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Covid 19 Vaccines: Clinical Trials Status with Targeted Action

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ABSTRACT

Since November 2019, the World facing pandemic challenges of severe acute respiratory syndrome coronavirus 2 (SARS-Co-2). Initially, the infectivity of the virus was identified at Wuhan city of China. The virus officially named COVID-19 causes respiratory tract infections in humans. Tyrrell and Bynoe identified the first strain of the human coronavirus in 1965. Covid -19 develops faster than its two predecessors the SARS COV-2 and Middle East respiratory affection coronavirus (MERS – COV) but have lower mortality. Currently, most of the pharmaceutical industries were in a race to developing antiviral drugs and vaccines against COVID-19. Companies conducting the experiments and clinical trials of various vaccines are ongoing to ensure effectiveness and safety in humans. In this review, we provide an overview of Covid-19 history, types of vaccine and mechanism of actions, the current status of a clinical trial, future therapeutic drugs, and patents. Relative with the mechanism of actions such as an inactivated vaccine, vector vaccines, DNA and RNA based vaccine and antiviral drugs already entered in (Phase II and III) clinical trials. Furthermore, we summarize various trending vaccines having more effectiveness on humans in the future. A scientist may face challenges during the post-marketing clinical trial because the time taken for developing the drug was very less and so they may observe new interactions and toxicity worldwide. But this is also a good opportunity for upcoming scientists to improve the quality, and minimize the adverse effects. This report shows the current status of vaccines.

INTRODUCTION:

Coronavirus caused an infectious disease by severe acute respiratory syndrome (SARS-COV-2). It is a group of RNA viruses that causes diseases in humans, mammals, and birds[1]. Covid-19'sfirst case was being identified in Wuhan, China, in November 2019 [2,3]. In humans, they cause respiratory tract infections. Covid-19 constituents on the family of coronavirus and subfamily *Coronavirinae*. It is an enveloped or enclosed type virus with a positive-sense single-stranded RNA genome and nucleocapsid of helical symmetry [4]. About 26-32 Kilo bases size of the genome of the coronavirus. In electron micrographs coronavirus structure will be seen as large, club-shaped, or spherical shape structure and spikes present in their structure[4]. Its structure will be seen the same as to solar corona structure. Covid-19 affects people in different ways. Symptoms will be seen in mild to moderate conditions such as Dry cough, tiredness, headache, loss of taste, fever. Loss of speech, loss of movement, Difficulty in breathing, chest pain will be serious symptoms seen in Covid-19[1- 3].

HISTORY of (SARS-COV-19):

In 1965 Firstly Identified Human Corona Virus by the Scientists [5, 6]. The main Symptoms identify the human coronavirus is the Common Cold [6]. Again, New Corona Virus was identified in 2019 in Wuhan, China Market. China is the first country in the world to identify the First patient or Virus Infected patient [5, 6]. The researcher said that it's a big Familiar disease and again Common cold main symptoms present infected patient [5]. Newly identify Coronavirus officially name SARS-CoV-2 (Severe acute respiratory syndrome) by the International Committee on Taxonomy of Virus researcher said novel coronavirus originated in bats [5]. The Main contained identify researcher is the Virus is rapidly transferred from animals to the human body. And the human body to again next human body continuously transforms because this virus is very dangerous, rapidly transform one body into another body. Coronavirus is the fifth Pandemic disease. Shortly Pandemic Information mention in (Table 1). As per WHO on 2020 December 10, Active Case 69.1% and mortality rate 1.57% all over the world.

Table No. 1: History of pandemic disease

Sr.No	Year	Name of Virus
1	1918	SpanishFlu(H1N1)(InfluenzaAVirus)[9]
2	1957	AsianFlu(H2N2)(InfluenzaAvirus)[9]
3	1968	HongKongFlu(H3N3)(InfluenzaAVirus)[7]
4	1976	ZaireEbolavirus(EBOV)
5	2009	PandemicFlu(H1N1)(InfluenzaAVirus)[10]
6	2019	Covid-19(SARS-COV-2)Coronavirus

VACCINES:

1. Pfizer BioNTech Covid 19 vaccine:

Pfizer BioNTech has like Moderna, provide vaccine that uses mRNA to bring about the immune system to identify the coronavirus. Pfizer vaccine needs to store at 70 degrees Celsius. BNT162b2 was 90 % effective against Covid 19 after28days [11,]. The vaccine is injected into human cells to produce the SARS-COV -2 spike protein the immune system's main target against coronavirus.

Mechanism:

This vaccine can be developed by mRNA. The mRNA carries information between different parts of a cell, providing instructions like which protein to make. BNT162b2 uses messenger RNA that report one of the spike protein that dotted the outer surface of SARS-coV-2[15]. Even so, human body cells don't make spike protein, they can still read viral messenger RNA and follow its rules [13,14]. Spike protein generates by dose but only the spike protein and no other parts of the virus[13]. Human body cell has mRNA of genes for the spike protein on the surface of Covid 19. After the mRNA lipids of the synthetic mRNA is a collection of lipids nanoparticles that the instruction a cells membrane to cell [14]. The mRNA gives a message to manufacturing the viral protein. That surface of the cell and restoratives immune system feedback [12]. After this process antigen is formed and T cells are produced [16]. An mRNA

vaccine is relatively new on the scene but has the potential to be safe and more effective than other vaccine types. There is no risk of getting Covid 19 from a vaccine, as the virus is never present in the body [12].

Clinical Trials Status:

Preclinical trial: In the preclinical study, BNT162b2 demonstrated a protective antiviral effect in rhesus macaques, with concomitant high neutralizing antibody titers and a TH-1 based cellular response in rhesus macaques and mice [15]. In a Covid viral infection, macaques that received two control injections were challenged 55 days after the 2nd immunization with very high viral inoculums of approximately, million plaque-forming units of SARS –COV-2, via both nose and lungs routes [15,16].

Phase I: After preclinical trials, the vaccine passes for phases I trial and it will check the efficacy and safety of the trial in the animals so that animals will develop a strong immune system it will help to found out it was suitable for humans being and or not [15].

Phase II-III: The final stage of the vaccine BNT162b2 began in late June and has enrolled 44,543 participants to date, 90 % of who have received a second dose of the vaccine candidate as of December 2020[16]. The phase 2-3 study is an event-driven trial that is planned to enroll up to 40,000 participants between 18 to 85 years of age [13].

