity).

280717 **ALB - albumin (cattle)**
4F5S Crystal Structure of Bovine Serum Albumin
Serum albumin first appeared in early vertebrates and is present in the plasma of all mammals. Its canonical structure supported by a conserved set of disulfide bridges is maintained in all mammalian serum albumins and any changes in sequence are highly correlated with evolution of the species. Previous structural investigations of mammalian serum albumins have only concentrated on human serum albumin (HSA), most likely as a consequence of crystallization and diffraction difficulties. Here, the crystal structures of serum albumins isolated from bovine, equine and leporine blood plasma are reported.
https://www.rcsb.org/structure/4F5S

100009195 **ALB - albumin (rabbit)**
Interactions and Pathways Chemical-Target Interactions: 1-Chloro-2,4-dinitrobenzene

Substances - Toxic Substances – toxic and/or corrosive/combustible – Health: Health: TOXIC
Inhalation, ingestion, or skin contact with material may cause severe injury or death. Contact with molten substance may cause severe burns to skin and eyes. Avoid any skin contact. Effects of contact or inhalation may be delayed. Fire may produce irritating, corrosive and/or toxic gases. Runoff from fire control or dilution water may be corrosive and/or toxic and cause pollution.

Attention - Extremely Dangerous Chemical Compound that is connected
1-Chloro-2,4-dinitrobenzene
THE CONJUGATION OF DRUGS AND OTHER FOREIGN CMPD /SUCH AS 1-CHLORO-2,4-DINITROBENZENE/ WITH GLUTATHIONE LEADS TO THE FORMATION OF N-ACETYLCYSTEINE (OR MERCAPTURIC ACID) DERIVATIVES.

Danger: GHS Hazard Statements
H301: Toxic if swallowed [Danger Acute toxicity, oral]
H311: Toxic in contact with skin [Danger Acute toxicity, dermal]
H331: Toxic if inhaled [Danger Acute toxicity, inhalation]
H373 **: Causes damage to organs through prolonged or repeated exposure [Warning Specific target organ toxicity, repeated exposure]
H400: Very toxic to aquatic life [Warning Hazardous to the aquatic environment, acute hazard]

H410: Very toxic to aquatic life with long lasting effects [Warning Hazardous to the aquatic environment, long-term hazard]
https://pubchem.ncbi.nlm.nih.gov/patent/US-4000256-A

Effects of Short-Term Exposure
The substance is severely irritating to the skin and eyes. The substance may cause effects on the blood. This may result in the formation of methaemoglobin. Exposure to high concentrations could cause death.
ILO-WHO International Chemical Safety Cards (ICSCs)

Effects of Long-Term Exposure
Repeated or prolonged contact may cause skin sensitization. The substance may have effects on the blood. This may result in a decrease in hemoglobin and a decrease of blood cells.
ILO-WHO International Chemical Safety Cards (ICSCs)
https://pubchem.ncbi.nlm.nih.gov/compound/6

***2,4-Dinitrochlorobenzene**
Is a potent sensitizer that has been applied topically in the evaluation of delayed hypersensitivity. It has also been used as an immunostimulant in various conditions including some forms of cancer, and in the treatment of alopecia and warts. It has also been investigated in HIV infection and leprosy.

11. Hepatitis A Hepatitis A Vaccine (HepA)
***Associated Disorders and Diseases available at the end of report**
Havrix® HAVRIX (Hepatitis A Vaccine) injectable suspension, for intramuscular use
HAVRIX (hepatitis A vaccine, inactivated) is a sterile suspension containing formaldehyde-inactivated hepatitis A virus **(HM175 hepatitis A virus strain**) adsorbed onto aluminium hydroxide.

Nonmedicinal Ingredients - ***Aluminium** (as aluminium hydroxide), amino acids for injection, disodium phosphate, monopotassium phosphate, polysorbate 20, potassium chloride, sodium chloride, water for injection. Residue *neomycin sulphate. ******Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component[3]including neomycin and yeast.
https://ca.gsk.com/media/6243/havrix.pdf

***Variants of hepatitis A virus (pHM175 virus)**
Recovered from persistently infected green monkey kidney (BS-C-1) cells induced a cytopathic effect during serial passage in BS-C-1 or fetal rhesus kidney (FRhK-4) cells.
https://pubmed.ncbi.nlm.nih.gov/1705995/

***Aluminum - GHS Hazard Statements Danger: flammable solid**
The main targets of aluminum are the central nervous system and bones. Aluminum binds to dietary phosphorus and impairs gastrointestinal absorption of aluminum. The decreased phosphate body burden results in osteomalacia and rickets. Aluminum neurotoxicity is believed to involve different mechanisms. Changes in cytoskeletal protein functions as a result of altered phosphorylation, proteolysis, transport, and synthesis are believed to be one cause. Aluminum may induce neurobehavioral effects by affecting permeability of the blood-brain barrier, cholinergic activity, signal transduction pathways. It has been suggested that aluminum's interaction with estrogen receptors increases the expression of estrogen-related genes and thereby contributes to the progression of breast cancer. Certain aluminum salts induce immune responses by activating inflammasomes.

Associated Disorders and Diseases (there are 36 listed, please find at the end of report)
https://pubchem.ncbi.nlm.nih.gov/compound/5359268

12. Tdap: ≥7 yrs.
Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed and Inactivated Poliovirus Vaccine
Tradename: KINRIX Manufacturer: GlaxoSmithKline Biologicals
*Epinephrine and other appropriate agents used for the control of immediate allergic reactions must be immediately available should an acute anaphylactic reaction occur.

