IN THE SUPREME COURT OF INDIA

CIVIL ORIGINAL JURISDICTION

WRIT PETITION (CIVIL) NO. OF 2021

(PIL UNDER ART. 32 OF THE CONSTITUTION OF INDIA)

IN THE MATTER OF:

Dr. Ridhi Arora & Others ...PETITIONERS

Versus

Union of India ...RESPONDENT

WITH

I.A. No. 169056 **of 2021**	Application for permission to file lengthy synopsis and list of dates
I.A. No. 169057 **of 2021**	Application for Exemption from filing duly affirmed copy of the Affidavit

[VOLUME-I Page No: A - 264]

PAPER BOOK

(FOR INDEX PLEASE SEE INSIDE)

Filed on: 30.10.2021

ADVOCATE FOR THE PETITIONER: SATYA MITRA

MASTER INDEX

Sl.No.	Particulars	Page No. of Part to which it belongs	Remarks	
		Part I	Part II	
(i)	(ii)	(iii)	(iv)	(v)
1.	Listing Performa	A-A1		
2.	Cover Page of Paper Book		A2	
3.	Index of Record of Proceeding		A3	
4.	Defect List		A4	
5.	Note Sheet		A5	
6.	Synopsis and List of Dates and Events	B - FF		
7.	Writ Petition under Article 32 of Constitution of India along with supporting Affidavit	1-67		
8.	**Annexure P-1** True Copy of Operational Guidance for COVID-19 Vaccination of Pregnant Women dated 02.07.2021	68-80		

9.	**Annexure P-2** True Copy of Relevant pages of Clinical Trial Details of BBV152 (Covaxin), Gam-COVID-Vac (Sputnik V) and ChAdOx1nCoV-19 (Covishield)	81-86		
10.	**Annexure P-3** True copy of the typed factsheet of Covaxin	87-89		
11.	**Annexure P-4** True copy of the Summary of Product Characteristic of Covaxin	90-97		
12.	**Annexure P-5** True copy of the typed Product Insert of Covishield	98-109		
13.	**Annexure P-6** True copy of the typed Fact Sheet of Sputnik V	110-116		
14.	**Annexure P-7** True Copy of Sputnik V Summary of Product Characteristics	117-125		
15.	**Annexure P-8** True copy of RTI CDSCO/R/T/21/00670 dated 27.07.2021	126-127		
16.	**Annexure P-9**			

	True Copy of the FAQ downloaded from MOHFW website	128-132		
17.	**Annexure P-10** True typed copy of relevant extracts from Elsevier Peer Reviewed Study	133-154		
18.	**Annexure P-11** True Copy of Testimonial of Dr. Michael Yeadon	155-162		
19.	**Annexure P-12** True Copy of the Petition of concern filed by Wolfgang Wodarg and Dr. Michael Yeadon with the European Medicines Agency	163-205		
20.	**Annexure P-13** True Copy of relevant portions of Op-Ed by Steve Kirsch	206-213		
21.	**Annexure P-14** True Copy of Dr. Byram Bridle's Article in London Times	214-215		
22.	**Annexure P-15** True copy of the letter dated 19.06.2021 by Dr. Robert Malone	216-217		
23.	**Annexure P-16** True Copy of Article published in Global Research	218-221		

24.	**Annexure P-17** True copy of the Syncytin Study	222-235		
25.	**Annexure P-18** True Copy of the Report by 57 leading experts on Covid-19 vaccine	236-247		
26.	**Annexure P-19** True Copy of news report of the petition by medical experts	248-253		
27.	**Annexure P-20** True Copy of Paper on Precautionary Principle by Judy Wilyman dated 28.11.2020	254-264		
28.	**Annexure P-21** True Copy of Grant Report on Adverse Event Reporting System	265-271		
29.	**Annexure P-22** True Copy of compilation of news reports of deaths after Covid vaccination	272-567		
30.	**Annexure P-23** True Copy of Report of Deaths reported to CDC	568-577		
31.	**Annexure P-24** True Copy of letter by Indian Doctors for Truth	578-621		
32.	**I.A. No. _____ of 2021** Application for permission to file lengthy synopsis and list of dates	622-623		
33.	**I.A. No. _____ of 2021**			

	Application for Exemption from filing duly affirmed copy of the Affidavit.	624-625		
34.	F/M		626	
35.	VAKALATNAMA		627	
36.	MEMO OF APPEARANCE		627	

VOLUME-I INDEX

Sl.No.	Particulars	Page No. of Part to which it belongs	Remarks	
		Part I	Part II	
(i)	(ii)	(iii)	(iv)	(v)
1.	Listing Performa	A-A1		
2.	Cover Page of Paper Book		A2	
3.	Index of Record of Proceeding		A3	
4.	Defect List		A4	
5.	Note Sheet		A5	
6.	Synopsis and List of Dates and Events	B - FF		
7.	Writ Petition under Article 32 of Constitution of India along with supporting Affidavit	1-67		
8.	**Annexure P-1** True Copy of Operational Guidance for COVID-19 Vaccination of Pregnant Women dated 02.07.2021	68-80		

9.	**Annexure P-2** True Copy of Relevant pages of Clinical Trial Details of BBV152 (Covaxin), Gam-COVID-Vac (Sputnik V) and ChAdOx1nCoV-19 (Covishield)	81-86		
10.	**Annexure P-3** True copy of the typed factsheet of Covaxin	87-89		
11.	**Annexure P-4** True copy of the Summary of Product Characteristic of Covaxin	90-97		
12.	**Annexure P-5** True copy of the typed Product Insert of Covishield	98-109		
13.	**Annexure P-6** True copy of the typed Fact Sheet of Sputnik V	110-116		
14.	**Annexure P-7** True Copy of Sputnik V Summary of Product Characteristics	117-125		
15.	**Annexure P-8** True copy of RTI CDSCO/R/T/21/00670 dated 27.07.2021	126-127		
16.	**Annexure P-9**			

	True Copy of the FAQ downloaded from MOHFW website	128-132		
17.	**Annexure P-10** True typed copy of relevant extracts from Elsevier Peer Reviewed Study	133-154		
18.	**Annexure P-11** True Copy of Testimonial of Dr. Michael Yeadon	155-162		
19.	**Annexure P-12** True Copy of the Petition of concern filed by Wolfgang Wodarg and Dr. Michael Yeadon with the European Medicines Agency	163-205		
20.	**Annexure P-13** True Copy of relevant portions of Op-Ed by Steve Kirsch	206-213		
21.	**Annexure P-14** True Copy of Dr. Byram Bridle's Article in London Times	214-215		
22.	**Annexure P-15** True copy of the letter dated 19.06.2021 by Dr. Robert Malone	216-217		
23.	**Annexure P-16** True Copy of Article published in Global Research	218-221		
24.	**Annexure P-17**			

	True copy of the Syncytin Study	222- 235		
25.	**Annexure P-18** True Copy of the Report by 57 leading experts on Covid-19 vaccine	236-247		
26.	**Annexure P-19** True Copy of news report of the petition by medical experts	248-253		
27.	**Annexure P-20** True Copy of Paper on Precautionary Principle by Judy Wilyman's dated 28.11.2020	254-264		

Kindly See Volume II

PROFORMA FOR FIRST LISTING

SECTION: PIL

The case pertains to (Please tick/check the correct box):

☒ Central Act: (Title) Art. 32, Constitution of India

☒ Section(s): N.A

☒ Central rule: (Title) N.A

☒ Rule No.(s):

☒ State Act (Title)

☒ Section:

☒ State Rule: N.A

☒ Rule No(s): N.A

☒ Impugned Interim Order: (Date) N.A

☒ Impugned Final Order/Decree: (Date) N.A

☒ High Court: N.A

☒ Name of Judges: N.A

☒ Tribunal/Authority: N.A

1. Name of matter: ☑ Civil ☐ Criminal
2. (a) Petitioner/Appellant no. 1: Dr. Ridhi Arora
   (b) E-mail ID: ridhiarora27@gmail.com
   (c) Mobile Phone Number: 8427005997
3. (a) Respondent : Union of India
   (b) E-mail ID: _____N.A._____
   (c) Mobile Phone Number: _____N.A._____
4. (a) Main category classification: 18
   (b) Sub classification: 1807

5. Not to be listed before: _____N.A._____

6. (a) Similar disposed of matter with citation, if any. & case details. – No similar disposed of matter.

(b) Similar pending matter with case details: No similar matter pending.

7. Criminal Matters:

a. Whether accused/convict has surrendered: N.A.

b. FIR No. N.A. Date: N.A

c. Police Station: N.A

d. Sentence Awarded: N.A

e. Period of sentence N.A

8. Land Acquisition Matters:

(a) Date of Section 4 notification: _____N.A._____

(b) Date of Section 6 notification: _____N.A._____

(c) Date of Section 17 notification: _____N.A._____

9. Tax Matters: State the tax effect: _____N.A._____

10. Special Category (first petitioner/appellant only):

☐ Senior Citizen>65yrs; ☐ SC/ST; ☐ Woman/Child;

☐ Disabled; ☐ Legal Aid case; ☐ In custody

11. Vehicle Number (in case of Motor Accident Claim matters):

Date: 30/10/2021

Satya Mitra

AOR for Petitioner(s)/Appellant(s)

Registration No. 1852

Email: satyamitra2003@yahoo.co.in

IN THE SUPREME COURT OF INDIA

CIVIL ORIGINAL JURISDICTION

WRIT PETITION (CIVIL) NO. OF 2021

(PIL UNDER ART. 32 OF THE CONSTITUTION OF INDIA)

IN THE MATTER OF:

Dr. Ridhi Arora & Others ...PETITIONERS

Versus

Union of India ...RESPONDENT

WITH

I.A. No. _____ of 2021	Application for permission to file lengthy synopsis and list of dates
I.A. No. _____ of 2021	Application for Application for Exemption from filing duly affirmed copy of the Affidavit.

PAPER BOOK

(FOR INDEX PLEASE SEE INSIDE)

ADVOCATE FOR THE PETITIONER: SATYA MITRA

RECORD OF PROCEEDINGS

S.NO.	Date	Description	Pages

SYNOPSIS

1. The present Writ Petition is being filed in the public interest under Article 32 of the Constitution of India in the backdrop of MoHFW guidelines dated 2nd July 2021, as per which, pregnant women will be eligible to get vaccinated for Covid-19. The present Petition seeks urgent reliefs to prevent vaccination of pregnant women, for the reasons elaborated hereinafter.

2. This Writ Petition is entirely different from the pending Writ Petition vide no. WPC No. 572 of 2021 which seeks to categorise Pregnant Women and Lactating mothers as belonging to the high-risk category and be given priority in vaccination. While on the other hand our petition relates to prevent vaccination of pregnant women as emphasised herein:

Background

3. COVID vaccines in India, i.e. COVAXIN, COVISHIELD and more recently SPUTNIK have been released under EUA (Emergency Use Authorisation) for COVID 19. Therefore, under EUA, the Vaccines are 'EXPERIMENTAL' which means they are NOT 'APPROVED'. It is, therefore, prohibited by law for the Indian Government to state that they are "safe and effective". Yet, these statements are frequently made by WHO and the Indian Government and carried nationwide in the mainline media including newspapers. The Local Government Bodies (LGB) and State Governments have gone to the extent of using coercive measures by denying entry to public spaces, to force people to get vaccinated, even to the extent of mandating them.

4. These COVID 19 Vaccines have been manufactured at warp speed of about 3-4 months, as against the 9-10 years it takes in the normal course, to manufacture Vaccines and release them to the public after the completion of biosafety tests and peer review. In the present situation, it is straightforwardly abhorrent to subject pregnant women to these untested vaccines and it is urged that they may not be subjected to a biologically active agent.

5. Women are advised to avoid all medication in pregnancy, as far as possible and this prohibition extends also to most vaccines except for vaccines to prevent tetanus in the baby. Their safety is the gold standard of biomedical ethics and pregnant women invite the most rigorous scrutiny for safety. And there is therefore, absolutely no basis and no cause for these vaccines to be injected into pregnant women who are also unsuspecting and uninformed of the double dangers that these vaccines pose, both to themselves and to the unborn child they are carrying. In the present situation, it is straightforwardly abhorrent to subject pregnant women to these untested vaccines and it is urged that they may not be subjected to a biologically active agent.

6. Furthermore, Covishield (Astra Z), Covaxin (Bharat Biotech) and Sputnik V (Dr. Reddy's), are experimental vaccines under Emergency Use Authorisation (EUA), which means that they have not been approved and their non-approval status is because their Phase III trial is either not complete and it has not been subjected to peer review. Therefore, it is obvious that real safety data can be known only after the trial is completed many months into

the future. Covishield is a DNA vaccine. The vector vaccine has not been used in this manner in any human trial before. The same is unknown for Covaxin as not much has been disclosed about it in the public domain. However, the most recent data states that it too has spike proteins/will produce spike proteins.

7. In particular, the biosafety protocols demand the publication of long term data for chronic toxicity (long term testing, more than 90 days) in animal models, which as per Petitioners' knowledge, have not been done. There is also no reproductive toxicity studies nor genotoxicity studies, which are precisely long term. Pertinently, pregnant women were not included in any of the trials – not even in animal studies. It would have been too dangerous a risk for the vaccine manufacturers to test pregnant women in the absence first of animal models.

8. Furthermore, there is no briefing by and to anyone with regard to these risks; neither nursing staff administering vaccines or those being vaccinated. It is submitted that such understanding of risks is the domain of trained medical personnel in conjunction with a thorough knowledge of these experimental vaccines. It can never be that experimental vaccines are injected in the casual way that they are being administered at clinics. Clearly, there is no informed consent.

Caution by manufacturers on who should not get the vaccine

9. It is submitted that fact sheet of Bharat Biotech COVAXIN website, put out by manufacturers itself states that:

WHAT IF I AM PREGNANT?

If you are pregnant, you should not get the vaccine as the safety of the vaccine has not been studied in pregnant women."

As per Summary of Product Characteristic available with Central Drugs Standard Control Organisation (CDSCO), relevant section is reproduced below:

"*4.3 Contraindications*

- *Pregnant and lactating mothers.*"

10. Similarly, COVISHIELD Product Insert mentions the pregnancy should only be considered when the potential benefits outweigh any potential risks for the mother and fetus. The risk assessment has not been made:

"*Pregnancy*

There is a limited experience with the use of ChAdOx1 nCoV-19 Corona Virus Vaccine (Recombinant) in pregnant women. Preliminary animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryofoetal development, parturition or postnatal development; definitive animal studies have not been completed yet. The full relevance of animal studies to human risk with vaccines for COVID-19 remains to be established.

Administration of COVISHIELD™ in pregnancy should only be considered when the potential benefits outweigh any potential risks for the mother and fetus."

11. Even in the case of Sputnik V, the fact sheet of Sputnik V Vaccine categorically clarifies the use in Pregnant Women. The relevant part of the Fact sheet states:

"*WHAT IF I AM PREGNANT OR BREASTFEEDING?*

The product is not for use during pregnancy, since its effectiveness and safety during this period have not been studied."

Moreover, as per Summary of Product Characteristic available with CDSCO, relevant section is reproduced below:

"*4.3 Contraindications:*

Contraindications for the injection of component I

- *Pregnant and lactating mothers.*"

12. Therefore, it is evident that even as per the caution given by vaccine manufacturers themselves, it would be seriously harmful, unconscionable, ethically abhorrent on the part of the State, to subject pregnant women to an experimentation of this kind.

13. It is also pertinent to mention that in one RTI No. CDSCO/R/T/21/00670 dated 27.07.2021 (as annexed in the Petition) a request was made as following:

"Please provide documents of all safety trials conducted on the Covid vaccines which shows its safety for people with existing conditions, pregnant women and breast feeding women. Please provide peer reviewed scientific research showing, beyond reasonable doubt that Covid vaccines are safe for

people with pre-existing conditions, pregnant women and breast feeding women."

The Response received is as hereunder:

"The brief of interim clinical trial results containing safety, immunogenicity and efficacy results along with side-effects, contraindications, precautions of approved COVID-19 vaccines are available in Summary of Product Characteristics (SmPC) & factsheet which are publicly available on CDSCO website i.e.www.cdsco.gov.in.

CDSCO has not granted permission to conduct clinical trials on pregnant women and breast feeding women."

Hence, it is evident that absolutely no safety assessment can be made as the Trials have not been conducted as per the response received to the RTI query.

Hidden Vaccine Ingredients in Covishield

14. It is also pertinent to note that Covishield Factsheet does not mention Aluminium Hydroxide Gel as part of the ingredients' list and it is not yet known what it's effects might be, whereas on the Ministry of Health and Family Welfare website, under Frequency Asked Questions, following query shows that the composition does contain the same:

"*What is the composition of both the vaccines?* ***Composition of Covishield*** *includes inactivated adenovirus with segments of Coronavirus, Aluminium Hydroxide Gel, L-Histidine, L-Histidine Hydrochloride Monohydrate, Magnesium Chloride*

Hexahydrate, Polysorbate 80, Ethanol, Sucrose, Sodium Chloride, and Disodium Edetate Dihydrate (EDTA).

Composition of Covaxin *includes inactivated Coronavirus, Aluminum Hydroxide Gel, TLR 7/8 Agonist, 2-Phenoxyethanol and Phosphate Buffered Saline [NKA1].*"

Background of Vaccine Technology of COVID Vaccines Administered in India – All Vaccines approved in India under EUA produce the Spike Protein of SARS CoV-2/COVID 19

15. **Covaxin**: As mentioned in the Summary of Product Characteristics of Covaxin, each Single human dose (0.5 mL) of Covaxin contains:

Whole Virion Inactivated Corona Virus Antigen 6 micrograms. Produced using a Vero cell-based platform, that propagates the virus, expressing the viral spike (S) protein of SARS-CoV-2.

16. **Covishield**: As mentioned in the Summary of Product Characteristics of Covishield, each dose (0.5 ml) Covishield contains:

ChAdOx1 nCoV- 19 Corona Virus Vaccine (Recombinant) 5 × 10 to the power 10 viral particles (vp).

Recombinant, replication-deficient chimpanzee adenovirus vector encoding the SARS-CoV-2 Spike (S) glycoprotein.

17. **Sputnik V:** As mentioned in the Summary of Product Characteristics of Sputnik V, each dose of Sputnik V contains:

Gam-COVID-Vac Combined vector vaccine (Component I) - 0.5 ml/dose & (Component II) -0.5 ml/dose

Component I - Gam-COVID-Vac Combined vector vaccine (Recombinant adenovirus serotype 26 particles containing the SARS-CoV-2 protein S gene, in an amount of (1.0 ± 0.5) x 10 to the power 11 particles / dose) to prevent SARS-CoV-2-induced coronavirus infection.

Component II - Gam-COVID-Vac Combined vector vaccine (Recombinant adenovirus serotype 5 particles containing the SARS-CoV-2 protein S gene, in an amount of (1.0 ± 0.5) x 10 to the power 11 particles / dose) to prevent SARS-CoV-2-induced coronavirus infection.

18. Covid-19 vaccines are unlike any previous vaccine & have been inadequately studied. This description includes (a) mRNA/DNA gene-base vaccines ie Pfizer, Moderna and Astrazeneca or Covishield, along with Johnson & Johnson (DNA); and (b) Covaxin (Bharat Biotech) and Sputnik. The mode of action of all these COVID vaccines' for the production of antigens include and involve the Spike Protein of the virus SARS-CoV-2/COVID19.

Traditional vs. Covid Vaccines

19. Before turning to the critical issue of spike proteins, because of their singular contribution to the serious lack of safety of COVID 19 vaccines, it is relevant to clarify the difference between traditional vaccines and COVID 19 vaccines. This is of particular importance because of the implicit trust of the people in the former and the unfortunate fact that Covid 19 vaccines are drawing undue advantage and riding on this psychological trust. The

complete lack of information feeds into this phenomenon of rushing to be vaccinated in order to survive the mistaken ravages of the virus.

20. Traditional Vaccines were developed and tested over 10-12 years before being released to the Public and market commercialisation. The medicinal agents, which are being called vaccines against covid-19 all utilise new technology. Traditional vaccines comprise a small amount of the pathogen (disease-causing agent) mixed with a material called an adjuvant, which is a substance which induces mild inflammation and thereby alerts the immune system to the presence of a foreign protein. The small amount of pathogen is traditionally 'killed' by heating or by chemical treatment so that it cannot cause the disease against which immunity it sought. Alternatively, the pathogen is grown on by repeatedly infecting one cell culture after another, during which process the lethality of the virus reduces. This is called attenuation and some vaccines use so-called 'live attenuated' material to bring about immunisation. Vaccines of these basic designs cover almost every vaccine ever developed and in use in the population today. It bears repetition that these were developed and tested for 10-12 years before being released to the Public and market commercialisation.

21. Traditional vaccines, like any product, can occasionally malfunction and recognising this, regulatory authorities around the world usually maintain a public record of adverse events (AE) noted after vaccination, without necessarily attributing causation to the noted adverse event. However, the collection of event types and their frequency, coupled with a description of

the alleged injured party, taken together with the relationship in time after vaccination that the adverse event is alleged to have occurred does permit linkages sometimes to be made. For instance, the swine flu vaccine marketed in 2009-10 was eventually withdrawn because the Swedish regulatory authorities noted a striking incidence in young people of a neurological condition, narcolepsy, which was reported in many citizens.

22. On the other hand, COVID -19 vaccines work in an entirely different way to conventional vaccines and therefore have a radically different set of potential safety concerns. It is to be noted that Regulatory oversight of COVID vaccines lacks scrutiny and rigour and is marked by significant gaps in biosafety, and have even so, been released under EUA (emergency use authorisation) globally, including in India. Furthermore, it is pertinent to note that the conspicuous lack of sound data records (adverse effects or AE) in all countries and in India in particular, is also a cause of great concern, disallowing rigorous follow-up for: identification of the problem, Post Mortem pathology reports without which problems will not be identified, and medical treatment and analyses to adequately and responsibly inform the situation and action required. COVID vaccines were also developed at warp speed in 3-4 months/certainly less than a year. What that means is that it is wholly inappropriate to treat them like other vaccines. However, as a result of the new-technology products called Covid-19 vaccines, working quite differently from prior products, (traditional vaccines, which are appropriately termed vaccines), leading medical experts & scientists are of

the considered opinion that the regulatory standard has fallen woefully short of the tests required to adequately assess and assure safety, while further recognising that there was an "ongoing failure of the regulatory standard, given the technical novelty of the covid-19 vaccines".

COVID Vaccines: the synthetic Spike Protein of the vaccines is cytotoxic, pathogenic and biologically active.

23. An Elsevier Toxicology Report, a peer-reviewed study states the following: "*We believe that mid-or long-term adverse effects are possible based on the recent emergence of evidence that would support the probability of mid-and long-term adverse effects from the COVID-19 inoculants, such as:*

- *The spike protein itself can be a toxin/pathogenic protein.*
- *S protein alone can damage vascular endothelial cells (ECs) by downregulating ACE2 and consequently inhibiting mitochondrial function.*
- *it is concluded that ACE2 and endothelial damage is a central part of SARS-CoV2 pathology and may be induced by the spike protein alone.*
- *the spike protein of SARS-CoV-1 (without the rest of the virus) reduces ACE2 expression, increases angiotensin II levels, exacerbates lung injury, and triggers cell signaling events that may promote pulmonary vascular remodeling and Pulmonary Arterial Hypertension (PAH) as well as possibly other cardiovascular complications.*
- *the recombinant S protein alone elicits functional alterations in cardiac vascular pericytes (PCs). This was documented as:*

- *increased migration*
- *reduced ability to support EC network formation on Matrigel*
- *secretion of pro-inflammatory molecules typically involved in the cytokine storm*
- *production of pro-apoptotic factors responsible for EC death. Furthermore, the S protein stimulates the phosphorylation/activation of the extracellular signal-regulated kinase 1/2 (ERK1/2) through the CD147 receptor, but not ACE2, in cardiac PCs, the S protein may elicit vascular cell dysfunction, potentially amplifying, or perpetuating, the damage caused by the whole corona-virus.*
- *"even in the absence of the angiotensin-converting enzyme 2 receptors, the S1 subunit from SARS-CoV-2 spike protein binding to neutral phospholipid membranes leads to their mechanical destabilization and permeabilization. A similar cytotoxic effect of the protein was seen in human lung epithelial cells.".*
- *The LNP layer encapsulating the mRNA of the inoculant is highly inflammatory in both intradermal and intranasal inoculation and "Polyethylene glycol (PEG) is a cause of anaphylaxis to the Pfizer/BioNTech mRNA COVID-19 vaccine". "Humans are likely developing PEG antibodies because of exposure to everyday products containing PEG. Therefore, some of the im-mediate allergic responses observed with the first shot of mRNA-LNP vaccines might be related to pre-existing PEG anti-bodies. Since these vaccines often require*

a booster shot, anti-PEG antibody formation is expected after the first shot. Thus, the allergic events are likely to increase upon re-vaccination".

There is also the possibility that the components of the LNP shell could induce the ASIA Syndrome (auto-immune/inflammatory syndrome induced by adjuvants), as shown by studies on post-inoculation thyroid hyperactivity and post-inoculation subacute thyroiditis.

- *The spike protein has been found in the plasma of post- inoculation individuals, implying that it could circulate to, and impact adversely, any part of the body.*
- *The spike protein of SARS-CoV-2 crosses the blood-brain barrier in mice, and "the SARS-CoV-2 spike proteins trigger a pro-inflammatory response on brain endothelial cells that may contribute to an altered state of BBB function".*
- *The spike proteins manufactured in vivo by the present COVID-19 inoculations could potentially "precipitate the onset of autoimmunity in susceptible subgroups, and potentially exacerbate autoimmunity in subjects that have pre-existing autoimmune diseases", based on the finding that anti-SARS-CoV-2 protein antibodies cross-reacted with 28 of 55 diverse human tissue antigens.*
- *"The biodistribution of ChaAdOx1 [Astra Zeneca's recombinant adenovirus vaccine candidate against SARS-CoV-2] in mice confirmed the delivery of vaccine into the brain tissues. The vaccine may therefore*

spur the brain cells to produce CoViD spike proteins that may lead to an immune response against brain cells, or it may spark a spike protein-induced thrombosis. This may explain the peculiar incidences of the fatal cerebral venous sinus thrombosis (CVST) observed with viral vector-based CoViD-19 vaccines". A complementary perspective to explain adenovirus-based vaccine-induced thrombocytopenia is that "transcription of wildtype and codon-optimized Spike open reading frames enables alternative splice events that lead to C-terminal truncated, soluble Spike protein variants. These soluble Spike variants may initiate severe side effects when binding to ACE2-expressing endothelial cells in blood vessels."

- *A Pfizer Confidential study performed in Japan showed that "modRNA encoding luciferase formulated in LNP comparable to BNT162b2" injected intramuscularly concentrated in many organs/tissues in addition to the injection site. The main organs/sites identified were adrenal glands, liver, spleen, bone marrow, and ovaries. While damage to any of these organs/sites could be serious (if real for humans), adverse effects on the ovaries could be potentially catastrophic for women of child-bearing or pre-childbearing age."*

24. The Covid-19 vaccines currently released and subject to emergency use authorisation (EUA), share a commonality: they cause the recipients' cells to manufacture a portion of the SARS-CoV-2 virus called the spike protein and its subunit S1. It is known conclusively that the spike protein is the

causative factor for serious disease in the body and causes disease on its own and apart from the presence of the virus.

25. In this regard, a testimony has been provided by Dr. Michael Yeadon "Concerning information in relation to covid-19 vaccination and fertility" which is annexed with the Petition. Dr. Michael Yeadon, PhD, is an independent life sciences researcher. His first degree was in biochemistry & toxicology, followed by his research-based PhD in respiratory pharmacology. His early work was in appointments to secret government facilities at Porton Down (Chemical Defence Establishment) and at Aldermaston (Forensic Science Service HQ). His subsequent career in the biopharmaceutical industry spanned almost 30 years leading project teams seeking new pharmacological treatments for asthma and COPD. He held positions of increasing responsibility and was, until 2011, Chief Scientific Officer, responsible for allergy & respiratory research worldwide within Pfizer, UK until that facility was closed. Dr. Yeadon then spent the next decade as an independent consultant, assisting 30 biotechnology companies in the fields of new medicines discovery for inflammatory and immunological diseases of lung and skin, largely during their start-up phase. During that time he also founded and led as CEO his own biotech (Ziarco) which was acquired by Novartis in 2017.