2. ZycoV-D Vaccine:

ZycoV-D vaccine is India's second vaccine candidate to start the human trials & developed by the Institute of Zydus Cedila [17, 19]. It consists of the genetic material of SARSCoV-2 proteins that human cells make a SARScoV-2 antigen and will inform to immune response.

Mechanism:

This vaccine can be developed by plasmid DNA Vaccine. It will develop DNA vaccine by viral proteins and it is present on virus [17]. Extract the RNA from the corona Virus and forming a complementary DNA structure by dNTPs (Deoxynucleoside triphosphates). This Complementary DNA structure is the gene in which add the promoter and Poly A. tail group. The promoteris made up of two main regions coding region and noncoding region. The coding region is used for the formation of the gene product, and the Non-coding region is used for the Controlling of transcription of the coding region. The promoter is added to the

gene because the gene works well in a human cell. Also added the poly A. tail group because in the prokaryotic cell the messenger RNA is formed but it does not move in the cell but in the case of eukaryotic cell the messenger RNA is the move from nucleus to the cytoplasm by various enzymes & this enzyme are very harmful. After modifying the gene cut the plasmid by Restriction endonuclease mechanism and inserts the modified gene in Plasmid, which is called a recombinant plasmid. After the formation of one recombinant plasmid makes copies by PCR and formed a vaccine. Inject the vaccine to the human body by needles, gene gun, CO2 Bioinjector, Electroporation. Injecting the vaccine into the human body, the recombinant plasmid enters the human cell and forming the gene product inside, outside the cell. Gene product formed inside the cell it represents as an MHC-I (Intracellular antigen representation) & activates the helper T cell. Gene product formed outside the cell, & engulfs by the antigen-presenting cell it represents as an MHC-II (Extracellular antigen representation) & activate the Cytotoxic T cell. Helper T cell and Cytotoxic T cell forms the memory B cell and memory T cell which can form a strong immune system and fight against coronavirus.

Clinical Trials Status:

Preclinical trial: After developing the vaccine it will be passed for preclinical trials at which will be performed the vaccine trials on animals. The rats, guinea pigs, rabbits, the mouse can participate in trials [20]. For two animals take 28 days for the vaccine trial. This trial will check the efficacy and safety of the vaccine candidate. The result of the trial is the pigs, rabbit animals devolved a strong immune system it will help to induce a high level of neutralizing antibodies in animals, vaccine demonstration for favorable studies also, and it will check the tolerability [17]. **Phase I:** After preclinical trial, the vaccine passes to DCGI for phase I trial on human consists of 1000 volunteers participated for vaccine trial [19,20]. The result for phase I is this vaccine developed the antibodies amount check by antibody titer test in which the person's blood calculates the strength of the immune response [18]. **Phase II and III:** In this phase II 1000 volunteers can be participating and this trial conduct on Nov- Dec 2020 [19].

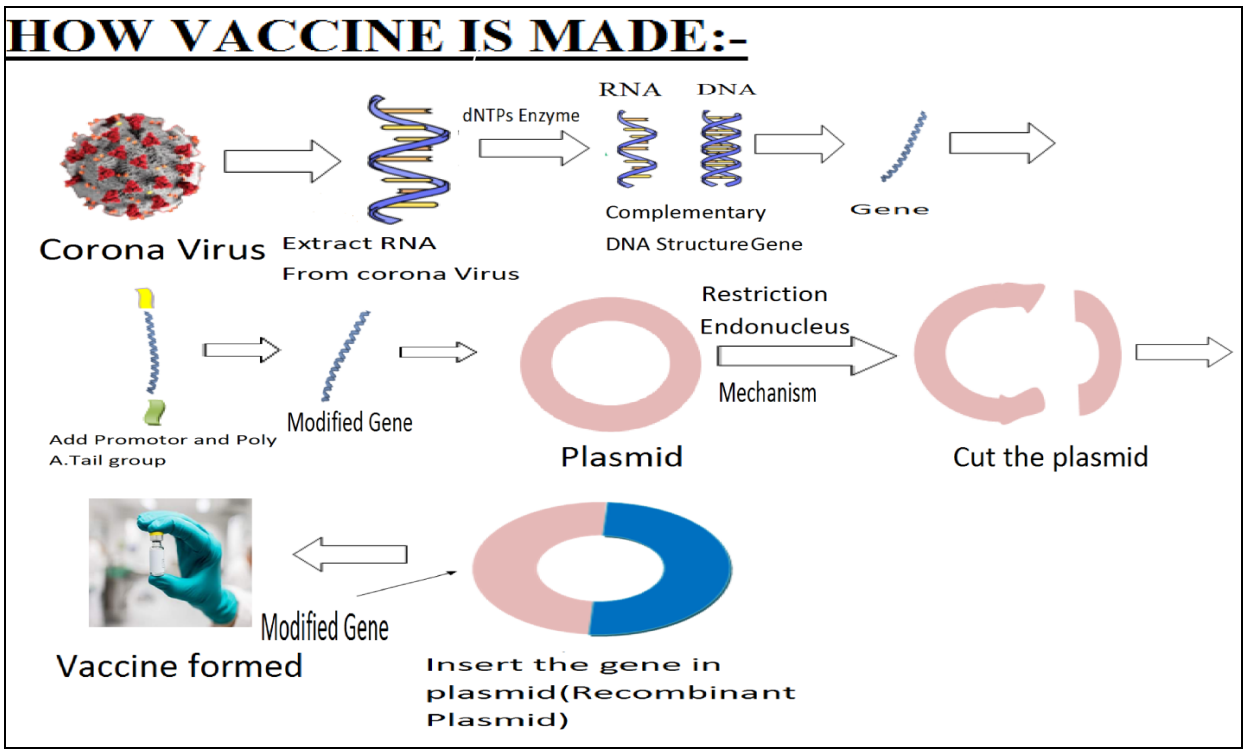

Figure No.1 (a): Development of ZycoV-D vaccine[34].

