



A Review Article on: “General Vaccine”

Miss. Mayuri D. Thakare and Miss. Chaitali G. Borase

SSBT's Institute of Pharmacy

ABSTRACT:

The human immune system has various lines of defence that protect in case of infection. The first are physical and chemical problems such as skin, mucous membranes, and gastric acid. Still, a series of detectors are present to spot foreign agents or antigens and to spark the ingrained vulnerable system, if a pathogen bypasses these obstacles and causes infection. These detectors have evolved to distinguish between self and non-self and to detect conserved features of pathogens. Vaccination is regarded as one of the highest triumphs in the history of drugs. We're living in the most successful era of vaccine development. The accumulation of multidisciplinary knowledge and the investment of massive backing have enabled the development of vaccines against numerous contagious conditions including nasty Tumors. The clinical vaccine evaluation and licensure paradigm have also been efficient and grounded on scientific advancements and literal experience.

Ultramodern vaccine development is presently exploiting a wide array of new technologies to produce safer and more efficient vaccines including viral vectors produced in beast cells, contagion-such like patches made in inert or nonentity cells, polysaccharide conjugation to carrier proteins, DNA plasmids produced in E. coli, and remedial cancer vaccines produced by in vitro activation of patient leukocytes. Sanctification advances are adding effectiveness, while innovative logical styles are perfecting process understanding. New adjuvants similar to mono-phosphoryl lipid A, which acts on antigen-presenting cell receptors, are expanding the preliminarily conservative list of extensively accepted vaccine adjuvants. As in other areas of biotechnology, process characterization by sophisticated analysis is critical not only to ameliorate yields but also to determine the final product quality. From a nonsupervisory perspective, Quality by Design (QbD) and Process Analytical Technology (PAT) are important enterprises that can be applied effectively to numerous vaccine processes.

Keywords: Eradication, Vaccination, vaccines, public understanding.

VACCINE:

INTRODUCTION:

A mild form of a disease that's fitted into a person's or a beast's blood using an injection to cover the body against that disease. A vaccine is a natural medication that gives actively acquired immunity to a particularly contagious disease.^[1] A vaccine generally contains an agent that resembles a disease-causing microorganism and is frequently made from incapacitating or killing forms of the microbe. The agent stimulates the body's immune system to detect the agent as trouble and destroy it and to further detect and destroy any of the microorganisms associated with that agent that it may destroy in the future. Vaccines can be precautionary or remedial.^{[2][3][4][5]} Some vaccines offer full-altering immunity, in which infection is averted fully.^[6]

The administration of vaccines is called vaccination. wide immunity due to vaccination is mainly responsible for the worldwide eradication of smallpox and the restriction of conditions similar to diseases such as polio, measles, and tetanus from the world.^[7] The efficacy of vaccination has been widely studied and verified;^[8] for example, vaccines that have proven effective include the influenza vaccine,^[9] the HPV vaccine,^[10] and the chickenpox vaccine.^[11] The World Health Organization (WHO) announced that licensed vaccines are now available for twenty-five different preventable infections.^[12]



Fig no. 1 VACCINE

HISTORY:

First-generation vaccines are whole-organism vaccines - either live and incapacitate or killed forms. Live, attenuated vaccines, such as smallpox and polio vaccines, can induce killer T-cell responses, helper T-cell (TH) responses, and antibody immunity. Still, attenuated forms of a pathogen can convert to a dangerous form and may cause disease in immunocompromised vaccine donors (similar to those with AIDS). While killed vaccines don't have this threat, they cannot induce specific killer T-cell responses and may not work at all for some diseases.^[13]

Second-generation vaccines were developed to reduce the threat of live vaccines. These are subunit vaccines, conforming to specific protein antigens (similar to tetanus or diphtheria toxoids), or recombinant protein factors (similar to the hepatitis B face antigen). They can induce TH and antibody responses, but not killer T-cell responses.

RNA vaccines and DNA vaccines are examples of third-generation vaccines.^{[13][14][15]} In 2016 a DNA vaccine for the Zika virus began testing at the National Institutes of Health. Separately, Inovio Pharmaceuticals and Gene One Life Science started tests of a different DNA vaccine against Zika in Miami. Manufacturing the vaccines in volume was unsolved as of 2016.^[16] Clinical trials for DNA vaccines to help HIV are underway.^[17] mRNA vaccines similar to BNT162b2 were developed in the time 2020 with the help of Operation Warp Speed and largely stationed to combat the COVID-19 epidemic. In 2021, Katalin Karikó and Drew Weissman entered Columbia University's Horwitz Prize for their pioneering exploration of mRNA vaccine technology.^[18]



Fig no. 2 HISTORY OF VACCINE

TYPES:

Vaccines generally contain attenuated, inactivated, or dead organisms or purified products obtained from them. There are several types of vaccines in use.^[19] These represent different strategies used to try to reduce the threat of illness while retaining the capability to induce a favourable immune response.

Attenuated vaccine:

Some vaccines contain live, attenuated microorganisms. Some of these are active viruses that have been cultivated under conditions that disable their malign properties, or that use nearly connected but less dangerous organisms to produce a broad immune response. Although attenuated vaccines are viral, some are bacterial in nature. Examples include the viral disease of yellow fever, measles, mumps, and rubella, and the bacterial disease typhoid. The live *Mycobacterium tuberculosis* vaccine developed by Calmette and Guérin isn't made of a contagious strain but contains a malignantly modified strain called "BCG" used to evoke a vulnerable response to the vaccine. The live attenuated vaccine containing strain *Yersinia pestis* EV is used for pest immunization. Attenuated vaccines have some advantages and disadvantages. Attenuated, or live, weakened, vaccines generally provoke more durable immunological responses. But they may not be safe for use in immunocompromised individuals, and on rare occasions change to a malign form and cause disease.^[20]

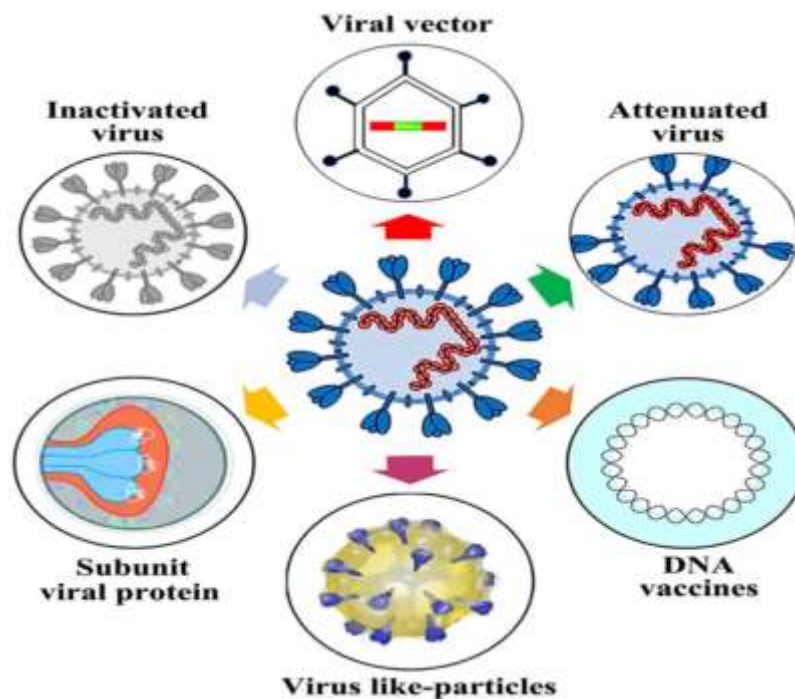


Fig no. 3 VIRUS

Inactivated vaccine:

Some vaccines contain inactivated, but preliminarily malign, micro-organisms that have been destroyed with chemicals, heat, or radiation.^[21] "ghosts", with complete but empty bacterial cell envelopes. They're considered an intermediate phase between the inactivated and downgraded vaccines.^[22] Examples include IPV (polio vaccine), hepatitis A vaccine, rabies vaccine, and utmost influenza vaccines.^[23]

Toxoid vaccine:

Toxoid vaccines are made from inactivated toxic compounds that cause illness rather than micro-organisms.^[24] Examples of toxoid-based vaccines include tetanus and diphtheria.^[23] Not all toxoids are for micro-organisms; for example, *Crotalus* toxoid is used to vaccinate dogs against rattlesnake bites.^[25]

Subunit vaccine:

Rather than initiating an inactivated or attenuated microorganism to a vulnerable system, a "whole-agent" vaccine or a subunit vaccine uses a scrap of it to produce a vulnerable response. One illustration is the subunit vaccine against hepatitis B, which is composed of only the face proteins of the contagion.^[26] Another example is edible algae vaccines, similar to the contagion-virus-like particle (VLP) vaccine against human papillomavirus (HPV), which is composed of the viral major capsid protein.^[27] Another illustration is the hemagglutinin and neuraminidase subunits of the influenza virus.^[23] A subunit vaccine is being used for pest immunization.^[28]

Conjugate vaccine:

Certain bacteria have a polysaccharide external coat that's poorly immunogenic. By linking these external coats to proteins, the immune system can be led to fete the polysaccharide as if it were a protein antigen. This approach is used in the Haemophilus influenzae type B vaccine.^[29]

Outer membrane vesicle:

Outer membrane vesicles (OMVs) are essentially immunogenic and can be manipulated to produce potent vaccines. The best-known OMV vaccines are those grown for serotype B meningococcal disease.^{[30][31]}

Heterologous vaccine:

Heterologous vaccines also known as "Jennerian vaccines", are vaccines that are pathogens of other animals that either don't cause disease or beget mild disease in the organism being treated. A classic example is Jenner's use of cowpox to cover against smallpox. A current illustration is the use of the BCG vaccine made from Mycobacterium bovis to cover against tuberculosis.^[32]

Viral vector vaccine:

Viral vector vaccines use a safe virus to put pathogen genes in the body to make specific antigens, such as surface proteins, to stimulate an immune response.^{[33][34]}

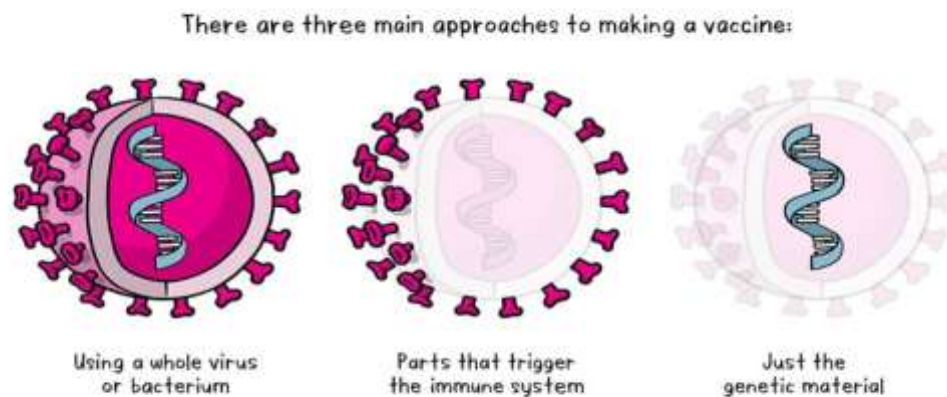


Fig no. 4 Approaches to making vaccine

RNA vaccine:

An mRNA vaccine (or RNA vaccine) is a novel type of vaccine that is composed of nucleic acid RNA, packaged within a vector such as lipid nanoparticles.^[35] Among the COVID-19 vaccines are some RNA vaccines under development to combat the COVID-19 pandemic and some have been approved or have received emergency use authorization in some countries. For example, the Pfizer-BioNTech vaccine and Moderna mRNA

PRODUCTION:



Fig no. 5 PRODUCTION OF VACCINE

Vaccine products are unnaturally different from other kinds of manufacturing—including regular pharmaceutical manufacturing in that vaccines are intended to be administered to millions of people of whom the vast majority are impeccably healthy. This fact drives an extraordinarily rigorous production process with strict compliance conditions far beyond what other products need.^[39]

Depending upon the antigen, it can bring anywhere from US \$50 to \$500 million to make a vaccine product installation, which requires largely technical types of equipment, clean apartments, and constraint apartments. There's a global failure of the labour force with the right combination of skill, expertise, knowledge, capability, and personality to staff vaccine product lines. With the notable exceptions of Brazil, China, and India, numerous developing countries' educational systems are unfit to give enough good campaigners, and vaccine makers grounded in similar countries must hire an aboriginal labour force to keep the product going.^[40]

Vaccine product has several stages. First, the antigen itself is generated. Contagions are grown moreover on primary cells similar to funk eggs or on nonstop cell lines similar to dressed mortal cells (e.g., for hepatitis A).^[41] Bacteria are developed in bioreactors (e.g., *Haemophilus influenzae* type b). Likewise, a recombinant protein deduced from contagions or bacteria can be generated in incentive, bacteria, or cell societies.

After the antigen is generated, it's insulated from the cells used to induce it. A contagion may need to be inactivated, conceivably with no further sanctification needed. Recombinant proteins need numerous functions involving ultrafiltration and column chromatography. After some time, the vaccine is formulated by adding adjuvants, stabilizers, and preservatives as demanded. The adjuvant enhances the vulnerable response to the antigen, stabilizers increase the storehouse life, and preservatives allow the use of multidose vials.^{[42][43]} Combination vaccines are harder to develop and produce, because of implicit incompatibilities and relations among the antigens and other constituents involved.

The last stage in vaccine manufacture before distribution is fill and finish, which is the process of filling vials with vaccines and packaging them for distribution. Although this is a conceptually simple part of the vaccine manufacturing process, it's frequently a tailback in distributing and administering vaccines. Vaccine product ways are evolving. dressed mammalian cells are anticipated to become decreasingly important, compared to conventional options similar to funk eggs, due to lesser productivity and low prevalence of problems with impurity. Recombination technology that produces genetically detoxified vaccines is anticipated to grow in fashionability for the product of bacterial vaccines that use toxoids. Combination vaccines are anticipated to reduce the amounts of antigens they contain, thereby dropping undesirable relations, by using pathogen-associated molecular patterns.^[44]

OTHER CONTENT:

A vaccine dose contains many constituents, veritably little of which is the active component, the immunogen. A single dose may have simply nanograms of micrograms of bacterial polysaccharides. A vaccine injection, oral drops, or nasal spray is substantially water. Other constituents are added to boost the vulnerable response, to ensure safety, or to help with the storehouse, and a tiny quantum of material is left over from the manufacturing process. veritably infrequently, these materials can beget an antipathetic response in people who are veritably sensitive to them.