26. On December 1, 2020, Dr. Wolfgang Wodarg and Dr. Michael Yeadon, expert reviewer in this field, filed a petition of concern with the European Medicines Agency. In his said Petition, the principal grounds of concern

were the excessive speed of clinical development, together with a limited series of specific concerns (which were not claimed to be exhaustive):

i. Determination of covid-19 'cases' relied on inadequately controlled PCR testing. It is very widely held by independent experts that the PCR tests used grossly over-estimate prevalence of truly infected 'cases' – in relation to which it is noteworthy that FDA has just announced that it is withdrawing approval from all PCR tests for detection of SARS-CoV-2 infection.

ii. The potential for antibody dependent enhancement, which process has caused the termination of all other prior vaccines against coronaviruses.

iii. The potential for precipitating acute allergic reactions upon administration of the lipid-encapsulated vaccines (Pfizer/BioNTech and Moderna products), which in fact did happen on the very first day of mass vaccination in UK & the label was soon changed to avoid administration to persons suspected of having had allergic responses to injected products in the past.

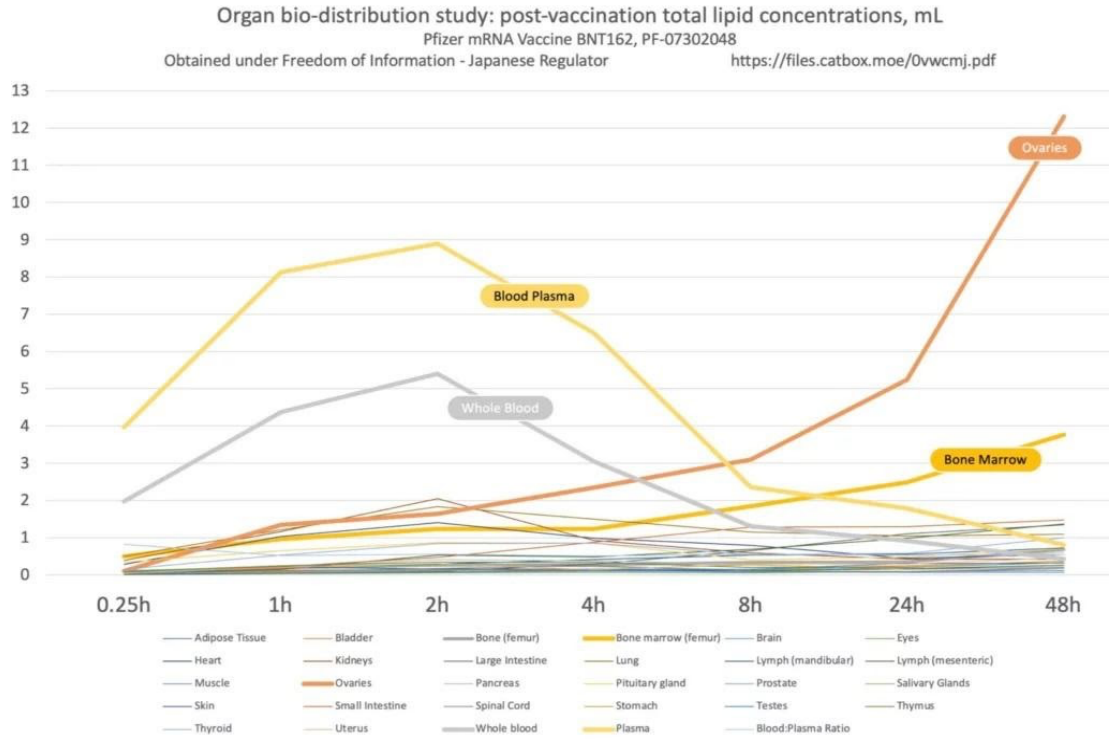
iv. The potential for cross-over immune responses to a protein essential to successful pregnancy. It is this latter concern to which the remainder of the instant Petition refers.

27. Further, as per the petition of Dr. Michael Yeadon, the Spike Protein is almost entirely responsible for the damage to the cardiovascular system, if it gets into circulation. If the Vaccines were like traditional bona fide vaccines, and did not leave the immediate site of vaccination, typically the shoulder

muscle, beyond the local draining lymph node, then the damage that the spike protein could cause might be limited. Spike proteins are biologically active and they initiate the blood coagulation cascade among other properties. It is stated that it is the induction of blood coagulation in various locations in the body which is responsible for a high proportion of the serious adverse events including deaths which are being reported to the Vaccine Adverse Event Reporting System (VAERS) in the USA and in analogous databases elsewhere. These are woefully inadequate, suggesting approximations ranging from less than 1% to say 10%, with proven falsification/cover-up in several cases of data reporting. In general terms, there is paucity in Indian data and no data connected with foetus and or maternal deaths. Furthermore, since no long term reproductive toxicology studies have been conducted, it will not be known in any case what the long term impacts might be. The rate of fatal outcomes following Covid-19 vaccination, usually from clotting or bleeding disorders, is extraordinary and exceeds that from any previous vaccine by a very large amount, which this reviewer estimates is of the order of 60-fold. This astonishingly high rate of adverse events after vaccination, is a consequence of two factors: (i) The manufacturers were simply not required to study the way the product moves around the body after injection and (ii) They were not required to study the functional effects of the genetic code within the product after administration.

28. It would be relevant to also point out the evidence obtained by Byram Bridle through a Freedom of Information Act (FOIA) request on confidential Pfizer data. Byram Bridle is a PhD, Viral Immunologist and Associate Professor at the University of Guelph. Bridle has obtained data from Pfizer's vaccine trial data in Japan.

Steve Kirsch, author of Op-ed "Should You get Vaccinated?" who is fully vaccinated, has reproduced the below graph using the aforementioned data.



Bio-distribution of lipid nanoparticles which carry the mRNA show that the ovaries get the highest concentration. This turns the ovaries into a very large manufacturing plant to turn out toxic spike protein. Accumulation in the bone marrow is likely not good either.

29. It may be further pointed out that as per Pfizer Data obtained by Dr. Byram Bridle through FOIA request:

    i. The graph (above) shows the distribution of Lipid Nano-particles which carry the mRNA to different areas of the body in 48 hours from the time of the injection.

    ii. The highest concentration at 48 hours is in the ovaries.

    iii. These are Pfizer data given to the regulator and kept secret up to now, and known to the FDA. They show that the injection does not remain at the injection site, but that within a few hours (as low as 4 hours), it has gone everywhere, to every organ, even the brain (crossing the blood brain barrier).

30. Dr. Robert Malone, MD, MS is an American virologist and immunologist who has written a letter dated 19th June 2021 in support of Dr. Bridle's findings. He states as follows:

> "*I have independently assessed most of the data which serves as the basis for Dr. Bridle's communications regarding safety risks associated with the COVID-19 genetic vaccines, concur with his findings, and have independently raised my concerns with the US FDA including speaking directly with CBER director Peter Marks. I*

am particularly alarmed and surprised by the bioethical positions being taken by the government of Canada regarding these experimental – stage vaccines, and very surprised. These policies appear contrary to what I have been trained as the bedrock principles of clinical research/human subjects bioethics. Please stop politicizing science. The scientific process requires dissent and discussion to arrive at truth. This is a central tenant. Dr. Bridle has spoken truth as he sees it. --- My assessment is very much aligned with that of Dr. Bridle."

31. Following further observations and submissions as culled out from the various scientific evidence mentioned in the Yeadon's testimonial, are noteworthy:

i. **The shadow of Thalidomide and changes to drug safety regulation in pregnancy**. The drug name 'Thalidomide', is, particularly in Europe, indelibly associated in the public mind with birth defects. Intended to treat nausea associated with early pregnancy, it was prescribed in 46 countries, but not the USA, between 1957 and 1962, when it was withdrawn, having been identified as the causative agent in 10,000 birth malformations involving reduced or absent limbs. Thalidomide is one of the most infamous case of failed drug safety evaluation. By contrast with regulators in dozens of other countries, the US drug regulatory agency, the Food & Drug Administration, did not approve thalidomide because the reviewer was not satisfied by the available information.

As a result, Drug safety was substantially reformed worldwide in the aftermath of this event, notably to require manufacturers to conduct what is broadly termed ‘reproductive toxicology’ and also almost always to include rabbits as a test species, because it was later discovered that thalidomide did cause birth defects in rabbits, but far less obviously in rodents. There was a realisation; the concept that the foetus was somehow protected from harm by being in the womb, was completely mistaken. On the contrary, the intricacies of embryo-foetal development started to be recognised as a period of extreme vulnerability.

ii. **Covid-19 vaccines have not been taken through reproductive toxicology tests.** It is essential to lay-out the backdrop to the current position with clinical use of covid-19 vaccines, for one reason: we have NEVER, since thalidomide, exposed ‘women of childbearing potential’ (WOCBP) and ESPECIALLY NEVER pregnant women to ANY novel, experimental pharmaceutical product, without that product first having completed a full battery of reproductive toxicology tests. Even after this crucial step, pilot studies are always conducted in a small number of pregnant women to minimise risk to the developing foetus. Neither of these essential steps have been undertaken.

iii. **No justification for taking risks with the health of unborn children.** It is the height of recklessness to allow WOCBP to receive covid-19 vaccines, which are of an entirely novel, (including gene-based technology, mRA/DNA), for which there is no prior human safety

experience in a large population. Worse, the active recommendation that these experimental agents should be administered to pregnant women is, criminally negligent. Furthermore, it is completely incomprehensible that these novel vaccines are recommended for use in pregnancy, most of which happen in women aged 40y or younger, since the dominant risk factor for poor outcomes from infection by SARS-CoV-2 is age. The mRNA/DNA, which are formulated in lipid nanoparticles, accumulate in the ovaries of mammals including humans.

iv. With reference to Dr. Bridle's biodistribution study and the concentration of NLP in the Ovaries, "the intended induction of immunity definitely does not require the presence of vaccine components in reproductive tissue. Most commonly, the concentrations of drugs in any tissue in the body peaks quickly after administration, after which they fall away gradually over time. In light of this, it is more troubling still that, instead of falling away gradually over time as expected, the tissue levels RISE over time, suggestive of an active process. The study was aborted 48 hours after administration of the test material, not unreasonably. After that much time, it would be normal to be expecting the peak of tissue concentrations to have passed. However, the highest concentrations were seen at the last time point, 48 hours post-dose, meaning it is not known when the peak time after administration actually is or whether concentrations in the ovaries and spleen rise even higher at extended

times --- What this means is immediately obvious to anyone experienced in the development of medical products:

- It is unsafe to make any assumptions at all about the safety profile, short or long, after administration to humans.
- We did not know, prior to the tragic lessons arising from Thalidomide that early in gestation, the developing embryo is exquisitely vulnerable to the adverse effects of environmental agents, including pharmaceuticals.
- It is unreasonable to assume that, because conventional vaccines are not generally considered to represent a safety issue in relation to fertility and pregnancy, that these novel, gene-based products and Covaxin and Sputnik with their spike proteins will be safe in pregnancy.
- The part of the SARS-CoV-2 virus called the spike protein is coded into these new technology products, such that they all induce the body of the recipient to manufacture that spike protein or a portion thereof.
- It is conventional good practise to review the scientific literature around chosen targets for use in vaccines, in this case, spike protein. This is required to ensure that the potential for unwanted effects, (when humans are caused to develop immune responses to it), is understood.

v. Dr. Yeadon has further noted, that *"in addition to the class- effect concerns we now have of immune responses to syncytin-1, (almost certainly this will not be limited to antibodies but also probably include cytotoxic T-lymphocytes directed against cells expressing syncytin-1), we also have concerns about vaccine carriers, in this case the lipid nanoparticle (LNP) concentrating in ovaries. I've just discovered that the phenomenon of ovarian concentration of carriers has been known since at least 2012. Furthermore, it extends beyond rats & the same problematic profile has been seen repeatedly in mice, too. It's literally so bad that it surely cannot be accidental". ---"They KNEW".*

vi. **Any experienced reviewer would call for a halt to the use of this vaccine in non-menopausal women.** Dr. Yeadon further notes *"in the absence of evidence that says this is not a predictor for humans, this is what I expect is happening to every female administered this agent. It is to be expected that the consequences of this concentration in reproductive will be adverse. Based on observations elsewhere in the body, where blood clots and bleeding have separately been reported. In my opinion, any reasonable reviewer would agree that these vaccines should not be administered to any female below menopause".*

vii. Additionally, antibodies raised against the spike protein might interact with the naturally occurring syncytin proteins, adversely affecting multiple steps in human reproduction. The manufacturers did not provide data on this subject despite knowing about the spike protein's similarity

to syncytin proteins for more than one year. There are now a very high number of pregnancy losses in VAERS. A study recently published in the New England Journal of Medicine, 'Preliminary Findings of mRNA COVID-19 Vaccine Safety in Pregnant Persons,' exposes that pregnant women receiving Vaccines during their first or second trimesters suffer an 82% spontaneous abortion rate, killing 4 out of 5 unborn babies. There are worldwide reports of irregular vaginal bleeding without clear explanation. Scientists are concerned that the Vaccines pose a substantial risk to a woman's reproductive system. This increased risk of sterility stems from an increased concentration of the spike proteins in various parts of the reproductive system after vaccination. Not enough is known to determine the risk of sterility, but it is beyond question that the risk is increased. Billions of aggressive spike proteins are accumulating in very delicate ovarian tissues, the one place in the human body where females carry a finite number of fertile eggs.

More Views of Leading Scientists, Doctors and Policy Experts

32. It is further submitted that 57 leading scientists, doctors and policy experts from North and South America have released a report calling into question the safety and efficacy of the current COVID-19 vaccines and are now calling for an immediate end to COVID 19 vaccination drive, which is annexed with this Petition.

33. Furthermore, twenty Seven health experts have written to FDA – "slow down and get the science right before approving vaccines". This important

letter exposes the WHO myth of the safety of COVID Vaccines. Authored by 27 leading medical experts (various countries), including Dr. Peter McCullough (leading cardiologist, intensivist, epidemiologist) is a signatory, it exposes the cover-up, the gaps in safety testing, but also, why these mRNA and DNA vaccines pose serious potential harm to people and global health. RNA/DNA vaccine safety testing, therefore, requires rigorous and diligent oversight by independent experts, who are proven to have no conflict of interest. The letter is also annexed with the Petition.

Vaccinations are resulting in deaths and Serious Adverse Events which are wilfully not reported and therefore underestimated.

34. There have been thousands of cases of deaths and serious adverse events following vaccination reported in the newspapers in India as of 19th October 2021. The Compilation has approximately 5132 newspaper reports reporting deaths alone after administration of vaccine, has been annexed with this Petition.

35. Moreover, nearly 11,000 Deaths after COVID Vaccines have been reported to CDC, as FDA Adds New Warning to J&J Vaccine. Furthermore, the website https://johnplatinumgoss.com/covid-19-vaccination-statistics/ pools Adverse Event Data from USA, EU and UK. These are official statistics and those who produce them, MHRA, EMA and FDA, concede that they are much higher, (10 to 100 times higher) than the figures they have released. Given that India's AEFI monitoring and reporting mechanism has

serious lapses, if one extrapolates the USA, UK and EU numbers for India, the figures could be potentially shocking as vaccination coverage increases.

Precautionary Principle (PP)

36. The application of the Precautionary Principle is completely and absolutely relevant to the question of vaccinating pregnant women. These vaccines do not even offer reasonable certainty of no harm. By some estimates, the number of deaths attributable to COVID vaccines have exceeded the total 40 year data of deaths of all vaccines put together. In a real sense therefore, we have gone beyond the notion of mere caution and precaution in this matter. It would be ethically unconscionable, and would invite the opprobrium of medical insanity to vaccinate pregnant women and in view of the Syncytin evidence, also WOCBA. It is worth adding for the record that based on the vaccine leaflets and on their own admission, several other groups qualify for exclusion.

37. The technology of COVID 19 vaccines is a textbook case for the application of the Precautionary Principle. The precautionary principle necessitates that if there are reasonable scientific grounds for believing that a new process or product may not be safe, it should not be introduced until we have convincing evidence of reasonable certainly of no harm.

38. The above matters and in their application in particular to the current policies being implemented in India defy belief; are shocking, and unconscionable, a serious indictment of Regulatory bodies worldwide including India. The evidence of a lack of rigour and scrutiny in the regulatory oversight of the

safety of Covid 19 vaccines, must put into question the entire policy of the release under EUA, of these vaccines. The problem gets compounded when innate or natural immunity is factored into the matter of vaccines administered to pregnant women. Furthermore, and despite the clear evidence of the orchestrated attempts to minimise Adverse Effects (AE), the deliberate cover-up, under-reporting etc, the record of AE that has nevertheless emerged including deaths, is medically and humanly shocking and have led many scientists to call for an immediate stop to the mass vaccination drive, particularly in pregnant women.

39. Therefore, keeping in mind the above scientific evidence, indicating that there is a significant population, including pregnant women, that has already been infected, there is a need to conduct elaborate tests and trials without conducting which, it will be completely abhorrent and unconscionable to vaccinate pregnant women, and expose them as well as the unborn child to serious adverse effects, which will be in violation of their fundamental right to health.

40. Hence, this Writ Petition.

LIST OF DATES

24.04.20	Ministry of Home Affairs vide Order, dated 24.03.2020, addressed to The Secretaries of All Ministries/ Dept of GoI and Chief Secretaries of all States/Administrator of States/Union Territories, issued guidelines to take effective measures to prevent the spread of Covid-19 in the country.
30.06. 2020	The Drugs Controller General of India (DCGI) approved Phase I and II clinical trial of Covaxin.
26.08.20	Clinical trials of Covishield developed by Oxford University and AstraZeneca were initiated
23.10.2020	The Drugs Controller General of India (DCGI) granted permission for conducting phase-3 clinical trial of COVAXIN.
03.01.2021	Drugs Controller General of India (DCGI) granted emergency approval to Covaxin And Covishield
14.01.2021	Letter by Additional Secretary, MoHFW, regarding Contraindications and Comparative Sheet for Covishield and Covaxin, clearly mentions "Pregnant & Lactating women have not been part of any Covid-19 Vaccine clinical trial so far.

	Therefore, women who are pregnant or not sure of their pregnancy; and lactating women should not receive Covid-19 vaccine at this time."
16.01.21	Government of India started the Covid-19 Vaccination Program for Healthcare and Frontline Workers and People above the age of 60 years or those with certain comorbidities.
01.04.21	Covid-19 Vaccination available for everyone above the age of 45 years.
01.05.21	Covid-19 Vaccination available for everyone above the age of 18 years.
19.05.21	In a letter to all Chief Secretaries/Administrators of all States & UTs, Secretary of MoHFW states "Covid-19 Vaccination is recommended for all lactating women"
02.07.21	In a Press Release by MoHFW dated 2nd July, 2021, GoI informs that "Based on recommendation from National Technical Advisory Group on Immunization (NTAGI), the Union Ministry of Health and Family Welfare (MoHFW) today approved the vaccination of pregnant women against Covid-19.

27.07.21	In an RTI reply for CDSCO/R/T/21/00670 filed by Rushil Tamboli, it is stated "CDSCO has not granted permission to conduct clinical trials on Pregnant Women and breast feeding women
08.10.21	In an RTI reply for CDSCO/R/E/21/00423 filed by Brian Fernandes, it is stated "As per information available, the applicants have enrolled healthy participants in the various clinical trials of Covid-19 vaccines and as per exclusion criteria, Pregnant and lactating/breast feeding women were excluded."
	Hence, this Writ Petition.

IN THE SUPREME COURT OF INDIA

CIVIL ORIGINAL JURISDICTION

WRIT PETITION (CIVIL) NO. OF 2021

(PIL UNDER ART. 32 OF THE CONSTITUTION OF INDIA)

IN THE MATTER OF:

Dr. Ridhi Arora
D/o Mr. Gulshan Arora,
R/o 237, Sector 4,
MDC, Panchkula, Haryana – 134112 …Petitioner No. 1

Mathukutty John,
S/o Mr. John J.,
R/o Thyparambil House, Anakullu
P.O. Kanjirappally – 686508 …Petitioner No. 2

Suman Kumari Chouhan,
D/o Mr. Bhim Chouhan,
R/o Chinsura Station Road,
Lenin Nagar, Dharampur (CT), Hooghly,
Chinsurah RS, West Bengal – 712102 …Petitioner No. 3

Versus

Union of India through Secretary,
Department of Health & Family Welfare,
Nirman Bhawan, Maulana Azad Road,
New Delhi 110011 …Respondent

WRIT PETITION OF MANDAMUS UNDER ARTICLE 32

OF THE CONSTITUTION OF INDIA

To,

THE HON'BLE CHIEF JUSTICE OF INDIA AND

HIS COMPANION JUSTICES OF

THE HON'BLE SUPREME COURT OF INDIA

THE HUMBLE PETITION OF THE

PETITIONERS ABOVE NAMED

MOST RESPECTFULLY SHOWETH:

1. The present Writ Petition is being filed in the public interest under Article 32 of the Constitution of India in the backdrop of MoHFW guidelines dated 2nd July 2021, suggesting pregnant women will be eligible to get vaccinated for Covid-19 to take certain steps to ensure the protection of Fundamental Rights guaranteed to the citizens under the Constitution of India.

   The true copy of the MoHFW Guidelines dated 2nd July 2021 regarding vaccination against pregnant women is annexed herewith and marked as Annexure P-1, Pg. 68-80.

1 A. The Petitioners have not approached any other authority for the same relief.

PARTIES

2. That, Petitioner No. 1 is an MBBS doctor, an ex-Medical Officer obstetrician-gynaecologist at Government Hospital in Chandigarh. She runs a private practice and she actively does and promotes normal birth or natural birthing. S[redacted]

[redacted]. By virtue of her profession Petitioner No. 1 has faced several queries by pregnant women. She has given consultation to her patients and pregnant women. The Petitioner No. 1 has approached this Hon'ble Court in public interest and is not seeking any relief for personal interest or for herself. The petitioner is not involved in any civil, criminal or revenue litigation which has/ could have a legal nexus with the issues involved in PIL.

3. That, Petitioner no. 2 is an Evangelist by profession and by education he has [redacted]. He is the father of 31 year old Mahima Mathews, who passed away 13 days after taking Covid-19 vaccine. Mahima was 7 weeks pregnant and expecting twins. She was asked to take the Covid vaccine by her Gynecologist and was told that as per the Government of India, it is advisable for pregnant women to take the vaccine. The Petitioners [redacted] No. 2 is an aggrieved party, he has approached this Hon'ble Court in public

interest and is not seeking any relief for personal interest or for himself. The petitioner is not involved in any civil, criminal or revenue litigation which has/ could have a legal nexus with the issues involved in PIL.

4. That, Petitioner No. 3 is a Housewife and is 20 weeks and 10 days pregnant as on 10.10.21. By Education she has completed a Diploma in Computer Science. [redacted] She is the daughter of [redacted] Although the Petitioner No. 3 is a pregnant woman and may be an aggrieved party, she has approached this Hon'ble Court in public interest and is not seeking any relief for personal interest or for herself. The petitioner is not involved in any civil, criminal or revenue litigation which has/ could have a legal nexus with the issues involved in PIL.

5. That, Respondent No. 1 is the Union of India through Secretary, Department of Health and Family Welfare, which is responsible for recommending Covid-19 vaccination for Pregnant and Lactating Women as per Letter dated 19th May 2021 for lactating women and Press release dated 2nd July 2021 for Pregnant Women.

6. That, the present Writ Petition has been filed by the Petitioners in public interest under Article 32 of the Constitution of India and the Petitioners have no personal interest herein.

7. That, the petitioners are seeking inter alia the issuance of the writ of Mandamus or any other appropriate order or direction against the respondents, directing them to actively follow up to record and investigate instances of deaths/serious adverse events of the pregnant and lactating women within 30 days following immunization, to advertise extensively in newspaper, television, radio (during prime time) and on social media that any pregnant or lactating woman dying or suffering serious adverse events within 30 days of vaccination may complain directly to officials and to further direct the authorities to mandatorily record all the cases being reported, to frame extensive programme for the reasonable compensation for those dying or experiencing serious adverse events within 30 days of vaccination, to publish all information related to the phase 1, 2 and 3 trials of the vaccine and to further direct the public authorities and all private establishments to prevent vaccination of pregnant women and bring an end to the adverse events caused by vaccinating pregnant women, under judicial oversight.

8. That, the Petitioners are filing the present Petition on their own and the litigation cost is being borne by the Petitioners.

9. That, a thorough research has been conducted in the matter raised through the present Writ Petition/PIL and the relevant available matters in this regard are being annexed herewith.

10. That, to the best of the Petitioner's knowledge and research, the issue raised herein was not dealt with or decided by this Hon'ble Court and that a similar or identical petition was not filed earlier by the Petitioners.

SUMMARY OF ISSUES

11. A summary of the key issues involved in the present Petition are as hereunder:

i. COVID 19 Vaccines to prevent infections and stop the spread of the SARS CoV-2 have been manufactured at warp speed of about 3-4 months, as against the 9-10 years it takes in the normal course, to manufacture Vaccines and release them to the public after the completion of biosafety tests and peer review.

ii. Given Governments' perceptions worldwide, and under WHO directions and the announcement of a pandemic in March 2020, COVID vaccines in India, COVAXIN, COVISHIELD and more recently SPUTNIK have been released under EUA (Emergency Use Authorisation) for COVID 19. Therefore, under EUA, the Vaccines are "EXPERIMENTAL" which means they are NOT 'APPROVED'. It is, therefore, prohibited by law for the Indian Government to state that they are "safe and effective". Yet, these statements are frequently

made by WHO and the Indian Government and carried nationwide in the mainline media including newspapers.

iii. It is unclear that by what authority the Local Government Bodies (LGB) and State Governments have gone to the extent of using coercive measures by denying entry to public spaces, to force people to get vaccinated, even to the extent of mandating them. These 'mandates' are entirely illegal and must invite appropriate legal action using the full authority of the Law.

The above issues are germane to the objectives of this PIL to prevent the vaccination of pregnant women on an urgent basis. Women are advised to avoid all medication in pregnancy, as far as possible and this prohibition extends also to most vaccines except for vaccines to prevent tetanus in the baby. Their safety is the gold standard of biomedical ethics. In the present situation, it is straightforwardly abhorrent to subject pregnant women to these untested vaccines and it is urged that they may not be subjected to a biologically active agent. It may be noted that all the vaccines mentioned above, produce Spike Proteins in the body, which can have serious adverse effects.

FACTUAL BACKGROUND

Vaccine Approval Status

12. The basic principle of the Hippocratic Oath is to do NO HARM. Pregnant women invite the most rigorous scrutiny for safety. And there is therefore, absolutely no basis and no cause for these vaccines to be injected into

pregnant women who are also unsuspecting and uninformed of the double dangers that these vaccines pose, both to themselves and to the unborn child they are carrying. There are also these added reasons why these vaccines in particular may not be given in good conscience without violating the most basic principles of medical bioethics:

i. Covishield (Astra Z), Covaxin (Bharat Biotech) and Sputnik V (Dr. Reddy's), are experimental vaccines under Emergency Use Authorisation (EUA), which means that they have not been approved. Their non-approval status is because their Phase III trial is either not complete and it has not been subjected to peer review. Therefore, it is obvious that real safety data can be known only after the trial is completed many months into the future.