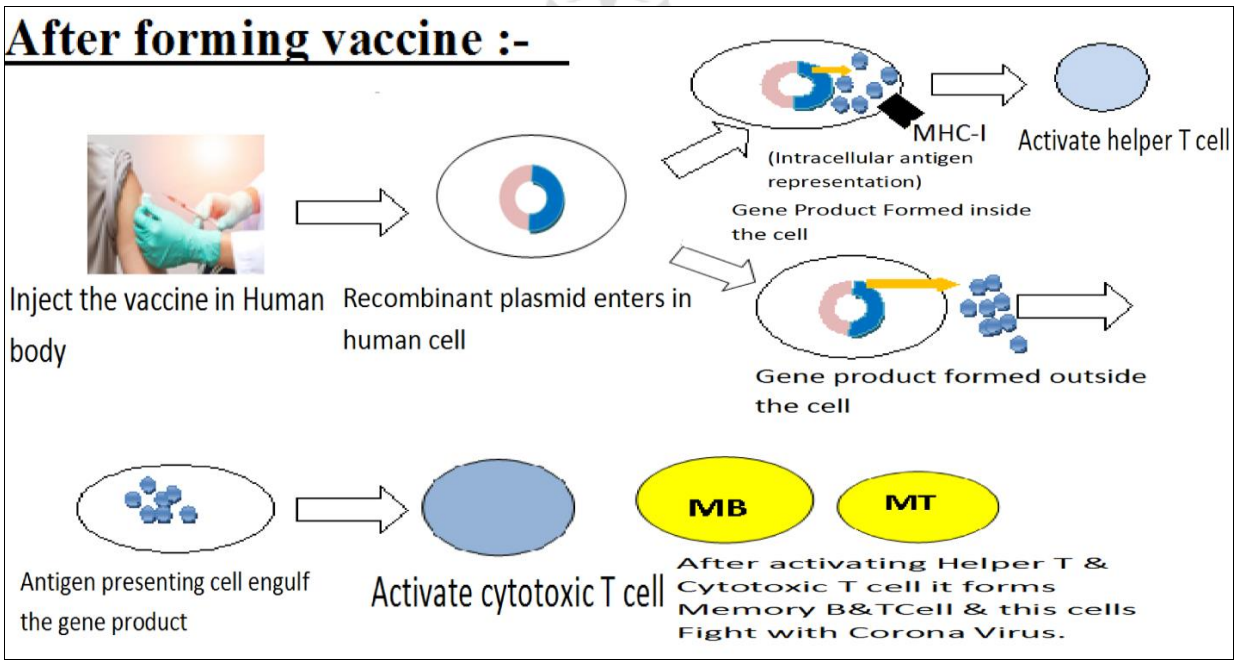

Figure No. 1(b): Formation of T cell for destroying Covid -19 virus[35].

3. SARS Cov2 Vaccine (AZD1222)

AZD1222 vaccine was come about by Oxford University "Jenner Institute and Oxford Vaccine group [21-23].The AZD1222 corona vaccine knows as ChAdox 1n Cov-19 is made

from Chadox1[25] Its Vaccines needs to keep that 2-8°C (For at least 6 months) [21]. The new version of a common cold virus (adenovirus) that causes due to Chimpanzee [21,25].

Mechanisms:

AZD1222 Vaccine works by use viral vector (syndrome) and produced T cells [22,24,25]. After vaccination spike protein is produced in the human body [22]. Immune system attacks on the virus, if it later infects the body protect it against Covid -19 through the body [25].The immune system of healthy volunteers is strong and the body induced a large amount of T-cells [25,26]. AZD1222 vaccine develops by generating immunity power to the body [26]. After get vaccination power generates in the human body they are affected as spike protein gene is purified [22]. Then next step genetic material is added through AZD1222 the body produces spike protein. AZD1222 vaccination produced Antibodies through the healthy volunteer's body [21].

Clinical Trials Status:

Trail phase I/II start in country Southern England on 2020 April 23 [21]. Healthy Volunteers (1077) age group of 18 to 55 years [22,23, 25]. Across the southern centers, the centers AZD1222 vaccine access safety, immunogenicity, and efficacy [25,26]. In the trial 543 participate received the First dose, AZD1222 (and 56 volunteers also received Prophylactic Paracetamol), and the next 534 volunteers received MenAcWY, a comparator meininological conjugate vaccine. 10 Volunteers received two doses of AZD1222 vaccines a part of 1 month [25]. AZD1222 vaccine single dose results are very good and appreciate in volunteers [22,25]. After vaccination produces four-fold antibodies increase to the SARS-CoV-2, then Virus spike proteins in 95% of volunteers one month after applying vaccination AZD1222 [21,25]. Mainly on healthy volunteers researched observed that T-cell response was induced by 14 day and good T-cell response, after 2 months vaccinations [22,23]. Researchers told that no serious effect produced AZD1222 and reactions were less the use of prophylactic paracetamol tablet[25]. And 328 volunteers who received AZD1222 without paracetamol (67%) reported mild to moderate pain after vaccinations and 403 (83%) volunteers reported site tenderness [25]. AZD1222 without paracetamol group added the observed systematic reaction was common in volunteers [21,22]. After vaccinations, 340 (70%) reporting volunteers fatigue and 31 (68%) reported headache after getting AZD1222. Other reaction reported in the group includes muscle aches (60%), malaise (61%) chills (56%), and feeling

feverish (51%) and other are experienced Fever, 18% reported temperatures of at least 38% and 2% reported temperature at least 39 degree Celsius. The systematic reaction was highest on and after vaccination AZD1222. After protective responses through the l/2 phase the next phase automatically approval by FDA [22,24]. II/III phase trial centers UK and Brazil [21,22, 23].

4. Sputnik -V vaccine (Gam-kOVID-Vak)

The Gam-kOVID-Vak Vaccine was developed by Gamaleya Research Institute of Epidemiology and Microbiology [27,29]. 11 Aug 2020 Registered Vaccines COVID -19 By the Russian Ministry of Health[27]. Is the first world country quick approval Sputnik V (Gam-kOVID-Vak) to claim to production COVID-19 Vaccine [27,29]? After a good response, vaccine developer claim that it to be the best vaccine COVID-19 and recently World Health Organization present list and this vaccine (Gam-kOVID-Vak) among top 10 candidate vaccine approaching the end of clinical trial and start a large amount of vaccine production [27].