Immunologic adjuvant:

Vaccines generally contain one or further adjuvants, used to boost the immune response. Tetanus toxoid, for case, is generally adsorbed onto alum. This presents the antigen in such a way as to produce a lesser action than the simple waterless tetanus toxoid. People who have an adverse response to adsorbed tetanus toxoid may be specified the simple vaccine when the time comes for a supporter.^[45]

In preparation for the 1990 Persian Gulf campaign, the whole-cell pertussis vaccine was used up as an adjuvant for the anthrax vaccine. This produces a more rapid immune reaction than giving only the anthrax vaccine, which is of some benefit if exposure might be approaching.^[46]

Preservatives:

Vaccines may also contain preservatives to help impurity with bacteria or fungi. Until recent times, the preservative thiomersal was used in numerous vaccines that didn't contain live contagions. As of 2005, the only nonage vaccine in the U.S. that contains thiomersal in lesser than trace quantities is the influenza vaccine,^[47] which is presently recommended only for children with certain threat factors.^[48] Single-cure influenza vaccines supplied in the UK don't list thiomersal in the constituents. Preservatives may be used at colourful stages of the product of vaccines, and the most sophisticated styles of dimension might describe traces of them in the finished product, as they may in the terrain and population as a whole.^[49]

Numerous vaccines need preservatives to help serious adverse goods similar to *Staphylococcus* infection, which in one 1928 incident killed 12 of 21 children invested with a diphtheria vaccine that demanded a preservative.^[50] Several preservatives are available, including thiomersal, phenoxyethanol, and formaldehyde. Thiomersal is more effective against bacteria, has a better shelf-life, and improves vaccine stability, energy, and safety; but, in the U.S., the European Union, and many other rich countries, it's no longer used as a preservative in nonage vaccines, as a preventative measure due to its mercury content.^[51] Although controversial claims have been made that thiomersal contributes to autism, no satisfying scientific substantiation supports these claims.^[52] likewise, a 10-11-time study of, 461 children set up that the MMR vaccine doesn't beget autism and reduced the threat of autism by seven per cent.^{[53][54]}

Excipients:

Besides the active vaccine itself, the following excipients and residual manufacturing compounds are present or may be present in vaccine preparations:^[55] Aluminum salts or gels are added as adjuvants. Adjuvants are added to encourage an earlier, more powerful response, and more persistent

immune response to the vaccine; they allow for a lower vaccine dosage. Antibiotics add up to some vaccines to block the growth of bacteria during the production and storage of the vaccine.

Egg protein is present in the influenza vaccine and unheroic fever vaccine as they're prepared using funk eggs. Other proteins may be present. Formaldehyde is used to disable bacterial products for toxoid vaccines. Formaldehyde is also used to inactivate unwanted contagions and kill bacteria that might pollute the vaccine during the product. Monosodium glutamate (MSG) and 2-phenoxyethanol are used as stabilizers in many vaccines to support the vaccine and remain unchanged when the vaccine is exposed to heat, light, acidity, or moisture. Thiomersal is a mercury-containing antimicrobial that's added to vials of vaccines that contain more than one cure to help impurity and the growth of potentially dangerous bacteria. Due to the contestation girding thiomersal, it has been removed from utmost vaccines except for multi-use influenza, where it was reduced to situations so that a single cure contained lower than a microgram of mercury, a position analogous to eating ten grams of canned tuna.^[56]

DELIVERY SYSTEM:



Fig no. 6 DELIVERY SYSTEM

One of the most common styles of delivering vaccines into the mortal body is injection. The development of new delivery systems raises the stopgap of vaccines that are safer and more effective to deliver and administer. Lines of exploration include liposomes and ISCOM (vulnerable stimulating complex).^[57] Notable developments in vaccine delivery technologies have included oral vaccines. Beforehand attempts to apply oral vaccines showed varying degrees of promise, beginning in the 20th century, at a time when the veritable possibility of an effective oral antibacterial vaccine was controversial.^[58] By the 1930s there was adding interest in the precautionary value of an oral typhoid fever vaccine for illustration.^[59]

An oral polio vaccine turned out to be effective when vaccinations were administered by levy staff without formal training; the results also demonstrated increased ease and effectiveness of administering the vaccines. Effective oral vaccines have numerous advantages; for illustration, there's no threat of blood impurity. Vaccines intended for oral administration need not be liquid, and as solids, they generally are more stable and less prone to damage or corruption by indurating in transport and storehouses.^[60] Similar stability reduces the need for a " cold chain " of the coffers needed to keep vaccines within a defined temperature range from the manufacturing stage to the point of administration, which, in turn, may drop the costs of vaccines.^[61]

A microneedle approach, which is still in stages of evolution, uses " pointed protrusions fabricated into arrays that can produce vaccine delivery pathways through the skin ".^[62] An experimental needle-free vaccine delivery system is witnessing beast testing.^{[63][64]} A stamp-size patch analogous to a tenacious girth contains about, 000 bitsy protrusions per forecourt cm.^[65] This dermal administration potentially increases the effectiveness of vaccination while taking a lower vaccine than injections.^[66]

EFFECTS:

There's inviting scientific agreement that vaccines are a veritably safe and effective way to fight and annihilate contagious conditions.^{[67][68][69][70]} The vulnerable system recognizes vaccine agents as foreign destroys them, and " remembers " them. When the malign interpretation of an agent is encountered, the body recognizes the protein fleece on the contagion and therefore is set to respond, by first negating the target agent before it can enter cells, and secondly by feting and destroying infected cells before that agent can multiply to vast figures.^{[71][72]}

Once antibodies are produced, they may promote immunity in several ways, depending on the class of antibodies involved. Their success in clearing or inactivating a pathogen will depend on the number of antibodies produced and on the extent to which those antibodies are effective at countering the strain of the pathogen involved, since different strains may be differently susceptible to a given immune reaction.^[73] In some cases, vaccines may result in partial immune protection (in which immunity is less than 100% effective but still reduces the risk of infection) or in temporary immune protection (in which immunity wanes over time) rather than full or permanent immunity. They can still raise the reinfection threshold for the population as a whole and make a substantial impact.^[74] They can also mitigate the severity of infection, resulting in a lower mortality rate, lower morbidity, faster recovery from illness, and a wide range of other effects.^{[75][76]}

Those who are aged frequently display lower responses than those who are young, a pattern known as immuno-anility.^[77] Adjuvants generally are used to boost vulnerable responses, particularly for aged people whose vulnerable response to a simple vaccine may have weakened.^[78] The efficacy or performance of the vaccine is dependent on several factors.