A true copy of the Trials Protocol for each of the 3 vaccines is annexed herewith and marked as Annexure P-2, Pg. 81-86.

ii. That in particular, the biosafety protocols demand the publication of long term data for chronic toxicity (long term testing, more than 90 days) in animal models, which as per Petitioners' knowledge, have not been done. There are also no reproductive toxicity studies nor genotoxicity studies, which are precisely long term. Pertinently, pregnant women were not included in any of the trials – not even in animal studies. It would have been too dangerous a risk for the vaccine manufacturers to test pregnant women in the absence first of animal models.

iii. Covishield is a DNA vaccine. The vector vaccine has not been used in this manner in any human trial before. The same is unknown for Covaxin as not much has been disclosed about it in the public domain. However, the most recent data states that it too has spike proteins/will produce spike proteins.

iv. Vaccines in the normal course take as long as 10 years to fulfil all the safety protocols. The present vaccines have been produced at warp speed, in 3-4 months, but certainly less than a year.

v. For any manufacturer of vaccines to put out a list of conditions which invite a 'caution' tag, means, that the caution warning better approximates a risk reality that is several amplifications higher. This is how it is in such matters. All 3 Vaccines carry a caution for giving these vaccines to pregnant women. There is nothing in the literature regarding WOCBA.

Furthermore, there is no briefing by and to anyone with regard to these risks; neither nursing staff administering vaccines or those being vaccinated. It is submitted that such understanding of risks is the domain of trained medical personnel in conjunction with a thorough knowledge of these experimental vaccines. It can never be that experimental vaccines are injected in the casual way that they are being administered at clinics. Clearly, there is no informed consent.

Caution by manufacturers on who should not get the vaccine

13. COVAXIN

It is submitted that fact sheet Bharat Biotech Covaxin website, put out by manufacturers itself states that:

> ***WHAT IF I AM PREGNANT?***
>
> *If you are pregnant, you should not get the vaccine as the safety of the vaccine has not been studied in pregnant women."*

A true copy of the typed factsheet of Covaxin is annexed herewith and marked as Annexure P-3, Pg. 87-89.

As per Summary of Product Characteristic available with Central Drugs Standard Control Organisation (CDSCO), relevant section is reproduced below:

> "*4.3 Contraindications*
>
> - *Pregnant and lactating mothers.*"

A true copy of the Summary of Product Characteristic of Covaxin is annexed herewith and marked as Annexure P-4, Pg. 90-97.

14. COVISHIELD - Product Insert mentions the pregnancy should only be considered when the potential benefits outweigh any potential risks for the mother and foetus. The risk assessment has not been made:

> "*Pregnancy*
>
> *There is a limited experience with the use of ChAdOx1 nCoV-19 Corona Virus Vaccine (Recombinant) in pregnant women. Preliminary animal studies do not indicate direct or indirect harmful*

effects with respect to pregnancy, ***embryofoetal development, parturition or postnatal development; definitive animal studies have not been completed yet.*** *The full relevance of animal studies to human risk with vaccines for COVID-19 remains to be established.*

Administration of COVISHIELD™ in pregnancy should only be considered when the potential benefits outweigh any potential risks for the mother and fetus."

A true copy of the typed Product Insert of COVISHIELD vaccine is annexed herewith and marked as Annexure P-5, Pg. 98-109.

15. Sputnik V:

The fact sheet of Sputnik V Vaccine categorically clarifies the use in Pregnant Women. The relevant part of the Fact sheet is as under

"*WHAT IF I AM PREGNANT OR BREASTFEEDING?*

The product is not for use during pregnancy, since its effectiveness and safety during this period have not been studied."

A true copy of the typed fact sheet of Sputnik is annexed herewith and marked as Annexure P-6, Pg. 110-116.

Moreover, as per Summary of Product Characteristic available with CDSCO, relevant section is reproduced below:

"*4.3 Contraindications:*

Contraindications for the injection of component I

- *Pregnant and lactating mothers.*"

A true copy of the Summary of Product Characteristic of Sputnik V is annexed herewith and marked as Annexure P-7, Pg. 117-125.

16. Therefore, in the light of the caution given by the vaccine manufacturers themselves, it would be seriously unconscionable, ethically abhorrent on the part of the State, to subject pregnant women to an experimentation of this kind, specifically when the right to health is a fundamental right protected under the Constitution of India.

17. It is also pertinent to mention that in one RTI No. CDSCO/R/T/21/00670 dated 27.07.2021 (as annexed in the Petition) a request was made as following:

"Please provide documents of all safety trials conducted on the Covid vaccines which shows its safety for people with existing conditions, pregnant women and breast feeding women. Please provide peer reviewed scientific research showing, beyond reasonable doubt that Covid vaccines are safe for people with pre-existing conditions, pregnant women and breast feeding women."

The Response received is as hereunder:

"The brief of interim clinical trial results containing safety, immunogenicity and efficacy results along with side-effects, contraindications, precautions of approved COVID-19 vaccines are available in Summary of Product Characteristics (SmPC) & factsheet which are publicly available on CDSCO website i.e.www.cdsco.gov.in.

CDSCO has not granted permission to conduct clinical trials on pregnant women and breast feeding women."

A true copy of the RTI No. CDSCO/R/T/21/00670 dated 27.07.2021 is annexed herewith and marked as Annexure P-8, Pg. 126-127.

Hidden Vaccine Ingredients in Covishield

18. On the Ministry of Health and Family Welfare website, under Frequency Asked Questions, following query is pertinent to be noted:

"*What is the composition of both the vaccines?* ***Composition of Covishield*** *includes inactivated adenovirus with segments of Coronavirus, Aluminium Hydroxide Gel, L-Histidine, L-Histidine Hydrochloride Monohydrate, Magnesium Chloride Hexahydrate, Polysorbate 80, Ethanol, Sucrose, Sodium Chloride, and Disodium Edetate Dihydrate (EDTA).*

Composition of Covaxin *includes inactivated Coronavirus, Aluminum Hydroxide Gel, TLR 7/8 Agonist, 2-Phenoxyethanol and Phosphate Buffered Saline [NKA1].*"

A true copy of the FAQ downloaded from MOHFW website is annexed herewith and marked as Annexure P-9, Pg. 128-132.

It is also pertinent to note that Covishield Factsheet does not mention Aluminium Hydroxide Gel as part of the ingredients' list and it is not yet known what it's effects might be.

Vaccine Technology of COVID Vaccines Administered in India – All Vaccines approved in India under EUA ie, Covaxin, Covishield and Sputnik V produce the Spike Protein of SARS CoV-2/COVID-19.

19. **Covaxin**: As mentioned in the Summary of Product Characteristics of Covaxin, each Single human dose (0.5 mL) of Covaxin contains:

Whole Virion Inactivated Corona Virus Antigen 6 micrograms. produced using a Vero cell-based platform, that propagates the virus, expressing the viral spike (S) protein of SARS-CoV-2.

20. **Covishield**: As mentioned in the Summary of Product Characteristics of Covishield, each dose (0.5 ml) Covishield contains:

ChAdOx1 nCoV- 19 Corona Virus Vaccine (Recombinant) 5 × 10 to the power 10 viral particles (vp).

Recombinant, replication-deficient chimpanzee adenovirus vector encoding the SARS-CoV-2 Spike (S) glycoprotein.

21. **Sputnik V:** As mentioned in the Summary of Product Characteristics of Sputnik V, each dose of Sputnik V contains:

Gam-COVID-Vac Combined vector vaccine (Component I) - 0.5 ml/dose & (Component II) -0.5 ml/dose

Component I - Gam-COVID-Vac Combined vector vaccine (Recombinant adenovirus serotype 26 particles containing the SARS-CoV-2 protein S gene, in an amount of (1.0 ± 0.5) x 10 to the power 11 particles / dose) to prevent SARS-CoV-2-induced coronavirus infection.

Component II - Gam-COVID-Vac Combined vector vaccine (Recombinant adenovirus serotype 5 particles containing the SARS-CoV-2 protein S gene, in an amount of (1.0 ± 0.5) x 10 to the power 11 particles / dose) to prevent SARS-CoV-2-induced coronavirus infection.

Background of Vaccines

22. Covid-19 vaccines are unlike any previous vaccine & have been inadequately studied. Petitioners include under this description (a) mRNA/DNA gene-base vaccines ie Pfizer, Moderna and Astrazeneca or Covishield (As per News Reports, both Pfizer and Moderna are being actively considered by the Government for approval under EUA (Emergency Use Authorisation) in India), along with Johnson & Johnson (DNA); and (b) Covaxin (Bharat Biotech) and Sputnik. The mode of action of all these COVID vaccines' for the production of antigens include and involve the Spike Protein of the virus SARS-CoV-2/COVID19.

i. **Traditional vs. Covid Vaccines**: Before turning to the critical issue of spike proteins, because of their singular contribution to the serious lack of safety of COVID 19 vaccines, it is relevant to clarify the difference between traditional vaccines and COVID 19 vaccines. This is of particular importance because of the implicit trust of the people in the former and the unfortunate fact that Covid 19 vaccines are drawing undue advantage and riding on this psychological trust. The complete lack of information feeds into this phenomenon of

rushing to be vaccinated in order to survive the mistaken ravages of the virus.

The former have been in use for over 4 decades and they form the basis of the trust and acceptance of traditional vaccines in the general public and the medical profession. On the other hand, Covid-19 vaccines are unlike any previous vaccine because the DGCI gave approval for the vaccine without completing third phase trial which is crucial to determine the effectiveness, adverse effects, reactions against the composition.

ii. **Traditional Vaccines** were developed and tested over 10-12 years before being released to the Public and market commercialisation. The medicinal agents, which are being called vaccines against covid-19 all utilise new technology. Traditional vaccines comprise a small amount of the pathogen (disease-causing agent) mixed with a material called an adjuvant, which is a substance which induces mild inflammation and thereby alerts the immune system to the presence of a foreign protein. The small amount of pathogen is traditionally 'killed' by heating or by chemical treatment so that it cannot cause the disease against which immunity it sought. Alternatively, the pathogen is grown on by repeatedly infecting one cell culture after another, during which process the lethality of the virus reduces. This is called attenuation and some vaccines use so-called 'live attenuated'

material to bring about immunisation. Vaccines of these basic designs cover almost every vaccine ever developed and in use in the population today. It bears repetition that these were developed and tested for 10-12 years before being released to the Public and market commercialisation.

Traditional vaccines, like any product, can occasionally malfunction and recognising this, regulatory authorities around the world usually maintain a public record of adverse events (AE) noted after vaccination, without necessarily attributing causation to the noted adverse event. However, the collection of event types and their frequency, coupled with a description of the alleged injured party, taken together with the relationship in time after vaccination that the adverse event is alleged to have occurred does permit linkages sometimes to be made.

For instance, the swine flu vaccine marketed in 2009-10 was eventually withdrawn because the Swedish regulatory authorities noted a striking incidence in young people of a neurological condition, narcolepsy, which was reported in many citizens.

iii. **COVID Vaccines:** The COVID -19 vaccines work in an entirely different way to conventional vaccines and therefore have a radically different set of potential safety concerns. It is noted that Regulatory oversight of COVID vaccines lacks scrutiny and rigour and is marked by significant gaps in biosafety, and have even so, been released

under EUA (emergency use authorisation) globally, including in India. Furthermore, it is pertinent to note that the conspicuous lack of sound data records (adverse effects or AE) in all countries and in India in particular, is also a cause of great concern, disallowing rigorous follow-up for: identification of the problem, Post Mortem pathology reports without which problems will not be identified, and medical treatment and analyses to adequately and responsibly inform the situation and action required. COVID vaccines were also developed at warp speed in 3-4 months/certainly less than a year. What that means is that it is wholly inappropriate to treat them like other vaccines. However, as a result of the new-technology products called Covid-19 vaccines, working quite differently from prior products, (traditional vaccines, which are appropriately termed vaccines), leading medical experts & scientists are of the considered opinion that the regulatory standard has fallen woefully short of the tests required to adequately assess and assure safety, while further recognising that there was an "ongoing failure of the regulatory standard, given the technical novelty of the covid-19 vaccines".

COVID Vaccines: the synthetic Spike Protein of the vaccines is cytotoxic, pathogenic and biologically active.

23. An Elsevier Toxicology Report, a peer-reviewed study states the following: We believe that mid-or long-term adverse effects are possible based on the

recent emergence of evidence that would support the probability of mid-and long-term adverse effects from the COVID-19 inoculants, such as:

- The spike protein itself can be a toxin/pathogenic protein.
- S protein alone can damage vascular endothelial cells (ECs) by downregulating ACE2 and consequently inhibiting mitochondrial function.
- It is concluded that ACE2 and endothelial damage is a central part of SARS-CoV2 pathology and may be induced by the spike protein alone.
- The spike protein of SARS-CoV-1 (without the rest of the virus) reduces ACE2 expression, increases angiotensin II levels, exacerbates lung injury, and triggers cell signaling events that may promote pulmonary vascular remodeling and Pulmonary Arterial Hypertension (PAH) as well as possibly other cardiovascular complications.
- The recombinant S protein alone elicits functional alterations in cardiac vascular pericytes (PCs). This was documented as:
- increased migration
- reduced ability to support EC network formation on Matrigel
- secretion of pro-inflammatory molecules typically involved in the cytokine storm
- Production of pro-apoptotic factors responsible for EC death. Furthermore, the S protein stimulates the phosphorylation/activation of the extracellular signal-regulated kinase 1/2 (ERK1/2) through the CD147 receptor, but not ACE2, in cardiac PCs, the S protein may elicit

vascular cell dysfunction, potentially amplifying, or perpetuating, the damage caused by the whole corona-virus.

- “Even in the absence of the angiotensin-converting enzyme 2 receptors, the S1 subunit from SARS-CoV-2 spike protein binding to neutral phospholipid membranes leads to their mechanical destabilization and permeabilization. A similar cytotoxic effect of the protein was seen in human lung epithelial cells.”
- The LNP layer encapsulating the mRNA of the inoculant is highly inflammatory in both intradermal and intranasal inoculation and “Polyethylene glycol (PEG) is a cause of anaphylaxis to the Pfizer/BioNTech mRNA COVID-19 vaccine”. “Humans are likely developing PEG antibodies because of exposure to everyday products containing PEG. Therefore, some of the immediate allergic responses observed with the first shot of mRNA-LNP vaccines might be related to pre-existing PEG anti-bodies. Since these vaccines often require a booster shot, anti-PEG antibody formation is expected after the first shot. Thus, the allergic events are likely to increase upon re-vaccination”.

  There is also the possibility that the components of the LNP shell could induce the ASIA Syndrome (auto-immune/inflammatory syndrome induced by adjuvants), as shown by studies on post-inoculation thyroid hyperactivity and post-inoculation subacute thyroiditis.

- The spike protein has been found in the plasma of post- inoculation individuals, implying that it could circulate to, and impact adversely, any part of the body.
- The spike protein of SARS-CoV-2 crosses the blood-brain barrier in mice, and “the SARS-CoV-2 spike proteins trigger a pro-inflammatory response on brain endothelial cells that may contribute to an altered state of BBB function”.
- The spike proteins manufactured in vivo by the present COVID-19 inoculations could potentially "precipitate the onset of autoimmunity in susceptible subgroups, and potentially exacerbate autoimmunity in subjects that have pre-existing autoimmune diseases", based on the finding that anti-SARS-CoV-2 protein antibodies cross-reacted with 28 of 55 diverse human tissue antigens.
- “The biodistribution of ChaAdOx1 [Astra Zeneca’s recombinant adenovirus vaccine candidate against SARS-CoV-2] in mice confirmed the delivery of vaccine into the brain tissues. The vaccine may therefore spur the brain cells to produce CoViD spike proteins that may lead to an immune response against brain cells, or it may spark a spike protein-induced thrombosis. This may explain the peculiar incidences of the fatal cerebral venous sinus thrombosis (CVST) observed with viral vector-based CoViD-19 vaccines”. A complementary perspective to explain adenovirus-based vaccine-induced thrombocytopenia is that “transcription of wildtype and codon-optimized Spike open reading

frames enables alternative splice events that lead to C-terminal truncated, soluble Spike protein variants. These soluble Spike variants may initiate severe side effects when binding to ACE2-expressing endothelial cells in blood vessels."

- A Pfizer Confidential study performed in Japan showed that "modRNA encoding luciferase formulated in LNP comparable to BNT162b2″injected intramuscularly concentrated in many organs/tissues in addition to the injection site. The main organs/sites identified were adrenal glands, liver, spleen, bone marrow, and ovaries. While damage to any of these organs/sites could be serious (if real for humans), adverse effects on the ovaries could be potentially catastrophic for women of child-bearing or pre-childbearing age.

True typed copy of relevant extracts from Elsevier Peer Reviewed Study is annexed herewith and marked as Annexure - P-10, Pg. 133-154

24. The Covid-19 vaccines currently released and subject to emergency use authorisation (EUA), share a commonality: they cause the recipients' cells to manufacture a portion of the SARS-CoV-2 virus called the spike protein and its subunit S1. It is known conclusively that the spike protein is the causative factor for serious disease in the body and causes disease on its own and apart from the presence of the virus.

25. Dr. Michael Yeadon, PhD, is an independent life sciences researcher. His first degree was in biochemistry & toxicology, followed by his research-based PhD in respiratory pharmacology. His early work was in appointments

to secret government facilities at Porton Down (Chemical Defence Establishment) and at Aldermaston (Forensic Science Service HQ). His subsequent career in the biopharmaceutical industry spanned almost 30 years leading project teams seeking new pharmacological treatments for asthma and COPD. He held positions of increasing responsibility and was, until 2011, Chief Scientific Officer, responsible for allergy & respiratory research worldwide within Pfizer, UK until that facility was closed. Dr. Yeadon then spent the next decade as an independent consultant, assisting 30 biotechnology companies in the fields of new medicines discovery for inflammatory and immunological diseases of lung and skin. Largely during their start-up phase. During that time he also founded and led as CEO his own biotech (Ziarco) which was acquired by Novartis in 2017.

A testimony has been provided by Dr. Michael Yeadon "Concerning information in relation to covid-19 vaccination and fertility".

A true copy of testimonial is annexed herewith and marked as Annexure P-11, Pg. 155-162.

26. On December 1, 2020, Dr. Wolfgang Wodarg and Dr. Michael Yeadon, expert reviewer in this field, filed a petition of concern with the European Medicines Agency.

A true copy of the Petition is annexed herewith and marked as Annexure P-12, Pg. 163-205.

27. In his said Petition, the principal grounds of concern were the excessive speed of clinical development, together with a limited series of specific concerns (which were not claimed to be exhaustive):

i. **Determination of covid-19 'cases' relied on inadequately controlled PCR testing**. It is very widely held by independent experts that the PCR tests used grossly over-estimate prevalence of truly infected 'cases' – in relation to which it is noteworthy that FDA has just announced that it is withdrawing approval from all PCR tests for detection of SARS-CoV-2 infection.

ii. **The potential for antibody dependent enhancement, which process has caused the termination of all other prior vaccines against coronaviruses.**

iii. **The potential for precipitating acute allergic reactions upon administration of the lipid-encapsulated vaccines** (Pfizer/BioNTech and Moderna products), which in fact did happen on the very first day of mass vaccination in UK & the label was soon changed to avoid administration to persons suspected of having had allergic responses to injected products in the past.

iv. **The potential for cross-over immune responses to a protein essential to successful pregnancy**. It is this latter concern to which the remainder of the instant Petition refers.

28. Further, as per the petition of Dr. Michael Yeadon, the Spike Protein is almost entirely responsible for the damage to the cardiovascular system, if it

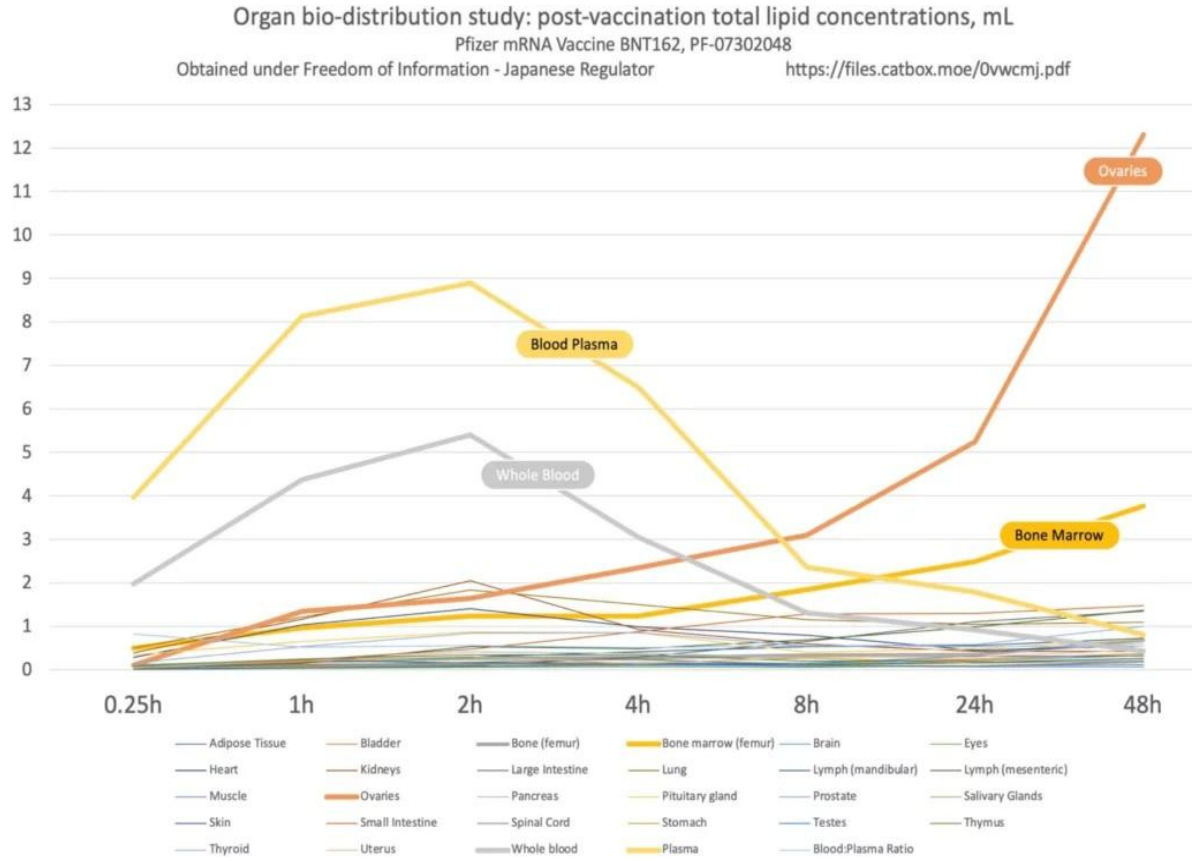
gets into circulation. If the Vaccines were like traditional bona fide vaccines, and did not leave the immediate site of vaccination, typically the shoulder muscle, beyond the local draining lymph node, then the damage that the spike protein could cause might be limited. Spike proteins are biologically active and they initiate the blood coagulation cascade among other properties. It is stated that it is the induction of blood coagulation in various locations in the body which is responsible for a high proportion of the serious adverse events including deaths which are being reported to the Vaccine Adverse Event Reporting System (VAERS) in the USA and in analogous databases elsewhere. These are woefully inadequate, suggesting approximations ranging from less than 1% to say 10%, with proven falsification/cover-up in several cases of data reporting. In general terms, there is paucity in Indian data and no data connected with foetus and or maternal deaths. Furthermore, since no long term reproductive toxicology studies have been conducted, it will not be known in any case what the long term impacts might be. The rate of fatal outcomes following Covid-19 vaccination, usually from clotting or bleeding disorders, is extraordinary and exceeds that from any previous vaccine by a very large amount, which this reviewer estimates is of the order of 60-fold. This astonishingly high rate of adverse events after vaccination, is a consequence of two factors: (i) The manufacturers were simply not required to study the way the product moves around the body after injection and (ii) They were not required to study the functional effects of the genetic code within the product after administration.

29. Dr. Yeadon further notes in Yeadon's Testimonial, that "*There are no products on the mass market which operate in this way. This is the greatest failure of medicinal product regulation in relation to reproductive health since thalidomide and is very much greater in terms of societal impact. It is imperative that all these products be suspended until improved safety testing can determine whether there are any groups in whom the benefits outweigh the risks*".

30. It would be appropriate at this stage to also point out the evidence obtained by Byram Brydle through a Freedom of Information Act (FOIA) request on confidential Pfizer data. Byram Brydle is a PHd, Viral Immunologist and Associate Professor at the University of Guelph. Brydle has obtained data from Pfizer's vaccine trial data in Japan.

    Steve Kirsch, author of Op-ed "Should You get Vaccinated?" who is fully vaccinated, has reproduced the below graph using the aforementioned data. **A true copy of the relevant portions of the Op-ed is annexed herewith and marked as Annexure P-13, Pg. 206-213.**

    Biodistribution of lipid nanoparticles which carry the mRNA show that the ovaries get the highest concentration. This turns the ovaries into a very large manufacturing plant to turn out toxic spike protein. Accumulation in the bone marrow is likely not good either. What are the long term implications of that?



31. It may be further pointed out that as per Pfizer Data obtained by Dr. Byram Bridle through FOIA request:

- The graph (above) shows the distribution of Lipid Nano-particles which carry the mRNA to different areas of the body in 48 hours from the time of the injection.
- The highest concentration at 48 hours is in the ovaries.
- These are Pfizer data given to the regulator and kept secret up to now, and known to the FDA. They show that the injection does not remain at the injection site, but that within a few hours (as low as 4 hours), it

has gone everywhere, to every organ, even the brain (crossing the blood brain barrier).

32. **A true copy of article from London Times is reproduced below, also annexed herewith and marked as Annexure P-14, Pg. 214-215.**

Article of Dr. Byram Bridle based on the Biodistribution Study referenced earlier, shares:

Audio from a radio show has emerged wherein Dr. Byram Bridle reveals the scientists behind the COVID-19 "Vaccine" made a terrible mistake.

According to the Doctor, who cites a brand new, peer-reviewed research study out of Japan "They made a mistake – they thought the spike protein was a great target antigen, only to discover it is a toxin that can travel to many organs of the body, causing severe damage."

WORSE, the spike proteins generated by mRNA vaccines don't stay in the shoulder muscle, but spread to the brain, heart, ovaries, etc.

They also know that the spike protein is what causes the damage with COVID—and now it is clear how it is causing so much damage in other parts of the bodies of the vaccinated.

Spike protein, on its own, is the cause of the vascular, neurodegenerative, problems, not the virus. In the original theory it stays in deltoid, goes to local draining lymph node, and activates immune system. But a new bio-distribution study from Japan tracked the vax and spike proteins. It gets into the blood within days of vax, accumulates in spleen, brain, bone marrow, liver, adrenal glands, with high concentrations in ovaries.

Spike protein is a pathogenic toxin that causes damage if in circulation, binds to platelets, epithelial cells of blood vessels, clotting, bleeding, heart problems, brain blood clotting.

Conclusion is “We made a big mistake, and didn’t realize it till now.” “We thought the spike protein was a great target antigen but never knew the spike protein itself was a pathogenic toxin protein.” “By vaccinating people we are inadvertently inoculating them with a toxin.”

33. Dr. Robert Malone, MD, MS is an American virologist and immunologist who has written a letter dated 19th June 2021 “to support Dr. Bridle’s good character”. **A true copy of the letter is annexed herewith marked as Annexure P-15, Pg. 216-217.**

This letter provides the impressive credentials of Dr Malone, the original inventor of mRNA vaccines and DNA vaccines and who has been granted “secret” clearance for the DoD”. (US Department of Defence):

US-based physician and scientist with an extensive record of successful innovation in basic and applied science, pathology, molecular virology, immunology, vaccine development, biodefense, project management, clinical development, regulatory affairs, and bioethics since 1984.

He states: “I have independently assessed most of the data which serves as the basis for Dr. Bridle’s communications regarding safety risks associated with the COVID-19 genetic vaccines, concur with his findings, and have independently raised my concerns with the US FDA including speaking directly with CBER director Peter Marks. I am particularly alarmed and

surprised by the bioethical positions being taken by the government of Canada regarding these experimental – stage vaccines, and very surprised. These policies appear contrary to what I have been trained as the bedrock principles of clinical research/human subjects bioethics.