Mechanism:

Sputnik v (Gam-kOVID-Vak) is based on viral two vector vaccine, the human adenovirus -a - common cold virus - (rAD5 C, rAd26 [27,29]. Steps after vaccination: Sputnik V (Gam-kOVID-Vak) Vaccine binding with the gene that encoding. The spike protein of SARS-CoVID-2 (Novel Corona Virus) stimulates an immune response [27,28,29]. In the vaccine, the recombinant adenovirus type -5 (AD-5) and adenovirus type -26 (Ad26), used as a vector in the vaccine and immunity response [27]. 1st Day vaccination: Vector with gene Coding S proteins of Coronavirus gets into a cell. The body synthesizes S proteins in response to the production of immunity Response [29]. 21st Day vaccination: The vaccine based on another adenovirus vector unknown to the body boosts the immune for long testing immunity[29].

Clinical Trials Status:

Phase l/2 clinical trials of the Russian countries officially registered COVID-19 vaccine Sputnik V [27]. According to the result phase, l/2 vaccines are safe and effective, with strong antibodies and cellular immune responses. After vaccination to healthy volunteers, they observed that T -Cells and immunity boost response [27]. Then also RDIF said that the level of neutralizing antibodies with the vaccine (Gam-COVID-Vak) was 1.4 to 1.5 times higher

compared to those patients who had recovered Form COVID -19 [27,28]. After l/2 clinical trial according to good results by healthy volunteers [29]. RDIF starts the phase 2/3 trial on Belarus, UAE, Venezuela, and other countries, while it is a phase 2/3 in India. According to result phase 2/3 trial Sputnik V 92% effective, show interim trial result [28]. Earlier in this month's Russian said that 40000 volunteers as a part of it are large phase 3 Trials. experience from phases 1and 2[27].

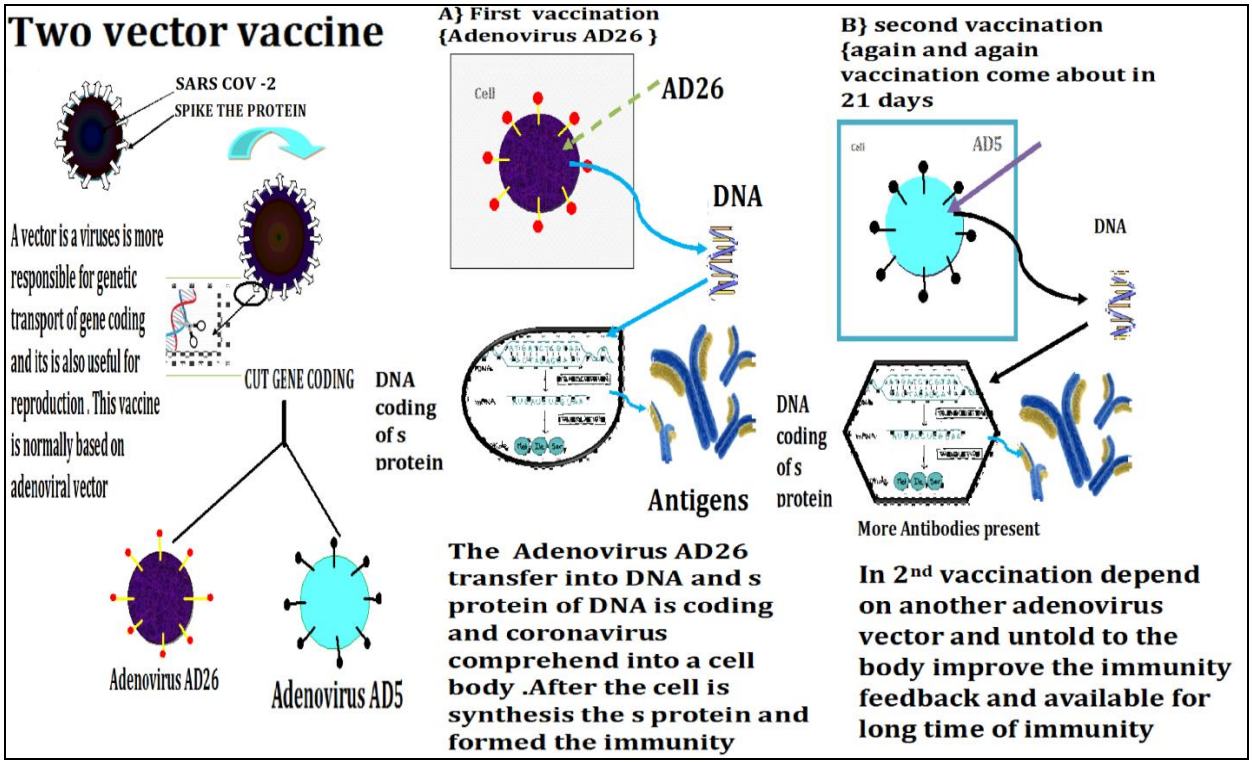

Figure No. 2: Method of developing a vaccine.[29]

5. Covaxin:

Covaxin is India's first Indigenous Covid-19 vaccine and developed by the Bharat Biotech International Limited collaborated with the National Institute of Virology (NIV) [30,32]. Alhydroxiquim-II adjuvant drug used to boost immune response. We use adjuvant that elucidates mechanisms of action inducing greater antibody response to vaccine antigens and protect against pathogens [30]. Also adjuvant will enhance the sustainability ofthe vaccine to provide antigens sparing effect [30]. The reason behind developing the vaccine is to recognize your immunity system and fight with novel coronavirus in our body being at risk of an actual infection[33].

