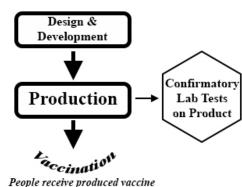


## Update: COVID-19 Vaccine Candidates and Abortion-Derived Cell Lines

Accurate information about the development and production of COVID-19 vaccines is essential, especially because many proposed candidates use newer molecular technologies for production of a viral vaccine. One concern regarding the ethical assessment of viral vaccine candidates is the potential use of abortion-derived cell lines in the development, production or testing of a vaccine. This analysis utilizes data from the primary scientific literature when available, along with data from clinical trial documents, reputable vaccine tracking websites, and published commercial information.<sup>1</sup> It is the hope that by providing accurate data, recipients can make well-informed decisions regarding vaccine choices.

For additional background and guidance, please see:

- \* A Visual Aid to Viral Infection and Vaccine Production for a visual primer on the various strategies for viral vaccine production.
- \* COVID-19 Vaccines & Fetal Cell Lines for an infographic description of how fetal cell lines are sometimes used to produce vaccines.
- \* Chart of Operation Warp Speed Vaccines streamlined view of the leading vaccine candidates.



## Flow Chart for Creation and Testing of Vaccines

<u>Design & Development</u>: conceptualization, preparatory experiments, and specification for how vaccine will be constructed and produced.

Production: process used to manufacture final vaccine to be given to people.

<u>Confirmatory Lab Tests on Product</u>: tests to analyze quality, nucleic acid or protein sequence, protein confirmation, antibody reactivity, etc. of final vaccine product.

Vaccination: giving final produced vaccine to people.

Analysis of SARS-CoV-2 (COVID-19) Vaccine Candidates Last Updated 3 December 2020					DOES USE	USE abortion-derived ce abortion-derived cell lin DO NOT use abortion-d	e
					•	ndetermined	, 
Sponsor(s) <sup>1</sup>	Country	Strategy <sup>2</sup>	Clinical Trial Status <sup>3</sup>	Public Funding⁴	Design & Development	Production	Confirm- atory Lab Tests
WHOLE VIRUS VACCINI	E – LIVE A'	<b>FTENUATED or INACT</b>	IVATED				
Beijing Institute of Biological Products/ Sinopharm	China	Inactivated virus "BBIBP-CorV" Given: Intramuscular	Phase 3 Phase 3		Vero monkey cells	Vero monkey cells	Cytopathic test

			<u>Phase 1/2</u>	Wang <i>et al., Cell</i> <u>182, P713,</u> <u>6Aug2020</u>	<u>Wang et al., Cell</u> <u>182, P713,</u> <u>6Aug2020</u>	Vero monkey cells <u>Wang et al.</u> , <u>Cell 182</u> , <u>P713</u> ,
Wuhan Institute of Biological Products/ Sinopharm	China	Inactivated virus "New Crown COVID-19" Given: Intramuscular	<u>Phase 3</u> <u>Phase 1/2</u>	Vero monkey cells <u>Xia <i>et al., JAMA</i> 324, 951, 13Aug2020</u>	Vero monkey cells <u>Xia <i>et al., JAMA</i> 324, 951, 13Aug2020</u>	6Aug2020 Plaque reduction neutralization test Vero monkey cells Xia et al., JAMA 324, 951, 13Aug2020
Bharat Biotech/Indian Council of Medical Research	India	Inactivated virus "BBV152" Given: Intramuscular	Phase 3 Phase 1/2 Phase 1/2 Phase 1/2	Vero monkey cells <u>Yadav et al.,</u> <u>ResearchSquare</u> <u>10Sept2020</u>	Vero monkey cells Yadav et al., <u>ResearchSquare</u> <u>10Sept2020</u>	Antibody ELISA Plaque reduction Vero monkey cells <u>Yadav et al.</u> , <u>ResearchSquar</u> e 10Sept2020
John Paul II Medical Research Institute	USA	Live attenuated virus	Pre-clinical	Ethical cell lines as a matter of policy	Perinatal human cells (term umbilical cord and placental)	•••••••••••••••••••••••••••••••••••••••
Sinovac Biotech Co., Ltd.	China	Inactivated virus "PiCoVacc" Given: Intramuscular	Phase 3 Phase 3 Phase 1/2 Phase 1/2 Phase 1/2	Vero monkey cells	Vero monkey cells Gao et al., Science 369, 77, 3July2020	protein test HEK293 cells Supplement Gao et al., Science 369, 77, 3July2020
Valneva and Dynavax	France USA UK	Inactivated Virus "VLA2001" plus adjuvant CpG1018 Given: Intramuscular	Pre-clinical	Vero monkey cells	Vero monkey cells Same platform as <u>IXIARO, Valneva</u> press release, <u>22April2020</u>	Ø
VIRAL VECTOR-BASED	VACCINE					