Please stop politicizing science. The scientific process requires dissent and discussion to arrive at truth. This is a central tenant. Dr. Bridle has spoken truth as he sees it. –'My assessment is very much aligned with that of Dr. Bridle.

34. Inventor of mRNA Technology: Vaccine Causes Lipid Nanoparticles to Accumulate in 'High Concentrations' in Ovaries. **The true copy of article published in Global Research is annexed herewith and marked as Annexure P-16, Pg. 218-221.**

This is a short outtake from the full podcast of the "Dark Horse Podcast' (which was taken down by YouTube). On June 10, Dr. Robert Malone, creator of mRNA vaccine technology, joined evolutionary biologist Bret Brownstein, Ph.D., tech entrepreneur Steve Kirsch for a 3-hour conversation on the "Dark Horse Podcast" to discuss multiple safety concerns related to the Pfizer and Moderna vaccines. Their focus was the implications of the controversial Japanese Pfizer biodistribution study, which made public earlier this month by Dr. Byram Bridle, a viral immunologist. Bridle received a copy of a Japanese biodistribution study — which had been kept from the public — as a result of a freedom of information request made to the Japanese government for Pfizer data.

(Malone) -- Prior to the study's disclosure, the public was led to believe by regulators and vaccine developers that the spike protein produced by mRNA COVID vaccines stayed in the shoulder where it was injected and was not biologically active — even though regulators around the world had a copy of the study, which showed otherwise. Malone said the original data packages contained this biodistribution information. "This data has been out there a long time" within the protected, non-disclosed, purview of regulators across the world. The FDA knew the COVID spike protein was biologically active and could travel from the injection site and cause adverse events, and that the spike protein, if biologically active, is very dangerous.

In fact, Malone was one of many scientists to warn the FDA about the dangers of the free spike protein.

They also discuss the lack of proper animal studies for the new mRNA vaccines. Malone said there needed to be monitoring of vaccine recipients for leukaemia and lymphomas as there were concentrations of lipid nanoparticles in the bone marrow and lymph nodes. But those signals often don't show up for six months to three or nine years down the road. Usually, signals like this are picked up in animal studies and long-term clinical trials, but this didn't happen with mRNA vaccines.

Autoimmune issues may also be related to free-circulating spike protein which developers assured would not happen. To pick up autoimmune issues, a 2- to 3- year follow-up period in phase 3 patients would be required to monitor for potential autoimmune consequences from vaccines — but that

monitoring didn't happen with the Pfizer and Moderna vaccines. Pfizer and Moderna didn't conduct proper animal studies, Brownstein said. What the animal models give us is a signal that alerts us to what we need to follow up on in humans.

Malone further stated that there are two adverse event signals that are becoming apparent to the U.S. Food and Drug Administration (FDA). One of them is thrombocytopenia — not having enough platelets, which are manufactured in the bone marrow. The other is re-activation of latent viruses.

And furthermore, earlier this year, Dr Vanden Bossche put out a call to the World Health Organization, supported by a 12-page document, that described the "uncontrollable monster" that a global mass vaccination campaign could potentially unleash; that mass vaccination could produce ever more transmissible and potentially deadly variants.

(Malone). "Vanden Bossche got it right". Vanden Bossche's concern is not theoretical. It is real and we have the data. We're stuck with this virus or its downstream variants pretty much for the rest of our lives and it's going to become more like the flu. We will have continuing evolution and circulation of variants, and that is an 'escape.' " (petitioner clarification – mutant escape or emergence of new variants).

35. Following further observations and submissions as culled out from the various scientific evidence mentioned in the Yeadon testimonial, are noteworthy:

i. **The shadow of Thalidomide and changes to drug safety regulation in pregnancy**. The drug name ‘Thalidomide’, is, particularly in Europe, indelibly associated in the public mind with birth defects. Intended to treat nausea associated with early pregnancy, it was prescribed in 46 countries, but not the USA, between 1957 and 1962, when it was withdrawn, having been identified as the causative agent in 10,000 birth malformations involving reduced or absent limbs. Thalidomide is one of the most infamous case of failed drug safety evaluation. By contrast with regulators in dozens of other countries, the US drug regulatory agency, the Food & Drug Administration, did not approve thalidomide because the reviewer was not satisfied by the available information.

As a result, Drug safety was substantially reformed worldwide in the aftermath of this event, notably to require manufacturers to conduct what is broadly termed ‘reproductive toxicology’ and also almost always to include rabbits as a test species, because it was later discovered that thalidomide did cause birth defects in rabbits. But far less obviously in rodents. There was a realisation; the concept that the foetus was somehow protected from harm by being in the womb, was completely mistaken. On the contrary, the intricacies of embryo-foetal development started to be recognised as a period of extreme vulnerability.

ii. **Covid-19 vaccines have not been taken through reproductive toxicology tests.** It is essential to lay-out the backdrop to the current position with clinical use of covid-19 vaccines, for one reason: we have NEVER, since thalidomide, exposed ‘women of childbearing potential’ (WOCBP) and ESPECIALLY NEVER pregnant women to ANY novel, experimental pharmaceutical product, without that product first having completed a full battery of reproductive toxicology tests. Even after this crucial step, pilot studies are always conducted in a small number of pregnant women to minimise risk to the developing foetus. Neither of these essential steps have been undertaken.

iii. **No justification for taking risks with the health of unborn children.** The expert reviewer is astonished at the current position. It is the height of recklessness to allow WOCBP to receive covid-19 vaccines, which are of an entirely novel, (including gene-based technology, mRA/DNA), for which there is no prior human safety experience in a large population. Worse, the active recommendation that these experimental agents should be administered to pregnant women is, in my opinion, ---- criminally negligent. Furthermore, it is completely incomprehensible that these novel vaccines are recommended for use in pregnancy, most of which happen in women aged 40y or younger, since the dominant risk factor for poor outcomes from infection by SARS-CoV-2 is age. The mRNA/DNA,

which are formulated in lipid nanoparticles, accumulate in the ovaries of mammals including humans.

iv. The Petitioners reiterate here that Covaxin and Sputnik both have the spike protein. Both manufacturers state in the vaccine literature that they are contraindicated for pregnant women.

v. With reference to Dr. Bridle's biodistribution study and the concentration of NLP in the Ovaries, "the intended induction of immunity definitely does not require the presence of vaccine components in reproductive tissue. Most commonly, the concentrations of drugs in any tissue in the body peaks quickly after administration, after which they fall away gradually over time. In light of this, it is more troubling still that, instead of falling away gradually over time as expected, the tissue levels RISE over time, suggestive of an active process. The study was aborted 48 hours after administration of the test material, not unreasonably. After that much time, it would be normal to be expecting the peak of tissue concentrations to have passed. However, the highest concentrations were seen at the last time point, 48 hours post-dose, meaning it is not known when the peak time after administration actually is or whether concentrations in the ovaries and spleen rise even higher at extended times --- What this means is immediately obvious to anyone experienced in the development of medical products:

- It is unsafe to make any assumptions at all about the safety profile, short or long, after administration to humans.
- We did not know, prior to the tragic lessons arising from Thalidomide that early in gestation, the developing embryo is exquisitely vulnerable to the adverse effects of environmental agents, including pharmaceuticals.
- It is unreasonable to assume that, because conventional vaccines are not generally considered to represent a safety issue in relation to fertility and pregnancy, that these novel, gene-based products and Covaxin and Sputnik with their spike proteins will be safe in pregnancy.
- The part of the SARS-CoV-2 virus called the spike protein is coded into these new technology products, such that they all induce the body of the recipient to manufacture that spike protein or a portion thereof.
- It is conventional good practise to review the scientific literature around chosen targets for use in vaccines, in this case, spike protein. This is required to ensure that the potential for unwanted effects, (when humans are caused to develop immune responses to it), is understood.

vi. **Syncytins**: Two outstanding findings were identified from this scientific literature search:

- First, spike proteins are able to initiate blood platelet aggregation and this to trigger blood coagulation, which calls into serious doubt the wisdom of having selected spike protein in all the vaccines to date.
- Second, syncytins: there is a weak, but obvious similarity of the coronavirus spike protein and a family of human proteins called syncytins. It is wrong to decide the level of similarity solely by reference to the primary amino acid sequence of two proteins and important also to consider the similarity of their 3-dimensional structure.
- The Syncytin family of proteins are considered critical for the formation and successful maintenance of the placenta. Therefore, no matter how weak the homology between spike protein and syncytins, the concern arose that, upon making a strong immune response to spike protein, some women might generate an immune response to their own placental proteins. This concern would, in Dr. Yeadon's experience of over 30 years in the pharmaceutical industry, be met technically with a small series of studies to examine, hopefully to rule out, this concern. There are a number of ways in which this could be done. It is not difficult to devise a clinical study to evaluate whether or not women administered a covid-19 vaccine develop circulating antibodies to syncytin-1.

A true copy of such a Study, reported as a pre-print, is annexed herewith and marked as Annexure P-17, Pg. 222-235.

- The authors of this paper have no basis to claim that the amount of antibodies to syncytin-1 is too small to matter. They appear to be unaware of the thalidomide lessons, which show that periods of exquisite sensitivity exist during early development where the presence of a toxin for periods of as little as two days can terminate development processes which are then never repaired. It is sobering to recall again the lessons from thalidomide. It turns out that if the mother, early in pregnancy, took her first dose of thalidomide on day 20 after conception, their baby was likely to be born with brain damage; If on day 21, blind; if on day 24, limbs were often shortened or missing; no damage occurred if taken after day 42 since conception.
- This new data, which shows that women do raise antibodies to a component of their placenta after vaccination with the Pfizer/BioTech product, raises serious concerns for foetal safety. It is not safe to assume that this will not have adverse consequences on successful pregnancy. It is not safe to assume that the other vaccines will not have similar effects. Again, as with the biodistribution study, a presumption of risk, potentially severe, arises from these clinical observations, and there isn't an aware person who wouldn't call a halt at this point.

vii. Dr. Yeadon has further noted, that *"in addition to the class- effect concerns we now have of immune responses to syncytin-1, (almost certainly this will not be limited to antibodies but also probably include cytotoxic T-lymphocytes directed against cells expressing syncytin-1), we also have concerns about vaccine carriers, in this case the lipid nanoparticle (LNP) concentrating in ovaries. I've just discovered that the phenomenon of ovarian concentration of carriers has been known since at least 2012. Furthermore, it extends beyond rats & the same problematic profile has been seen repeatedly in mice, too. It's literally so bad that it surely cannot be accidental"*. ---*"They KNEW"*.

viii. **Any experienced reviewer would call for a halt to the use of this vaccine in non-menopausal women.** Dr. Yeadon further notes *"in the absence of evidence that says this is not a predictor for humans, this is what I expect is happening to every female administered this agent. It is to be expected that the consequences of this concentration in reproductive will be adverse. Based on observations elsewhere in the body, where blood clots and bleeding have separately been reported. In my opinion, any reasonable reviewer would agree that these vaccines should not be administered to any female below menopause"*.

ix. Additionally, antibodies raised against the spike protein might interact with the naturally occurring syncytin proteins, adversely

affecting multiple steps in human reproduction. The manufacturers did not provide data on this subject despite knowing about the spike protein's similarity to syncytin proteins for more than one year. There are now a very high number of pregnancy losses in VAERS. A study recently published in the New England Journal of Medicine, 'Preliminary Findings of mRNA COVID-19 Vaccine Safety in Pregnant Persons,' exposes that pregnant women receiving Vaccines during their first or second trimesters suffer an 82% spontaneous abortion rate, killing 4 out of 5 unborn babies. There are worldwide reports of irregular vaginal bleeding without clear explanation. Scientists are concerned that the Vaccines pose a substantial risk to a woman's reproductive system. This increased risk of sterility stems from an increased concentration of the spike proteins in various parts of the reproductive system after vaccination. Not enough is known to determine the risk of sterility, but it is beyond question that the risk is increased. Billions of aggressive spike proteins are accumulating in very delicate ovarian tissues, the one place in the human body where females carry a finite number of fertile eggs.

36. The above matters and in their application in particular to the current policies being implemented in India defy belief; are shocking, and unconscionable, a serious indictment of Regulatory bodies worldwide including India. The evidence of a lack of rigour and scrutiny in the regulatory oversight of the safety of Covid 19 vaccines, must put into question the entire policy of the

release under EUA, of these vaccines. The problem gets compounded when innate or natural immunity is factored into the matter of vaccines administered to pregnant women.

More Views of Leading Scientists, Doctors and Policy Experts

37. It is further submitted that 57 leading scientists, doctors and policy experts from North and South America have released a report calling into question the safety and efficacy of the current COVID-19 vaccines and are now calling for an immediate end to COVID 19 vaccination drive. The relevant portion of the report is reproduced hereunder:

> "*The lack of thorough testing in animals prior to clinical trials, and authorization based on safety data generated during trials that lasted less than 3.5 months, raise questions regarding the safety of these vaccines. The recently identified role of SARS-CoV-2 glycoprotein Spike for inducing endothelial damage characteristic of COVID-19, <u>even in absence of infection</u>, is extremely relevant given that most of the authorized vaccines (mRNA/DNA – including Astra Zeneca (DNA) and Sputnik) induce the production of Spike glycoprotein in the recipients. Given the high rate of occurrence of adverse effects, and the wide range of types of adverse effects that have been reported to date, as well as the potential for vaccine-driven disease enhancement, Th2-immunopathology, autoimmunity, and immune evasion, there is a need for a better understanding of the benefits and*

risks of mass vaccination, particularly in the groups that were excluded in the clinical trials."

"Furthermore, even in the absence of SARS-CoV-2 virus, Spike glycoprotein alone causes endothelial damage and hypertension in vitro and in vivo in Syrian hamsters by down-regulating angiotensin-converting enzyme 2 (ACE2) and impairing mitochondrial function [26]. Although these findings need to be confirmed in humans, the implications of this finding are staggering, as all vaccines authorized for emergency use are based on the delivery or induction of Spike glycoprotein synthesis. In the case of mRNA vaccines and adenovirus-vectorized vaccines, not a single study has examined the duration of Spike production in humans following vaccination. Under the cautionary principle, it is parsimonious to consider vaccine-induced Spike synthesis could cause clinical signs of severe COVID-19, and erroneously be counted as new cases of SARS-CoV-2 infections. If so, the true adverse effects of the current global vaccination strategy may never be recognized unless studies specifically examine this question. There is already non-causal evidence of temporary or sustained increases in COVID-19 deaths following vaccination in some countries (Fig. 1) and in light of Spike's pathogenicity, these deaths must be studied in depth to determine whether they are related to vaccination"

"Some adverse reactions, including blood-clotting disorders, have already been reported in healthy and young vaccinated people. These cases led to the suspension or cancellation of the use of adenoviral vectorized ChAdOx1-nCov-19 and Janssen vaccines in some countries. It has now been proposed that vaccination with ChAdOx1-nCov-19 can result in immune thrombotic thrombocytopenia (VITT) mediated by platelet-activating antibodies against Platelet factor-4, which clinically mimics autoimmune heparin-induced thrombocytopenia [29] Unfortunately, the risk was overlooked when authorizing these vaccines, although adenovirus-induced thrombocytopenia has been known for more than a decade, and has been a consistent event with adenoviral vectors [30]. The risk of VITT would presumably be higher in those already at risk of blood clots, including women who use oral contraceptives [31], making it imperative for clinicians to advise their patients accordingly."

A true copy of the Report is annexed herewith and marked as Annexure P-18, Pg. 236-247.

38. Furthermore, twenty Seven health experts have written to FDA – "slow down and get the science right before approving vaccines". This important letter exposes the WHO myth of the safety of COVID Vaccines. Authored by 27 leading medical experts (various countries), including Dr. Peter McCullough (leading cardiologist, intensivist, epidemiologist) is a signatory, it exposes the cover-up, the gaps in safety testing, but also, why

these mRNA and DNA vaccines pose serious potential harm to people and global health. RNA/DNA vaccine safety testing, therefore, requires rigorous and diligent oversight by independent experts, who are proven to have no conflict of interest.

A true copy of the news report of the petition by medical experts is annexed herewith and marked as Annexure P-19, Pg. 248- 253.

The relevant portion of the letter is reproduced herewith:

"3. Require data on the safety and pharmacokinetic (the study of the time course of drug absorption, distribution, metabolism). profiles of the spike protein.

Rationale:

a. In-situ production of SARS-CoV-2 spike protein is the target mechanism of action of all COVID-19 vaccines with an EUA at present. Therefore, the safety profile of spike protein itself (i.e., in the absence of virus) must be thoroughly understood in the range of populations on the indications list.

b. Recently, evidence of systemic circulation of spike protein or its components in subjects post-immunization was reported. All studies we are aware of to date raise concerns about the safety of spike protein, and the concentration of circulatory spikes was correlated to the disease severity in COVID-19 patients.

c. Required studies must, at a minimum, address these concerns:

i. Coagulopathy issues, including blood clots, haemorrhage, thrombocytopenia, heart attack, and strokes. According to the VAERS, as of May 21, 2021, there have been a total of 1,222 reports of thrombocytopenia/low platelets; and 6,494 (112 in 0-24 year-olds) reports of blood clots/strokes.

ii. Reproductive issues, including menstrual irregularities, reduced fertility, miscarriages, and preterm births. According to VAERS, as of May 21, 2021, there were 511 reports of miscarriage and 522 reports of uterine haemorrhage (including 88 in women older than 50 years). The vaccines induce the generation of antibodies to attack spike protein, which are genetically similar to proteins produced by the placenta. To date, no vaccine sponsors have conducted immunologic studies of spike protein involvement with proteins involved in placental development.

iii. Carcinogenesis. There is preliminary and theoretical evidence that the spike protein may promote cancer. Considering the potential for annual booster vaccinations, COVID-19 vaccines should be treated similarly to medication taken for chronic conditions on a long term basis. Carcinogenic potential is important to characterize.

iv. Transmission of spike protein (or its fragments) from vaccinated individuals, such as through breast milk and associated risk in neonates and infants. According to the UK Medicines & Healthcare products Regulatory Agency, there are 921 reports of exposure via

breast milk following AstraZeneca's vaccine and 215 reports following Pfizer's vaccine.

v. Neurological disorders, including Guillain-Barré syndrome, acute disseminated encephalomyelitis, transverse myelitis, encephalitis, myelitis, encephalomyelitis, meningoencephalitis, meningitis, encephalopathy, demyelinating diseases, and multiple sclerosis.

vi. Cardiac issues, including myocardial infarction, myocarditis and pericarditis, among others. According to the VAERS, as of May 21, 2021, there have been a total of 1,598 reports of heart attacks (24 reported in 0-24 year-olds; 501 resulted in death).

vii. Autoimmune diseases, including thyroiditis and diabetes mellitus, immune thrombocytopenia, autoimmune hepatitis, primary biliary cholangitis, systemic sclerosis, autoimmune disease for skeletal muscles (myasthenia gravis, myositis such as polymyositis, dermatomyositis, or other inflammatory myopathies)

viii. Studies should be conducted in individuals of both sexes and all ages. We cannot assume that the effects of spike protein are the same across populations of all ages, sex, and across pre-existing conditions.

4. Require data from biodistribution studies investigating the actual COVID-19 vaccines.

Rationale:

a. Data from the biodistribution studies submitted by Moderna and Pfizer suggests that the vaccines distribute widely in the body, including to the liver, brain, heart, lung, adrenals, ovaries, and testes, among many other tissues.34,35 (See Tables 1a, 1b, and 2 below for studies R-[?]-0072 and 185350 submitted by Pfizer and study 5002121 submitted by Moderna.)

b. However these were not studies of the currently authorized products: Pfizer's BNT162b2, Moderna's mRNA-1273, or Janssen's Ad26.COV2.S.34–36

c. Instead of presenting novel biodistribution studies of the COVID-19 vaccine formulations, sponsors presented substitute studies to FDA for an EUA during the pandemic.

d. Therefore, novel biodistribution studies investigating the actual COVID-19 vaccines are necessary.

e. Biodistribution studies would be required for any small molecule pharmaceutical drug submitted for approval (i.e. New Drug Application), and should be conducted on the COVID-19 vaccines as well as these novel vaccines which work on the premise of gene delivery--very different to conventional vaccines.

f. Biodistribution studies help inform an understanding of vaccine transfection to various tissues (away from injection site) spurring various distant tissues to produce spike proteins and consequent autoimmune response against the body's cells. These studies will therefore help enhance our understanding of the nature of potential short

and long term adverse events. At this point in time, in which other data sources exist to characterize short term harms of COVID-19 vaccines with an EUA, the utility of biodistribution studies to characterize long term adverse effects and better understand potential mechanism(s) of action of short and long term harms, remains critically important. g. Necessary studies must, at a minimum, address these concerns

7. Ensure the inclusion of experts in gene therapy in the VRBPAC.

Rationale:

a. The COVID-19 vaccines produced by Pfizer, Moderna, and Janssen (as well as AstraZeneca, CanSinoBio (China) and Gamaleya Research Institute (Russia)) are gene based vaccines. Their mechanism of action differs substantially from all other vaccines that have been used on populations globally, as these novel vaccines work on the premise of gene delivery, and may therefore be considered a type of gene therapy. These gene based vaccines involve entering the cell, where the overwhelming majority of critical body activities occur, and utilizing the host's cells to produce spike protein. This is an entirely different mechanism than that utilized by traditional vaccines such as inactivated, attenuated, subunit or protein-based (that are not intended to invade cells). Therefore, there is a need to consider safety with the informed perspectives of those with expertise in gene therapies.

8. Ensure that the analysis of data and decisions regarding any COVID-19 vaccine BLA application are informed by experts with no financial or

research relationships with any vaccine manufacturers within the last 36 months, both within FDA and amongst the composition of the VRBPAC. (This is the CBER - The Center for Biologics Evaluation and Research-- Vaccines and Related Biological Products Advisory Committee)."

Precautionary Principle (PP)

39. The application of the PP is completely and absolutely relevant to the question of vaccinating pregnant women. These vaccines do not even offer reasonable certainty of no harm. Furthermore, and despite the clear evidence of the orchestrated attempts to minimise Adverse Effects (AE), the deliberate cover-up, under-reporting etc, the record of AE that has nevertheless emerged including deaths, is medically and humanly shocking and have led many scientists to call for an immediate stop to the mass vaccination drive, particularly in pregnant women.

40. By some estimates, the number of deaths attributable to COVID vaccines have exceeded the total 40 year data of deaths of all vaccines put together. In a real sense therefore, we have gone beyond the notion of mere caution and precaution in this matter. It would be ethically unconscionable, and would invite the opprobrium of medical insanity to vaccinate pregnant women and in view of the Syncytin evidence, also WOCBA; and it is not understood how such mindlessness is occurring in the vaccine roll-out to include both these categories. It is worth adding for the record that based on the vaccine leaflets and on their own admission, several other groups qualify for exclusion.

41. The technology of COVID 19 vaccines is a textbook case for the application of the Precautionary Principle. The precautionary principle necessitates that if there are reasonable scientific grounds for believing that a new process or product may not be safe, it should not be introduced until we have convincing evidence of reasonable certainly of no harm.

42. This Hon'ble Court in *A.P. Pollution Control Board v. M.V. Nayudu [1999 (2) SCC 718]* held that that precautionary principle is applicable to India. The principle mandates that when a new technology or process can cause serious and irreversible harm to human health and the environment, precautionary measures should be taken even if some cause and effect relationships are not fully established scientifically. In this context, the proponent of the novel and uncertain activity rather than the public should bear the burden of proof. As, if one is embarking on something new, one should go ahead only and until one is reasonably convinced that it is safe. Pushing forward with untested, inadequately researched technologies, and insisting that it is for the society to prove conclusively that they are harmful before they can be stopped, is self- defeating and extremely dangerous.

43. Misapplication of the Precautionary Principle has Misplaced the Burden of Proof of Vaccine Safety – by Judy Wilyman, Principia Scientific International (PSI) & Citizens for Health Awareness published on 28 November 2020, states:

"*Human health can be protected in government policies if the precautionary principle is used in the correct format that puts the onus of proof of*

harmlessness on the government and pharmaceutical industry, and not the general public. This has not been done in current vaccination programs and we cannot rule out the possibility that the increased use of vaccines is destroying the genetic fabric of society as MacFarlane Burnet postulated."- **A true copy of the Full Paper is Annexed herewith and marked as Annexure P-20, Pg. 254-264.**

44. It is further submitted that Vaccinations are resulting in deaths and Serious Adverse Events which are wilfully not reported and therefore underestimated, and is in stark contrast to the appropriate Reporting system. **A true Copy of Grant Report on Adverse Event Reporting System is annexed herewith and marked as Annexure P-21, Pg. 265-271.**

45. There have been thousands of cases of deaths and serious adverse events following vaccination reported in the newspapers in India as of 19th October 2021. The Compilation has approximately 5132 newspaper reports reporting deaths alone after administration of vaccine.

A true copy of the compilation of Reports of deaths after Covid vaccination is annexed herewith and marked as Annexure P-22, Pg.272-567

46. Moreover, nearly 11,000 Deaths after COVID Vaccines have been reported to CDC, as FDA Adds New Warning to J&J Vaccine.

A true copy of the report is annexed herewith and marked as Annexure P-23, Pg. 568-577.

47. Furthermore, the website https://johnplatinumgoss.com/covid-19-vaccination-statistics/ pools Adverse Event Data from USA, EU and UK.

These are official statistics and those who produce them, MHRA, EMA and FDA, concede that they are much higher, (10 to 100 times higher) than the figures they have released. In some of the tables on this page a more realistic picture is illustrated. Given that India's AEFI monitoring and reporting mechanism has serious lapses, if one extrapolates the USA, UK and EU numbers for India, the figures could be potentially shocking as vaccination coverage increases.

48. The table below shows the Reported Fatalities, Injuries and Total number of reports for USA, UK and EU as on 5.8.21. The table also estimates the number of cases if the Reported numbers were just 1% or 10% of the actual cases (unreported).

Covid-19 Injection Damage: EU, UK AND US SUMMARY		Estimated Numbers if those reported were just:	
		1%	10%
Region and data entry cut off date	Total Reported	Total	Total
UK Fatalities - 29th September 2021	1,698	169,800	16,980
EUdra Fatalities- 9th October 2021	27,242	2,724,200	272,420
US Fatalities -1st October 2021	16,310	1,631,000	163,100
Total Fatalities	**45,250**	**4,525,000**	**452,500**
UK Injuries -29th September 2021	1,222,566	122,256,600	12,225,660
EUdra Injuries -9th October 2021	2,536,526	253,652,600	25,365,260
US Injuries -1st October 2021	3,659,888	365,988,800	36,598,880
Total Injuries	**7,418,980**	**741,898,000**	**74,189,800**
UK Reports -29th September 2021	370,574	37,057,400	3,705,740
EUdra Reports -9th October 2021	1,038,776	103,877,600	10,387,760
US Reports -1st October 2021	778,221	77,822,100	7,782,210
Total Number of Reports	***2,187,571***	***218,757,100***	***21,875,710***

The above table is reproduced from the blog of John Goss. The true copy of the compiled data has been procured from the following sources:

- Medicines and Healthcare products Regulatory Agency (MHRA), UK

- Vaccine Adverse Event Reporting System, USA
- EudraVigilance by European Medicines Agency (EMA), EU
- VigiBase Data, WHO

Natural Immunity vs. Vaccine Immunity

49. 20 Doctors from India, representing a group called Indian Doctors for Truth, have written a letter to the Hon'ble Prime Minister requesting an urgent need to stop the overzealous vaccination drive against Covid -19.

A true copy of the letter is annexed herewith and marked as Annexure P-24, Pg. 578-621.