- ❖ the complaint itself (for some conditions vaccination performs better than for others)
- ❖ the strain of vaccine (some vaccines are specific to, or at least most effective against, particular strains of the complaint).^[79]
- ❖ whether the vaccination schedule has been duly observed.
- ❖ idiosyncratic response to vaccination; some individuals are "non-responders" to certain vaccines, meaning that they don't induce antibodies after being vaccinated correctly.
- ❖ varied factors similar to race, age, or inheritable predilection.
 - Still, the complaint is likely to be less malign than in unvaccinated cases, If a vaccinated existent does develop the complaint vaccinated against (advanced infection). Important Considerations in an effective vaccination program.^[80]
- ❖ careful modelling to anticipate the effect that an immunization crusade will have on the epidemiology of the complaint in the medium to long term.
- ❖ ongoing surveillance for the applicable complaint following the preface of a new vaccine.
- ❖ conservation of high immunization rates, indeed when a complaint has come rare.

ADVERSE EFFECT:

Vaccinations given to children, adolescents, or adults are normally safe.^{[81][82]} Adverse effect, are normally mild. The rate of effect depends on the vaccine in question. Some common side effects include fever, pain around the injection site, and muscle aches.^[83] Additionally, some individuals may be allergic to ingredients in the vaccine.^[84] MMR vaccine is rarely associated with febrile seizures.^[82]

Host- ("vaccinee")-related determinants that render a person susceptible to infection, similar to genetics, health status (underpinning complaint, nutrition, gestation, perceptivity or disinclinations), vulnerable capability, age, and profitable impact or artistic terrain can be primary or secondary factors affecting the inflexibility of infection and response to a vaccine. Elderly (above age 60), allergen-hypersensitive, and fat people have a vulnerability to compromised immunogenicity, which prevents or inhibits vaccine effectiveness, conceivably taking separate vaccine technologies for these specific populations or repetitious supporter vaccinations to limit contagion transmission.^[86] Severe side goods are extremely rare. Varicella vaccine is infrequently associated with complications in immunodeficient individualities, and rotavirus vaccines are relatively associated with intussusception.^[82] At least 19 countries have no-fault compensation programs to give compensation for those with severe adverse goods of vaccination.^[85]

INVETERINARY MEDICINES:



Fig no. 7 IN VETERINARY MEDICINE

Vaccinations of creatures are used both to help their constricting conditions and to help the transmission of complaints to humans.^[87] Both creatures kept as faves and creatures raised as beasts are routinely vaccinated. In some cases, wild populations may be vaccinated. This is occasionally fulfilled with vaccine-bejewelled food spread in a complaint-prone area and has been used to control rabies in raccoons.

Where rabies occurs, rabies vaccination of tykes may be needed by law. Other canine vaccines include canine illness, canine parvovirus, contagious canine hepatitis, adenovirus-2, leptospirosis, Bordetella, canine parainfluenza contagion, and Lyme complaint, among others.

Cases of veterinary vaccines used in humans have been proven, whether purposeful or accidental, with some cases of attendant illness, most especially with brucellosis. still, the reporting of similar cases is rare, and veritably little has been studied about the safety and results of similar practices. With the arrival of aerosol vaccination in veterinary conventions, mortal exposure to pathogens not naturally carried in humans, similar to Bordetella bronchiseptica, has probably increased in recent times.^[88]

DIVA vaccines:

DIVA (Differentiation of Infected from Vaccinated Animals), also known as **SIVA** (Segregation of Infected from Vaccinated Animals) vaccines, allows one to distinguish between infected and vaccinated animals. DIVA vaccines carry at least one antigenic determinant less than the equal uncultivated microorganism. An accompanying diagnostic test that detects the antibody against that antigenic determinant assists in identifying whether the animal has been vaccinated or not.

The first DIVA vaccines-formerly manufacturer vaccines and since 1999 coined as DIVA vaccines and companion diagnostic tests were developed by J. T. van Oirschot and colleagues at the Central Veterinary Institute in Lelystad, The Netherlands.^{[89][90]} They found that some live vaccines against pseudorabies (also termed Aujeszky's disease) had deletions in their viral genome (among which was the gE gene). Monoclonal antibodies were produced against those eliminations and selected to develop an ELISA that demonstrated antibodies against gE. In addition, novel genetically engineered gE-negative vaccines were constructed.^[91] Along the same lines, DIVA vaccines and companion diagnostic tests against bovine herpesvirus 1 infection have been developed.^{[90][91][92]}

The DIVA strategy has been applied in several countries to eradicate pseudorabies virus from those countries. Swine populations were intensively vaccinated and monitored the companion diagnostic test and, subsequently, the infected pigs were removed from the population. Bovine herpesvirus 1 DIVA vaccines are also popularly used in practice. Considerable efforts are ongoing to apply the DIVA principle to a wide range of infectious diseases, such as classical swine fever,^[93] avian influenza,^[94] Actinobacillus pleuropneumonia^[95] and Salmonella infections in pigs.^[96]

PATENTS:

According to the World Health Organization, the biggest hedge to vaccine products in lower developed countries has not been patents, but the substantial fiscal, structure, and pool conditions demanded request entry. Vaccines are complex fusions of natural composites, and unlike the case for traditional medicines, there are no true general vaccines. The vaccine produced by a new installation must undergo complete clinical testing for safety and efficacy by the manufacturer. For utmost vaccines, specific processes in technology are patented. These can be circumvented by indispensable manufacturing styles, but this requires an R&D structure and a suitably professed pool. In the case of many fairly new vaccines, similar to the mortal papillomavirus vaccine, the patents may put a fresh hedge.^[97]

When increased manufacturing of vaccines was urgently needed during the COVID-19 pandemic in 2021, the World Trade Organization and governments around the world evaluated whether to waive intellectual property rights and patents on COVID-19 vaccines, which would "remove all potential obstacles to the appropriate access of cost-effective COVID-19 medical products, involving vaccines and medicines, and scale up the manufacturing and supply of essential medical products."^[98]

LICENSING:

Vaccine licensure occurs after the successful conclusion of the evaluation cycle and further, the clinical trials and another plane of action involved through Phases I-III demonstrating safety, immunoactivity, immunogenetic safety at a given specific cure, proven effectiveness in precluding infection for target populations, and enduring preventative effect (time abidance or need for revaccination must be estimated).^[99] Because preventative vaccines are generally estimated in healthy population cohorts and distributed among the general population, a high standard of safety is needed.^[100] As part of the transnational licensing of a vaccine, the World Health Organization Expert Committee on Biological Standardization developed guidelines of transnational norms for manufacturing and quality control of vaccines, a process intended as a platform for public nonsupervisory agencies to apply for their licensing process.^[99] Vaccine manufacturers don't admit licensing until a complete clinical cycle of development and trials proves the vaccine is safe and has long-term effectiveness, following scientific review by a transnational or public nonsupervisory association, similar to the European Medicines Agency (EMA) or the US Food and Drug Administration (FDA).^{[101][102]}