Drug: Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed and Inactivated Poliovirus Vaccine Ingredient (UNII): Poliovirus Type 3 Antigen (Formaldehyde inactivated) (UNII:459ROM8M9M); Poliovirus Type 1 Antigen (Formaldehyde inactivated) (UNII:0LVY784C09); Bordetella Pertussis Toxoid Antigen (Glutaraldehyde inactivated) (UNII:QSN5XO8ZSU); Poliovirus Type 2 Antigen (Formaldehyde inactivated) (UNII:23JE9KDF4R); Clostridium Tetani Toxoid Antigen (Formaldehyde inactivated) (UNII:K3W1N8YP13); Bordetella Pertussis Pertactin Antigen (Formaldehyde inactivated) (UNII:I05O535NV6); Corynebacterium Diphtheriae Toxoid Antigen (Formaldehyde inactivated) (UNII:IRH51QN26H); Bordetella Pertussis Filamentous Hemagglutinin Antigen (Formaldehyde inactivated) (UNII:8C367IY4EY)

*Attention
Component of KINRIX, including neomycin and polymyxin B (Please see breakdowns of these ingredients above.)
https://www.fda.gov/media/80128/download?attachment

***Contradictions** (summary of each available in link)
Severe allergic reaction (e.g., anaphylaxis) after a previous dose of any diphtheria toxoid-, tetanus toxoid-, pertussis- or poliovirus-containing vaccine, or to any component of KINRIX, including neomycin and polymyxin B. (4.1)
Encephalopathy within 7 days of administration of a previous pertussis- containing vaccine. (4.2)
Progressive neurologic disorders. Hypersensitivity, Encephalopathy
*Component of KINRIX, including neomycin and polymyxin B. (Please see breakdowns of these ingredients above.
https://www.fda.gov/media/80128/download?attachment

***Serious Adverse Effects**
Within the 31-day period following study vaccination in 3 studies (Studies 046, 047, and 048) in which all subjects received concomitant MMR vaccine (U.S.-licensed MMR vaccine [Merck & Co., Inc.] in Studies 047 and 048, non—U.S.-licensed MMR vaccine in Study 046), 3 subjects (0.1% [3/3,537]) who received KINRIX reported serious adverse events (dehydration and hypernatremia; cerebrovascular accident; dehydration and gastroenteritis) and 4 subjects (0.3% [4/1,434]) who received INFANRIX and inactivated poliovirus vaccine (Sanofi Pasteur SA) reported serious adverse events (cellulitis, constipation, foreign body trauma, fever without identified etiology).

***Postmarketing Experience**
In addition to reports in clinical trials for KINRIX, the following adverse reactions have been identified during post approval use of KINRIX. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccination.

***General Disorders and Administration Site Conditions Injection site vesicles.**
Nervous System Disorders, Syncope, Skin and Subcutaneous Tissue Disorders, Pruritus. and Progressive neurologic disorders. Hypersensitivity, Encephalopathy
Additional adverse reactions reported following post marketing use of INFANRIX, for which a causal relationship to vaccination is plausible, are: Allergic reactions, including anaphylactoid reactions, anaphylaxis, angioedema, and urticaria; apnea; collapse or shock-like state (hypotonic- hyporesponsive episode); convulsions (with or without fever); lymphadenopathy; and thrombocytopenia.
https://pubchem.ncbi.nlm.nih.gov/compound/Diphtheria-and-Tetanus-Toxoids-and-Acellular-Pertussis-Adsorbed-and-Inactivated-Poliovirus-Vaccine

13. (HPV) Human Papillomavirus (Human Papillomavirus (HPV) Vaccine
***Linked Proteins available at the end of report**
Three HPV vaccines - 9-valent HPV vaccine (Gardasil 9, 9vHPV), quadrivalent HPV vaccine (Gardasil, 4vHPV), and bivalent HPV vaccine (Cervarix, 2vHPV)
Anyone with an allergic reaction SHOULD NOT receive: A previous dose of GARDASIL 9, A previous dose of GARDASIL®, Yeast (severe allergic reaction), Amorphous aluminum hydroxy phosphate sulfate Polysorbate 80

Adverse side effects
difficulty breathing, wheezing (bronchospasm), hives, rash, vomiting, swollen glands (neck, armpit, or groin) joint pain unusual tiredness, weakness, or confusion, chills, generally feeling unwell, leg pain, shortness of breath, chest pain, aching muscles, muscle weakness, seizure, bleeding or bruising more easily than normal, skin infection.

****FDA Pharmacological Classification**
Non-Proprietary Name: INFLIXIMAB-AXXQ
Pharmacological Classes: Tumor Necrosis Factor Receptor Blocking Activity [MoA]; Tumor Necrosis Factor Blocker
AVSOLA (infliximab-axxq) for injection, for intravenous use - Initial U.S. Approval: 2019
AVSOLA (infliximab-axxq) is biosimilar* to REMICADE (infliximab). AVSOLA (infliximab-axxq) is biosimilar* to REMICADE (infliximab).
https://www.fda.gov/media/90070/download?attachment

*WARNING
Serious Infections and Malignancy - See full prescribing information for complete boxed warning.

*Increased risk of serious infections leading to hospitalization or death, including tuberculosis (TB), bacterial sepsis, invasive fungal infections (such as histoplasmosis) and infections due to other opportunistic pathogens. (5.1)
Discontinue AVSOLA if a patient develops a serious infection.