The relevant excerpts from the letter are reproduced hereinbelow:

> "*There is enough and robust evidence available now that those who have recovered from Covid 19 develop robust and long-lasting immunity against SARS CoV2, even after mild or asymptomatic infections, and that chances of reinfection among these people, even from the emerging variants of the same virus, are extremely rare or non-existent.*"
>
> *"There is no evidence to show that those who have recovered from the infection will get any additional benefit from vaccination."*
>
> *"In India, recent sero-surveys at Delhi and Mumbai have reported a positivity of 50-70%, indicating that a significant proportion of our people have already been infected, reaching the levels of herd immunity, and will not need the vaccine."*

"A very important development that has taken place because of 4 latest studies that proves that almost 99.9% population has the memory from previous corona infection and that whether to the actual corona infection or to vaccine it is our same immune memory gets activated and vaccines in fact are more harmful in an already immune population".

50. Hence, keeping in mind the above scientific evidence, indicating that there is a significant population, including pregnant women, that has already been infected, there is a need to conduct elaborate tests and trials without conducting which, it will be completely abhorrent and unconscionable to vaccinate pregnant women, and expose them as well as the unborn child to serious adverse effects, which will be in violation of their fundamental right to health.

51. Upon being extremely disturbed and aggrieved by the evasive response and the inaction of the respondents, and the illegal and arbitrary campaigns and guidelines, the Petitioners beg to move this Petition under Article 32 of the Constitution of India on following amongst other:

GROUNDS

A. BECAUSE the impugned MoHFW Guidelines dated 02.07.2021 have absolutely no basis to advise Covid-19 vaccination for pregnant women and is not based on any new scientific or medical research which could conclude that these vaccines are safe for pregnant women. On the other hand, there is

plethora of medical evidence indicating that the guidelines are inconsistent and contrary to the medical and expert opinion on the issue of vaccination for pregnant and lactating women, and that they may not be subjected to a biologically active agents.

B. BECAUSE the Covid-19 vaccines in India, i.e. Covishield, Covaxin and Sputnik V, are experimental vaccines under Emergency Use Authorisation (EUA), which means that they have not been approved and their non-approval status is because their Phase III trial is either not complete and it has not been subjected to peer review. As is also evident from the material presented, these vaccines have not been tested on pregnant women and as such, it will be abhorrent to subject pregnant women to these untested vaccines.

C. BECAUSE there is absolutely no basis and no cause for these vaccines to be injected into pregnant women who are also unsuspecting and uninformed of the double dangers that these vaccines pose, both to themselves and to the unborn child they are carrying, therefore, there being no ‘informed consent’.

D. BECAUSE the biosafety protocols demand the publication of long term data for chronic toxicity (long term testing, more than 90 days) in animal models, which has not been done and there is also no long term reproductive toxicity studies nor genotoxicity studies. Pertinently, pregnant women were not included in any of the trials – not even in animal studies.

E. BECAUSE the vaccine manufacturers in the Product insert/Factsheet of these vaccines have themselves cautioned against vaccination of pregnant

women and have admitted that the same have not been studied in pregnant women. In the light of the caution given by the vaccine manufacturers themselves, it would be seriously unconscionable and ethically abhorrent on the part of the State, to subject pregnant women to an experimentation of this kind.

F. BECAUSE as per the Summary of Product Characteristic of these vaccines available with Central Drugs Standard Control Organisation (CDSCO), Pregnant and lactating mothers have been included under the section 'contraindications'.

G. BECAUSE as per the response received to an RTI query dated 27.07.2021, admittedly CDSCO has not granted permission to conduct clinical trials on pregnant women and breast feeding women.

H. BECAUSE unlike Traditional vaccines which have been in use for over 4 decades and form the basis of the trust and acceptance of traditional vaccines in the general public and the medical profession, Covid-19 vaccines have received EUA without completing third phase trial which is crucial to determine the effectiveness, adverse effects, reactions against the composition.

I. BECAUSE in case of traditional vaccines, regulatory authorities around the world usually maintain a public record of serious Adverse Effects noted after vaccination, which allows some linkages to be made between the vaccine and its effects. However, no such public record of adverse effects has been maintained for these EUA Covid-19 vaccines.

J. BECAUSE the Covid-19 vaccines approved in India produce Spike Protein as evident from their Summary of Product Characteristics, which is cytotoxic, pathogenic and biologically active, and can be severely harmful to pregnant women as well as the unborn child.

K. BECAUSE there have been thousands of cases of deaths and serious adverse events following vaccination reported in the newspapers in India as of 19th October 2021 and there is a staggering compilation of approximately 5132 newspaper reports reporting deaths alone after administration of vaccine, as annexed with this Petition.

L. BECAUSE the technology of Covid-19 vaccines is a textbook case for the application of the Precautionary Principle, which necessitates that if there are reasonable scientific grounds for believing that a new process or product may not be safe, it should not be introduced until we have convincing evidence of reasonable certainly of no harm. This Hon'ble Court in *A.P. Pollution Control Board v. M.V. Nayudu [1999 (2) SCC 718]* has held as follow:

> *"31. The "uncertainty" of scientific proof and its changing frontiers from time to time has led to great changes in environmental concepts during the period between the Stockholm Conference of 1972 and the Rio Conference of 1992. In Vellore Citizens' Welfare Forum v. Union of India 2 a three-Judge Bench of this Court referred to these changes, to the "precautionary principle" and the new concept of "burden of proof" in environmental matters. Kuldip Singh, J. after referring to the*

principles evolved in various international conferences and to the concept of "sustainable development", stated that the precautionary principle, the polluter-pays principle and the special concept of onus of proof have now emerged and govern the law in our country too, as is clear from Articles 47, 48-A and 51-A(g) of our Constitution and that, in fact, in the various environmental statutes, such as the Water Act, 1974 and other statutes, including the Environment (Protection) Act, 1986, these concepts are already implied. The learned Judge declared that these principles have now become part of our law. The relevant observations in the Vellore case 2 in this behalf read as follows: (SCC p. 660, para 14)

"14. In view of the above-mentioned constitutional and statutory provisions we have no hesitation in holding that the precautionary principle and the polluter-pays principle are part of the environmental law of the country."

M. BECAUSE this Hon'ble Court in plethora of cases such as *Consumer Education and Research Centre vs. Union of India* [1995 AIR 922], CESC *Ltd. vs. Subash Chandra Bose* [(1992) 1 SCC 441], has held that right to health is an integral fact of a meaningful right to life.

N. BECAUSE in terms of Article 21 of the Constitution of India, the State is under an obligation to take every measure to preserve life, as has been held by this Hon'ble Court in the *Paschim Banga Khet Mazdoor Samity & Ors. Vs. State of West Bengal & Ans* [(1996) 4 SCC 37].

O. BECAUSE this Hon'ble Court in *Common Cause vs. Union of India* [(2018) 5 SCC 1], while discussing an individual's right over his/her own body and the right to decide the medical treatment for themselves, held asunder:

> "*169. In the context of health and medical care decisions, a person's exercise of self-determination and autonomy involves the exercise of his right to decide whether and to what extent he/she is willing to submit himself/herself to medical procedures and treatments, choosing amongst the available alternative treatments or, for that matter, opting for no treatment at all which, as per his or her own understanding, is in consonance with his or her own individual aspirations and values.*"

P. BECAUSE this Hon'ble Court in plethora of cases has held that maternal, reproductive and sexual health is a right of a woman which flows from the right to life protected under Article 21 of the Constitution of India. As such in view of the overwhelming evidence, it will be completely abhorrent and unconscionable to vaccinate pregnant women, and expose them as well as the unborn child to serious adverse effects, which will be in violation of their fundamental right to health.

52. The Petitioners crave leave to add, alter or delete averments or grounds mentioned above.

53. The Petitioners state that in the facts and circumstances stated hereinabove, he has made out a strong prima facie case which warrants judicial review.

54. The balance of convenience and/or inconvenience rests in favour of the Petitioners for grant of reliefs as prayed for hereinafter and such reliefs, if

granted, would provide adequate remedy to the petitioner and the public at large.

55. The Public at Large shall suffer irreparable loss, injury and prejudice if orders as prayed for hereinafter are not granted.

56. The Petition is bonafide and made in the interest of justice.

57. The Petitioners have not filed a similar petition before this Hon'ble Court or before any other Court for similar reliefs prayed by the Petitioner herein.

PRAYER

Therefore, in view of the facts and circumstances mentioned herein above, it is humbly requested to this Hon’ble Court to grant the following reliefs:

i. Issue a direction, order or writ, including writ in the nature of mandamus directing the Respondents as well as their concerned departments to forthwith categorize pregnant and lactating women as non-eligible for Covid-19 vaccination, excepting under a doctor’s prescription;

ii. Issue a direction, order or writ, including writ in the nature of mandamus commanding the Respondent as well as its concerned departments to forthwith stop vaccination of pregnant and lactating women, unless under a doctor’s prescription.

iii. Issue a direction, order or writ, including writ in the nature of mandamus commanding the Respondent as well as its concerned departments to suitably issue guidelines for standard operating

procedure to track and monitor pregnant women, who may have already received Covid-19 vaccination;

iv. Issue any other direction or order which this Hon'ble Court may deem fit and proper in the facts of the present case and in the interest of justice.

And for this act of kindness, the petitioner as in duty bound shall ever pray.

Drawn on: 30.10.2021

Drawn By:

Varsha Gumashta

FILED BY:

(Satya Mitra)

Advocate for the Petitioners

IN THE SUPREME COURT OF INDIA

CIVIL ORIGINAL JURISDICTION

WRIT PETITION (CIVIL) NO. OF 2021

(PIL UNDER ART. 32 OF THE CONSTITUTION OF INDIA)

IN THE MATTER OF:

Dr. Ridhi Arora & Others ...PETITIONERS

Versus

Union of India ...RESPONDENT

AFFIDAVIT

I, Dr. Ridhi Arora, aged about 40 years, [redacted], do hereby solemnly affirm and state as under:

1. That I am the Petitioner No. 1 in the above captioned Writ Petition/PIL, and in such capacity, I am well conversant with the facts of the Petition and competent to swear this affidavit.

2. That the statement of the facts contained in Synopsis and list of dates at pages __B_ to __FF__ and Paragraph 1 to 57 at pages 1 to _61_ of the Writ Petition/PIL and the contents of the accompanying applications are true and correct to my knowledge and belief nothing material has been concealed.

3. That the Annexures annexed with this Writ Petition/PIL are true copies of their respective originals.

4. This Writ Petition is being filed under my instructions and the contents thereof are true to the best of my knowledge and there is no personal gain, private motive or oblique reason in filing the Public Interest Litigation.

DEPONENT

VERIFICATION:

Verified at New Delhi on this the 30th day of October, 2021 that the contents of the above affidavit are true and correct to my knowledge, that no part of it is false and that nothing material has been concealed.

DEPONENT

IN THE SUPREME COURT OF INDIA

CIVIL ORIGINAL JURISDICTION

WRIT PETITION (CIVIL) NO. OF 2021

(PIL UNDER ART. 32 OF THE CONSTITUTION OF INDIA)

IN THE MATTER OF:

Dr. Ridhi Arora & Others ...PETITIONERS

Versus

Union of India & Another ...RESPONDENTS

AFFIDAVIT

I, Mathukutty John, aged about 64 years, S [redacted] A [redacted], do hereby solemnly affirm and state as under:

1. That I am the Petitioner No. 2 in the above captioned Writ Petition/PIL, and in such capacity, I am well conversant with the facts of the Petition and competent to swear this affidavit.

2. That the statement of the facts contained in Synopsis and list of dates at pages __B_ to _FF___ and Paragraph 1 to 57 at pages 1 to __61__ of the Writ Petition/PIL and the contents of the accompanying applications are true and correct to my knowledge and belief nothing material has been concealed.

3. That the Annexures annexed with this Writ Petition/PIL are true copies of their respective originals.

4. This Writ Petition is being filed under my instructions and the contents thereof are true to the best of my knowledge and there is no personal gain, private motive or oblique reason in filing the Public Interest Litigation.

DEPONENT

VERIFICATION:

Verified at New Delhi on this the 30th day of October, 2021 that the contents of the above affidavit are true and correct to my knowledge, that no part of it is false and that nothing material has been concealed.

DEPONENT

IN THE SUPREME COURT OF INDIA

CIVIL ORIGINAL JURISDICTION

WRIT PETITION (CIVIL) NO. OF 2021

(PIL UNDER ART. 32 OF THE CONSTITUTION OF INDIA)

IN THE MATTER OF:

Dr. Ridhi Arora & Others ...PETITIONERS

Versus

Union of India & Another ...RESPONDENTS

AFFIDAVIT

I, Suman Kumari Chouhan, aged about 29 years, [redacted], do hereby solemnly affirm and state as under:

1. That I am the Petitioner No. 3 in the above captioned Writ Petition/PIL, and in such capacity, I am well conversant with the facts of the Petition and competent to swear this affidavit.

2. That the statement of the facts contained in Synopsis and list of dates at pages __B_ to __FF__ and Paragraph 1 to 57 at pages 1 to _61__ of the Writ Petition/PIL and the contents of the accompanying applications are true and correct to my knowledge and belief nothing material has been concealed.

3. That the Annexures annexed with this Writ Petition/PIL are true copies of their respective originals.

4. This Writ Petition is being filed under my instructions and the contents thereof are true to the best of my knowledge and there is no personal gain, private motive or oblique reason in filing the Public Interest Litigation.

Suman Chauhan

DEPONENT

VERIFICATION:

Verified at New Delhi on this the 30th day of October, 2021 that the contents of the above affidavit are true and correct to my knowledge, that no part of it is false and that nothing material has been concealed.

Suman Chauhan

DEPONENT

ANNEXURE P-1

Operational Guidance for COVID-19 Vaccination of Pregnant Women

Background

02/07/2021

COVID-19 infection during pregnancy may result in rapid deterioration of health of pregnant women and could also affect the fetus. Experts are of the view that the benefits of vaccination to the pregnant women outweigh its potential risks. Based on the recommendations from National Technical Advisory Group on Immunization (NTAGI), MoHFW has approved vaccination of pregnant women against COVID-19 with the condition that the pregnant women may be informed about the risks of exposure to COVID-19 infection along with the risks and benefits associated with the COVID-19 vaccines available in the country. Based on the information provided, a pregnant woman will have the choice to take the vaccination.

The COVID-19 vaccination has been expanded to include all citizens from 18 years of age onwards, making more than 69% of population eligible, of which nearly half (48%) are women. Pregnant women who develop COVID-19 are more likely to require intensive care than their non-pregnant counterparts. COVID-19 infection during pregnancy may result in rapid deterioration of health of pregnant women and might affect the fetus also. Information related to COVID-19, the impact of the disease on pregnancy and data related to COVID-19 vaccines are rapidly evolving. In the context of current situation of the SARS-CoV-2 pandemic, experts have suggested that the COVID-19 vaccine may be offered to the pregnant women if no contraindications exist. The intent is to weigh risk versus benefit on individualized basis, so that a pregnant woman can take an informed decision. This decision is based on the woman's understanding that the risk of infection and/or morbidity from COVID-19 outweighs the undescribed risk of being vaccinated during pregnancy.

In India, at present three vaccines have received approval for restricted use in emergency situation. One of them is an inactivated vaccine (Covaxin) and other two are based on non-replicating viral vector platform (Covishield and Sputnik V).

A pregnant woman who opts for vaccination, could be vaccinated at any time of the pregnancy. To help pregnant women make an informed decision to be vaccinated, they should

be provided with information about the risks of COVID-19 infection in pregnancy, the benefits of vaccination, along with the likely side effects of vaccination.

This guidance note enables states to develop a Counseling and Vaccination plan for pregnant women.

Section I: Preparing for COVID-19 vaccination of pregnant women

(i) Orientation and Capacity Building

Orientation of programme staff: States would undertake an orientation of programme managers responsible of the COVID vaccination programme at district, block and sub block levels, including Health and Wellness Centres and vaccinators at the health facilities in the public and private sector and also of all FLWs and health care providers at all the levels including medical colleges, DH, SDH, CHCs, PHCs, private clinics etc. who provide ANC services to women. The orientation would be conducted virtually and would broadly cover the areas in the attached sheet (Annexure I).

Training of FLWs and Vaccinations: From the above category, states would identify a pool of individuals (PHC-MOs, Staff Nurses, District Programme managers, and Community Health Officers etc.) who would be directly be responsible for training of frontline workers and vaccinators on counseling of pregnant women and providing them with accurate information regarding the benefits and risks of the vaccine, including guiding them on registration and the location of the appropriate vaccination site. This training can be accomplished in two hours. It would need to be conducted in small batch (10-15) at the level of the PHC, ensuring COVID appropriate behaviors. The material to be used is at Annexure II.

(ii) Engagement of medical professionals in the private sector

The state would conduct an orientation of members from professional bodies such as FOGSI, IMA, IAP & NNF, and any other state specific professional bodies they would be requested to ensure that this information is transmitted to all membeers. This could also be done virtually.

Section II: Counseling pregnant women for COVID Vaccination

There are several points at which interface of the pregnant woman and the FLW occurs and where pregnant women could be counselled. These include:

- Household visits by frontline workers;
- Antenatal checkup at health facility, outreach immunization sessions, Village Health and Nutrition Days (VHNDs) and Urban Health and Nutrition Days (UHNDs).
- Facility visits by pregnant women for other reasons;
- Any other site where there is interaction with the pregnant woman
- COVID-19 Vaccination Centers (CVCs);

During the counselling, the FLW or vaccinator (if the women reaches the CVC directly and has questions related to COVID 19 vaccination) should explain to the pregnant women the potential risks of COVID-19 on their health or that of the baby, benefits of vaccination, potential side effects and precautions they need to take following vaccination.

Section III: Vaccination of Pregnant Women

If the pregnant woman decides to get vaccinated, the process of registration for COVID-19 vaccination needs to be explained to her and the accompanying family member. She also needs to be informed about the nearest COVID vaccination center

The modality for registration of beneficiaries, reporting of vaccination, generation of certificate etc. remains the same as general population. Operational guidelines and standard operating procedures for COVID-19 vaccination are available at:

https://www.mohfw.gov.in/pdf/COVID19VaccineOG111Chapter16.pdf

https://www.mohfw.gov.in/pdf/GuidancedocCOWIN2.pdf

Section IV: Adverse Events following Vaccination

The full impact of COVID-19 disease on pregnancy outcomes for mother and fetus as well as for new-born is still unclear. Therefore, pregnant women require special considerations and systematic reporting of adverse events following immunization (AEFI). National AEFI surveillance operational guidelines and Covid-19 vaccination operational guidelines will be

followed for AEFI surveillance related to Covid-19 vaccination of pregnant women. Following are the additional specific activities and action points under this:

1. Obstetrician and gynecologist, pediatrician or neonatologist to be included in AEFI committees and be sensitized on Covid-19 vaccination of pregnant women
2. Members of local FOGSI chapter and IAP should be oriented on Covid-19 vaccination of pregnant women
3. All the medical officers, private practitioners and frontline health workers to be trained on their role in AEFI surveillance related to Covid-19 vaccination of pregnant women.

During vaccination:

1. The vaccinator or medical officer must consider the fact that women in reproductive age group might be unaware of the pregnancy at the time of vaccination. Therefore, the vaccinator must inform her for immediate reporting of AEFI, if any, following Covid-19 vaccination. In such cases, women will need to report immediately to the vaccinator or nearest health facility.

Reporting:

1. The pregnancy status of women should be recorded into the AEFI notification form while reporting AEFI cases.
2. All Adverse Event following vaccination of pregnant women should be reported immediately into Co-WIN.
3. All serious and severe adverse events following vaccination of pregnant women should be reported immediately to concerned Medical Officer / District Immunization Officer.

Investigation of cases:

1. Obstetrician and gynecologist, pediatrician or neonatologist should be part of District AEFI Committee investigating all serious and severe AEFI cases following vaccination of pregnant women.
2. The investigation of all such cases to be expedited. Cytopathological examination of aborted/ perinatal death if any occurring in vaccinated women may be done.
3. The adverse event and the pregnancy outcome must be noted on the ANC/MCH card. Pregnancy registry can be used to track such cases and to determine pregnancy outcome.

4. All antenatal, post-natal and other relevant clinical records must be sought for and collected during investigation and gathered from the treating physician.

Causality assessment:

Causality assessment of all adverse events following Covid-19 vaccination of pregnant women to be expedited.

Section V: Monitoring (as for current vaccination for COVID)

State Task forces (STF) will review planning, capacity building and implementation of pregnant women vaccination in the state.

District Task Forces (DTF) / Urban Task Forces (UTF) will be responsible for ensuring training of health workers, sensitization of professional bodies, and monitoring of vaccination activities for pregnant women.

*****

Annexure I

Counselling pregnant women for COVID vaccines

Fact-Sheet to guide the Medical Officers

As a Medical Officer, you need to build capacity of Frontline Workers and Vaccinators to counsel pregnant women and their families about the risks of COVID-19 in pregnancy (including, for example, that some pregnant women are at increased risk of infection, or have comorbidities that add to their risk of severe disease and adverse pregnancy outcomes), the likely benefits of vaccination in the current epidemiological context, and the current limitations of the safety data in pregnant women. Based on it the pregnant woman can choose to get vaccinated or not for COVID-19. This would empower pregnant women to make an informed decision. This note provides you with the information to help you educate and support Frontline Workers and Vaccinators, so that they can assist pregnant women and their families make an informed decision on getting the COVID-19 vaccine.

1. Why is COVID 19 vaccine being recommended for pregnant women?

- Pregnancy does not increase the risk to COVID-19 infection, but current evidence indicate that pregnant women are at an increased risk for severe illness from COVID-19 compared to non-pregnant women in case they get infected.
- Additionally, pregnant women with COVID-19 are at increased risk for preterm birth and might have an increased risk of other adverse pregnancy outcomes[1] including higher chances of neonatal morbidity[2]
- Most pregnant women will be asymptomatic or have mild disease, BUT their health may deteriorate rapidly and that might affect the foetal outcome.
- It is important that they take all precautions to protect themselves from acquiring COVID-19, including taking vaccination against COVID-19.
- WHO recommends vaccination in pregnant women when the benefits of vaccination to the pregnant woman outweigh the potential risks, such as pregnant women at high risk of exposure to COVID-19andpregnant women with comorbidities that place them in a high-risk group for severe COVID-19 disease.
- It is therefore advised that a pregnant woman should take COVID-19 vaccine.

[1]Wei SQ, Bilodeau-Bertrand M, Liu S, Auger N. The impact of COVID-19 on pregnancy outcomes: a systematic review and meta-analysis. CMAJ. 2021 Apr 19;193(16):E540-E548. doi: 10.1503/cmaj.202604. Epub 2021 Mar 19. PMID: 33741725; PMCID: PMC8084555.

[2] Outcomes of Neonates Born to Mothers with Coronavirus Disease 2019 (COVID-19) – National Neonatology Forum (NNF) India COVID-19 Registry; early online version, Indian pediatrics

2. Who are at Higher Risk of getting infected with COVID-19?
   - Someone who is a health care worker or a frontline worker.
   - Community having high or increasing rate of COVID-19 infections.
   - Frequently exposed to people outside the household.
   - Difficulty in complying with social distancing if living in a crowded household.

3. How does COVID 19 affect the health of the pregnant woman?
   - Although most (>90 percent) infected pregnant women recover without need for hospitalization, rapid deterioration in health may occur in a few.
   - Symptomatic pregnant women appear to be at increased risk of severe disease & death.
   - Compared with pregnant women without COVID-19, those with symptomatic COVID-19 are at increased risk of adverse pregnancy outcomes, including admission to the ICU, iatrogenic preterm birth, pre-eclampsia-like symptoms, Caesarean section and death [3].

4. How does COVID 19 infection of pregnant women affect the baby?
   - Most (over 95 percent) of newborns of COVID-19 positive mothers have been in good condition at birth.
   - However, Covid-19 in pregnancy increases the chances of preterm birth, increasing the possibility of hospitalization for the neonate and in some cases even death.

5. Which pregnant women are at higher risk of developing complication after COVID 19 infection?

   Risk factors for developing complication after COVID 19 infection during pregnancy are:
   - Pre-existing co-morbidities, advanced maternal age, and high body mass index are risk factors for severe COVID -19 in pregnancy[4].
   - Pregnant women with certain high-risk conditions have greater risk of severe illness from COVID-19 such as
     - Pre-existing medical conditions e.g. Diabetes
     - Organ transplant recipients
     - Chronic respiratory conditions like COPD, Asthma, Cystic Fibrosis
     - Homozygous sickle cell disease

[3] https://www.heart.org/en/coronavirus/coronavirus-questions/questions-about-covid-19-vaccination

[4] SAGE guidance for the development of evidence-based vaccination-related recommendations. Geneva: World Health Organization; 2017 (https://www.who.int/immunization/sage/Guidelines_development_recommendations.pdf, accessed 19 April 2021).

- Receiving immunosuppression therapies (enough to significantly increase risk of infection)
- Dialysis or advanced chronic kidney disease
- Congenital or acquired heart disease

6. If a pregnant woman has already had COVID-19, when should she be vaccinated?
   - In case a woman has been infected with COVID-19 infection during the current pregnancy, then she should be vaccinated soon after the delivery.

7. Are there any side effects of the COVID 19 vaccines that can either harm the pregnant women or her foetus?
   - COVID 19 vaccines available are safe and vaccination protects pregnant women against COVID 19 illness/disease like other individuals.
   - Based on current knowledge, experts believe that COVID -19 vaccines are unlikely to pose a risk to the pregnant person or foetus[5].
   - Like any medicine a vaccine may have side effects which are normally mild. After getting the vaccine, she can get mild fever, pain at injection site, or feel un-well for 1-3 days.
   - The long-term adverse effects and safety of vaccine for foetus and child is not established yet.
   - Very rarely, (one in 1-5 lakh persons) the beneficiary may after COVID 19 vaccination, experience some of the following symptoms within 20 days after getting the injection which may need immediate attention

Symptoms occurring within 20 days after receiving any COVID 19 vaccine

- Shortness of breath (difficulty in breathing)
- Chest Pain
- Pain in limbs / pain on pressing the limbs or swelling in the limbs (arm or calf)
- Small pinpoint haemorrhages (petechial) or bruising of the skin beyond the vaccination site
- Persistent abdominal pain with or without vomiting
- Seizures in the absence of previous history of seizures with or without vomiting
- Severe and persistent headaches with or without vomiting (in the absence of previous history of migraine or chronic headache)
- Weakness/paralysis of limbs or any particular side of the body
- Persistent vomiting without any obvious reason
- Blurred vision/ pain in eyes

Any other symptom or health condition which is of concern to the recipient or the family

5 Interim Clinical Considerations for Use of COVID -19 Vaccines Currently Authorized in the United States; Centers for Disease Control and Prevention; https://www.cdc.gov/vaccines/Covid -19/info-by-product/clinical-considerations.html#pregnant; accessed on 16 May 2021.

8. Are there any specific contraindications for vaccination in Pregnancy?

   As for the general population, pregnant women should avoid vaccination in the following conditions:

   - Anaphylactic or allergic reaction to the previous dose of COVID-19 vaccine
   - Anaphylaxis or allergic reaction to vaccines or injectable therapies, pharmaceutical products, food-items etc.
   - Vaccine is temporarily contraindicated in the following conditions:
     - Diagnosed COVID-19 infection – defer for 12 weeks from infection or 4 to 8 weeks from recovery
     - Active COVID-19 infection
     - COVID-19 infection treated with anti-COVID-19 monoclonal antibodies or convalescent plasma

9. What are the global recommendations and practices on vaccination of pregnancy women in other countries?

   Given the potential benefits and risks of the vaccine, International professional bodies have taken a positive stand on the COVID-19 vaccine in pregnancy. These bodies acknowledged lack of data in pregnancy.