Altimmune	USA	Replication-deficient Adenovirus vector	Pre-clinical		•		
		"Adenovirus vector "AdCOVID" Given: Intranasal			PER.C6 cells	PER.C6 cells Same platform as NasoVAX	
						NasoVAX uses <u>PER.C6</u> Licensed PER.C6 from Janssen	
AstraZeneca	USA	Replication-deficient	Phase 3	Operation Warp			
University of Oxford	UK	Adenovirus vector	Phase 3	Speed	HEK293 cells	HEK293 cells	•
		"AZD1222"	Phase 3	HHS-BARDA		van Doremalen et	
		"ChAdOX1nCoV-19" Given: Intramuscular	Phase 2/3 Phase 2/3	\$1.2 Billion		al., Nature preprint, 30July2020	
		Given: Intramuscular	Phase 2/3 Phase 1/2	CEPI up to		<u>5054192020</u>	
			Phase 1/2	\$384 Million			
CanSino Biologics, Inc.	China	Replication-deficient	Phase 3				
Beijing Institute of		Adenovirus vector	Phase 3		HEK293 cells	HEK293 cells	
Biotechnology, Academy of		"Ad5-nCoV"	Phase 2		HER293 cells	Biospace,	
Military Medical Sciences,		Given: Intramuscular	Phase 2			<u>12May2020</u>	
PLA of China			Phase 2				
			Phase 1 Phase 1				
Gamaleya Research Institute	Russia	Replication-deficient	Phase 3				
	itassia	Adenovirus vectors	Early				-
		(rAd26-S+rAd5-S)	approval in		HEK293 cells	HEK293 cells	
		"Sputnik V"	Russia				
		Given: Intramuscular	August 2020				
			<b>Phase 1/2</b>				
			Phase 1/2		•	•	
ImmunityBio and NantKwest	USA	Replication-deficient	Phase 1				$\bullet$
		Adenovirus vector recombinant			E.C7 cells	E.C7 cells	Protein and
		"hAd5 S-Fusion + N-			(derivative of	(derivative of	antibody tests HEK293T
		ETSD"			HEK293 cells) Rice et al., bioRxiv	HEK293 cells) Rice et al., bioRxiv	cells
		Given: Subcutaneous			<u>30July2020</u>	<u>30July2020</u>	Rice et al.,
							<u>bioRxiv</u> <u>30July2020</u>
							<u>Seiling et al.,</u> <u>medRxiv</u>
							<u>6Nov2020</u>