Upon developing countries adopting WHO guidelines for vaccine development and licensure, each country has its responsibility to issue national licensure, and to manage, deploy, and monitor the vaccine throughout its use in each country.^[99] Gaining confidence and acceptance of a licensed vaccine among the public is a task of communication by governments and healthcare personnel to ensure a vaccination campaign proceeds easily, saves lives and enables economic recovery.^{[103][104]} When a vaccine is licensed, it will initially be in limited supply due to variable manufacturing, distribution, and logistical factors, requiring an allocation plan for the finite supply and which population segments should be prioritized to first receive the vaccine.^[103]

World Health Organization:

Vaccines developed for international distribution via the United Nations Children's Fund (UNICEF) require pre-qualification by the WHO to make sure international standards of quality, safety, immunogenicity, and efficacy for adoption by numerous countries. The process requires manufacturing consistency at WHO-contracted laboratories following Good Manufacturing Practice (GMP).^[99] When UN agencies are involved in vaccine licensure, individual countries collaborate by 1) issuing marketing authorization and a national license for the vaccine, its manufacturers, and distribution partners; and 2) conducting post-marketing surveillance, including records for adverse events after the vaccination program. The WHO works with national agencies to monitor inspections of manufacturing facilities and distributors for compliance with GMP and regulatory oversight.^[96] Some countries choose to buy vaccines licensed by reputable national organizations, such as EMA, FDA, or national agencies in other affluent countries, but such purchases typically are costly and may not have distribution resources suitable to local conditions in developing countries.^[99]

CONCLUSION:

Inconceivable progress has been made in the field of mRNA vaccines in the last decade. Optimization in mRNA design, and LNP composition, as well as in manufacturing processes have led to mRNA vaccines that are well-permitted and immunogenic in humans, stable, and can be gauged up to hundreds of millions of boluses. The use of standardized processes and reagents, the capability to combine multiple mRNA antigens in the same LNP thus targeting multi-pathogens contemporaneously, the lack of vector impunity, and the robust vulnerable responses verified in several clinical studies make mRNA vaccines a disruptive technology that may change vaccine development in the incoming times. In addition, due to the relatively recent operation of mRNA for large-scale vaccine operations, there's important room for advancements and new developments.

Another focus is to ameliorate the efficacy and safety of vaccines indeed further beyond the inviting successes of vaccines in the once several centuries. The most important keyword from the efficacy standpoint is 'adjuvant'. Some vaccine products are certified or under development in the form of an admixture of a vaccine and a certain adjuvant. utmost of the presently certified adjuvanted vaccine products target influenza. The emphasis on the significance of adjuvants is gradationally added with the ageing of the population. Because they grease the vulnerable response to vaccination in aged people, numerous experts anticipate that adjuvants will be an essential element for wide vaccine use in entire populations.

REFERENCE:

- 1) "Expanded Practice Standards" (PDF). Iowa Administrative Code. 2019.
- 2) Melief CJ, van Hall T, Arens R, Ossendorp F, van der Burg SH (September 2015). "Therapeutic cancer vaccines". *The Journal of Clinical Investigation*. 125 (9): 3401–3412. doi:10.1172/JCI80009. PMC 4588240. PMID 26214521.
- 3) Bol KF, Aarntzen EH, Pots JM, Olde Nordkamp MA, van de Rakt MW, Scharenborg NM, de Boer AJ, van Oorschot TG, Croockewit SA, Blokk WA, Oyen WJ, Boerman OC, Mus RD, van Rossum MM, van der Graaf CA, Punt CJ, Adema GJ, Figdor CG, de Vries IJ, Schreibelt G (March 2016). "Prophylactic vaccines are potent activators of monocyte-derived dendritic cells and drive effective anti-tumor responses in melanoma patients at the cost of toxicity". *Cancer Immunology, Immunotherapy*. 65 (3): 327–339. doi:10.1007/s00262-016-1796-7. PMC 4779136. PMID 26861670.
- 4) Brotherton J (2015). "HPV prophylactic vaccines: lessons learned from 10 years experience". *Future Virology*. 10(8): 999–1009. doi:10.2217/fv.15.60.
- 5) Frazer IH (May 2014). "Development and implementation of papillomavirus prophylactic vaccines". *Journal of Immunology*. 192 (9): 4007–4011. doi:10.4049/jimmunol.1490012. PMID 24748633.
- 6) Ledford, Heidi (2020-08-17). "What the immune response to the coronavirus says about the prospects for a vaccine". *Nature*. 585 (7823): 20–21. Bibcode:2020Natur.585...20L. doi:10.1038/d41586-020-02400-7. PMID 32811981. S2CID 221180503.
- 7) *United States Centers for Disease Control and Prevention (2011). A CDC framework for preventing infectious diseases. Archived 2017-08-29 at the Way back Machine Accessed 11 September 2012. "Vaccines are our most effective and cost-saving tools for disease prevention, preventing untold suffering and saving tens of thousands of lives and billions of dollars in healthcare costs each year."
- 8) Zimmer, Carl (20 November 2020). "2 Companies Say Their Vaccines Are 95% Effective. What Does That Mean? You might assume that 95 out of every 100 people vaccinated will be protected from Covid-19. But that's not how the math works". *The New York Times*. Retrieved 21 November 2020.
- 9) Fiore AE, Bridges CB, Cox NJ (2009). "Seasonal influenza vaccines". *Vaccines for Pandemic Influenza*. *Curr. Top. Micro bio I. Immunol. Current Topics in Microbiology and Immunology*. Vol. 333. pp. 43–82. doi:10.1007/978-3-540-92165-3_3. ISBN 978-3-540-92164-6. PMID 19768400. S2CID 33549265.
- 10) Chang Y, Brewer NT, Rinas AC, Schmitt K, Smith JS (July 2009). "Evaluating the impact of human papillomavirus vaccines". *Vaccine*. 27 (32): 4355–4362. doi: 10.1016/j.vaccine.2009.03.008. PMID 19515467.
- 11) Liesegang TJ (August 2009). "Varicella zoster virus vaccines: effective, but concerns Linger". *Canadian Journal of Ophthalmology*. 44 (4): 379–384. doi:10.3129/i09-126. PMID 19606157. S2CID 662998.