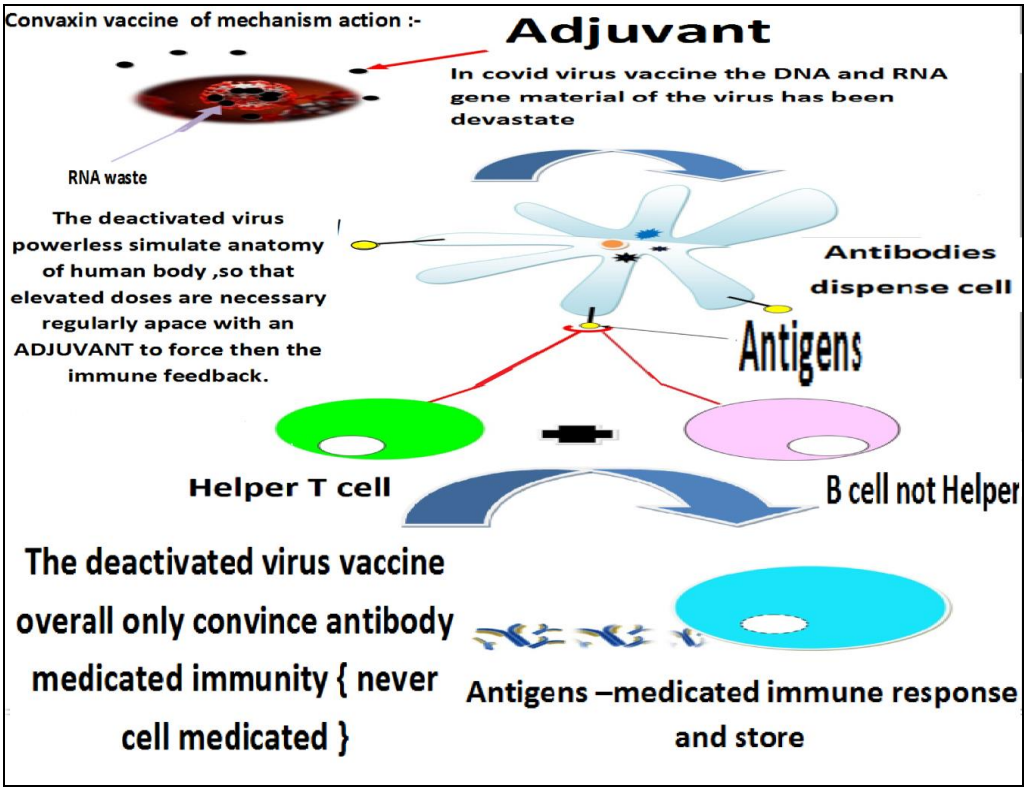

Figure No. 3: formation of antibodies dispenser[33]

Mechanism:

Covaxin is the inactivated vaccine & enhances the antibody response [30,31]. In that vaccine, the dead virus is used & genetic material RNA, DNA present in the virus that has been destroyed. After destroying the genetic material, the vaccine injects into the human cell by injections and there it has no potential to replicate or infect inside the body and needed higher doses [30]. Also, use adjuvant (Alhydroxiquim-II) to strengthen the immune response.

Clinical Trials Status:

Preclinical trial: After producing the vaccine BBIL passes this vaccine to preclinical trial in animals [30].The preclinical trial will be conducted on the animal such as mice, guinea pigs and results to be seen as the news say for years and it boosts the immune response and preventing to any infection or diseases [30].

Phase-I: after the pre-clinical trial CDSCO approving the coaxin for human trial on phase I [30]. This trial conducts a small group of people and the people can be divided into four groups. The first three groups will receive the coaxin vaccine but the fourth group can receive the Japanese encephalitis vaccine that would be previously developed and this fourth group is

called a controller group [33]. The people were divided into four groups because to see the comparable property to other vaccine and the good effects of the coaxin vaccines [33]. Phase-I trial results in it will check the Covaxin is safe for use and the rate of effectiveness of their immunity towards the virus [33].

Phase-II: In phase -II trial around 750 to 800 people participate in this trial and this trial will be conducted the same as in phase-I means conducted in four groups [33]. In the phase-II trial, it will check the Covaxin vaccine's ability to enhance necessary immunity response towards novel coronavirus [33].

Phase-III: after performing the phase-II trial around 26,000 people participate in this trial [32]. Approximately 22 sites such as Delhi, Haryana, and Odisha in the country started Phase-III on 16th November [32].

LISTS OF COVID 19 VACCINES:[13-19]

Table No.2: Brief information of different vaccines and stages of clinical trial

Agents	**Sponsor**	**Mechanisms action**	**Institute**	**Trial phase**	**Country [critical trial]**	**Reference**
Bacillus calmette Guerin [BCG] vaccine	i.university of Melbourne and Murdoch children research institute [austrelia] ii.Radboud university medical center [nethorland] iii.Faustomon Labatt Massachusetts General hospital [America]	Live attenuated vaccine	1.university of Melbourne and Murdoch children research institute [Australia] 2.Radboud university medical center [nethorland] 3.Faustomon Labatt Massachusetts	Phase 2/3	Japan	https://scholar.google.co.in/scholar?q=bacillus+calmette+guerin+vaccine&hl=en&as_sdt=0&as_vis=1&oi=scholart

			General hospital [America]			
India imunologides	Hyderabad headquartered	Use of an innovative codon – deoptimization tech	1.indian immunologidestd [IIL] 2.Griffth university ,Australia	Phase 3	India	https://m.hindustantimes.com/india-news/7-indian-firms-in-race-to-develop-covid-19-vaccine-who-stands-where/story-KKiXGhuhkPTki5ZtM0YshN.html
HGCO19	i.Genova ii.Hdtbioin us, Brazil and South-Africa	mRNA recreate the covid -19 spike protein	Gennova biopharmaceutical –HDT bio	Started clinical trial	USA	https://gennova.bio/mrna-vaccines/
LUNAR – COVID 19 [ARCT-021]	i.ArcturusTheraputics Inc. ii.Duke-NVS	Self-replicating RNA vaccine	Arcturus Therapeutics and DukeNUs medical school	Phase2	Singapore	https://m.economictimes.com/news/international/business/singapore-

						developed-covid-19-vaccine-injected-into-first-group-of-volunteers/articleshow/77524083.cms
LNP-n COVsa RNA	Imperial College of London	Self-amplifying RNA vaccine	Imperial College of London	Phase 2	England	https://go.drugbank.com/drugs/DB15799
bacTRL-spike	Symviva	Monovalent oral vaccine [bifidobacteria]	Symvivo corporation	Phase 1	Canada	https://www.genengnews.com/covid-19-candidates/symvivo-bactrl-spike/
GX-19	Genexine Inc.	DNA Vaccine	Genexine Inc.	Phase2	Korea	https://clinicaltrials.gov/ct2/show/NCT04445389
Adimrsc -2f	Adimmune	Protein subunit vaccine	Adimmune	Phase 1	Taiwanese	https://www.raps.org/news-and-articles/news-articles/20