   - WHO recommends use of recombinant vaccine in pregnant women, provided the benefits of vaccination outweigh the potential risk. Pregnant women may also be exposed to COVID-19 vaccine before the woman knows she is pregnant.
   - WHO does not recommend pregnancy testing prior to vaccination and delaying pregnancy or terminating pregnancy because of vaccination.
   - International Federation of Gynecology and Obstetrics (FIGO) believes that risk-based approach to immunization might be of disadvantage to the pregnant woman.
   - The Royal College of Obstetricians and Gynecologists (RCOG) states that pregnant women should be offered the vaccine as the general population[6].
   - The American College of Obstetricians and Gynecologists (ACOG) states that pregnancy testing should not be required prior to receiving vaccine and vaccine may be administered to the people who may consider future pregnancy. Women under age 50 including pregnant women can receive any COVID-19 vaccine. However, they should be

[6] Royal College of Obstetricians and Gynecologists (RCOG). COVID -19 vaccines, pregnancy and breastfeeding. [Online] 16 April 2021. https://www.rcog.org.uk/en/guidelines-research-services/coronavirus-Covid -19-pregnancy-and-womens-health/Covid -19-vaccines-and-pregnancy/Covid -19-vaccines-pregnancy-and-breastfeeding/; Accessed: 16 May April 2021

aware of the rare risk of thrombosis with thrombocytopenia syndrome after receipt of mRNA vaccines.

- Countries such as **Australia, Canada, Israel, Singapore, United Kingdom and United State of America** are vaccinating pregnant women with COVID-19 vaccines.

Annexure II

Counselling pregnant women for COVID-19 vaccines

Fact-Sheet to guide the Frontline Health Care Workers and Vaccinators

As a Frontline Worker or a Vaccinator, you need to counsel pregnant women about the availability, value and precautions regarding COVID vaccine. This note provides you with the information that you need to educate and support pregnant women, so that they can take an informed decision on getting the COVID vaccine. Based on it the pregnant woman can choose to get vaccinated or not for COVID-19. The note is structured in the form of questions & answers to make it easier for you to inform pregnant women and their families about most important issues related COVID-19 vaccination.

For additional information please contact: Medical Officer of nearest Health Centre

1. **Why is COVID-19 vaccine being recommended for pregnant women?**
   - Pregnancy does not increase the risk to COVID-19 infection
   - Most pregnant women will be asymptomatic or have mild disease, **BUT their health may deteriorate rapidly and that might affect the foetus too.**
   - It is important that they take all precautions to protect themselves from acquiring COVID-19, including taking vaccination against COVID-19.
   - It is therefore advised that a pregnant woman should take COVID-19 vaccines.

2. **Who are at higher risk of getting infected with COIVD-19?**
   - Someone who is a health care worker or a frontline worker
   - Community having high or increasing rate of COVID-19 infections
   - Frequently exposed to people outside the household
   - Difficulty in complying with social distance if living in a crowded household

3. **How does COVID-19 affect the health of the pregnant woman?**
   - Although most (>90 percent) infected pregnant women recover without need for hospitalization, rapid deterioration in health may occur in a few.

- Symptomatic pregnant women appear to be at increased risk of severe disease and death. In severe disease, like all other patients, pregnant women may also need hospitalization.
- Pregnant women with underlying medical conditions e.g., high blood pressure, diabetes, obesity, age over 35 years are at higher risk of severe illness due to COVID-19.

4. **How does COVID-19 infection of pregnant women affect the baby?**
   - Most (over 95 percent) of newborns of COVID-19 positive mothers have been in good condition at birth.
   - In some cases, COVID-19 infections in pregnancy may increase the possibility of pre-mature delivery, baby's weight might be less than 2.5 KG and in rare situations, baby might die before birth.

5. **Which pregnant women are at higher risk of developing complication after COVID-19 infection?**
   - Pregnant women who are:
     - Older than 35 years of age
     - Obese
     - Have an underlying medical conditions such as diabetes or high blood pressure
     - Have a history of clotting in the limbs

6. **If a pregnant woman has already had COVID, when should she be vaccinated?**
   - In case a woman has been infected with COVID during the current pregnancy, then she should be vaccinated soon after the delivery.

7. **Are there any side effects of the COVID-19 vaccines that can either harm the pregnant women or her foetus?**
   - COVID-19 vaccines available are safe and vaccination protects pregnant women against COVID 19 illness/disease like other individuals.
   - Like any medicine a vaccine may have side effects which are normally mild After getting the vaccine injection, she can get mild fever, pain at injection site, or feel un-well for 1-3 days.

- The long-term adverse effects and safety of vaccine for foetus and child is not established yet.
- Very rarely, (one in 1 to 5 lakh persons) the beneficiary may afterCOVID19 vaccination, experience some of the following symptoms within 20 days after getting the injection which may need immediate attention.

Symptoms occurring within 20 days after receiving any COVID 19 vaccine

- Shortness of breath (difficulty in breathing)
- Chest Pain
- Pain in limbs / pain on pressing the limbs or swelling in the limbs (arm or calf)
- Small pinpoint haemorrhages (petechial) or bruising of the skin beyond the vaccination site
- Persistent abdominal pain with or without vomiting
- Seizures in the absence of previous history of seizures with or without vomiting
- Severe and persistent headaches with or without vomiting (in the absence of previous history of migraine or chronic headache)
- Weakness/paralysis of limbs or any particular side of the body
- Persistent vomiting without any obvious reason
- Blurred vision/ pain in eyes

Any other symptom or health condition which is of concern to the recipient or the family

8. **When should the vaccine be given to the pregnant woman?**
   - The COVID-19 vaccination schedule can be started anytime during pregnancy.

9. **What other precautions need to be advised to the pregnant woman after vaccination?**
   - You must counsel the pregnant woman and her family members to continue to practice COVID appropriate behaviour: wearing double mask, frequent handwashing, maintaining physical distance, and avoiding crowded areas, to protect themselves and those around from spreading the COVID-19 infection.

10. **How does a pregnant woman register herself for Covid-19 vaccination?**
    - All pregnant women need to register themselves on Co-WIN portal or may get themselves registered on-site at the COVID-19 vaccination centre. The process of registration for pregnant women remains same as of the general population and as per the latest guidance provided by MoHFW from time to time.

Myth buster: You cannot get COVID-19 infection from vaccination

ANNEXURE P-2 81

COVID-19 Information

Public health information (CDC)

Research information (NIH)

SARS-CoV-2 data (NCBI)

Prevention and treatment information (HHS)

Español

NIH U.S. National Library of Medicine

ClinicalTrials.gov

An Efficacy and Safety Clinical Trial of an Investigational COVID-19 Vaccine (BBV152) in Adult Volunteers

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Read our disclaimer for details.

ClinicalTrials.gov Identifier: NCT04641481

Recruitment Status : Active, not recruiting
First Posted : November 23, 2020
Last Update Posted : March 19, 2021

Sponsor:
Bharat Biotech International Limited

Collaborators:
Indian Council of Medical Research
Iqvia Pty Ltd

Information provided by (Responsible Party):
Bharat Biotech International Limited

Study Details | Tabular View | No Results Posted | Disclaimer | How to Read a Study Record

82

Actual Study Start Date :

November 16, 2020

Actual Primary Completion Date :

January 8, 2021

Estimated Study Completion Date :

December 2022

Resource links provided by the National Library of Medicine

Genetic and Rare Diseases Information Center resources: Severe Acute Respiratory Syndrome

U.S. FDA Resources

Arms and Interventions

Go to

Arm	Intervention/treatment
Experimental: Study vaccine BBV152B (6µg-Algel-IMDG)	Biological: BBV152 BBV152 (6µg-Algel - Imidazoquinoline)
Placebo Comparator: Placebo Phosphate buffered saline with Alum (without antigen)	Biological: Placebo Placebo (PBS+Alum, without antigen)

Outcome Measures

Go to

Primary Outcome Measures :

1. First occurrence of Virologically confirmed (RT-PCR positive) symptomatic cases of COVID-19. [Time Frame: Day 42 to Month 12]

   (RT-PCR positive) symptomatic cases of COVID-19.

Secondary Outcome Measures :

1. First occurence of Virologically confirmed (RT-PCR positive) symptomatic cases of COVID-19 based on the case definition for the secondary efficacy symptomatic endpoint. [Time Frame: Day 42 to Month 12]

   (RT-PCR positive) symptomatic cases of COVID-19.

Clinical Trial to Assess Safety and Immunogenicity of Gam-COVID-Vac Combined Vector Vaccine for Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-Cov-2) Infection

ClinicalTrials.gov Identifier: NCT04640233

Recruitment Status : Active, not recruiting

First Posted : November 23, 2020

Last Update Posted : June 2, 2021

Sponsor:

Dr. Reddy's Laboratories Limited

Collaborators:

Gamaleya Research Institute of Epidemiology and Microbiology, Health Ministry of the Russian Federation

Additionally, the subjects will be able to have remote consultations with the study physician through the weekly telephonic follow-up.

Blood samples will be taken from immunogenicity group of phase II (all 100) and phase III (284 out of 1500) trials during the following visits to assess the immunogenicity parameters.

Study Design

Go to

Study Type :

Interventional (Clinical Trial)

Actual Enrollment :

1600 participants

Allocation:

Randomized

Intervention Model:

Parallel Assignment

Masking:

Double (Participant, Investigator)

Primary Purpose:

Prevention

Official Title:

Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Phase II/III Adaptive Clinical Trial to Assess the Safety and Immunogenicity of **Gam-COVID-Vac** Combined Vector Vaccine for SARS-Cov-2 Infection in Indian Healthy Subjects

Actual Study Start Date :

November 30, 2020

Estimated Primary Completion Date :

August 2021

Estimated Study Completion Date :

September 2021

85

COVID-19 Information

Public health information (CDC)

Research information (NIH)

SARS-CoV-2 data (NCBI)

Prevention and treatment information (HHS)

Español

Trial record **2 of 5** for: Covishield

Previous Study | Return to List | Next Study

Characterization and Durability of COVID-19 Vaccine Induced Immune Responses in Healthcare/Frontline Workers

ClinicalTrials.gov Identifier: NCT05049187

Recruitment Status : Recruiting
First Posted : September 20, 2021
Last Update Posted : September 22, 2021

See Contacts and Locations

Sponsor:
Tuberculosis Research Centre, India

Collaborator:
National Institute of Epidemiology

Information provided by (Responsible Party):

Observational Model:

Cohort

Time Perspective:

Prospective

Official Title:

Characterization and Durability of COVID-19 Vaccine Induced Immune Responses in Healthcare/Frontline Workers

Actual Study Start Date :

May 21, 2021

Estimated Primary Completion Date :

August 20, 2023

Estimated Study Completion Date :

August 20, 2023

Groups and Cohorts

Go to

Group/Cohort
Group 1 **COVISHIELD** Participants will receive one dose of COVID-19 vaccine (**Covishield**) at baseline and one second dose after 28 days (Window period of +3 days) intra muscularly.
Group 2 COVAXIN Participants will receive one dose of COVID-19 vaccine (Covaxin) at baseline and one second dose after 28 days (Window period of +3 days) intra muscularly.

Outcome Measures

Go to

Primary Outcome Measures :

1. Antibody titers [Time Frame: 2 years]

   IgM and IgG SARS-Cov2 specific antibody titres and IgA and IgE (total)

2. Ratio of immune biomarker production [Time Frame: 2 years]

   The ratio of immune biomarkers production between pre and post COVID-19 vaccination

Eligibility Criteria

Go to

RESTRICTED USE IN EMERGENCY SITUATION OF COVID- 19

COVAXIN®

SARS-CoV-2 VACCINE BY BHARAT BIOTECH

The Bharat Biotech COVID-19 Vaccine (COVAXIN®) is administered to prevent Coronavirus Disease 2019 (COVID-19) caused by SARS-CoV-2. This Fact Sheet contains information to help you understand the risks and benefits of the Bharat Biotech COVID-19 Vaccine (COVAXIN®**).**

REPORTING OFSIDE EFFECTS

As with any new medicine, this vaccine will be closely monitored to allow quick identification of any new safety information. You can help by reporting any side effects you may get after vaccination to Bharat Biotech who is the manufacturer of COVAXIN® vaccine on 24x7 Toll-Free Number: 18001022245 or at email at pvg@bharatbiotech.com. For more information, please read this Information Sheet carefully.

Please read this Fact Sheet for information about the Bharat Biotech COVID-19 Vaccine (COVAXIN®). Talk to Vaccinator/ Officer supervising your vaccination if you have any questions. It is your choice to receive COVAXIN®. COVAXIN® is administered as a 2-dose series, 4 weeks apart, into the deltoid muscle of the upper arm.

WHAT IS COVID-19?

COVID-19 disease is caused by a Coronovirus called SARS-CoV-2. This type of Coronavirus has not been seen before. You can get COVID-19 through contact with another person who has the virus. It is predominantly a respiratory illness that can affect other organs. People with COVID-19 may experience wide range of symptoms from mild to severe category. Symptoms may appear 2 to 14 days after exposure to the virus. Symptoms may include fever or chills; cough; shortness of breath; fatigue; muscle or body aches; headache; loss of taste or smell of recent onset; sore throat; congestion or runny nose; nausea or vomiting; diarrhea.

WHAT ISTHE BHARAT BIOTECH COVID-19 VACCINE (COVAXIN®)?

The Bharat Biotech COVID-19 Vaccine (COVAXIN®) is a vaccine with approval for emergency use that may prevent COVID-19. The Central Licensing Authority has granted permission for the sale or distribution of COVAXIN® for emergency use in public interest.

WHAT SHOULD YOU MENTION TO YOUR VACCINATION PROVIDER BEFORE YOU GET COVAXIN®

Tell the Vaccinator/ Officer supervising your vaccination about all of your medical conditions, including if you:

- Are on regular medication for any illness, for how long and for which condition.
- Have any allergies
- Have fever
- Have a bleeding disorder or are on a blood thinner
- Are immunocompromised or are on a medicine that affects your immune system
- Are pregnant
- Have received another COVID-19 vaccine

WHO SHOULD GET COVAXIN®?

COVAXIN® has been approved for restricted use in emergency situation in individuals 18 years of age and older.

WHO SHOULD NOT GET COVAXIN®?

You should not get COVAXIN® if you:

- Had a severe allergic reaction to any ingredients of the vaccine.
- Had a severe allergic reaction after a previous dose of this vaccine. • Currently have an acute infection or fever.

WHAT ARE THE INGREDIENTS IN THE COVAXIN®?

COVAXIN® includes the following ingredients: COVAXIN® contains *6µg* of whole-virion inact ivated SARS- CoV-2 antigen (Strain: NIV-2020-770), and the other inactive ingredients such as aluminum hydroxide gel (250 µg), TLR 7 /8 agonist (imidazoquinolinone) 15 *µg*, 2-phenoxyethanol 2.5 mg, and phosphate buffer saline up to 0.5 ml. The vaccine (COVAXIN®) thus has been developed by using inactivated/ killed virus along with the above mentioned chemicals.

HOW ISTHE BHARAT BIOTECH COVID-19VACCINE (COVAXIN®) GIVEN?

The Bharat Biotech COVID-19 (COVAXIN®) will be given to you as on injection into the deltoid muscle of the upper arm. COVAXIN® vaccination series is 2 doses given 4 weeks apart.

HAS COVAXIN® BEEN USED BEFORE?

The Central Licensing Authority has granted permission for the sale or distribution of COVAXIN® for

emergency use in public interest. In Phase 1 and Phase 2 clinical trials, about 680 (300 in Phase 1, and ®. Phase 3 clinical trial conducted in 25,800

380 in Phase 2) were administered with 2-doses of COVAXIN participants, with an interim ana lysis results showing vaccine efficacy of 78 %.

WHAT ARE THE BENEFITS OF COVAXIN®)?

In an ongoing clinical trial, COVAXIN® has been shown to generate immunity following 2 doses given 4 weeks apart. Phase 3 clinical trial conducted in 25,800 participants, with an interim analysis results showing vaccine efficacy of 78%.

Hence, it is important to appreciate that receiving the vaccine does not mean that other precautions related to COVID-19 need not be followed.

WHAT ARE THE RISKS OF BHARAT BIOTECH COVID-19 VACCINE (COVAXIN®)?

Side effects that have been reported with the Bharat Biotech COVID-19 (COVAXIN®) include:

- Injection site pain / Swelling / Redness / Itching
- Headache
- Fever
- Malaise / bodyache
- Nausea
- Vomiting
- Rashes

A severe allergic reaction may very rarely occur after getting a dose of COVAXIN®.

These may not be all the possible side effects of COVAXIN®. Serious and unexpected side effects may occur. COVAXIN® is still being studied in clinical trials.

WHAT SHOULD I DO ABOUT SIDE EFFECTS?

If you experience any side effect(s), please contact/visit your health provider/ Vaccinator / Officer supervising your vaccination or immediately go to the nearest hospital. In addition, you con report side effects after vaccination to Bharat Biotech International Limited who is the manufacturer of COVAXIN® on 24x7 Toll- Free Number: 18001022245 or email at pvg@bharotbiotech.com.

WHAT IF I DECIDE NOT TO GET COVAXIN®?

It is your choice to receive or not receive COVAXIN®.

CAN I RECEIVE COVAXIN° WITH OTHER VACCINES?

There is no scientific information yet available on the appropriateness of use of COVAXIN® along with other vaccines.

WHAT IF I AM PREGNANT?

Available data on COVAXIN® Vaccine administered to pregnant women are insufficient to inform vaccine associated risks in pregnancy.

WHAT IF I AM ON A BLOOD THINNER OR COAGULANT?

Individuals on stable anticoagulation therapy (warfarin, or a new anticoagulant [apixaban or rivaroxaban]) who are up-to-date with their scheduled international normalized ratio **(INR)** testing and whose latest INR was below the upper threshold of their therapeutic range, can receive intramuscular vaccination. Individuals on simple blood thinners (Aspirin and / or clopidogrel) who have a stable medical disease condition assessed by the vaccination provider may receive intramuscular vaccination.

The bleeding may take a little longer to stop in these individuals, and may lead to increased bruising on the upper arm. The immunization of patients with bleeding disorders differs from that of the average population concerning the risk of haematoma formation. A fine needle (23 - 25 gauge) should be used for the vaccination in these individuals, followed by firm pressure applied to the site without rubbing for at least 2 minutes. In case of any doubt, consult with the clinician responsible for prescribing or monitoring the individual's anticoagulant therapy. Individuals with bleeding disorders may be vaccinated intramuscularly if, in the opinion of a doctor familiar with the individual's bleeding risk the vaccine can be administered with reasonable safety by Intramuscular route.

WHAT IF I HAVE ALLERGIES?

Individuals who have a known severe allergy to any component of COVAXIN® are NOT advised to be vaccinated. COVAXIN® contains 6µg of whole-virion inactivated SARS-CoV-2 antigen (Strain: NIV-2020- 770), and the other inactive ingredients such as aluminium hydroxide gel 250 *µg*, TLR 7 / 8 agonist (imidazo quinolinone) 15 *µg*,

2-phenoxyethonol 2.5 mg, and phosphate buffer saline upto 0.5 ml.) Individuals with a history of severe allergic reactions NOT related to vaccines or injectable medications such as environmental allergies,

allergies to food, pet dander, venom, or latex- may still get vaccinated. Individuals with a history of allergies to oral medications or a family history of allergic reactions, or who might have a mild allergy to vaccines (but no anaphylaxis) may still get vaccinated.

WHAT IF I AM IMMUNOCOMPROMISED?

Individuals with HIV infection or other immunocomprom1smg conditions, or who take immunosuppressive medications or therapies might be at increased risk for severe COVID-19. However, data is NOT currently available to establish vaccine safety and efficacy in these groups. Individuals with immunosuppression may not generate a full immune response to COVID-19.

Transplant recipients should be counselled that the vaccine's effectiveness and safety profile for them is not currently known. As it is not a live virus vaccine, it is unlikely to pose a safety risk. Transplant recipients may have a weakened immune response compared to the general population. Thus, they should be advised regarding the importance of maintaining all current guidance to protect themselves even after vaccination. Immunocompromised individuals may receive COVID-19 vaccination if they have no contraindications to vaccination.

WILL THE BHARAT BIOTECH COVID-19 VACCINE (COVAXIN®) GIVE ME COVID-19?

No. BHARAT BIOTECH COVID-19 VACCINE (COVAXIN®) is an inactivated (killed) vaccine, and hence, there is no chance of getting COVID-19.

ANNEXURE P-4

SUMMARY OF PRODUCT CHARACTERISTICS

BHARAT BIOTECH Lead Innovation

COVAXIN™

1. NAME OF THE MEDICINAL PRODUCT

Whole Virion Inactivated Corona Virus Vaccine

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

This is a single or multidose vial and injected in intra-muscular route.

Each Single human dose (0.5 mL) contains

Whole Virion Inactivated Corona Virus Antigen 6 micrograms. produced using a Vero cell-based platform, that propagates the virus, expressing the viral spike (S) protein of SARS-CoV-2.

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

The vaccine is a white translucent liquid and free from extraneous particulate matter containing 6 µg of Whole Virion Inactivated Corona Virus Antigen (strain: NIV-2020-770) for injection (sterile), pH: 7.00 - 8.00.

4. CLINICAL PARTICULARS

It is indicated for active immunization to prevent COVID-19 caused by SARS-CoV-2 virus, in individuals 18 years of age and older. The use of this vaccine should be in accordance with official recommendations. This vaccine is permitted for restricted use in Emergency situation in Clinical Trial mode, as per provisions of New Drugs and Clinical Trials Rules, 2019, under Drugs & Cosmetics Act 1940.

4.1 Therapeutic indication

COVAXIN™ is indicated for active immunization against SARS-CoV-2 Virus infection for age ≥18years.

4.2 Posology and method of administration.

COVAXIN™ should be administered as two doses on Day 0 and Day 28.
Method of administration: intramuscular injection (IM).

4.3 Contraindications

- Hypersensitivity to any constituents of the vaccine.
- Pregnant and lactating mothers.
- During fever or severe infection.
- Individuals below 18 years.

4.4 Special warnings and precautions for use

- Do not administer intravenously, intradermally, or subcutaneously.
- Like all other vaccines, supervision and appropriate medical treatment should always be available to treat any anaphylactic reactions following immunization.
- The vaccine should remain under medical supervision for at least 30 minutes after vaccination.

Before use, COVAXIN™ should be shaken well to obtain a uniform, whitish translucent suspension. Vial should be visually checked for the presence of any particulate matter or other coloration, if any, prior to its administration. If in doubt, do not use the contents of the vial.

COVAXIN™ should not be mixed with other vaccines.

4.5 Interaction with other medicinal products.

Chloroquine and Corticosteroids as they may impair the antibody response.

4.6 Pregnancy and Lactation

Safety and effectiveness have not been established in pregnant women and in nursing mothers.

4.7 Effects on ability to drive and use machines

No studies on the effect of COVAXIN™ on the ability to drive and use machines have been performed.

4.8 Undesirable effects

Clinical Trial Experience

Safety of the COVAXIN™ vaccine was established in Phase 1 and Phase 2 studies.

Phase 1 clinical trial was conducted in India in 375 adult healthy volunteers. The most common local adverse event reported was Injection site Pain. The most common systemic adverse events reported were headache, followed by fatigue, fever, body ache, abdominal pain, nausea, and vomiting. The other less common adverse events were dizziness/giddiness, tremor, sweating, cold, cough, and injection site swelling. No vaccine related serious adverse events (SAE) were reported.

A Phase 2 clinical trial was conducted in India in 380 adolescents and adult healthy volunteers. Similar adverse events were reported in the phase 2 clinical trial. No serious adverse events (SAE) were reported.

A Phase 3 efficacy study is on-going in 25,800 participants and administered with 1st dose of vaccination with COVAXIN™, no vaccine related adverse events were observed.

4.9 Immune Response

COVID-19 disease is caused due to SARS-CoV-2 virus infection.

In Phase 1 clinical trial a total of 375 healthy participants were enrolled across the three groups and received three vaccine formulations, BBV152A (3µg with Algel-IMDG (Aluminium hydroxide gel- Imidazo quinolin gallamide (IMDG); a TLR 7/8 agonist), BBV152B (6µg with Algel-IMDG), and BBV152C (6µg with Algel). None of the participants had detectable neutralizing antibodies at baseline analyzed by MNT_{50}. The proportion of participants seroconverted post 2 weeks after 2nd dose was 87.9%, 91.9%, and 82.8% in the BBV152A, B, and C groups, respectively.

In Phase 2 clinical trial a total of 380 healthy participants were enrolled among two groups and received two vaccine formulations, BBV152 A and BBV152B. None of the participants had detectable neutralizing antibodies at baseline analyzed by MNT_{50}. The proportion seroconverted participants of Group 1 and Group 2, post 4 weeks of 2nd dose was 88.0% and 96.6% respectively.

4.10 Overdose

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

COVID-19 disease is caused due to SARS-CoV-2 virus infection. **COVAXIN™** is a whole virion inactivated SARS-CoV-2 virus vaccine, has been studied in Phase 1 and 2 clinical studies for safety and immunogenicity and found to be safe and immunogenic. **COVAXIN™** has been shown to prevent COVID-19 following 2 doses given 4 weeks apart. The duration of protection against COVID-19 is currently unknown.

5.2 Pharmacokinetic properties

Evaluation of pharmacokinetic properties is not required for vaccines.

5.3 Preclinical safety data

All the formulations were tested for immunogenicity in mice, rats, and rabbits. Mice, rats, and rabbits were vaccinated on days 0, 7, and 14 (n+1 doses). Further these formulations are tested for immunogenicity, safety, and protective efficacy in Syrian Hamster challenge model and Non-Human Primates (*Rhesus macaque*) challenge model. The Hamsters were vaccinated on Days 0, 14, and 35 (n+1 doses), the live SARS-CoV-2 virus was challenged through intranasal route on Day 50. Likewise, the Rhesus macaques were vaccinated on Days 0 and 14, and live SARS-CoV-2 virus was challenged through intranasal and intratracheal routes on Day 28. All the formulations were found to be safe, immunogenic, and provided effective protection to both upper and lower respiratory tract.

PHARMACEUTICAL PARTICULARS

6.1 List of excipients and composition

Each 0.5 mL (single human dose) contains

Whole Virion Inactivated Corona Virus Antigen …….6 µg

Aluminium hydroxide gel equivalent to Al^{+3}……...250 µg

TLR 7/8 Agonist……15 µg

2-phenoxyethanol……...2.5 mg

Phosphate buffered saline……..q.s. to 0.5 mL

Note: TLR 7/8 agonist is an Imidazo quinolin gallamide (IMDG)

6.2 Incompatibilities

The product should not be mixed with any other medicinal products or active immunizing agents.

6.3 Shelf life

The expiry date of COVAXIN™ is indicated on the label and carton of the product. Do not use the product after the expiration date shown on the label and carton of the product.

6.4 Special precautions for storage

Store at +2° to +8 °C, do not freeze. Discard if frozen.

Shake well before use. Keep out of reach of children. Protect from light.

Do not use the vaccine after the expiration date as shown on the label.

6.5 Nature and contents of container

COVAXIN™ is presented as Single dose (0.5 mL) and multidose (5 mL and 10 mL) in transparent vial (type I glass) with a stopper (butyl rubber) and a flip-off plastic cap with aluminium seal. Each vial of single dose contains 0.5 mL, each vial of multidose contains 10 doses (5 mL) and 20 doses (10 mL) respectively.

6.6 Handling of multi-dose vials

Opened vials should be used as soon as possible and within 6 hrs when kept between 2 - 8 ºC.