- 12) World Health Organization, Global Vaccine Action Plan 2011-2020. Archived 2014- 04-14 at the Way back Machine Geneva, 2012.
- 13) Alarcon JB, Waine GW, McManus DP (1999). "DNA Vaccines: Technology and Application as Anti-parasite and Anti-microbial Agents". *Advances in Parasitology* Volume 42. *Advances in Parasitology*. Vol. 42. pp. 343–410. doi:10.1016/S0065-308X (08)60152-9. ISBN 9780120317424. PMID 10050276.
- 14) Robinson HL, Pertmer TM (2000). DNA vaccines for viral infections: basic studies and applications. *Advances in Virus Research*. Vol. 55. pp. 1–74. doi:10.1016/S0065-3527(00)55001-5. ISBN 9780120398553. PMID 11050940.
- 15) Naftalis, Kramer Levin; Royzman, Frankel LLP-Irena; Pineda, ré (30 November 2020). "Third-Generation Vaccines Take Center Stage in Battle Against COVID-19 | Lexology". www.lexology.com. Retrieved 24 January 2021.
- 16) Regalado, Antonio. "The U.S. government has begun testing its first Zika vaccine in humans". Retrieved 2016-08-06.
- 17) Chen Y, Wang S, Lu S (February 2014). "DNA Immunization for HIV Vaccine Development". *Vaccines*. 2 (1): 138–159. doi:10.3390/vaccines2010138. PMC 4494200. PMID 26344472.
- 18) "Katalin Karikó and Drew Weissman Awarded Horwitz Prize for Pioneering Research on COVID-19 Vaccines". Columbia University Irving Medical Center. 2021-08-12. Retrieved 2021-09-07.
- 19) "Vaccine Types". National Institute of Allergy and Infectious Diseases. 2012-04-03. Archived from the original on 2015-09-05. Retrieved 2015-01-27.
- 20) Sinha JK, Bhattacharya S. *A Text Book of Immunology* (Google Books Preview). Academic Publishers. p. 318. ISBN 978-81-89781-09-5. Retrieved 2014-01-09.
- 21) "Types of Vaccines". Archived from the original on 2017-07-29. Retrieved October 19, 2017.
- 22) Batah, Aly; Ahmad, Tarek (2020-06-15). "The development of ghost vaccines trials". *Expert Review of Vaccines*. 19 (6): 549–562. doi:10.1080/14760584.2020.1777862. ISSN 1476-0584. PMID 32500816. S2CID 219331100.
- 23) "Different Types of Vaccines | History of Vaccines". www.historyofvaccines.org. Retrieved 2019-06-14.
- 24) "Different Types of Vaccines | History of Vaccines". www.historyofvaccines.org. Retrieved 2019-05-03.
- 25) "Types of Vaccines". coastalcarolinaresearch.com. Retrieved 2019-05-03.
- 26) Philadelphia, The Children's Hospital of (2014-08-18). "A Look at Each Vaccine: Hepatitis B Vaccine". www.chop.edu. Retrieved 2019-06-14.
- 27) "HPV Vaccine | Human Papillomavirus | CDC". www.cdc.gov. 2019-05-13. Retrieved 2019-06-14.
- 28) Williamson, E. D.; Eley, S. M.; Griffin, K. F.; Green, M.; Russell, P.; Leary, S. E.; Oyston, P. C.; Easterbrook, T.; Reddin, K. M. (December 1995). "A new improved sub-unit vaccine for plague: the basis of protection". *FEMS Immunology and Medical Microbiology*. 12 (3–4): 223–230. doi:10.1111/j.1574-695X.1995.tb 00196.x. ISSN 0928-8244. PMID 8745007.
- 29) "Polysaccharide Protein Conjugate Vaccines". www.globalhealthprimer.emory.edu. Retrieved 2019-06-14.
- 30) Pollard AJ, Bijker EM (2020-12-22). "A guide to vaccinology: from basic principles to new developments". *Nature Reviews Immunology*. 21 (2): 83–100. doi:10.1038/s41577-020-00479-7. ISSN 1474-1741. PMC 7754704. PMID 33353987.
- 31) Pol L, Stork M, Ley P (2015-11-11). "Outer membrane vesicles as platform vaccine technology". *Biotechnology Journal*. 10 (11): 1689–1706. doi:10.1002/biot.201400395. ISSN 1860-7314. PMC 4768646. PMID 26912077.
- 32) Scott (April 2004). "Classifying Vaccines" (PDF). *BioProcesses International*: 14–23. Archived (PDF) from the original on 2013-12-12. Retrieved 2014-01-09.
- 33) "Vaccine Types". Vaccines.org. Office of Infectious Disease of the United States Department of Health and Human Services. Retrieved 13 March 2021.
- 34) "Understanding and Explaining Viral Vector COVID-19 Vaccines". Centers for Disease Control and Prevention. Retrieved 13 March 2021.
- 35) Garde, Damian; Feuerstein, Adam (1 November 2020). "How nanotechnology helps mRNA Covid-19 vaccines work". *STAT*. Retrieved 21 December 2020.
- 36) CDC (11 February 2020). "COVID-19 and Your Health". Centers for Disease Control and Prevention. Retrieved 21 December 2020.
- 37) Banks, Marcus A. (16 July 2020). "What Are mRNA Vaccines, and Could They Work Against COVID-19?". *Smithsonian Magazine*. Retrieved 21 December 2020.
- 38) Branswell, Helen (19 December 2020). "FDA grants authorization to Moderna's Covid-19 vaccine". *STAT*. Retrieved 21 December 2020.

- 39) Gomez, Phillip L.; Robinson, James M.; Rogalewicz, James (2008). "Chapter 4: Vaccine Manufacturing". In Plotkin, Stanley A.; Orenstein, Walter A.; Offit, Paul A. (eds.). *Vaccines* (5th ed.). New York: Saunders Elsevier. pp. 45–58. ISBN 9781437721584. Retrieved March 26, 2021.
- 40) Plotkin, Stanley; Robinson, James M.; Cunningham, Gerard; Iqbal, Robyn; Larsen, Shannon (24 July 2017). "The complexity and cost of vaccine manufacturing – An overview". *Vaccine*. 35 (33): 4064–4071. doi: 10.1016/j.vaccine.2017.06.003. PMC 5518734. PMID 28647170.
- 41) "Three ways to make a vaccine" (infographic). Archived from the original on 2015-12-23. Retrieved 2015-08-05, in Stein, Rob (24 November 2009). "Vaccine system remains antiquated". *The Washington Post*. Archived from the original on 19 October 2017.
- 42) Muzumdar JM, Cline RR (2009). "Vaccine supply, demand, and policy: a primer". *Journal of the American Pharmacists Association*. 49 (4): e87–99. doi:10.1331/JAPhA.2009.09007. PMC 7185851. PMID 19589753.
- 43) "Components of a vaccine". Archived from the original on 2017-06-13.
- 44) Bae K, Choi J, Jang Y, Ahn S, Hur B (April 2009). "Innovative vaccine production technologies: the evolution and value of vaccine production technologies". *Archives of Pharmacal Research*. 32 (4): 465–480. doi:10.1007/s12272-009-1400-1. PMID 19407962. S2CID 9066150.
- 45) Engler, Renata J. M.; Greenwood, John T.; Pittman, Phillip R.; Grabenstein, John D. (2006-08-01). "Immunization to Protect the US Armed Forces: Heritage, Current Practice, and Prospects". *Epidemiologic Reviews*. 28 (1): 3–26. doi:10.1093/epirev/mxj003. ISSN 0193-936X. PMID 16763072.
- 46) Sox, Harold C.; Liverman, Catharyn T.; Fulco, Carolyn E.; War, Institute of Medicine (US) Committee on Health Effects Associated with Exposures During the Gulf (2000). *Vaccines*. National Academies Press (US).
- 47) "Institute for Vaccine Safety – Thimerosal Table". Archived from the original on 2005-12-10.
- 48) Wharton, Melinda E.; National Vaccine Advisory committee "U.S.A. national vaccine plan" Archived 2016-05-04 at the Way back Machine
- 49) "Measurements of Non-gaseous air pollutants > Metals". npl.co.uk. National Physics Laboratory. Archived from the original on 29 September 2007. Retrieved 28 June 2020.
- 50) "Thimerosal in vaccines". Center for Biologics Evaluation and Research, U.S. Food and Drug Administration. 2007-09-06. Archived from the original on 2013-01-06. Retrieved 2007-10-01.
- 51) Bigham M, Copes R (2005). "Thiomersal in vaccines: balancing the risk of adverse effects with the risk of vaccine-preventable disease". *Drug Safety*. 28 (2): 89–101. doi:10.2165/00002018-200528020-00001. PMID 15691220. S2CID 11570020.
- 52) Offit PA (September 2007). "Thimerosal and vaccines – a cautionary tale". *The New England Journal of Medicine*. 357 (13): 1278–1279. doi:10.1056/NEJMp078187. PMID 17898096. S2CID 36318722.
- 53) March 5, Reuters Updated; 2019 (2019-03-05). "Another study, this one of 657k kids, finds MMR vaccine doesn't cause autism | Montreal Gazette". *National Post*. Retrieved 2019-03-13.
- 54) Hoffman J (2019-03-05). "One More Time, With Big Data: Measles Vaccine Doesn't Cause Autism". *The New York Times*. ISSN 0362-4331. Retrieved 2019-03-13.
- 55) CDC (2018-07-12). "Ingredients of Vaccines – Fact Sheet". Archived from the original on December 17, 2009. Retrieved December 20, 2009.
- 56) The mercury levels in the table, unless otherwise indicated, are taken from *Mercury Levels in Commercial Fish and Shellfish* (1990-2010) Archived 2015-05-03 at the Way back Machine U.S. Food and Drug Administration. Accessed 8 January 2012.
- 57) Morein B, Hu KF, Abusugra I (June 2004). "Current status and potential application of ISCOMs in veterinary medicine". *Advanced Drug Delivery Reviews*. 56 (10): 1367–1382. doi: 10.1016/j.addr.2004.02.004. PMID 15191787.
- 58) *American Medicine*. American-Medicine Publishing Company. 1926.
- 59) South African Institute for Medical Research (1929). Annual report [Jaarverslag]. South African Institute for Medical Research – Suid-Afrikaanse Instituut vir Mediese Navorsing.
- 60) Khan FA (2011-09-20). *Biotechnology Fundamentals*. CRC Press. p. 270. ISBN 978-1-4398-2009-4.
- 61) Giudice EL, Campbell JD (April 2006). "Needle-free vaccine delivery". *Advanced Drug Delivery Reviews*. 58 (1): 68–89. doi: 10.1016/j.addr.2005.12.003. PMID 16564111.
- 62) WHO to trial Nanopatch needle-free delivery system| ABC News, 16 Sep 2014| "Needle-free polio vaccine a 'game-changer'". ABC News. 2014-09-16. Archived from the original on 2015-04-02. Retrieved 2015-09-15.
- 63) "Australian scientists develop 'needle-free' vaccination". *The Sydney Morning Herald*. 18 August 2013. Archived from the original on 25 September 2015.