*Perform test for latent TB; if positive, start treatment for TB prior to starting AVSOLA. Monitor all patients for active TB during treatment, even if initial latent TB test is negative. (5.1)

*Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with tumor necrosis factor (TNF) blockers, including infliximab products. (5.2)

*Postmarketing cases of fatal hepatosplenic T-cell lymphoma (HSTCL) have been reported in patients treated with TNF blockers including infliximab products. Almost all had received azathioprine or 6-mercaptopurine concomitantly with a TNF blocker at or prior to diagnosis. The majority of cases were reported in patients with Crohn's disease or ulcerative colitis, most of whom were adolescent or young adult males. (5.2)
https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761086s001lbl.pdf

*Patent: Vaccine against HPV - There are 85 Papillomavirus type strains (including non -human strains) linked to the CDC Recommended Vaccine List included at the end of report
https://pubchem.ncbi.nlm.nih.gov/patent/EP-2318042-B1

Clinical Trials
*Immunogenicity of GlaxoSmithKline Biological's Human Papillomavirus (HPV) Vaccine (580299) Versus Merck's Gardasil® in Healthy Females 18-45 Years of Age – 2020
https://clinicaltrials.gov/study/NCT00423046?tab=results

*Immunogenicity and Safety Study of GlaxoSmithKline Biologicals' Human Papillomavirus (HPV) Vaccine (GSK-580299) and Merck's Gardasil Vaccine When Administered According to Alternative 2-dose Schedules in 9-14 Year Old Females - 2019
https://clinicaltrials.gov/study/NCT01462357

14. Meningococcal (MenACWY-D: ≥9 mos, MenACWY-CRM: ≥2 mos, MenACWY-TT: ≥2years) Meningococcal group A, C, Y and W-135 conjugate vaccine
Menactra is contraindicated in persons who have had a severe allergic reaction (e.g., anaphylaxis) after a previous dose of a meningococcal capsular polysaccharide-, diphtheria toxoid-, or CRM_{197}-containing vaccine, or to any component of the vaccine.

LABEL: Menactra *Attention: please see vaccines # 3, 4, 5 - Identical TOXIC ingredients
Menactra is a sterile, intramuscularly administered vaccine that contains **Neisseria meningitidis** serogroup A, C, Y and W-135 capsular polysaccharide antigens individually conjugated to diphtheria toxoid protein. N meningitidis A, C, Y and W-135 strains are cultured on Mueller Hinton agar and grown in Watson Scherp media containing casamino acid. The polysaccharides are extracted from the N meningitidis cells and purified by centrifugation, detergent precipitation, alcohol precipitation, solvent extraction and diafiltration. To prepare the polysaccharides for conjugation, they are depolymerized, derivatized, and purified by diafiltration. Diphtheria toxin is derived from **Corynebacterium diphtheriae** grown in modified culture medium containing hydrolyzed casein (5) and is detoxified using formaldehyde. The diphtheria toxoid

protein is purified by ammonium sulfate fractionation and diafiltration. The derivatized polysaccharides are covalently linked to diphtheria toxoid and purified by serial diafiltration. The four meningococcal components, present as individual serogroup-specific glycoconjugates, compose the final formulated vaccine. No preservative or adjuvant is added during manufacture. Each 0.5 mL dose may contain residual amounts of formaldehyde of less than 2.66 mcg (0.000532%), by calculation. Potency of Menactra is determined by quantifying the amount of each polysaccharide antigen that is conjugated to **diphtheria toxoid protein and** the amount of unconjugated polysaccharide present.
Menactra is manufactured as a sterile, clear to slightly turbid liquid. Each 0.5 mL dose of vaccine is formulated in sodium phosphate buffered isotonic sodium chloride solution to contain 4 mcg each of meningococcal A, C, Y and W-135 polysaccharides conjugated to approximately 48 mcg of diphtheria toxoid protein carrier. The serum bactericidal assay (SBA) used to test sera contained an exogenous complement source that was either human (SBA-H) or baby rabbit (SBA-BR).
https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=4d8781ff-9366-462c-8161-6e958f44fcb4&audience=consumer - S11

***Post Marketing ADVERSE EFFECTS - Menactra®, Meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine**
*Blood and Lymphatic System Disorders Lymphadenopathy
*Immune System Disorders
*Hypersensitivity reactions such as anaphylaxis/anaphylactic reaction, wheezing, difficulty breathing, upper airway swelling, urticaria, erythema, pruritus, hypotension
*Nervous System Disorders
*Guillain-Barré syndrome, paresthesia, vasovagal syncope, dizziness, convulsion, facial palsy, acute disseminated
*encephalomyelitis, transverse myelitis
*Musculoskeletal and Connective Tissue Disorders Myalgia
*General Disorders and Administrative Site Conditions
*Large injection site reactions, extensive swelling of the injected limb (may be associated with erythema, warmth, tenderness or pain at the injection site).

Menactra®, Meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine
https://www.vaccineshoppe.com/assets/pdf/vsh/pi/menactrapi.pdf

Adverse effects
***Diphtheria toxin** currently used as a carrier protein for polysaccharides and haptens to make them immunogenic. There is some dispute about the toxicity of **CRM197,** with evidence that it is toxic to yeast cells and some mammalian cell lines.[3]
https://en.wikipedia.org/wiki/CRM197

***Haptens**
Are small molecules that elicit an immune response only when attached to a large carrier such as a protein Haptens initially activate innate immune responses by complex mechanisms involving inflammatory cytokines, damage-associated molecular patterns (DAMP), or the inflammasome.
https://en.wikipedia.org/wiki/Hapten