Institut Pasteur and Themis and	USA	Replication-competent	Phase 1	CEPI up to \$4.9	0		P
Merck	France	recombinant measles virus "TMV-083" Given: Intramuscular		Million	•	Vero monkey cells	U
Israel Institute for Biological Research (IIBR)	Israel	Replication-competent recombinant vesicular stomatitis virus (VSVΔG) "IIBR-100" Given: Intramuscular	Phase 1		BHK hamster cells Vero monkey cells <u>Yahalom-Ronen <i>et</i></u> <u>al., bioRxiv</u> <u>19June2020</u>	Vero monkey cells <u>Yahalom-Ronen <i>et</i></u> <u>al., bioRxiv</u> <u>19June2020</u>	Plaque reduction; immunofluore: cence Vero monkey cells <u>Yahalom- Ronen et al.,</u> <u>bioRxiv</u> 19June2020
Janssen Research & Development, Inc. Johnson & Johnson	USA	Replication-deficient Adenovirus vector "Ad26.COV2-S" Given: Intramuscular	Phase 3 Phase 1/2	Operation Warp Speed HHS-BARDA \$1,457,887,081 total	PER.C6 cells	PER.C6 cells <u>Tostanoski et al.,</u> <u>Nature Medicine,</u> <u>3Sept2020;</u> <u>Mercado et al.,</u> <u>Nature 30July2020</u> <u>J&amp;J, 30March2020;</u> <u>Janssen Vaccine</u> <u>Technologies</u>	•
Merck and IAVI	USA	Replication-competent recombinant vesicular stomatitis virus (VSV∆G) "V590" Given: Intramuscular	Phase 1	Operation Warp Speed HHS-BARDA \$38,033,570	Vero monkey cells	Vero monkey cells <u>Use rVSV Ervebo</u> <u>platform</u> <u>Ervebo uses Vero</u> <u>cell culture-11</u> Description	P
Shenzhen Geno-immune Medical Institute	China	Lentivirus minigenes + Adult human APC (antigen-presenting cells)	Phase 1		¢		P
Shenzhen Geno-immune Medical Institute	China	Lentivirus minigenes + Adult human CD/T cells (dendritic cells and T cells) "LV-SMENP-DC"	<u>Phase 1/2</u>		œ		0
Vaxart	USA	Replication-deficient Adenovirus vector "VXA-CoV2-1"	Phase 1		HEK293 cells	HEK293 cells	•

INSTITUTE		plus dsRNA adjuvant Given: Oral				<u>Moore et al.,</u> <u>bioRxiv 6Sept2020</u>	
PROTEIN-BASED VACCI	NE						
Anhui Zhifei Longcom Biopharmaceutical/Institute of Microbiology, Chinese Academy of Sciences	China	Protein vaccine Recombinant RBD dimer plus adjuvant Given: Intramuscular	Phase 2 Phase 1/2 Phase 1		HEK293T cells Dai et al., Cell 6Aug2020	CHO hamster cells <u>Dai et al., Cell</u> <u>6Aug2020</u>	Pseudovirus HEK293T cells Dai et al., Cell
Clover Biopharmaceuticals, Inc.	China	Protein vaccine "SCB-2019" plus adjuvant CpG 1018 Given: Intramuscular	Phase 1	CEPI up to \$69.5 Million	cDNA in expression vector; transfect CHO hamster cells <u>Liang et al.</u> <u>bioRxiv</u> , <u>24Sept2020</u> <u>Trimer-Tag system;</u> <u>Liu et al., Scientific</u> <u>Reports 2017</u>	CHO hamster cells Liang et al., bioRxiv, 24Sept2020	6Aug2020 Pseudovirus HEK293 cells Ref'd: Nie et al., Emerging <u>Microbes &amp;</u> <u>Infections</u> 24Mar2020 Cytopathic effect Vero monkey cells Liang et al., <u>bioRxiv</u> , 24Sept2020
Federal Budgetary Research Institution State Research Center of Virology and Biotechnology "Vektor"	Russia	Protein vaccine "EpiVacCorona" chemically synthesized peptide antigens of SARS-CoV-2, conjugated to a carrier protein adsorbed on an aluminum-containing adjuvant Given: Intramuscular	Early approval in Russia Oct 2020 <u>Phase 1</u> <u>Phase 1</u>		•	chemically synthesized peptide antigens	
John Paul II Medical Research Institute	USA	Recombinant Protein Perinatal human cells (term umbilical cord and placental)	Pre-clinical		Ethical cell lines as a matter of policy	Perinatal human cells (term umbilical cord and placental)	ß
Kentucky BioProcessing, Inc. (British American Tobacco)	USA	Protein vaccine "KBP-201" Plant-expressed RBD Given: Intramuscular	Phase 1/2		Recombinant DNA sequence for RBD of SARS-CoV-2	Plant expression of RBD peptide	•