- 64) "Vaxxas raises \$25m to take Brisbane's Nanopatch global". Business Review Weekly. 2015-02-10. Archived from the original on 2015-03-16. Retrieved 2015-03-05.
- 65) "Australian scientists develop 'needle-free' vaccination". The Hindu. Chennai, India. 28 September 2011. Archived from the original on 1 January 2014.
- 66) "Needle-free nanopatch vaccine delivery system". News Medical. 3 August 2011. Archived from the original on 11 May 2012.
- 67) Orenstein WA, Bernier RH, Dondero TJ, Hinman AR, Marks JS, Bart KJ, Sirotkin B (1985). "Field evaluation of vaccine efficacy". *Bulletin of the World Health Organization*. 63 (6): 1055–1068. PMC 2536484. PMID 3879673.
- 68) Jan 11, Hub staff report / Published; 2017 (2017-01-11). "The science is clear: Vaccines are safe, effective, and do not cause autism". The Hub. Retrieved 2019-04-16.
- 69) Ellenberg SS, Chen RT (1997). "The complicated task of monitoring vaccine safety". *Public Health Reports*. 112 (1): 10–20, discussion 21. PMC 1381831. PMID 9018282.
- 70) "Vaccine Safety: The Facts". HealthyChildren.org. Retrieved 2019-04-16.
- 71) Mak, Tak W.; Saunders, Mary E.; Jett, Bradley D. (2014). "Chapter 1 - Introduction to the Immune Response". *Primer to The immune response* (2nd ed.). Burlington, MA: Academic Cell. pp. 3–20. ISBN 978-0-12-385245-8. Retrieved 18 April 2022.
- 72) Clem, Angela S (2011). "Fundamentals of Vaccine Immunology". *Journal of Global Infectious Diseases*. 3 (1): 73–78. doi:10.4103/0974-777X.77299. ISSN 0974-777X. PMC 3068582. PMID 21572612.
- 73) Bonanni, Paolo; Picazo, Juan José; Rémy, Vanessa (12 August 2015). "The intangible benefits of vaccination – what is the true economic value of vaccination?". *Journal of Market Access & Health Policy*. 3: 10.3402/jmahp. v3.26964. doi:10.3402/jmahp. v3.26964. ISSN 2001-6689. PMC 4802696. PMID 27123182.
- 74) Stanciu, Stefan G. (24 August 2016). *Micro and Nanotechnologies for Biotechnology*. BoD – Books on Demand. ISBN 978-953-51-2530-3. Retrieved 19 April 2022.
- 75) Frasca, Daniela; Diaz, Alain; Romero, Maria; Garcia, Denisse; Blomberg, Bonnie B. (6 October 2020). "B Cell Immunosenescence". *Annual Review of Cell and Developmental Biology*. 36 (1): 551–574. doi:10.1146/annurev-cellbio-011620-034148. ISSN 1081-0706. PMC 8060858. PMID 33021823. Retrieved 18 April 2022.
- 76) Neighmond P (2010-02-07). "Adapting Vaccines For Our Aging Immune Systems". Morning Edition. NPR. Archived from the original on 2013-12-16. Retrieved 2014-01-09. open access
- 77) Schlegel M, Osterwalder JJ, Galeazzi RL, Vernazza PL (August 1999). "Comparative efficacy of three mumps vaccines during disease outbreak in Eastern Switzerland: cohort study". *BMJ*. 319 (7206): 352. doi:10.1136/bmj.319.7206.352. PMC 32261. PMID 10435956.
- 78) Préziosi MP, Halloran ME (September 2003). "Effects of pertussis vaccination on disease: vaccine efficacy in reducing clinical severity". *Clinical Infectious Diseases*. 37 (6): 772–779. doi:10.1086/377270. PMID 12955637.
- 79) Miller, E.; Beverley, P. C. L.; Salisbury, D. M. (2002-07-01). "Vaccine programmes and policies". *British Medical Bulletin*. 62 (1): 201–211. doi:10.1093/bmb/62.1.201. ISSN 0007-1420. PMID 12176861.
- 80) Orenstein WA, Papania MJ, Wharton ME (May 2004). "Measles elimination in the United States". *The Journal of Infectious Diseases*. 189 Suppl 1 (Suppl 1): S1-3. doi:10.1086/377693. PMID 15106120.
- 81) Dudley, Matthew Z; Halsey, Neal A; Omer, Saad B; Orenstein, Walter A; O'Leary, Sean T; Limaye, Rupali J; Salmon, Daniel A (May 2020). "The state of vaccine safety science: systematic reviews of the evidence". *The Lancet Infectious Diseases*. 20 (5): e80–e89. doi:10.1016/s1473-3099(20)30130-4. ISSN 1473-3099. PMID 32278359. S2CID 215751248.
- 82) Maglione MA, Das L, Raaen L, Smith A, Chari R, Newberry S, Shanman R, Perry T, Goetz MB, Gidengil C (August 2014). "Safety of vaccines used for routine immunization of U.S. children: a systematic review". *Pediatrics*. 134 (2): 325–337. doi:10.1542/peds.2014-1079. PMID 25086160.
- 83) "Possible Side-effects from Vaccines". Centers for Disease Control and Prevention. 2018-07-12. Archived from the original on 17 March 2017. Retrieved 24 February 2014.
- 84) "Seasonal Flu Shot – Seasonal Influenza (Flu)". CDC. 2018-10-02. Archived from the original on 2015-10-01. Retrieved 2017-09-17.
- 85) Looker C, Heath K (2011). "No-fault compensation following adverse events attributed to vaccination: a review of international programmes". *Bulletin of the World Health Organization*. World Health Organisation. 89 (5): 371–378. doi:10.2471/BLT.10.081901. PMC 3089384. PMID 21556305. Archived from the original on August 11, 2013.
- 86) https://en.wikipedia.org/wiki/Vaccine#cite_ref-wied_22-3.