***Diphtheria Toxin Binds to the Epidermal Growth Factor (EGF)-like Domain of Human Heparin-binding EGF-like Growth Factor/Diphtheria Toxin Receptor and Inhibits Specifically Its Mitogenic Activity (∗)**
https://www.jbc.org/article/S0021-9258(18)82959-3/fulltext

***Neisseria meningitidis – chemical compound summary**
https://pubchem.ncbi.nlm.nih.gov/compound/Neisseria-meningitidis

FDA National Drug Code Directory: *This is not FDA approved
0268-6710 1965-01-01 INJECTION, SOLUTION .05 g/mL ALK-Abello, Inc.
Product ndc": "0268-6710", generic name": "Chinese Elm" - brand name": "ULMUS PUMILA POLLEN"
https://api.fda.gov/drug/ndc.json?search=product_ndc:"0268-6710"

***WARNING**
This product is intended for use by physicians who are experienced in the administration of allergenic extracts and the emergency care of anaphylaxis, or for use under the guidance of an allergy specialist.
As with all allergenic extracts, severe systemic reactions may occur. In certain individuals these life-threatening reactions may result in death. Fatalities associated with skin testing have been reported. Patients should be observed for at least 20 - 30 minutes following testing. Emergency measures and adequately trained personnel should be immediately available in the event of a life-threatening reaction.
Patients with unstable asthma or steroid dependent asthmatics and patients with underlying cardiovascular disease are at greater risk to a fatal outcome from a systemic allergic reaction.
https://ndclist.com/ndc/0268-6710/label/

Pharmacologic Class
Allergens, Cell-mediated Immunity, Increased Histamine Release, Increased IgG Production, Non-Standardized Pollen Allergenic Extract - Pollen
https://pharmacygps.com/drug/non-standardized-allergenic/0268-6710/

Patent - METHOD OF PRODUCING MENINGOCOCCAL MENINGITIS VACCINE FOR NEISSERIA MENINGITIDIS SEROTYPES A,C,Y, and W-135
https://pubchem.ncbi.nlm.nih.gov/patent/US-2008020428-A1

Linked Genes
29760 BLNK - B cell linker (human)
17060 Blnk - B cell linker (house mouse)
499356 Blnk - B-cell linker (Norway rat)
395733 SH2D6 - SH2 domain containing 6 (chicken)

Linked Proteins
P80045 Ovary maturating parsin (migratory locust)
P80228 Major outer membrane protein P44 (Mannheimia haemolytica)

Linked Taxonomies
9606 Homo sapiens (human)
485 Neisseria gonorrhoeae
486 Neisseria lactamica
487 Neisseria meningitidis
1717 Corynebacterium diphtheriae

15. Meningococcal serogroup B vaccination (MenB-4C, MenB-FHbp) (minimum age: 10 years) [MenB-4C, Bexsero®; MenB-FHbp, Trumenba®])
Bexsero, Trumenba, (MenB)
Meningococcal disease is a bacterial infection that can infect the spinal cord and brain, causing meningitis that can be fatal or lead to permanent and disabling medical problems. Meningococcal group B vaccine is for use in children and young adults who are 10 to 25 years old. The Centers for Disease Control recommends that the best time to get this vaccine is between the ages of 16 and 18 years old.

Adverse effects
***Erythema** (multiforme)
Is a skin disorder that's considered to be an allergic reaction to medicine or an infection. Symptoms are symmetrical, red, raised skin areas that can appear all over the body. They do seem to be more noticeable on the fingers and toes. These patches often look like "targets" (dark circles with purple-grey centers). The skin condition may happen over and over again, and usually lasts for 2 to 4 weeks each time. Most often, this disorder is caused by the herpes simplex virus. It has also been associated with Mycoplasma pneumonia as well as fungal infections. *Erythema multiforme minor is not very serious and usually clears up with medicine to control infection or inflammation. However, if a person develops a more severe form of erythema multiforme (erythema multiforme major), the condition can become fatal. Erythema multiforme major is also known as Stevens-Johnson syndrome. It is usually caused by a medicine reaction rather than an infection.

https://www.hopkinsmedicine.org/health/conditions-and-diseases/erythema-multiforme

***Myalgia**
Myalgia describes muscle aches and pain, which can involve ligaments, tendons and fascia, the soft tissues that connect muscles, bones and organs. Injuries, trauma, overuse, tension, certain drugs and illnesses can all bring about myalgia. Symptoms include muscle cramps and joint pain. Myalgia is a sign of an injury, infection, disease or other health problem. You may feel a deep, steady ache or random sharp pains. Some people have muscle pain all over, while others have it in specific areas. Myalgia can cause fevers or chills if it is caused by an infection. It can also cause symptoms such as joint pain, or very weak (fatigue). Because of the pain, depression and feeling overly tired are common symptoms. This is true for most chronic pain conditions. Other symptoms can include tenderness, swelling, or redness.
https://www.hopkinsmedicine.org/health/conditions-and-diseases/myalgia

What is Myalgia: Causes, Symptoms, and Treatments
https://southernpainclinic.com/blog/what-is-myalgia-causes-symptoms-and-treatments/

Patent: ADJUVANTED VACCINES FOR SEROGROUP B MENINGOCOCCUS
Summary - An immunogenic composition comprises (i) an immune stimulatory oligonucleotide and a polycationic polymer, wherein the oligonucleotide and the polymer ideally associate with each other to form a complex, and (ii) a meningococcal serogroup B antigen. In most embodiments, the composition does not include an aluminium salt and does not include an oil-in-water emulsion.