						20/3/covid-19-vaccine-tracker
Epivac corona	Federal Budgetary Research institution state research center of virology and biotechnology	Peptide vaccine	Federal Budgetary Research institution state research center of virology and biotechnology	Phase 2	Russia	https://www.precisionvaccinations.com/vaccines/epivaccorona-vaccine
Sputnikv	Gamaleya Research institute,acellena contract drug research, and dev	Nonreplicating viral vector	Various institute work on this vaccine	Phase 3	Russia	https://en.m.wikipedia.org/wiki/Gam-COVID-Vac
AG0301 – COVID 19	AnGes, Increse	DNA vaccine	Japan agency for medical research and development	Phase 2	Japan	https://biorender.com/covid-vaccine-tracker/details/v-CV28/-43
INO-4800	Inoviopharmaceutical	DNA vaccine [plasmid]	Center for pharmacetical research,kanvas city, Univeristy of Pennsylvania ,Philadelphia	Phase3	America	https://www.precisionvaccinations.com/vaccines/ino-4800-dna-coronavirus-vaccine

INI - 78436735 [formerly AD26 CoV 2-5]	Johnson and Johnson	Non-replicating viral vector	Johnson and Johnson	Phase 3	America	https://www.precisionvaccinations.com/vaccines/ad26cov2-s-vaccine
mRNA - 1273	Moderna	mRNA based vaccine	Kaiser permanente washington health research instituent	Phase 3	America	https://www.modernatx.com/modernas-work-potential-vaccine-against-covid-19
NOVA VAX [NVX –C0V2373]	Novavax, Takeda	Non partical vaccine	Novavax	Phase 3	America	https://ir.novavax.com/news-releases/news-release-details/novavax-covid-19-vaccine-granted-fast-track-designation-us-fda
BNT 162	i.Biontech SE ii.pfizer iii.shanghaifosun	mRNA based vaccine	Multiple study sites in Europe and north	Phase 3	America	https://www.pfizer.com/news/p

	pharmaceutical Devlopmentco, Ltd		America			ress-release/press-release-detail/pfizer-and-biontech-conclude-phase-3-study-covid-19-vaccine
BBIBP – CorV	Beijing institute of biological products china National pharm. Grp [sinopharm]	Inactivated vaccine	Henan provincial center for disease control and prevention	Phase 3	China	https://www.sciencedirect.com/science/article/pii/S0092867420306954
Ad5-n-cov	cansin biologics	Recombinant vaccine [adenovirus type svedo]	Tongi hospital	Phase 3	*China*	https://www.raps.org/news-and-articles/news-articles/2020/3/covid-19-vaccine-tracker
Corona vac	Sinovac	Inactivated vaccine	Sinovac research and development co,Ltd	Phase 3	China	https://en.m.wikipedia.org/wiki/CoronaVac

AZD1222	The university oxford: Astra Zaneca; IQVIA;- SERUM institute of India	Replication deficient viral vector vaccine	The university of oxford the Jenner institute	Phase 3	India	https://en.m.wikipedia.org/wiki/AZD1222
Hydroxychloroquine	i.University of Oxford ii.University of Minnesota iii.University of Washington iv.Nacionaldecolombia	Antimalerial drug against Covid-19	Various Institute work on this drug	Phase4	India	https://www.medicoverhospitals.in/coronavirus/hydroxychloroquine/
Remedesivir	i.Gilead, world Health org. SOLIDARITY Trial ii. National Institute of Allergy & Infectious disease	Antiviral drug	Various Institute work on this drug	Phase3	South Asia	https://www.medscape.com/answers/2500114-197451/what-is-the-role-of-the-antiviral-drug-remdesivir-in-the-treatment-of-coronavirus-disease-2019-covid-19#qna

IMM101	i.Immodulon Therapeutics Ltd, BioCan Rx ii.Canadian Cancer Society Research Institute (CCSRI)	Marcolide antibiotic theraputic drug	Immodulon Therapeutics Ltd, BioCan Rx	Phase3	U.S,Canada	https://www.ajmc.com/view/drug-that-boosts-immunotherapy-studied-as-tool-to-battle-covid-19-in-patients-with-cancer
Measles,Mumps & Rubella vaccine	i.Kasr El Aini Hospital ii.Louisiana State University Health Sciences Center in New Orleans iii.Parsemus Foundation	Live attenuated vaccine	Louisiana State University Health Sciences Center in New Orleans	Phase3	Egypt, America, Netherland	https://www.webmd.com/lung/news/20200908/could-the-mmr-vaccine-help-prevent-covid-19-new-trial-may-tell
KBP-covid-19	Kentucky Bioprocessing Inc.	Antigen producing vaccine	Kentucky Bioprocessing Inc.	Phase 1/2	U.S., U.K.	https://clinicaltrials.gov/ct2/show/study/NCT044736

						90
Ebastine	Mjanyang central Hospital	Antiviral drug	Mjanyang central Hospital	Phase4	America	https://biorender.com/covid-vaccine-tracker/details/v-0035/rna-mrna-cv07050101
CoVLP	Medicago Inc.	Virus like particle-based vaccine	Medicago Inc.	Phase 2/3	Canada, U.S., America	https://biorender.com/covid-vaccine-tracker/details/v-0035/rna-mrna-cv07050101
INOpulse	BellerophonRegenero pharmaceutical Inc.	INOpulse device based drug	BellerophonRegenero pharmaceutical Inc.	Phase 2	Warren, NS,U.S.	https://www.bioworld.com/keywords/13807-inopulse
RTB101	RestorbioInc., National Institute of Aging	Inhibitory drug	RestorbioInc., National Institute of Aging	Phase 2	California&Boston	https://clinicaltrials.gov/ct2/show/NCT04584710
Sanofi	i.Sanofi	Recombinan	Sanofi	Phase1	French	https://ww

	ii.GSK	t DNA Technology		/2		w.sanofi.com/en/about-us/our-stories/sanofi-s-response-in-the-fight-against-covid-19
Heat biologics	i.Heatbiologics,Inc. (NASDAQ:HTBX) ii.waismanBio manufacturing	Potential of generating long term immune responses	Heat Biologics,Inc.	Phase1	U.S.	https://www.heatbio.com/news-media/news-releases/detail/669/heat-biologics-covid-19-vaccine-demonstrates-robust-t-cell
BNT162B2	i.BioNTech ii.pfizer	m-RNA based vaccine	Various Institute works on this vaccine	After phase3 clinical trial. It is used in an emergency	Germany	https://en.m.wikipedia.org/wiki/BNT162b2