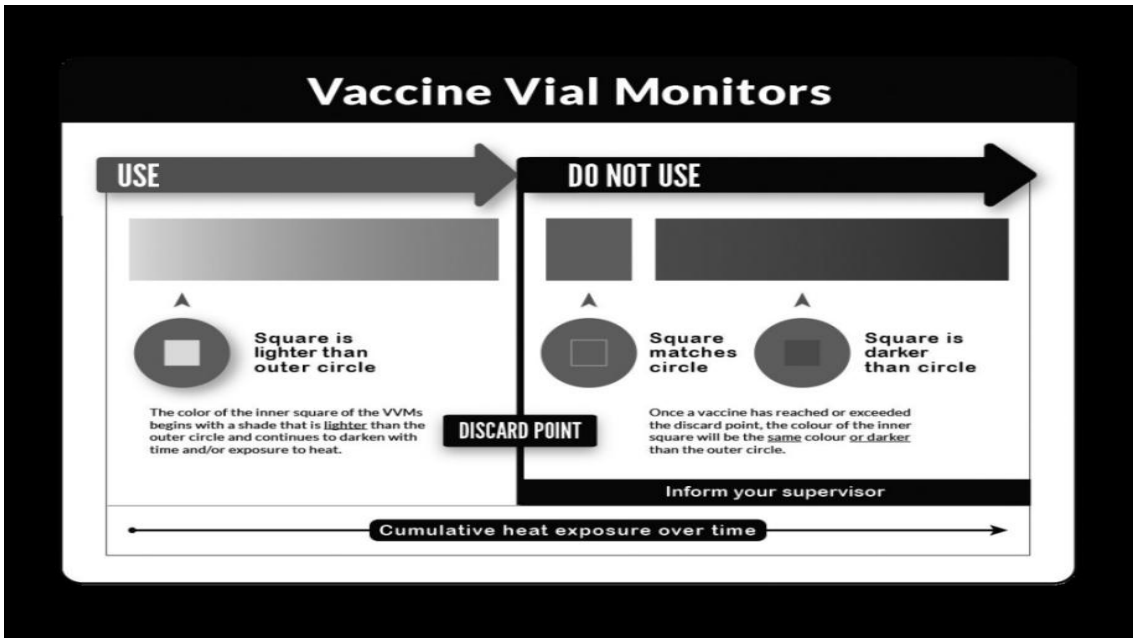
Disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. THE VACCINE VIAL MONITOR (OPTIONAL)

Presentation available with or without vaccine vial monitor

Vaccine Vial Monitors (VVM7) dot is a part of the label on **COVAXIN™** vials supplied through Bharat Biotech. VVM7 are supplied by TEMPTIME Corporation, USA. This is a time-temperature sensitive dot that provides an indication of the cumulative heat to which the vial has been exposed. It warns the end user when exposure to heat is likely to have degraded the vaccine beyond an acceptable level.



The interpretation of the VVM7 is simple: Focus on the central square; its colour will change progressively. As long as the colour of this square is lighter than the colour of the ring, the vaccine can be used. As soon as the colour of the central square is the same colour as the ring or of a darker colour than the ring, the vial should be discarded.

8. MARKETING AUTHORISATION NUMBER(S)

MF/BIO/21/000002, dated 3rd Jan, 2021

9. MARKETING AUTHORISATION HOLDER

Manufactured and Marketed by:

Bharat Biotech International Ltd.

Sy. No. 230, 231 and 235, Genome Valley, Turkapally, Shamirpet Mandal, Medchal-Malkajgiri District - 500 078, Telangana State, India.
E-mail: feedback@bharatbiotech.com; Website: www.bharatbiotech.com
For complaints and suggestions about the product, and any adverse event,
please email to feedback@bharatbiotech.com or call on Toll-free number: 1800 102 2245

10. DATE OF CREATION / REVISION OF THE TEXT

15th January, 2021

ANNEXURE P-5

For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory.

ChAdOx1 nCoV- 19 Corona Virus Vaccine (Recombinant)

COVISHIELD

1 NAME OF THE MEDICINAL PRODUCT

COVISHIELD™

ChAdOx1 nCoV- 19 Corona Virus Vaccine (Recombinant)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One dose (0.5 ml) contains:

ChAdOx1 nCoV- 19 Corona Virus Vaccine (Recombinant) 5×10^{10} viral particles (vp)

*Recombinant, replication-deficient chimpanzee adenovirus vector encoding the SARS-CoV-2 Spike (S) glycoprotein. Produced in genetically modified human embryonic kidney (HEK) 293 cells.

This product contains genetically modified organisms (GMOs). For the full list of excipients, see section 6.1.

Both **COVISHIELD™** (manufactured by Serum Institute of India Pvt Ltd) and COVID-19 Vaccine AstraZeneca (manufactured by AstraZeneca) are ChAdOx1 nCoV- 19 Corona Virus Vaccines (Recombinant).

3 PHARMACEUTICAL FORM

Solution for injection

The solution is colourless to slightly brown, clear to slightly opaque and particle free with a pH of 6.6.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

COVISHIELD™ is indicated for active immunisation of individuals ≥18 years old for the prevention of coronavirus disease 2019 (COVID-19).

4.2 Posology and method of administration

Posology

COVISHIELD™ vaccination course consists of two separate doses of 0.5 ml each. The second dose should be administered between 4 to 6 weeks after the first dose. However, there is data available for administration of the second dose up to 12 weeks after the first dose from the overseas studies (see section 5.1).

It is recommended that individuals who receive a first dose of **COVISHIELD™** complete the vaccination course with

COVISHIELD™ (see section 4.4).

Special populations

Elderly population

Efficacy and safety data are currently limited in individuals ≥ 65 years of age (see sections 4.8 and 5.1). No dosage adjustment is required in elderly individuals ≥ 65 years of age.

Paediatric population

The safety and efficacy of **COVISHIELD™** in children and adolescents (aged <18 years old) have not yet been established. No data are available.

Method of administration

COVISHIELD™ is for intramuscular (IM) injection only, preferably in the deltoid muscle. For instructions on administration, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and special precautions for use

Hypersensitivity

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of an anaphylactic event following the administration of the vaccine.

Concurrent illness

As with other vaccines, administration of **COVISHIELD™** should be postponed in individuals suffering from an acute severe febrile illness. However, the presence of a minor infection, such as cold, and/or low-grade fever should not delay vaccination.

Thrombocytopenia and coagulation disorders

As with other intramuscular injections, **COVISHIELD™** should be given with caution to individuals with thrombocytopenia, any coagulation disorder or to persons on anticoagulation therapy, because bleeding or bruising may occur following an intramuscular administration in these individuals.

Immunocompromised individuals

It is not known whether individuals with impaired immune responsiveness, including individuals receiving immunosuppressant therapy, will elicit the same response as immunocompetent individuals to the vaccine regimen. Immunocompromised individuals may have relatively weaker immune response to the vaccine regimen.

Duration and level of protection

The duration of protection has not yet been established.

As with any vaccine, vaccination with **COVISHIELD™** may not protect all vaccine recipients (See section 5.1).

Interchangeability

No data are available on the use of ChAdOx1 nCoV- 19 Corona Virus Vaccine (Recombinant) in persons that have previously received partial vaccine series with another COVID-19 vaccine.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

Concomitant administration of COVISHIELD™ with other vaccines has not been studied (see section 5.1)

4.6 Fertility, pregnancy and lactation

Fertility

Preliminary animal studies do not indicate direct or indirect harmful effects with respect to fertility.

Pregnancy

There is a limited experience with the use of ChAdOx1 nCoV-19 Corona Virus Vaccine (Recombinant) in pregnant women.

Preliminary animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryofetal development, parturition or postnatal development; definitive animal studies have not been completed yet. The full relevance of animal studies to human risk with vaccines for COVID-19 remains to be established.

Administration of COVISHIELD™ in pregnancy should only be considered when the potential benefits outweigh any potential risks for the mother and fetus.

Breastfeeding

It is unknown whether COVISHIELD™ is excreted in human milk.

4.7 Effects on ability to drive and use machines

ChAdOx1 nCoV- 19 Corona Virus Vaccine (Recombinant) has no or negligible influence on the ability to drive and use machines. However, some of the adverse reactions mentioned under section 4.8 may temporarily affect the ability to drive or use machines.

4.8 Undesirable effects

Overall summary of the safety profile from the Overseas studies:

The overall safety of COVID-19 Vaccine AstraZeneca [ChAdOx1 nCoV-19 Corona Virus Vaccine (Recombinant)] is based on an interim analysis of pooled data from four clinical trials conducted in the United Kingdom, Brazil, and South Africa. At the time of analysis, 23,745 participants ≥18 years old had been randomised and received either COVID-19 Vaccine AstraZeneca or control. Out of these, 12,021 received at least one dose of COVID-19 Vaccine AstraZeneca. The median duration of follow-up in the COVID-19 Vaccine AstraZeneca group was 105 days post dose 1, and 62 days post dose 2.

Demographic characteristics were generally similar among participants who received COVID-19 Vaccine AstraZeneca and those who received control. Overall, among the participants who received COVID-19 Vaccine AstraZeneca, 90.3% were aged 18 to 64 years and 9.7 % were 65 years of age or older. The majority of recipients were White (75.5%), 10.1% were Black and 3.5% were Asian; 55.8% were female and 44.2% male.

The most frequently reported adverse reactions were injection site tenderness (>60%); injection site pain, headache, fatigue (>50%); myalgia, malaise (>40%); pyrexia, chills (>30%); and arthralgia, nausea (>20%). The majority of adverse reactions were mild to moderate in severity and usually resolved within a few days of vaccination. By day 7 the incidence of subjects with at least one local or systemic reaction was 4% and 13%, respectively. When compared with the first dose, adverse reactions reported after the second dose were milder and reported less frequently.

Adverse reactions were generally milder and reported less frequently in older adults (≥65 years old).

If required, analgesic and/or anti-pyretic medicinal products (e.g. paracetamol-containing products) may be used to provide symptomatic relief from post-vaccination adverse reactions.

Adverse drug reactions

Adverse drug reactions (ADRs) are organised by MedDRA System Organ Class (SOC). Within each SOC, preferred terms are arranged by decreasing frequency and then by decreasing seriousness. Frequencies of occurrence of adverse reactions are defined as: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1000); very rare (<1/10,000) and not known (cannot be estimated from available data).

Table 1 – Adverse drug reactions

MedDRA SOC	**Frequency**	**Adverse reactions**
Blood and lymphatic system disorders	Uncommon	Lymphadenopathy
Metabolism and nutrition disorders	Uncommon	Decreased appetite
Nervous system disorders	Very common	Headache
	Uncommon	Dizziness
Gastrointestinal disorders	Very common	Nausea
	Common	Vomiting
	Uncommon	Abdominal pain
Skin and subcutaneous tissue disorders	Uncommon	Hyperhidrosisa, pruritisa, rash
Musculoskeletal and connective tissue disorders	Very common	Myalgia, arthralgia
General disorders and administration site conditions	Very common	Injection site tenderness, injection site pain, injection site warmth, injection site erythema, injection site pruritus, injection site swelling, injection site bruising, fatigue, malaise, pyrexia, chills
	Common	Injection site induration, influenza like illness

a Unsolicited adverse reaction

b Injection site bruising includes injection site haematoma (uncommon, unsolicited adverse reaction)

c Pyrexia includes feverishness (very common) and fever ≥38°C (common)

Very rare events of neuroinflammatory disorders have been reported following vaccination

with COVID 19 Vaccine AstraZeneca. A causal relationship has not been established.

Overall summary of the safety profile from the Indian study:

COVISHIELD™ was also safe and well tolerated in the phase II/III clinical trial in India. An interim analysis included data of all 1600 participants who received first dose [1200 in COVISHIELD™ group, 100 in Oxford/AZ-ChAdOx1 nCoV-19 vaccine group and 300 in Placebo group]. This interim analysis includes data collected until 14 Dec 2020 of all 1600 participants who received first dose and 1577 participants who received second dose.

Demographic characteristics were generally similar among participants across the three groups. Overall, among the participants who received COVISHIELD™, 87.33% were aged 18 to 59 years and 12.67% were 60 years of age or older.

Overall, the incidence of solicited reactions (injection site reactions such as pain, tenderness, redness, warmth, itch, swelling and induration; and systemic reactions include fever, chills, fatigue, malaise, headache, arthralgia and myalgia), unsolicited adverse events and serious adverse events (SAEs) was comparable in the study and control groups. No causally related SAE was caused by the study vaccine.

4.9 Overdose

Experience of overdose is limited.

There is no specific treatment for an overdose with ChAdOx1 nCoV-19 Corona Virus Vaccine (Recombinant). In the event of an overdose, the individual should be monitored and provided with symptomatic treatment as appropriate.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Mechanism of action

COVISHIELD™ is a monovalent vaccine composed of a single recombinant, replication-deficient chimpanzee adenovirus (ChAdOx1) vector encoding the S glycoprotein of SARS-CoV-2. Following administration, the S glycoprotein of SARS-CoV-2 is expressed locally stimulating neutralizing antibody and cellular immune responses.

Efficacy and immunogenicity data from the Overseas studies:

Clinical efficacy

Interim analysis of pooled data from COV001, COV002, COV003, and COV005

COVID-19 Vaccine AstraZeneca [ChAdOx1 nCoV-19 Corona Virus Vaccine (Recombinant)] has been evaluated based on an interim analysis of pooled data from four on-going randomised, blinded, controlled trials: a Phase I/II Study, COV001 (NCT04324606), in healthy adults 18 to 55 years of age in the UK; a Phase II/III Study, COV002 (NCT04400838), in adults

≥18 years of age (including the elderly) in the UK; a Phase III Study, COV003 (ISRCTN89951424), in adults ≥18 years of age (including the elderly) in Brazil; and a Phase I/II study, COV005 (NCT04444674), in adults aged 18 to 65 years of age in South Africa.

The studies excluded participants with history of anaphylaxis or angioedema; severe and/or uncontrolled cardiovascular, gastrointestinal, liver, renal, endocrine/metabolic disease, and neurological illnesses; as well as those with immunosuppression. In studies COV001 and COV002, licensed seasonal influenza and pneumococcal vaccinations were permitted (at least 7 days before or after their study vaccine). All participants are planned to be followed for up to 12 months, for assessments of safety and efficacy against COVID-19 disease.

Based on the pre-defined criteria for interim efficacy analysis, COV002 and COV003 exceeded the threshold of ≥5 virologically confirmed COVID-19 cases per study and therefore contributed to the efficacy analysis; COV001 and COV005 were excluded.

In the pooled analysis for efficacy (COV002 and COV003), participants ≥18 years of age received two doses of COVID-19 Vaccine AstraZeneca (N=5,807) or control (meningococcal vaccine or saline) (N=5,829). Because of logistical constraints, the interval between dose 1 and dose 2 ranged from 4 to 26 weeks.

Baseline demographics were well balanced across COVID-19 Vaccine AstraZeneca and control treatment groups. Overall, among the participants who received COVID-19 Vaccine AstraZeneca, 94.1% of participants were 18 to 64 years old (with 5.9% aged 65 or older); 60.7% of subjects were female; 82.8% were White, 4.6% were Asian, and 4.4% were Black. A total of 2,070 (35.6%) participants had at least one pre-existing comorbidity (defined as a BMI ≥ 30 kg/m2, cardiovascular disorder, respiratory disease or diabetes). At the time of interim analysis the median follow up time post-dose 1 and post- dose 2 was 132 days and 63 days, respectively.

Final determination of COVID-19 cases were made by an adjudication committee, who also assigned disease severity according to the WHO clinical progression scale. A total of 131 participants had SARS-CoV-2 virologically confirmed (by nucleic acid amplification tests) COVID-19 occurring ≥15 days post second dose with at least one COVID-19 symptom (objective fever (defined as ≥37.8ºC), cough, shortness of breath, anosmia, or ageusia) and were without evidence of previous SARS-CoV-2 infection. COVID-19 Vaccine AstraZeneca significantly decreased the incidence of COVID-19 compared to control (see Table 2a).

Table 2a – COVID-19 Vaccine AstraZeneca efficacy against COVID-19*

Population	**COVID-19 Vaccine AstraZeneca**		**Control**		**Vaccine efficacy % (95.84% CI)**
	N	**Number of COVID-19 casesb, n (%)**	**N**	**Number of COVID-19 casesb, n (%)**	
Primary (see above)	5807		5829		

COVID-19 cases		30 (0.52)		101 (1.73)	70.42 (58.84, 80.63)
Hospitalisations		0		5 (0.09)	
Severe diseasec		0		1 (0.02)	
Any dose	**10,014**		**10,000**		
COVID-19 cases after dose 1		108 (1.08)		227 (2.27)	52.69 (40.52, 62.37)
Hospitalisations after dose 1		2 (0.02)		16 (0.16)	
Severe disease after dose 1		0		2 (0.02)	

N = Number of subjects included in each group; n = Number of subjects having a confirmed event; CI = Confidence Interval; * This is a pooled data of LDSD + SDSD regimen with second dose given at dose intervals ranging from 4 to 12 weeks. LD – Low Dose, SD – Standard Dose.

a 95.84% CI; b WHO severity grading ≥4; c WHO severity grading ≥6; d 95% CI; e Two cases of hospitalisation occurred on Days 1 and 10 post vaccination.

Table 2b – COVID-19 Vaccine AstraZeneca efficacy against COVID-19

Population	**COVID-19 Vaccine AstraZeneca**		**Control**		**Vaccine efficacy % (95.84% CI)**
	N	Number of COVID-19 cases, n (%)	**N**	Number of COVID-19 cases, n (%)	
Primary analysis population					
Overall (SDSD + LDSD)	5807	30 (0.52)	5829	101 (1.73)	70.42 (58.84, 80.63)
Licensing regimen					
SDSD	4440	27 (0.61)	4455	71 (1.59)	62.10 (39.96, 76.08)
Exploratory analysis					
LDSD	1367	3 (0.22)	1374	30 (2.18)	90.05 (65.84, 97.10)

N = Number of subjects included in each group; n = Number of subjects having a confirmed event; CI = Confidence Interval; LD = Low dose; SD = Standard dose

Table 2c - COVID-19 Vaccine AstraZeneca efficacy against COVID-19 by Dose Interval (SDSD)

Dose interval	Participants with events, n (%)		Vaccine efficacy %	95% CI (%)	P-value
	AZD1222 n / N (%)	Control n / N (%)			
< 6 weeks	9 / 1702 (0.53)	19 / 1698 (1.12)	53.28	(-3.21, 8.86)	0.060
6-8 weeks	5 / 562 (0.88)	9 / 521 (1.73)	51.08	(-45.57, 3.56)	0.199
9-11 weeks	9 / 1056 (0.85)	24 / 1110 (2.16)	60.55	(15.23, 81.64)	0.017
≥ 12 weeks	4 / 1120 (0.36)	19 / 1126 (1.69)	78.79	(37.63, 92.79)	0.005

The level of protection gained from single dose of COVID-19 Vaccine AstraZeneca was assessed in an exploratory analysis that included participants who had received one dose. Participants were censored from the analysis at the earliest time point of when they received a second dose or at 12 weeks post-dose 1. In this population, vaccine efficacy from 22 days post dose 1 was 73.00% (95% CI: 48.79; 85.76 [COVID-19 Vaccine AstraZeneca 12/7,998 vs control 44/7,982]). Exploratory analyses showed that increased immunogenicity was associated with a longer dose interval (see Immunogenicity Table 3). Efficacy is currently demonstrated with more certainty for dose intervals from 8 to 12 weeks and a similar trend for efficacy. Data for intervals longer than 12 weeks are limited.

Participants who had one or more comorbidities had a vaccine efficacy of 73.43% [95% CI: 48.49; 86.29]; 11 (0.53%) vs 43 (2.02%) for COVID 19 Vaccine AstraZeneca (N=2,070) and control (N=2,113), respectively; which was similar to the vaccine efficacy observed in the overall population.

The number of COVID-19 cases (2) in 660 participants ≥ 65 years old were too few to draw conclusions on efficacy. However, in this subpopulation, immunogenicity data are available, see below.

Immunogenicity

Following vaccination with COVID-19 Vaccine AstraZeneca, in participants who were seronegative at baseline, seroconversion (as measured by a ≥4 fold increase from baseline in S-binding antibodies) was demonstrated in ≥98% of participants at 28 days after the first dose and >99% at 28 days after the second. Higher S-binding antibodies were observed with increasing dose interval (Table 3).

Generally similar trends were observed between analyses of neutralising antibodies and S-

binding antibodies. An immunological correlate of protection has not been established; therefore, the level of immune response that provides protection against COVID-19 is unknown.

Table 3 – SARS CoV-2 S-binding antibody response to COVID-19 Vaccine AstraZeneca

Population	Baseline	28 days after dose 1	28 days after dose 2
	GMT (95% CI)	GMT (95% CI)	GMT (95% CI)
Overall	(N=882) 57.18 (52.8, 62.0)	(N=817) 8386.46 (7758.6, 9065.1)	(N=819) 29034.74 (27118.2, 31086.7)
Dose Interval			
< 6 weeks	(N=481) 60.51 (54.1, 67.7)	(N=479) 8734.08 (7883.1, 9676.9)	(N=443) 22222.73 (20360.50, 24255.3)
6-8 weeks	(N=137) 58.02 (46.3, 72.6)	(N=99) 7295.54 (5857.4, 9086.7)	(N=116) 24363.10 (20088.5, 29547.3)
9-11 weeks	(N=110) 48.79 (39.6, 60.1)	(N=87) 7492.98 (5885.1, 9540.2)	(N=106) 34754.10 (30287.2, 39879.8)
≥ 12 weeks	(N=154) 52.98 (44.4, 63.2)	(N=152) 8618.17 (7195.4, 10322.3)	(N=154) 63181.59 (55180.1, 72343.4)

N = Number of subjects included in each group; GMT = Geometric mean titre; CI = Confidence interval; S = Spike

Immune response evaluated using a multiplex immunoassay. In individuals who received two recommended doses of vaccine.

The immune response observed in participants with one or more comorbidities was consistent with the overall population.

High seroconversion rates were observed in older adults (≥65 years) after the first (97.8% [N=136, 95% CI: 93.7; 99.5]) and the second recommended dose (100.0% [N=111, 95% CI: 96.7; NE]). The increase in S-binding antibodies was numerically lower for participants ≥65 years old (28 days after second dose: GMT=20,727.02 [N=116, 95% CI: 17,646.6; 24,345.2]) when compared to participants aged 18-64 years (28 days after second dose: GMT=30,695.30 [N=703, 95% CI: 28,496.2; 33,064.1]). The majority of participants ≥65 years old had a dose interval of <6 weeks, which may have contributed to the numerically lower titres observed.

In participants with serological evidence of prior SARS-CoV-2 infection at baseline (GMT=13,137.97 [N=29; 95% CI: 7,441.8; 23,194.1]), S-antibody titres peaked 28 days after dose 1 (GMT=175,120.84 [N=28; 95% CI: 120,096.9; 255,354.8).

Spike-specific T cell responses as measured by IFN- enzyme-linked immunospot (ELISpot) assay are induced after a first
dose of COVID-19 Vaccine AstraZeneca. These do not rise further after a second dose.

Immunogenicity data from the Indian study:

GMTs of IgG antibodies against spike (S) protein were comparable between the groups at baseline – Day 1. GMTs increased significantly after each dose of vaccine in both the groups and were comparable. There was 100% seroconversion in both the groups on Day 57. The immunogenicity data indicates that COVISHIELD is comparable in terms of anti-S IgG antibody titers and seroconversion rates to Oxford/AZ-ChAdOx1 nCoV-19 vaccine (see Tables 4 and 5).

Table 4 Summary of Anti-S IgG antibodies

Timepoint	**Statistic**	**COVISHIELD™ (N=291) n (%)**	**Oxford/AZ-ChAdOx1 nCoV-19 (N=97) n (%)**
Baseline	n GMT 95% CI	291 95.4 (77.8, 117.0)	97 80.7 (59.0, 110.4)
Visit 3 – Day 29 (+14)	n GMT 95% CI	289 9988.1 (8395.0, 11883.7)	97 6738.5 (4880.4, 9304.1)
Visit 4 - Day 57 (+14)	n GMT 95% CI	140 33331.6 (27756.0, 40027.2)	46 33263.6 (24383.1, 45378.3)

Table 5 Summary of Proportion of Participants with Seroconversion for Anti-S IgG Antibodies

Timepoint	**COVISHIELD™ (N=291) n (%) 95(%) CI**	**Oxford/AZ-ChAdOx1 nCoV-19 (N=97) n (%) 95(%) CI**
Visit 3 – Day 29 (+14)	279 (96.5) (93.7, 98.3)	89 (91.8) (84.4, 96.4)
Visit 4 – Day 57 (+14)	**140 (100.0)** (97.4, 100.00)	**46 (100.0)** (92.3, 100.0)

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Toxicity and local tolerance studies

Non-clinical data reveal no special hazard for humans based on a conventional study of repeat dose toxicity. Animal studies into potential toxicity to reproduction and development have not yet been completed.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

L-Histidine
L-Histidine hydrochloride monohydrate Magnesium chloride hexahydrate Polysorbate 80
Ethanol Sucrose
Sodium chloride
Disodium edetate dihydrate (EDTA)
Water for injection

(The names of inactive ingredients may vary according to geographical region)

6.2 Incompatibilities

In the absence of compatibility studies, this vaccine must not be mixed with other medicinal products.

6.3 Shelf-life

The expiry date of vaccine is indicated on the label and packaging.

Once opened, multi-dose vials should be used as soon as practically possible and within 6 hours when kept between
+2ºC and +25ºC. All opened multidose vials of **COVISHIELD™** should be discarded at the end of immunization session or within six hours whichever comes first.

6.4 Special precautions for storage Store in a refrigerator (+2ºC to +8ºC). Do not freeze. Protect from light.

Opened multidose vial

For storage conditions after first opening of the medicinal product, see section 6.3.

6.5 Nature and contents of container

COVISHIELD™ is supplied as ready for use liquid in rubber-stoppered multidose vial and single dose vial in below listed presentations
1 dose – 0.5 ml per vial 2 dose – 1.0 ml per vial 5 dose – 2.5 ml per vial 10 dose – 5.0 ml per vial
20 dose – 10 ml per vial

6.6 Instructions for use, handling and disposal

Administration

COVISHIELD™ is a colourless to slightly brown, clear to slightly opaque solution. The vaccine should be inspected visually prior to administration and discarded if particulate matter or differences in the described appearance are observed.

Do not shake the vial.

Each vaccine dose of 0.5 ml is withdrawn into a syringe for injection to be administered intramuscularly. Use a separate sterile needle and syringe for each individual. It is normal for

liquid to remain in the vial after withdrawing the final dose. The vaccine does not contain any preservative. Aseptic technique should be used for withdrawing the dose for administration.

Once opened, multi-dose vials should be used as soon as practically possible and within 6 hours when kept between +2ºC and +25ºC. Discard any unused vaccine.

To facilitate the traceability of the vaccine, the name and the batch number of the administered product must be recorded for each recipient.

Disposal

COVISHIELD™ contains genetically modified organisms (GMOs). Any unused vaccine or waste material should be disposed of in accordance with local requirements. Spills should be disinfected with an appropriate antiviral disinfectant (e.g. Hydrogen peroxide based disinfectants).

ANNEXURE P-6

Dr.Reddy's

ARTWORK APPROVAL FORM		
Unit : IPDO	Department: Packaging Development	Page: 1of 2

Component: Fact sheet	Product Name: Sputnik	Strength: Na	Counts: NA
Market/Customer: Domestic		Material Code: 102751	Supersedes: NA

Reference SOP No.	SOP-GL-OB-PG-0002	Legacy Document No.	FTCPD033/A02

SPUTNIK V

FACT SHEET FOR VACCINE RECIPIENTS AND CAREGIVERS APPROVED FOR RESTRICTED USE IN EMERGENCY SITUATION IN PUBLIC INTEREST THE DR. REDDY'S LABORATORIES COVID-19 VACCINE (SPUTNIK VTM) GAM-COVID-VAC COMBINED VECTOR VACCINE FOR THE PREVENTION OF CORONAVIRUS INFECTION CAUSED BY THE SARS-COV-2 VIRUS IN INDIVIDUALS ABOVE 18 YEARS

This vaccine has been given restricted use license for emergency situation. It does not have a marketing authorization, However, this approval for the restricted use in emergency situation grants permission for the vaccine to be used for active Immunization of individuals above 18 years for the prevention of coronavirus disease 2019 (COVID-19).

Reporting of side effects

As with any medicine, this vaccine will be closely monitored to allow quick identification of new safety information. You can help by reporting any side effects you may get after vaccination to the Dr. Reddy's Laboratories Ltd. On 24x7 Toll Free Number: +91-1800 425 0014 or at customercareservices@drreddys.com All adverse events reported will be entered in COWIN App by the health care provider. For more information read this fact sheet carefully.