Linked Genes
2217 FCGRT - Fc gamma receptor and transporter (human)
This gene encodes a receptor that binds the Fc region of monomeric immunoglobulin G. The encoded protein transfers immunoglobulin G antibodies from mother to fetus across the placenta. This protein also binds immunoglobulin G to protect the antibody from degradation. Alternative splicing results in multiple transcript variants.
Disease associated with FCGRT is Myasthenia gravis. Myasthenia gravis (MG) is a chronic autoimmune disorder in which antibodies destroy the communication between nerves and muscle, resulting in weakness of the skeletal muscles. Myasthenia gravis affects the voluntary muscles of the body, especially those that control the eyes, mouth, throat and limbs. The disease can strike anyone at any age. A myasthenia gravis crisis can involve difficulty in swallowing or breathing. The cause of myasthenia gravis is unknown and there is no cure, but early detection and prompt medical management can help people live longer, more functional lives. This gene is directly related to trigger (Microbial infection) Acts as an uncoating receptor for a panel of echoviruses including Echovirus 5, 6, 7, 9, 11, 13, 25 and 29. Echoviruses are in the family Enteroviruses including poliovirus, echovirus, coxsackievirus.

3075 CFH - complement factor H (human)
4150 MAZ - MYC associated zinc finger protein (human)
7099 TLR4 - toll like receptor 4 (human)
10202 DHRS2 - dehydrogenase/reductase 2 (human)
54106 TLR9 - toll like receptor 9 (human)
12628 Cfh - complement component factor h (house mouse)
14132 Fcgrt - Fc fragment of IgG receptor and transporter (house mouse)
17188 Maz - MYC-associated zinc finger protein (purine-binding transcription factor) (house mouse)
21898 Tlr4 - toll-like receptor 4 (house mouse)
71412 Dhrs2 - dehydrogenase/reductase member 2 (house mouse)
81897 Tlr9 - toll-like receptor 9 (house mouse)
29260 Tlr4 - toll-like receptor 4 (Norway rat)
155012 Cfh - complement factor H (Norway rat)
338457 Tlr9 - toll-like receptor 9 (Norway rat)
691464 Dhrs2 - dehydrogenase/reductase 2 (Norway rat)
34235 Toll-4 - Toll-4 (fruit fly)
43914 maz - matzerath (fruit fly)
393539 dhrs4 - dehydrogenase/reductase (SDR family) member 4 (zebrafish)
403128 tlr9 - toll-like receptor 9 (zebrafish)
553297 cfh - complement factor H (zebrafish)

403502 TLR9 - toll like receptor 9 (dog)
493839 TLR9 - toll like receptor 9 (domestic cat)
280816 CFH - complement factor H (cattle)
281536 TLR4 - toll like receptor 4 (cattle)
282602 TLR9 - toll like receptor 9 (cattle)

***Linked Proteins (there are a total of 172, human and non-humans sourced)**

Patent: Adjuvanted vaccines for serogroup b meningococcus
https://pubchem.ncbi.nlm.nih.gov/patent/US-2013071422-A1

16. (PPSV23) pneumococcal polysaccharides vaccine (PPSV), 23-valent

Pneumococcal disease is a serious infection caused by a bacteria that can infect the sinuses, inner ear, lungs, blood, and brain. These conditions can be fatal. Pneumococcal polysaccharides vaccine (PPSV) is used to help prevent disease caused by pneumococcal bacteria. This vaccine contains 23 different types of pneumococcal bacteria. PPSV is for use in adults 50 years and older, and in people at least 2 years old who have an increased risk of developing pneumococcal disease due to certain medical conditions. The Centers for Disease Control and Prevention (CDC) recommends this vaccine in adults 65 years and older even if they had a pneumococcal vaccine before the age of 65. Like any vaccine, pneumococcal polysaccharides vaccine may not provide protection from disease in every person.

Adverse effects
Get emergency medical help if you have signs of an allergic reaction: hives; difficult breathing; swelling of your face, lips, tongue, or throat. Additional adverse effects: wheezing, trouble breathing; chest pain; severe stomach pain, severe vomiting or diarrhea**;** tremors, muscle stiffness; or painful or difficult urination.

Serious health concerns
erythema Pruritus, ecchymosis Injection site cellulitis Cerebrovascular accident, lumbar radiculopathy Paresthesia, radiculomyelopathy, Guillain-Barre syndrome, febrile convulsion, Arthralgia, arthritis, Nausea, dyspepsia, Nausea, dyspepsia, diarrhea Ulcerative colitis, pancreatitis Upper respiratory infection, pharyngitis Anaphylactoid reactions, serum sickness, angioneurotic edema Lymphadenitis, lymphadenopathy, thrombocytopenia in patients with stabilized idiopathic thrombocytopenic purpura, hemolytic anemia in patients who have had other hematologic disorders, leukocytosis urticaria, cellulitis-like reactions, erythema multiforme, Angina pectoris, heart failure, chest pain, myocardial infarction resulting in death

PNEUMOVAX 23 is indicated to help prevent pneumococcal disease caused by 23 serotypes
https://www.merckvaccines.com/pneumovax23/

Pneumovax 23 Side Effects
Generic name: pneumococcal 23-polyvalent vaccine
https://www.drugs.com/sfx/pneumovax-23-side-effects.html

17. Dengue Virus (DEN4CYD: 9-16 yrs.)

Dengvaxia®
Sanofi Pasteur licensed the first dengue vaccine (Dengvaxia®) in Mexico in 2015, and more than 20 countries, thereafter, based on the safety and efficacy demonstrated in two phase III trials and a single season of disease surveillance. Unfortunately, the optimism that a dengue vaccine was finally available quickly became disappointment when a safety signal was observed in vaccine recipients who were dengue non-immune at the time of vaccine administration. In the third year of the phase III clinical trial, the youngest, non-immune vaccine recipients experienced increased rates of hospitalized and severe dengue compared to their unvaccinated peers.
https://www.nature.com/articles/s41541-023-00658-2

IMPORTANT: Limitations of use:
*DENGVAXIA is not approved for use in individuals not previously infected by any dengue virus serotype or for whom this information is unknown. *Those not previously infected are at increased risk for severe dengue disease when vaccinated and subsequently infected with dengue virus. *Previous dengue infection can be assessed through a medical

record of a previous laboratory-confirmed dengue infection or through serological testing prior to vaccination. The safety and effectiveness of DENGVAXIA have not been established in individuals living in dengue non-endemic areas who travel to dengue endemic areas.