				case		
Nasovax	Altiimmune,Inc.	Replication deficient adenovirus vector vaccine	Altiimmune,Inc.	Phase2	U.S.	https://clinicaltrials.gov/ct2/show/record/NCT04442230
Vaxart	i.SOUTHSANFRANCISCO,Calif. ii.Vaxart,Inc.	Non replicating adenovirus vaccine	NASDAQ:VXRT	Phase1	America	https://www.precisionvaccinations.com/vaccines/vaxart-covid-19-oral-vaccine
Emergent biosolution	i.EmergentBiosolution Inc. ii.National Institute of Allergy &Infectious disease. iii.Biomedical advanced research & Devlopment authority (BARDA)	Plasma based hyperimmune vaccine	Emergent Biosolution Inc.	Phase3	U.S.	https://investors.emergentbiosolutions.com/news-releases/news-release-details/emergent-biosolutions-covid-19-human-immune-globulin-product

FUTURE ASPECT DRUGS FOR COVID-19:

There are some patents, therapeutic drugs, diagnostic agents being developed for the treatment of Covid-19. About 80% of drugs can relative to the development of therapeutic drugs, 28% can relative to diagnostic agents. There are some drugs in research and development for the treatment of Covid-19 (Table 3). There are some patents associated with potential drugs for the treatment of Covid-19 like patent no. WO2009114512 (Incyte Corporation, USA) and JP5971830 (Shionogi and Co, Ltd, Japan).

Table No.3: Antiviral drugs in research and development for the treatment of Covid-19

Sr. No.	Drug name	Possible Mechanism of action on Covid-19	Targeted on	Reference
1.	C-21	An angiostensin AT-2receptor against to alleviate the virus induced lung injury	Target on AT2	https://pubs.acs.org/doi/10.1021/acscentsci.0c00272
2.	Aurine tricarboxylic acid	It is inhibitor that bind to viral RdRp, and tested against SARS-CoV	Target on RNA-dependent RNA polymerase	https://pubmed.ncbi.nlm.nih.gov/10976530/
3.	Benzopurpurin B	It is chemical inhibitor that suppress viral infectivity by inhibiting endoribonuclease NSP15, then testing against SARS-CoV in culture cells.	Target on NSP15 (poly(U)-specific endoribonuclease)	https://m.sigmaaldrich.com/IN/en/product/aldrich/s567620?lang=null&region=null
4.	L-163491	Functionally active as angiotensin AT1 partial antagonist and AT2agonist which alleviate the virus induced lung injury.	Target on AT1&AT2	https://g.co/kgs/YjD75h
5.	Rupintrivir	Cysteine proteases inhibitor that disrupt the function of 3CLpro or PLpro.	Target on viral proteases as 3CLpro and PLpro	https://g.co/kgs/4FF2Wr

CONCLUSION:

The coronavirus (COVID -19) spreads at a clockwise time rate all over the world. The outbreak of the virus has confronted the world's economic medical and public health infrastructure. Currently, there are documented cures for the virus and many countries have been vaccine created and some vaccine 90% more effective. Covid -19 is an RNA virus that poses a threat to public health. Currently, the disease has caused thousands of infections and death. Fundament 100% no confirmed medicine or vaccine has been created to improve the health of patients with the condition.

In acceptance of novel coronaviruses (Covid-19) vaccine very highly (dangerous) by the baseline effectiveness of the Covid-19 vaccine. Prepare and study the general population to acceptance a Covid-19 vaccine with relatively lower effectiveness may be very difficult. Vaccine trials result in bases allowing the candidate vaccine emergency use. Researchers finding out define of Covid-19 is immunological (immunity increase need) correlates of protection against novel coronavirus, which could involve growing characteristics, age groups. The world human cannot be affordable to any mistakes at the crucial juncture of the pandemic.

DECLARATION OF COMPETING INTEREST:

On behalf of all authors, the corresponding author states that there is no conflict of interest.

REFERENCES:

1. Coronavirus. 06/12/2020. In Wikipedia: https://en.wikipedia.org/wiki/Coronavirus
2. COVID-19 pandemic. 09/12/2020. In Wikipedia: https://en.wikipedia.org/wiki/COVID-19_pandemic
3. COVID-19. 07/12/2020. In Wikipedia: https://en.wikipedia.org/wiki/Coronavirus_disease_2019
4. Coronavirus. World Health Organization. 2020. Available from: https://www.who.int/health-topics/coronavirus
5. Bhargav HD, Coronavirus History. WebMD. 15/4/2020. Available from: https://www.webmd.com/lung/coronavirus-history
6. Shawna Williams, A Brief history of Humans coronavirus. TS. O2/6/2020. Available from: https://www.the-scientist.com/news-opinion/a-brief-history-of-human-coronaviruses-67600
7. Hong Kong flu. 07/12/2020. Available from: https://en.m.wikipedia.org/wiki/Hong_Kong_flu
8. 1957-1958 Influenza pandemic. 07/12/2020. Available from: https://en.wikipedia.org/wiki/1957%E2%80%931958_influenza_pandemic.
9. Spanish flu. 11/12/2020. In Wikipedia: https://en.m.wikipedia.org/wiki/Spanish_flu
10. Pandemic influenza, Available from: https://www.cdc.gov/flu/pandemic-resources/index.htm
11. Pfizer and BioNTech conclude phase 3 study COVID -19 vaccine candidate. 18/11/2020. Available from: https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-conclude-phase-3-study-covid-19-vaccine