- 87) Patel JR, Heldens JG (March 2009). "Immunoprophylaxis against important virus disease of horses, farm animals and birds". *Vaccine*. 27 (12): 1797–1810. doi: 10.1016/j.vaccine.2008.12.063. PMC 7130586. PMID 19402200.
- 88) Berkelman RL (August 2003). "Human illness associated with use of veterinary vaccines". *Clinical Infectious Diseases*. 37 (3): 407–414. doi:10.1086/375595. PMID 12884166.
- 89) van Oirschot JT, Rziha HJ, Moonen PJ, Pol JM, van Zaane D (June 1986). "Differentiation of serum antibodies from pigs vaccinated or infected with Aujeszky's disease virus by a competitive enzyme immunoassay". *The Journal of General Virology*. 67 (Pt 6) (6): 1179–1182. doi:10.1099/0022-1317-67-6-1179. PMID 3011974.
- 90) van Oirschot JT (August 1999). "DIVA vaccines that reduce virus transmission". *Journal of Biotechnology*. 73 (2–3): 195–205. doi:10.1016/S0168-1656(99)00121-2. PMID 10486928.
- 91) van Oirschot JT, Gielkens AL, Moormann RJ, Berns AJ (June 1990). "Marker vaccines, virus protein-specific antibody assays and the control of Aujeszky's disease". *Veterinary Microbiology*. 23 (1–4): 85–101. doi:10.1016/0378-1135(90)90139-M. PMID 2169682.
- 92) Kaashoek MJ, Moerman A, Madić J, Rijsewijk FA, Quak J, Gielkens AL, van Oirschot JT (April 1994). "A conventionally attenuated glycoprotein E-negative strain of bovine herpesvirus type 1 is an efficacious and safe vaccine". *Vaccine*. 12 (5): 439–444. doi:10.1016/0264-410X(94)90122-8. PMID 8023552.
- 93) Hulst MM, Westra DF, Wensvoort G, Moormann RJ (September 1993). "Glycoprotein E1 of hog cholera virus expressed in insect cells protects swine from hog cholera". *Journal of Virology*. 67 (9): 5435–5442. doi:10.1128/JVI.67.9.5435-5442.1993. PMC 237945. PMID 8350404.
- 94) Capua I, Terregino C, Cattoli G, Mutinelli F, Rodriguez JF (February 2003). "Development of a DIVA (Differentiating Infected from Vaccinated Animals) strategy using a vaccine containing a heterologous neuraminidase for the control of avian influenza". *Avian Pathology*. 32 (1): 47–55. doi:10.1080/0307945021000070714. PMID 12745380. S2CID 22827454.
- 95) Maas A, Meens J, Baltes N, Hennig-Pauka I, Gerlach GF (November 2006). "Development of a DIVA subunit vaccine against *Actinobacillus pleuropneumoniae* infection". *Vaccine*. 24 (49–50): 7226–7237. doi: 10.1016/j.vaccine.2006.06.047. PMID 17027123.
- 96) Leyman B, Boyen F, Van Parys A, Verbrugge E, Haesebrouck F, Pasmans F (May 2011). "Salmonella Typhimurium LPS mutations for use in vaccines allowing differentiation of infected and vaccinated pigs". *Vaccine*. 29 (20): 3679–3685. doi: 10.1016/j.vaccine.2011.03.004. hdl:1854/LU-1201519. PMID 21419163. Archived from the original on 2017-10-28.
- 97) "Increasing Access to Vaccines Through Technology Transfer and Local Production" (PDF). World Health Organization. 2011. Archived (PDF) from the original on 2015-11-23.
- 98) Christy Somos (7 May 2021). "Everything you need to know about the WTO's COVID-19 vaccine patent proposal". CTV News. Retrieved 23 May 2021.
- 99) "Principles and considerations for adding a vaccine to a national immunization programme" (PDF). World Health Organization. 1 April 2014. Archived (PDF)
- 100) Bok, Karin; Sitar, Sandra; Graham, Barney S.; Mascola, John R. (August 2021). "Accelerated COVID-19 vaccine development: milestones, lessons, and prospects". *Immunity*. 54 (8): 1636–1651. doi: 10.1016/j.immuni.2021.07.017. PMC 8328682. PMID 34348117.
- 101) Wijnans, Leonoor; Voordouw, Bettie (11 December 2015). "A review of the changes to the licensing of influenza vaccines in Europe". *Influenza and Other Respiratory Viruses*. 10 (1): 2–8. doi:10.1111/irv.12351. ISSN 1750-2640. PMC 4687503. PMID 26439108.
- 102) Offit, Paul A. (2020). "Making vaccines: Licensure, recommendations and requirements". Children's Hospital of Philadelphia. Archived from the original on 8 September 2020. Retrieved 20 August 2020.
- 103) Toner E, Barnill A, Krubiner C, Bernstein J, Privor-Dumm L, Watson M, et al. (2020). Interim Framework for COVID-19 Vaccine Allocation and Distribution in the United States (PDF) (Report). Baltimore, MD: Johns Hopkins Center for Health Security. Archived (PDF) from the original on 22 August 2020. Retrieved 24 August 2020.
- 104) Dooling K, Marin M, Wallace M, McClung N, Chamberland M, Lee GM, et al. (December 2020). "The Advisory Committee on Immunization Practices' Updated Interim Recommendation for Allocation of COVID-19 Vaccine – United States, December 2020". *MMWR. Morbidity and Mortality Weekly Report*. 69 (5152): 1657–1660. doi:10.15585/mmwr.mm695152e2. PMID 33382671. Archived from the original on 29 September 2020. Retrieved 17 August 2020.