*DENGVAXIA is a live, attenuated virus vaccine consisting of four chimeric yellow fever dengue (CYD) viruses (one CYD virus each corresponding to dengue serotypes 1, 2, 3, and 4). Each of the four CYD viruses (CYD-1, CYD-2, CYD-3, and CYD-4) in DENGVAXIA was constructed using recombinant DNA technology by replacing the sequences encoding the pre-membrane (prM) and envelope (E) proteins in the yellow fever (YF) 17D204 vaccine virus genome with those encoding the homologous prM and E gene sequences of dengue virus serotypes 1, 2, 3, or 4. Each CYD virus is cultured separately in Vero cells (African Green Monkey kidney) under serum-free conditions, harvested from the supernatant of the Vero cells and purified and concentrated by membrane chromatography and ultrafiltration. The purified and concentrated harvest of each CYD virus is then diluted in a stabilizer. (4) to produce each of the four monovalent CYD virus drug substances. The CYD virus drug substances can be stored at. (4) . To manufacture the final drug product, the four monovalent drug substances are mixed with stabilizer solution, filtered, filled into vials and freeze-dried.
https://www.fda.gov/media/125157/download

CYD Vaccine Efficacy Studies
"Sanofi Pasteur conducted extensive phase III efficacy trials of their CYD vaccine, now in their third–fourth year, involving over 35,000 children, 2–16 years of age, resident in 10 dengue-endemic countries During year 3, there was an overall efficacy against hospitalization of 16.7% (65 hospitalizations in vaccinees, 39 in placebo group), but a relative risk of hospitalization of 1.6 among children younger than 9 years and 4.95 in children 5 years of age and younger.6 Vaccination of seronegative children resulted in universal broad neutralizing antibody responses but poor protection against breakthrough dengue cases.

During year 3, clinical observations on vaccinated children and placebo controls showed the vaccine to be asymmetrically protective and enhancing, that is, some age groups were protected, whereas in others, disease accompanying breakthrough dengue infections was increased. *A review of published data suggests that "all or nearly all" hospitalizations of vaccinated children over the 3-year postvaccination period may have occurred in children who were susceptible when vaccinated, and are attributed to vaccine ADE."
https://www.ajtmh.org/view/journals/tpmd/95/4/article-p741.xml

***WHO Vero 10–87 cell line**
The live attenuated Tetravalent Dengue Vaccine (TDV) has been developed using Vero cell line as cell substrate. The WHO Vero cell line (10–87) has been subjected to broad range of tests to establish its suitability for vaccine production. Food and Drug Administration (FDA) is custodian of supply of WHO Vero 10–87 cell line. US-FDA has approved Panacea Biotec's request and forwarded the same to ATCC for shipping of WHO Vero cell line (10–87) to Panacea Biotec Limited. Accordingly, Panacea Biotec imported Vero cells and prepared Master Cell Bank (MCB) and Working Cell Bank (WCB) in a GMP facility. *Cells were grown in SFM4 MegaVir (Hyclone) medium and cultured in incubators set at 37 °C with 5% CO_2 and passaged every 2–3 days.

The WHO Vero RCB 10-87 was established in 1987 and was subjected to a broad range of tests to establish its suitability for vaccine production. This WHO RCB provides a unique resource for the development of future biological medicines where a cell substrate with a safe and reliable history of use is desired. The WHO Vero RCB 10-87 is considered suitable for use as a cell seed for generating a Master Cell Bank (MRC). The Vero cell line is the most widely used continuous cell line for the production of viral vaccines over the last two decades. The WHO Vero RCB 10-87 was established in 1987 and was subjected to a broad range of tests to establish its suitability for vaccine production. This WHO RCB provides a unique resource for the development of future biological medicines where a cell substrate with a safe and reliable history of use is desired. As concluded by an expert review in 2002, the WHO Vero RCB 10-87 is not considered suitable for direct use as MCB material. However, the WHO Vero RCB 10-87 is considered suitable for use as a cell seed for generating a MCB, and its status has changed from "WHO Vero cell bank 10-87" to "WHO Vero reference cell bank 10-87".
https://www.culturecollections.org.uk/products/celllines/generalcell/detail.jsp?refId=88020401&collection=ecacc_gc

Cellosaurus Vero RCB 10-87 (CVCL_JF53)
Species of Origin: Green monkey (Cercopithecus sabaeus) (NCBI Taxonomy: 60711)

Group: Non-human primate cell line.
Group: Vaccine production cell line.
Characteristics: WHO working cell bank of 1000 ampoules deposited at ECACC, derived from an original American Type Culture Collection (ATCC) ampoule. Available free of charge to organizations producing vaccines following receipt of approval to supply from WHO.
Omics: Genome sequenced.
Derived from site: In situ; Kidney, epithelium; UBERON=UBERON_0004819.