Medicago	Canada	Protein on Virus-Like Particle "CoVLP" Plant-expressed spike protein particle with adjuvant, CpG1018 or	Phase 1		Recombinant DNA sequence in <i>Agrobacterium</i> , transformation of plant cells	Plant expression of protein and VLP <u>Ward et al., medRxiv</u> <u>6Nov2020</u>	Pseudovirus HEK293 cells <u>Ward et al.,</u> <u>medRxiv</u> <u>6Nov2020</u>
Novavax	USA	AS03 Given: Intramuscular Protein vaccine "NVX-CoV2373" Baculovirus expression plus Matrix M adjuvant Given: Intramuscular	Phase 3 Phase 2 Phase 1	<i>Operation Warp</i> <i>Speed</i> HHS-BARDA \$1,600,434,523 CEPI up to \$388 Million		Sf9 insect cells Bangaru <i>et al.</i> , <i>bioRxiv</i> preprint, <u>6Aug2020</u> ; <u>Graphical view</u>	Pseudovirus HEK293 cells <u>Bangaru <i>et al.</i>,</u> <u>bioRxiv</u> preprint, <u>6Aug2020</u>
Sanofi and GSK Protein Sciences	USA France	Protein vaccine Baculovirus expression plus AS03 adjuvant Given: Intramuscular	Phase 1/2	<i>Operation Warp</i> <i>Speed</i> HHS-BARDA \$2,072,775,336 total		Sf9 insect cells <u>Baculovirus</u> <u>expressed</u> recombinant protein ;	Ø
Sorrento	USA	Protein vaccine "T-VIVA-19" SARS-Cov-2 spike protein S1 domain fused with human IgG-Fc Given: Intramuscular	Pre-clinical		DNA fragment developed in lab <u>Herrmann <i>et al.</i>, <i>bioRxiv</i> preprint, <u>30June2020</u></u>	CHO cells Herrmann <i>et al.,</i> <u>bioRxiv preprint,</u> <u>30June2020</u>	Antibody ELISA; Neutralization assays Vero monkey cells <u>Herrmann et</u> <u>al., bioRxiv</u> <u>preprint</u> , 30June2020
Sorrento	USA	Protein vaccine "STI-6991" SARS-Cov-2 spike protein expressed on K562 cells	Pre-clinical		œ	K562 cells <u>Concept</u> : Ji <i>et al</i> <u>Medicine in Drug</u> <u>Discovery</u> <u>March2020</u>	? <u></u> ?
University of Pittsburgh	USA	Protein vaccine Adenovirus-expressed recombinant proteins "PittCoVacc"	Pre-clinical		HEK293 cells	HEK293 cells Kim et al., EBioMedicine, 2April2020	•

INSTITUTE							
		Given: Microneedle arrays					
University of Queensland and CSL Ltd.	Australia	Protein vaccine "V451" Recombinant protein with proprietary molecular clamp Given: Intramuscular	<u>Phase 1</u> <u>Phase 1</u> <u>Phase 1</u>	CEPI up to \$4.5 Million		expiCHO hamster cells	P
RNA VACCINE							
Arcturus Therapeutics	USA	mRNA vaccine self-transcribing, replicating "LUNAR-CoV19" ("ARCT-021") <i>in vitro</i> transcription reaction with T7 RNA polymerase from STARR plasmid template LUNAR proprietary lipid nanoparticle encapsulated Given: Intramuscular	<u>Phase 1/2</u>		Sequence designed on computer	No cells used <u>de Alwis <i>et al.</i></u> <u>bioRxiv 3Sept2020</u>	protein test HEK293 de Alwis et al., bioRxiv 3Sept2020
CureVac	Germany	mRNA vaccine non-replicating "CVnCoV" <i>in vitro</i> transcription lipid nanoparticle encapsulated Given: Intramuscular	Phase 2 Phase 1	CEPI up to \$15.3 Million	Sequence designed on computer	No cells used Rauch et al., bioRxiv 23Oct2020	Protein test Reticulocyte Iysate, HeLa cells <u>Rauch et al.,</u> <u>bioRxiv</u> 23Oct2020
Moderna, Inc. with National Institutes of Health	USA	mRNA vaccine non-replicating "mRNA-1273" T7 RNA polymerase- mediated transcription from DNA plasmid template LNP (lipid nanoparticle) encapsulated Given: Intramuscular	FDA Emergency Use Authorization Requested Phase 3 Phase 2 Phase 1	<i>Operation Warp</i> <i>Speed</i> HHS-BARDA \$2,479,894,979 total CEPI up to \$1 Million	Sequence designed on computer	No cells used <u>Corbett <i>et al.</i></u> <i>Nature</i> , <u>5Aug2020</u>	protein test & pseudovirus HEK293 cells <u>Corbett <i>et al.</i>,</u> <u>Nature</u> , <u>5Aug2020</u>