12. Kevin Dunleavy, Fraiser Kansteiner. COVID-19 tracker: Novavax's raw materials shortage; Moderna's supply hiccup; Thermo Fisher's deal with Pfizer. 26/3/2021. Available from: https://www.fiercepharma.com/pharma/covid-19-tracker-johnson-johnson-aims-to-test-shot-kids-president-trump-talks-firing-fauci
13. Pfizer and BioNTech Announce Data from Preclinical Studies of mRNA-based Vaccine Candidate Against COVID-19. 09/9/2020. Available from: https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-announce-data-preclinical-studies-mrna
14. Coronavirus disease (COVID-19): VACCINE. World Health organization. 28/10/2020. Available from:https://www.googleadservices.com/pagead/aclk?sa=L&ai=DChcSEwi45IHWhKvuAhW9h0s
15. Brittney G. Borowiec, How does Pfizer's "90% effective" COVID-19 vaccine work?. Wilfrid Laurier University. 09/11/2020. Available from:https://massivesci.com/notes/pfizer-covid-vaccine-90-percent-effective-mrna-rna-bnt162b2/
16. Adele peters , How Pfizer and Moderna's COVID-19 vaccines work: mRNA. Coronavirus. 11/09/2020. Available from: https://www.fastcompany.com/90573488/how-pfizers-covid-19-vaccine-works-mrna
17. Zydus Cadila's Covid-19 vaccine enters Phase II testing. Clinical trials. 07/6/2020. Available from: https://www.clinicaltrialsarena.com/news/zydus-covid-vaccine-phaseii/
18. Deepali Sharma ,Zydus Cadila has announced that the phase-I clinical trial of its vaccine candidate ZyCoV-D was over and it has commenced phase-II clinical trials from August. 28/11/2020. Available from: https://www.hindustantimes.com/india- news/pm-modi-reaches-ahmedabad-to-review-coronavirus-vaccine-development-by-zydus-cadila/story-vC4HHM2RroxgtSjOCAZSgK.html
19. Viswanath pilla, Covid Vaccine: Zydus Cadila completes phase-2 trial, to submit data in November. 3/11/2020. Available from: https://www.moneycontrol.com/news/business/companies/covid-vaccine-zydus-cadila-completes-phase-2-trial-to-submit-data-in-november-6058811.html/amp
20. TIMESOFINDIA /Coronavirus Vaccine India: Covaxin, ZyCOV-D move to phase II clinical trials. 08/06/2020. Available from: https://m.timesofindia.com/life-style/health-fitness/health-news/coronavirus-vaccine-india-covaxin-zycov-d-move-to-phase-ii-clinical-trials/amp_articleshow/77367413.cms
21. AZD1222 vaccine met primary efficacy endpoint in preventing COVID-19. 23/11/2020. Available from: https://www.astrazeneca.com/media-centre/press-releases/2020/azd1222hlr.html
22. COVID-19 vaccine AZD1222 is better tolerated in older adults than younger adults with similar immune responses across all age groups. 19/11/2020. Available from: https://www.astrazeneca.com/media-centre/articles/2020/covid-19-vaccine-azd1222-is-better-tolerated-in-older-adults-than-younger-adults-with-similar-immune-responses-across-all-age-groups.html
23. Reynald Castaneda, AstraZeneca's quick Covid-19 vaccine trial restart splits experts. GlobalData Health care.12/10/2020. Available from: https://www.clinicaltrialsarena.com/comment/azd1222-covid-vaccine-trials-astrazeneca//
24. Adrian Kemp, AZD1222 vaccine met primary efficacy endpoint in preventing COVID-19. 23/11/2020. https://www.astrazeneca.com/media-centre/press-releases/2020/azd1222hlr.html
25. Pedro M Folegatti, Katie J Ewer, et. al. Safety and immunogenicity of the ChAdOx1nCoV-19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2, single-blind, randomized controlled trial. The Lancet journal. 15/08/2020. Volume 396, Issue 10249, P467-478. Available from: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31604-4/fulltext
26. Roadmap for evaluation of AstraZeneca AZD1222 Vaccine against Covid-19. World Health Organization. 30/10/2020. Available from: https://www.who.int/publications/m/item/roadmap-for-evaluation-of-astrazeneca-azd1222-vaccine-against-covid-19
27. Sputnik –v COVID -19 Vaccine. 13/3/2020. In Wikipedia: https://en.m.wikipedia.org/wiki/Gam-COVID-Vac
28. Dr. Reddy's India Trials for Russian's Sputnik-v vaccine could start in next few weeks executive. 22/09/2020. Available from: https://health.economictimes.indiatimes.com/amp/news/pharma/india-trials-for-russias-sputnik-v-vaccine-could-start-in-next-few-weeks%20executive/78256078#aoh=16073247033169&csi=1&referrer=https%3A%2F%2Fwww.google.com&amp_tf=From%20%251%24

29. Jacob koshy, The Hindu Explains | what do we know about Russia's COVID-19 vaccine candidate Sputnik V? 22/7/2020. Available from:https://www.thehindu.com/sci-tech/health/the-hindu-explains-what-do-we-know-about-russias-covid-19-vaccine-candidate-sputnik-v/article32651231.ece
30. Varinder Bhatia, Chandigarh. Anil Vij tests positive, days after taking trial Covid-19 vaccine shot, Indian express News. 06/12/2020. Available from:https://indianexpress.com/article/india/anil-vij-tests-covid-fortnight-after-getting-covaxin-vaccine-shot-7092625/
31. Anil Vij on Covid-19 vaccine: Got only 1st shot of Covaxin, antibodies develop after 2nd dose. 06/12/2020. Available from: https://www.livemint.com/news/india/anil-vij-on-covaxin-got-only-1st-shot-of-coronavirus-vaccine-antibodies-develop-after-2nd-dose-11607226928844.html
32. Coronavirus vaccine in India: List of states that have started phase 3 trials of Covaxin. 02/12/2020. Available from: https://www.livemint.com/news/india/coronavirus-vaccine-in-india-these-states-have-started-phase-3-trials-of-bharat-biotech-covaxin-11606908773897.html
33. Coronavirus Outbreak, Coronavirus vaccine update: 2 vaccines could be eligible for emergency use in India by Jan, says AIIMS chief. 5/12/2020. Available from: :https://www.indiatoday.in/coronavirus-outbreak/story/coronavirus-vaccine-update-2-vaccines-could-be-eligible-emergency-use-india-january-2021-aiims-chief-1746848-2020-12-05.
34. TIMEOFINDIA, Coronavirus India vaccine: Zydus developed ZyCov-D initiates phase I and II clinical trials; first Indian vaccine to do so.06/16/2020. Available from: https://m.timesofindia.com/life-style/health-fitness/health-news/coronavirus-vaccine-india-zydus-developed-zycov-d-initiates-phase-i-and-ii-clinical-trials-first-indian-vaccine-to-do-so/amp_articleshow/76996248.cms
35. How are vaccine developed, world health organization. 12/08/2020. Available from: https://www.who.int/news-room/feature-stories/detail/how-are-vaccines-developed