"Unless specified otherwise, at the European Collection of Authenticated Cell Cultures (ECACC) we routinely handle all of our cell lines at containment level 2 in accordance with the ACDP guidelines. ACDP = Advisory Committee on Dangerous Pathogens (UK). All cell cultures have the potential to carry as yet unidentified adventitious agents. It is the responsibility of the end user to ensure that their facilities comply with biosafety regulations for their own country."
https://www.cellosaurus.org/CVCL_JF53

Depositor's Note:
The WHO Vero reference cell bank 10-87 cells are not "approved" in any way for vaccine manufacture by WHO. These repository cells are provided for the purpose of establishing master cell banks (MCB) and master working cell banks (MWCB). Regardless of any previous testing, any cells transferred to and cultured in a new environment will require re-qualification. Therefore, it is the responsibility of each manufacturer to ensure appropriate handling, expansion, and maintenance of the cells and to perform the qualification tests necessary to establish a cell bank for vaccine manufacture.
https://www.culturecollections.org.uk/media/92187/eccw35103_world_health_organisation_who_cell_line_release_authorisation_form.pdf

*Safety Data sheet - SFM4MegaVirTM
Percentage of the mixture consisting of ingredient(s) of unknown acute oral toxicity: 55.4%
Percentage of the mixture consisting of ingredient(s) of unknown acute dermal toxicity: 80.2%
Percentage of the mixture consisting of ingredient(s) of unknown acute inhalation toxicity: 80.2%
Percentage of the mixture consisting of ingredient(s) of unknown hazards to the aquatic environment: 35.6%
https://us.vwr.com/assetsvc/asset/en_US/id/35605766/contents/sds_sh30587-01.pdf

***Cells were grown in SFM4 MegaVir (Hyclone) -**
HyCloneTM SFM4Insect is an animal-derived component-free, versatile cell culture medium developed through the HyClone Metabolic Pathway Design process (see box) to support the growth of multiple insect cell lines and production of a variety of recombinant proteins using the baculovirus expression vector system (BEVS).
https://cdn.cytivalifesciences.com/api/public/content/digi-17564-pdf?_gl=1*pht4qk*_gcl_au*MTU2NzgzODU1Mi4xNjk0NzQ3NTQ3

"Number of Clinically Severe VCD Cases Throughout the Trial Due to Any Serotype Following Injection With Either CYD Dengue Vaccine or a Placebo [Time Frame: Day 0 to the end of study (up to 72 months)]
The severity of VCD cases was assessed by an Independent Data monitoring Committee (IDMC) based on a medical review of cases and any of the following criteria:1) Platelet count <=100000 /µl and bleeding (tourniquet, petechiae or any bleeding) plus plasma leakage 2) Shock (pulse pressure <= 20 mmHg in a child, or hypotension [<= 90 mmHg] with tachycardia, weak pulse and poor perfusion) 3) Bleeding requiring blood transfusion 4) Encephalopathy i.e. unconsciousness or poor conscious state or fitting not attributable to simple febrile convulsion or focal neurological signs. Poor conscious state or unconsciousness must be supported by Glasgow Coma Scale (GCS) score 5) Liver impairment (AST >1000 IU/L or prothrombin time [PT] International normalized ratio [INR] >1.5) excluding other causes of viral hepatitis 6) Impaired kidney function (serum creatinine >= 1.5 mg/dL) 7) Myocarditis, pericarditis or clinical heart failure supported by CXR, echocardiography, ECG or cardiac enzymes."
https://classic.clinicaltrials.gov/ct2/show/NCT01374516

Safety and immunogenicity of a single dose, live-attenuated 'tetravalent dengue vaccine' in healthy Indian adults; a randomized, double-blind, placebo-controlled phase I/II trial
*As per WHO, the first and only licensed dengue vaccine, Sanofi Pasteur's Dengvaxia (CYD-TDV) has been shown to be efficacious and safe in clinical trials in persons who have had a dengue virus infection in the past (seropositive

individuals), but carries an increased risk of hospitalization and severe dengue in those who experience their first natural infection after vaccination (seronegative individuals) [13]
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8892502/

Hepatitis A Vaccine (HepA) - Associated Disorders and Diseases

Autism Spectrum Disorder
Multiple Sclerosis, Chronic Progressive
Bone Diseases, Metabolic
Cardiovascular Diseases
Brain Diseases
Anemia
Eye Diseases
Memory Disorders
Cognition Disorders
Granuloma
Heart Defects, Congenital
Epilepsy, Tonic-Clonic
Fragile X Syndrome
Inflammation
Lung Diseases
Osteomalacia
Lymphadenitis
Nerve Degeneration
Parkinson Disease
Neoplasms
Osteoporosis
Bronchial Hyperreactivity
Multiple Sclerosis, Relapsing-Remitting
Neurodegenerative Diseases
Chronic Kidney Disease-Mineral and Bone Disorder
Chemical and Drug Induced Liver Injury
Poisoning
Diabetes Complications
Dyslipidemias
Respiratory Tract Diseases
Neurotoxicity Syndromes
Weight Loss
Heavy Metal Poisoning

Human Papillomavirus (HPV) Vaccine - Linked Proteins

Patent - Vaccine against HPV - GLAXOSMITHKLINE BIOLOG SA (BE)