	TICA		ED4				
Pfizer and BioNTech	USA Germany	mRNA vaccine non-replicating "BNT- 162a1,b1,b2,b3,c2" nucleoside-modified mRNA <i>in vitro</i> transcribed by T7 polymerase from a plasmid DNA template LNP (lipid nanoparticle) encapsulated Given: Intramuscular	FDA Emergency Use Authorization Requested UK EUA granted Phase 2/3 Phase 1/2 Phase 1/2 Phase 1 Phase 1	Operation Warp Speed HHS-BARDA \$1.95 Billion	Sequence designed on computer	No cells used <u>Vogel et al., bioRxiv</u> <u>8Sept2020</u>	protein test & pseudovirus HEK293 cells <u>Vogel et al.,</u> <u>bioRxiv</u> <u>8Sept2020</u>
Sanofi Pasteur and Translate Bio	USA France	mRNA vaccine non-replicating "MRT5500" synthesized by in vitro transcription employing RNA polymerase with a plasmid DNA template LNP (lipid nanoparticle) encapsulated Given: Intramuscular	Pre-clinical		Sequence designed on computer	No cells used <u>Kalnin <i>et al.</i>,</u> <u>bioRxiv 14Oct2020</u> <u>mRNA production</u> <u>in the lab</u> ; <u>Translate Bio</u> <u>scientific platform</u>	protein test & pseudovirus HEK293 cells Kalnin <i>et al.</i> , <i>bioRxiv</i> <u>14Oct2020</u>
DNA VACCINE Genexine	Korea	DNA vaccine	Phase 1/2				•
		"GX-19" DNA synthesized in vitro, placed in plasmid vector Given: Intramuscular and Electroporation			Sequence designed on computer	No cells used <u>Seo et al., bioRxiv</u> <u>10Oct2020</u>	•
Inovio Pharmaceuticals	USA	DNA vaccine "INO-4800" DNA synthesized in vitro, placed in plasmid vector Given: Intradermal Electroporation	<u>Phase 1/2</u> <u>Phase 1</u>	Operation Warp Speed CEPI up to \$22.5 Million	Sequence designed on computer	No cells used Smith <i>et al., Nature</i> 20May2020	protein test & pseudovirus HEK293 cells Smith <i>et al.</i> , <i>Nature</i> 20May2020
Symvivo Corporation	Canada	DNA vaccine Genetically engineered <i>Bifidobacterium longum</i>	Phase 1		P	No cells used	¢



"bacTRL-spike" Given: Oral, bacteria bind			
to gut lining			

1. Data accumulated from primary literature as referenced in the Chart; <u>AND</u> "COVID-19 Treatment and Vaccine Tracker," Milken Institute, <u>https://covid-19tracker.milkeninstitute.org/</u>; <u>AND</u> "Draft landscape of COVID-19 candidate vaccines," World Health Organization (WHO), <u>https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines</u>

NOTE that patents are <u>not</u> considered because they are unreliable sources; even the most relevant patents are prospective documents that provide examples of potential use, but do not provide information about actual, current application of an invention or technology.

2. Prentice, DA and Sander Lee, T. June 15, 2020. A Visual Aid to Viral Infection and Vaccine Production. *On Science Series 1. Accessed 19 June 2020* at: <a href="https://lozierinstitute.org/a-visual-aid-to-viral-infection-and-vaccine-production/">https://lozierinstitute.org/a-visual-aid-to-viral-infection-and-vaccine-production/</a>

3. Phases of Clinical Trials: Pre-clinical- laboratory and animal studies; Phase I- 10-100 people, study safety and dosage; Phase II- tens to hundreds of people, study efficacy, dosage, side effects; Phase III- hundreds to thousands of people, study efficacy and adverse reactions.

4. HHS-BARDA = U.S. Health and Human Services-Biomedical Advanced Research and Development Authority; CEPI = Coalition of Epidemic Preparedness Innovations; BARDA's rapidly-expanding COVID-19 medical countermeasure portfolio. *Accessed 29 Sept 2020* at

https://www.medicalcountermeasures.gov/app/barda/coronavirus/COVID19.aspx; CEPI's COVID-19 Vaccine Portfolio, Accessed 29 Sept 2020 at https://cepi.net/COVAX/