P50805 Major capsid protein L1 (Xipapillomavirus 1)
P08341 Major capsid protein L1 (Bos taurus papillomavirus 4)
P50807 Major capsid protein L1 (Bos taurus papillomavirus 6)
P03104 Major capsid protein L1 (Deltapapillomavirus 2)
P11326 Major capsid protein L1 (Deltapapillomavirus 1)
P22163 Major capsid protein L1 (Alpha papillomavirus 12)
Q02273 Major capsid protein L1 (human papillomavirus 13)
Q02274 Major capsid protein L1 (Pygmy chimpanzee papillomavirus type 1)
P06456 Major capsid protein L1 (Chaffinch papillomavirus)
P06417 Major capsid protein L1 (Human papillomavirus type 8)
P04012 Major capsid protein L1 (human papillomavirus 11)
P03099 Major capsid protein L1 (Human papillomavirus type 1a)
P25486 Major capsid protein L1 (Human papillomavirus type 2a)
P17388 Major capsid protein L1 (human papillomavirus 31)

P06416 Major capsid protein L1 (human papillomavirus 33)
P27232 Major capsid protein L1 (human papillomavirus 35)
P24838 Major capsid protein L1 (human papillomavirus 39)
P27557 Major capsid protein L1 (Human papillomavirus type 41)
P27233 Major capsid protein L1 (human papillomavirus 42)
P50815 Major capsid protein L1 (human papillomavirus 43)
P50816 Major capsid protein L1 (human papillomavirus 44)
P36741 Major capsid protein L1 (human papillomavirus 45)
P22424 Major capsid protein L1 (human papillomavirus 47)
P26536 Major capsid protein L1 (human papillomavirus 51)
P36743 Major capsid protein L1 (human papillomavirus 56)
P26535 Major capsid protein L1 (human papillomavirus 58)
P26537 Major capsid protein L1 (Human papillomavirus type 5b)
P69899 Major capsid protein L1 (Human papillomavirus type 6b)
P27964 Major capsid protein L1 (Human papillomavirus type me180)
P36733 Major capsid protein L1 (human papillomavirus 12)
P36734 Major capsid protein L1 (human papillomavirus 14)
Q05137 Major capsid protein L1 (Human papillomavirus 15)
Q02514 Major capsid protein L1 (Human papillomavirus 17)
Q02050 Major capsid protein L1 (Human papillomavirus 19)
Q02051 Major capsid protein L1 (human papillomavirus 25)
Q02515 Major capsid protein L1 (human papillomavirus 30)
P36731 Major capsid protein L1 (Human papillomavirus 3)
P36740 Major capsid protein L1 (human papillomavirus 40)
P36742 Major capsid protein L1 (Human papillomavirus type 49)
Q07860 Major capsid protein L1 (Human papillomavirus 4)
Q05138 Major capsid protein L1 (human papillomavirus 52)
Q05136 Major capsid protein L1 (Human papillomavirus type 7)
Q02480 Major capsid protein L1 (Human papillomavirus 9)
Q07861 Major capsid protein L1 (Human papillomavirus type 63)
Q07874 Major capsid protein L1 (Human papillomavirus 65)
P50786 Major capsid protein L1 (human papillomavirus 20)
P50787 Major capsid protein L1 (human papillomavirus 21)
P03102 Major capsid protein L1 (Papillomavirus sylvilagi (STRAIN KANSAS))
P50791 Major capsid protein L1 (Human papillomavirus 28)
P50792 Major capsid protein L1 (Human papillomavirus 29)
P50820 Major capsid protein L1 (Human papillomavirus type 55)
P50822 Major capsid protein L1 (Human papillomavirus type 61)
P50824 Major capsid protein L1 (Human papillomavirus type 64)
Q80961 Major capsid protein L1 (human papillomavirus 66)
P50825 Major capsid protein L1 (human papillomavirus 67)
P50826 Major capsid protein L1 (human papillomavirus 69)
P69898 Major capsid protein L1 (Human papillomavirus type 6a)
P50788 Major capsid protein L1 (Human papillomavirus 22)
P50789 Major capsid protein L1 (Human papillomavirus 23)
P50790 Major capsid protein L1 (human papillomavirus 24)
P50812 Major capsid protein L1 (human papillomavirus 36)
P50813 Major capsid protein L1 (Human papillomavirus 37)
P50814 Major capsid protein L1 (Human papillomavirus 38)
P50793 Major capsid protein L1 (Human papillomavirus type 70)
P50806 Major capsid protein L1 (Epsilon papillomavirus 1)
P50817 Major capsid protein L1 (Human papillomavirus type 48)
P50818 Major capsid protein L1 (Human papillomavirus type 50)
P50821 Major capsid protein L1 (Human papillomavirus type 60)
P54669 Major capsid protein L1 (human papillomavirus 68)

Q9IR52 Major capsid protein L1 (human papillomavirus 82)
P36736 Major capsid protein L1 (human papillomavirus 27)
P22162 Major capsid protein L1 (human papillomavirus 57)
P36732 Major capsid protein L1 (Human papillomavirus type 10)
P03101 Major capsid protein L1 (Human papillomavirus type 16)
P06794 Major capsid protein L1 (Human papillomavirus type 18)
P36735 Major capsid protein L1 (Human papillomavirus type 26)
P36737 Major capsid protein L1 (Human papillomavirus type 32)
P36738 Major capsid protein L1 (Human papillomavirus type 34)
Q05113 Major capsid protein L1 (Human papillomavirus type 53)
P06917 Major capsid protein L1 (Human papillomavirus 5)
P50823 Major capsid protein L1 (human papillomavirus 62)
P03103 Major capsid protein L1 (Deltapapillomavirus 4)
Q89828 Major capsid protein L1 (Canine oral papillomavirus (strain Y62))
P50819 Major capsid protein L1 (Human papillomavirus type 54)
P06458 Major capsid protein L1 (Bos taurus papillomavirus 2)