You are being offered the Dr. Reddy's Laboratories Ltd. (DRL) SPUTNIK Vaccine to prevent Coronavirus Disease 2019 (COVID-19) caused by SARS-CoV-2. This Fact Sheet contains information to help you understand the risks and benefits of the SPUTNIK V Vaccine, which you may receive because there is currently a pandemic of COVID-19 disease.

The SPUTNIK V is a vaccine and may prevent you from getting COVID-19 disease.

Please read this Fact Sheet for information about the Dr Reddys laboratories COVID-19 Vaccine (SPUTNIK V). Talk toVaccinator/ Officer supervising your vaccination if you have any questions.

It is your choice to receive the Dr Reddys laboratories COVID-19 Vaccine (SPUTNIK V).

The Dr Reddys laboratories COVID-19 Vaccine (SPUTNIK V) is carried out in two stages: rst with component I, then 3 weeks
later with component II. The product is administered intramuscularly: rst component I at a dose of 0.5 ml, then after 3 weeks
component II at a dose of 0.5 ml.

After the vaccine is administered, the patient should be monitored by a healthcare professional for 30 minutes.

The SPUTNIK V may not protect everyone.

WHAR YOU NEED TO KNOW BEFORE YOU GET THIS VACCINE

WHAT IS COVID-19?

COVID-19 disease is caused by a coronavirus called SARS-CoV-2. This type of coronavirus has not been seen before. You can get COVID-19 through contact with another person who has the virus. It is predominantly a respiratory illness that can affect other organs. People with COVID-19 have had a wide range of symptoms reported, ranging from mild symptoms to severe illness. Symptoms may appear 2 to 14 days after exposure to the virus. Symptoms may include: fever or chills; cough; shortness of breath; fatigue; muscle or body aches; headache; new loss of taste or smell; sore throat; congestion or runny nose; nausea or vomiting; diarrhea.

WHAT IS THE SPUTNIK VACCINE?

Sputnik V is Gam-COVID-Vac Combined vector vaccine for the prevention of coronavirus infection caused by the SARS-CoV-2 virus in individuals over 18 years.

WHAT YOU NEED TO KNOW BEFORE YOU USE SPUTNIK V

Tell your healthcare provider about all of your medical conditions, including:

- If you have kidney or liver problems, severe disorders of the endocrine system (diabetes mellitus), severe diseases ofthe hematopoietic system, epilepsy, strokes and other diseases of the central nervous system,
- If you have diseases of the cardiovascular system (history of myocardial infarction, myocarditis, endocarditis, pericarditis, ischemic heart disease),
- If you have primary and secondary immunode□ciency, autoimmune diseases
- If you have lung diseases, asthma and COPD, with allergic reactions, atopy, eczema
- If you are pregnant or plan to become pregnant
- If you have any other serious illnesses
- If you are taking any medicines (prescription, over-the-counter, vitamins, or herbal products).

You should consult your healthcare provider before deciding to take the vaccine.

WHO SHOULD GET THE SPUTNIK V VACCINE?
SPUTNIK V Vaccine has been approved for restricted use in emergency situation in individuals over 18 years.

WHO SHOULD NOT GET THE SPUTNIK V Vaccine?
If you have

- hypersensitivity to any component of a vaccine or a vaccine containing similar components
- history of severe allergic reactions
- if you are suffering from common cold, runny nose,fever, cough, bodyache or loose motions etc
- if you are pregnant
- age up to 18 years (due to lack of data on ef□cacy and safety)
- developed severe post-vaccination complications (anaphylactic shock, severe generalized allergic reactions, convulsive syndrome, temperature above 40°C, etc.) for the injection of component I of the vaccine

WHAT ARE THE INGREDIENTS IN THE SPUTNIK V VACCINE?

Component I contains:
Active substance: Recombinant adenovirus serotype 26 particles containing the SARS-CoV-2 protein S gene 1.0±0.5 x 1011
Particles.
Excipients: Tris (hydroxymethyl) aminomethane -1.21 mg, sodium chloride - 2.19 mg, sucrose -25.0 mg, magnesium chloride hexahydrate -102.0 µg, EDTA disodium salt dehydrate - 19.0 µg, polysorbate 80 - 250.0 µg, ethanol 95% - 2.50 µl, water for injection Q.s to 0.5 ml.

Component II contains:
Active ingredient: Recombinant adenovirus serotype 5 particles containing the SARS-CoV-2 protein S gene 1.0±0.5 x 1011 Particles.
Excipients: Tris (hydroxymethyl) aminomethane -1.21 mg, sodium chloride - 2.19 mg, sucrose -25.0 mg, magnesium chloride hexahydrate -102.0 µg, EDTA disodium salt dehydrate - 19.0 µg, polysorbate 80 - 250.0 µg, ethanol 95% - 2.50 µl, water for injection Q.s to 0.5 ml.

HOW IS THE SPUTNIK V GIVEN?
The SPUTNIK V Vaccine will be given to you as an intramuscular (IM) injection only, preferably in the deltoid muscle. The SPUTNIK V vaccination course consists of two separate doses of 0.5 Ml each.

If you receive first dose of the sputnik v vaccine, then the second dose should be administered after 3 weeks with second dose.

SPUTNIK V 102751

ARTWORK APPROVAL FORM		
Unit : IPDO	Department: Packaging Development	Page: 1of 2

Component: Fact sheet	Product Name: Sputnik	Strength: Na	Counts: NA
Market/Customer: Domestic		Material Code: 102751	Supersedes: NA

Reference SOP No.	SOP-GL-OB-PG-0002	Legacy Document No.	FTCPD033/A02

After the vaccine is administered, you will be monitored by a healthcare professional for 30 minutes.

If you miss your second dose
If you forget to go back at the scheduled time, ask your healthcare provider for advice.

HAS THE SPUTNIK V VACCINE BEEN USED BEFORE?
The SPUTNIK V is used in clinical trials, a number of participants received one or two doses in overseas and Indian trials.

WHAT ARE THE BENEFITS OF THE SPUTNIK V VACCINE?
In ongoing clinical trials, the SPUTNIK V Vaccine has been shown to prevent COVID-19 disease following 2 doses given at 3 weeks interval i.e. days 1 and 21. The duration of protection against COVID-19 disease is currently unknown.
You may get protective immune response within 1 to 3 weeks after the second dose of SPUTNIK V vaccine. Hence, you must practice the COVID-19 precautions recommended to prevent SARS-COV-2 infection till 3 weeks after the second dose of the vaccine i.e. day 42 from the □rst dose of vaccine.

WHAT ARE THE RISKS OF THE SPUTNIK V VACCINE?
Side effects that have been reported with the SPUTNIKV Vaccine include:
Very common (may affect more than 1 in 10 people)
- Tenderness, pain, warmth, redness, itching, swelling or bruising where the injection is given
- flu-like symptoms, such as high temperature, sore throat, runny nose, cough and chills

Common (may affect 1 in 10 people)
- Headache
- Feeling tired
- Feeling feverish or chills
- Muscle pain
- Runny nose
- Cough

Uncommon (may affect upto 1 in 100people)
- Feeling sick(Nausea)
- Being sick(Vomiting)
- Stomach ache
- Joint pain,
- Decrease appetite
- Sore throat
- Nasal congestion
- Impaired sense of taste
- Doubtfulness

These may not be all the possible side effects of the SPUTNIK V Vaccine. Serious and unexpected side effects may occur. SPUTNIK V Vaccine is still being studied in clinical trials and follow up on the trials is going on.

WHAT SHOULD I DO ABOUT SIDE EFFECTS?
If you experience a severe allergic reaction, call or go to the nearest hospital. Call the healthcare provider if you have any side effects that bother you or do not go away. In addition, you can report side effects after vaccination to Dr.REDDY'S LABORATORIES Ltd. as below.

- 24x7 Call Center Toll-Free Number (For Medical and Adverse Event Related Queries Only): Toll-Free Number: +91-1800 425 0014 or at customerservices@drreddys.com. All adverse events reported will be entered in COWINApp by the health care provider.

WHAT IF I DECIDE NOT TO GET THE SPUTNIK V VACCINE?
It is your choice to receive or not receive the SPUTNIK V Vaccine. You may prefer to consult your healthcare provider.

CAN I RECEIVE THE SPUTNIK V VACCINE WITH OTHER VACCINES?
There is no information on the use of the SPUTNIK V Vaccine with other vaccines.

WHAT IF I AM PREGNANT OR BREASTFEEDING?
The product is not for use during pregnancy, since its effectiveness and safety during this period have not been studied. Gam- COVID- Vac can be administered safely in lactating women.

WILL THE SPUTNIK V VACCINE GIVE ME COVID-19 INFECTION?
No. The SPUTNIK V COVID-19 Vaccine does not contain SARS-CoV-2 and cannot give you COVID-19 infection.

KEEP YOUR VACCINATION CARD
When you get your dose, please discuss with your healthcare provider regarding the option of your vaccination record on digital platform, if available.

HOW CAN I LEARN MORE?
Ask the healthcare provider. Contact your local or state public health department.

DETAILS OF MANUFACTURER

The Gamaleya National Center of Epidemiology and Microbiology of the Ministry of Health of the Russian Federation Manufactured at: GENERIUM Joint-Stock Company (GENERIUM JSC), 273 Zavodskaya Street, Volginsky, Petushinsky District, Vladimir Region, 601125 (Russia)
Fill Finish & Packed at: Open Joint Stock Company Pharmstandard-Ufa Vitamin Plant (d), 28, Khudayberdina Street., Ufa, Republic of Bashkortostan, 450077, Russia

IMPORTED AND MARKETED BY
M/s Dr. Reddy's Laboratories Ltd., Global Distribution Centre, Survey No. 41, Bachupally (V), Bachupally (M), Medchal - Malkajgiri(Dist.), Hyderabad – 500090, Telangana, INDIA
TMTrademark under registration.

Revised: 21st May 2021

ANNEXURE P-7

SUMMARY OF PRODUCT CHARACTERISTICS

SPUTNIK V
Gam-COVID-Vac

Combined vector vaccine for the prevention of coronavirus infection caused by the SARS-CoV-2 virus

1. NAME OF THE MEDICINAL PRODUCT

Gam-COVID-Vac Combined vector vaccine **(Component I) - 0.5 ml/dose & (Component II) - 0.5 ml/dose**

Component I - Gam-COVID-Vac Combined vector vaccine (Recombinant adenovirus serotype 26 particles containing the SARS-CoV-2 protein S gene, in an amount of $(1.0 \pm 0.5) \times 10^{11}$ particles / dose) to prevent SARS-CoV-2-induced coronavirus infection.

Component II - Gam-COVID-Vac Combined vector vaccine (Recombinant adenovirus serotype 5 particles containing the SARS-CoV-2 protein S gene, in an amount of $(1.0 \pm 0.5) \times 10^{11}$ particles / dose) to prevent SARS-CoV-2-induced coronavirus infection.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Composition per dose (0.5 ml):

Component I contains:

Active substance: Recombinant adenovirus serotype 26 particles containing the SARS-CoV-2 protein S gene $1.0 \pm 0.5 \times 10^{11}$ Particles.

Excipients: Tris (hydroxymethyl) aminomethane -1.21 mg, sodium chloride - 2.19 mg, sucrose - 25.0 mg, magnesium chloride hexahydrate -102.0 µg, EDTA disodium salt dehydrate - 19.0 µg, polysorbate 80 - 250.0 µg, ethanol 95% - 2.50 µl, water for injection Q.s to 0.5 ml.

Component II contains:

Active substance: Recombinant adenovirus serotype 5 particles containing the SARS-CoV-2 protein S gene $1.0 \pm 0.5 \times 10^{11}$ Particles.

Excipients: Tris (hydroxymethyl) aminomethane -1.21 mg, sodium chloride - 2.19 mg, sucrose - 25.0 mg, magnesium chloride hexahydrate -102.0 µg, EDTA disodium salt dehydrate - 19.0 µg, polysorbate 80 - 250.0 µg, ethanol 95% - 2.50 µl, water for injection Q.s to 0.5 ml.

3. PHARMACEUTICAL FORM

A solution for intramuscular injection. Component I - 0.5 ml / dose + component II - 0.5 ml / dose

4. CLINICAL PARTICULARS

4.1 Indications:

For the prevention of the novel Coronavirus infection (COVID-19) in adults aged over 18, when given in two separate doses three weeks apart.

Day 0: Component I (0.5 ml) & Day 21: Component II (0.5 ml)

4.2 Posology and Administration:

Sputnik V vaccination course consists of two separate doses of 0.5 ml each.

The vaccination is carried out in two stages: first with component I, then 3 weeks later with component II. The product is administered intramuscularly: first component I at a dose of 0.5 ml, then after 3 weeks component II at a dose of 0.5 ml.

After the vaccine is administered, the patient should be monitored by a healthcare professional for 30 minutes.

Special populations

Elderly population

Efficacy was similar in elderly population of more than 60 years of age as compared to adults less than 60 years of age.

Paediatric population

The safety and efficacy of SPUTNIK V in children and adolescents (aged <18 years old) have not yet been established. No data are available.

Method of administration:

The vaccine is intended for intramuscular injection only. Intravenous injection of the product is strictly prohibited. The vaccine is injected into the deltoid muscle (the upper third of the outer shoulder). If it is impossible to inject into the deltoid muscle, the product is injected into the vastus lateralis muscle.

For instructions on administration

Prior to vaccination with either Component I or Component II, take a vial of the intended component out of the freezer and keep at room temperature (15-25^{o}C) until completely thawed with no visible frozen inclusions. The vial may be held in hands to help it thaw.

Carefully mix the contents of the vial by swirling gently in an upright position for 10 seconds. Do not shake the vial.

Remove the protective plastic overlay from the vial and treat the rubber stopper with an alcohol wipe.

With a single-use syringe, draw 0.5 mL of the drug as a dose to administer to the patient.

After being thawed, the vaccine may be stored at room temperature (15-25^{o} C) for upto 2 hours. Unused contents after this period must be discarded.

4.3 Contraindications:

Contraindications for the injection of component I

- Hypersensitivity to any constituents of the vaccine.
- Severe allergic reactions in the past;
- Pregnant and lactating mothers.
- Individuals below 18 years.

- Acute infectious and non-infectious diseases, exacerbation of chronic diseases - vaccination is carried out 2-4 weeks after recovery or remission. In case of non-serious ARVI, acute gastrointestinal infections, vaccination is carried out after the temperature has returned to normal;

Contraindications for the injection of component II

- severe post-vaccination complications (anaphylactic shock, severe generalized allergic reactions, convulsive syndrome, temperature above 40 ° C, etc.) for the injection of component I of the vaccine;

4.4 Use with Caution

The vaccine should be used with caution in cases of chronic liver and kidney disease,endocrine disorders (apparent thyroid function abnormalities and diabetes mellitus in decompensation stage), serious diseases of the hematopoietic system, epilepsy and other CNS diseases, acute coronary syndrome, and acute cerebrovascular event,myocarditis, endocarditis, pericarditis.

Due to lack of data, vaccination may be a risk for the following groups of patients:

- With autoimmune diseases (stimulation of the immune system can lead to anexacerbation of the disease, special caution should be exercised with patients with an autoimmune disorder that tend to lead to severe and life-threatening conditions);
- With malignant neoplasms.

The decision to vaccinate should be based on the assessment of the benefit/risk ratio in each specific situation.

4.5 Interaction with other medicinal products

No interaction studies have been performed.

Concomitant administration of SPUTNIK V with other vaccines has not been studied

4.6. Fertility, Pregnancy and Lactation

It is not anticipated that there is a biologically plausible way in which the vaccine could cause infertility in any woman or man, developmental pathology, or affect offspring, since:

– The vaccine does not use adjuvants;

– The potentially toxic (in rats) excipient (polysorbate 80) used in the vaccine is used in a dose that cannot affect human fertility or the reproductive function

– The vaccine virus does not reproduce itself; after injection, the virus delivers the S protein gene to the cell and ceases to exist in the human body – The gene coding S protein in the body leads to the production of the viral S protein, and the development of an immune response to it

– Antibodies to the S protein produced in response to immunization are similar to the antibodies produced in response to a disease caused by SARS-CoV-2, therefore, the risk associated with immunization is not higher than that for infection

– Antibodies to adenovirus produced in response to immunization are similar to antibodies to adenoviruses produced in response to a disease caused by adenovirus with a widely spread pathogen; therefore, the risk associated immunization is not higher than that for infection.

– In preclinical studies of reproductive toxicity, a similar vaccine developed based on adenovirus vectors types 26 and 5 of identical composition was studied. No increased risk is expected with administering the drug in active reproductive populations given adherence to the restrictions indicated in the instructions for medical use.

Using during pregnancy and breastfeeding

The drug is contraindicated during pregnancy and breastfeeding, since its efficacy and safety in these conditions have not been studied.

4.7. Effects on Ability to Drive and Use Machines

There is no information regarding the effects on ability to drive and use machines.

4.8. Undesirable Effects

Adverse reactions specific to the use of the vaccine, revealed in clinical trials and studies of other vaccines based on a similar technological platform, are predominantly of mild or medium severity, and may develop during the first or second day following vaccination and usually abate within 3 subsequent days.

The most common include short-term general (a brief flu-like syndrome characterized by chills, fever, arthralgia, myalgia, asthenia, general discomfort, headache) or local (injection site tenderness, hyperemia, swelling) reactions. Non-steroidal anti-inflammatory drugs (NSAIDs) are recommended in case of post-vaccination fever and antihistamines for expressed local reactions.

Less common ones are nausea, dyspepsia, loss of appetite, occasionally - enlarged regional lymph nodes. Some patients may develop allergic reactions, short-term elevated liver transaminase levels, elevated serum creatinine and creatine phosphokinase levels.

Within the Gam-COVID-Vac safety, tolerability and immunogenicity clinical trials conducted to date the following AEs have been registered:

General injection site disorders and reactions: hyperthermia, vaccination site tenderness, edema and pruritus, asthenia, pain, malaise, pyrexia, increased vaccination site skin temperature, decreased appetite. Incidence rate - very common and common.

Respiratory, chest, and mediastinal disorders: oropharyngeal pain, nasal congestion, sore throat, rhinorrhea. Incidence rate – common

Nervous system disorders: common – headache; rare – dizziness, syncope

Gastrointestinal disorders: nausea, vomit, dyspepsia - common.

Lab test and instrumentation data: divergent deviations of immunological status indicators: increased count of T-lymphocytes, increase in the percentage of lymphocytes, decreased count of natural killer cells, increased count of CD4-lymphocytes, decreased count of CD4-lymphocytes, increased count of B-lymphocytes, decreased count of B-lymphocytes, increased count of natural killer cells, increased count of CD8 lymphocytes, increased level of immunoglobulin E (IgE) in the blood, increase in the CD4/CD8 ratio, decrease in the CD4/CD8 ratio, increased level of immunoglobulin A (IgA) in the blood, decrease in the percentage of CD8 lymphocytes. Abnormalities in the complete blood count: increase in the percentage of lymphocytes, decrease in the hematocrit, increased count of lymphocytes, increase in the erythrocyte sedimentation rate, increased leukocyte count, increased count of monocytes, increased platelet count, decreased count

of neutrophils, decreased platelet count. Deviations in common urine analysis: erythrocytes in the urine.

Most AEs ended in complete abatement, without any consequences. Lab test deviations were not of clinical significance (did not require additional diagnostics or therapy).

A safety analysis in Phase III Study conducted in Russia included **33,771** volunteers (all volunteers who were administered a dose of the study drug), which included 2990 volunteers > 60 years of age.

Incidence rate for Adverse Events (AE)
In the study, 26,405 cases of AE have been reported to date, developed in 12,080 volunteers (35.8%). The AE reported in association with vaccination were observed in 9,323volunteers (36.8%). Of which the commonly reported (>3%) were flu like illness (20.1%), injection site reaction (19.1%), headache (4.1%), increased body temperature (3.8%) and asthenia (3.2%).

The AE reported in association with vaccination were observed in 677 volunteers of age >60 years of age (30.2%). Of which the commonly reported (>3%) were injection site reaction (12.7%), flu like illness (12.1%), headache (3.5%) and asthenia (3.4%).

Serious Adverse Event (SAE) incidence rate
No SAE was reported in association with vaccination.

In the Multi-Centre Phase II/III Adaptive Clinical Trial is being conducted to assess the safety and immunogenicity of Gam-COVID Vac Combined Vector Vaccine for SARS-Cov-2 Infection in Indian healthy subjects. Of the 1,500 subjects (including 115 subjects > 60 years of age) enrolled in the phase III, 33.1% of the study cohort reported 1,784 AE. No SAE associated with vaccination is reported in this study. The commonly reported adverse events includes injection site pain, pyrexia, malaise, chills, asthenia, myalgia, decreased appetite, arthralgia and headache. Most of these events (88%) were of mild severity and transient (99% resolved by the time of interim data analysis). In subjects with > 60 years of age, 26 (21.8%) subjects reported 60 AE. The commonly reported ones include injection site reaction, fever and headache.

4.9 Overdose

Overdose cases were not reported.

Considering that the dispensing of product is allowed only for medical institutions, and the vaccination itself is carried out only by qualified medical personnel, the risk of overdose is extremely low. However, it can be assumed that with an accidental overdose, the development of the above toxic and toxic-allergic reactions to a more severe degree is possible. There are no specific antidotes to the product.

Therapeutic measures in this case will include symptomatic therapy in accordance with the indications (antipyretic /NSAID and desensitizing agents), corticosteroids - parenterally for severe toxic-allergic syndrome). The regimen for prescribing drugs should be selected according to the recommendations for use and dosages of this product.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: medical immunobiological vaccine.

ATC code: J07B

5.1 Pharmacodynamic properties

Mechanism of action

The vaccine induces the formation of humoral and cellular immunity against coronavirus infection caused by the SARS-CoV-2 virus.

The mechanism of the drug's action is based on the ability of Ad26 and Ad5-based recombinant viral particles carrying the SARS-CoV-2 S protein gene to transduce efficiently the cells of the vaccinated body; in this case, genetic sequences which code the antigen is delivered to the cells, so the transduced cells start to produce the antigen.

When the first dose (component 1) is administered (intramuscularly), the rAd26-based vector enters the cells of the body leading to the expression of SARS-CoV-2 S protein thus triggering the development of specific SARS-CoV-2 immunity. When the second dose (component 2) is administered (intramuscularly), the rAd5-based vector enters the cells of the body leading to the expression of SARS-CoV-2 S protein thus boosting efficiently the immune response to ensure a pronounced long-lasting immunity against SARS-CoV-2.

Immunogenicity and Vaccine effectiveness in Animals

Vaccine effectiveness and immunogenicity were studied in various animal models like mice, hamsters and primates. Hamster studies indicated that vaccination could achieve 100% survival in immunosuppressed hamsters when they are infected with SARS-COV-2 virus. Primate studies indicated that there was significant immunogenicity developed in vaccinated animals in terms of s-glycoprotein (spike protein) specific antibodies, virus neutralizing antibody and CD4/CD8 lymphocyte proliferation.

5.2 Pharmacokinetic properties

Target gene expression and content analysis for adenoviral DNA were evaluated in mice administered both components of the vaccine intramuscularly in thigh muscle. The gene expression peaked on day 2 to day 14 in mice organs. The adenoviral DNAs were found restricted to the thigh muscle (Adenovirus serotype 26 and 5) and local lymphnodes (Adenovirus serotype 5) only. No other pharmacokinetic studies were conducted with the product.

5.3 Preclinical Safety data

Systemic toxicity, allergenicity and immunotoxicity

Single-dose general toxicity studies were done on mice (each component separately), rabbits (components 1 and 2 in succession, with a reduced administration interval relative to planned clinical use), primates (components 1 and 2 in succession in a therapeutic dose for humans, with the administration interval that is planned for clinical use). Allergenicity tests were carried out on guinea pigs, and immunotoxicity tests on mice. There were toxicity, allergenicity or immunotoxicity was observed in this study with doses several folds high to the human equivalent dose. Studies conducted in primates also observed that there was no antibody dependent enhance reported in the vaccinated animals when they were exposed to SARS-COV-2 virus.

Carcinogenesis, Mutagenesis, Impairment of Fertility

No such studies were conducted with the product.

5.4 Clinical Studies

Phase I/II Clinical Trial in Russia (NCT04436471)

38 volunteers were recruited in this trial, of which 9 each received either component 1 or 2 and were observed for 28 days thereafter as part of Phase I study. Another 20 volunteers received component 1 followed by 2 at interval of 21 days and were followed up till day 42 (3 weeks after the second dose) as part of Phase II study. Phase I study indicated that both components of the vaccines were highly immunogenic and safe in the volunteers. Phase II indicated that humoral immunogenicity parameters s-glycoprotein (spike protein) specific antibodies and virus neutralizing antibodies increased over the observations at days, 14, 21, 28 and 42 with significantly superior titres to the convalescent plasma for the earlier parameter on days 28 and 42 as well as 100 seroconversion for both parameters by day 42. Cellular immunogenicity parameters of CD4/CD8 lymphocyte proliferation and interferon gamma secretion also increased over days 14 and 28 with 100% volunteers showing response in these parameters on day 28.

Phase III Clinical Trial in Russia (RESIST, NCT04530396)

As per the recent interim analysis, 33,771 volunteers [25,321 received Gam-COVID-Vac combined vector vaccine and 8,450 received placebo in 1:3 proportion] were enrolled in the study, which included subjects aged 18 to 92 years old (43.9±12 years), 33.6% females, 8.9% subjects > 60 years of age and 22.8% subjects with comorbidities.

Earlier interim analysis, which was published in Lancet. indicated that amongst 18,695 volunteers receiving both vaccine doses, there were 78 cases of COVID-19 reported [16 in vaccine arm and 62 in Placebo arm] from day 21 onwards with efficacy calculated at 91.6% (95% Confidence interval 85.6% - 95.2%). There were no significant differences in the efficacy across age groups or genders. In terms of moderate to severe COVID-19 cases, all 20 cases were reported in placebo arm indicating 100% protection against such disease. While considering the 60 COVID-19 cases reported from day 28 onwards (1 week after the second dose), the efficacy was calculated at 91.1% (95% confidence interval 83.8% to 95.1%).

In terms of humoral immunogenicity, s-glycoprotein (spike protein) specific antibody data from 980 volunteers (733 from the vaccine arm and 247 from the placebo arm), indicates that by day 42 (3 weeks after the second shot), 98.64% of volunteers in vaccine arm achieved seroconversion (with a geometric mean titre of 9818 fold) as compared to 12.55% ($P<0.001$) volunteers in placebo arm. As per earlier interim analysis, based on 100 volunteers (72 from the vaccine arm and 28 from the placebo arm), indicates that by day 42 (3 weeks after the second shot), 95.83% of volunteers in vaccine arm achieved seroconversion (with a geometric mean titre of 44.5 fold) as compared to 7.14% ($P<0.001$) volunteers in placebo arm. Further, on day 28 (1 week after the second dose) vaccinated arm reported significant proliferation of CD4 lymphocytes compared to CD8 lymphocytes and significant increase in interferon gamma secretion compared to placebo arm.

India Phase II/III adaptive study (NCT04640233)

Phase II part of the India study enrolled 100 subjects (75 in vaccine arm and 25 in placebo arm) and tested the immunogenicity as well as safety of the vaccine in Indian population. The

immunogenicity trends in the Phase II population closely correlated with Russia Phase II results as indicated by serial increase in immunogenicity parameters and similar seroconversion. Based on the same, go-ahead was given to Phase III part by the Drug Controller General (India).

Phase III part of the India study enrolled 1500 subjects (1125 in vaccine arm and 375 in placebo arm), of which 284 subjects are being evaluated for immunogenicity parameters. In terms of humoral immunogenicity, s-glycoprotein (spike protein) specific antibody data from 284 volunteers (213 from the vaccine arm and 71 from the placebo arm), indicates that by day 42 (3 weeks after the second shot), 99.5% of volunteers in vaccine arm achieved seroconversion (with a geometric mean titre of 8327.99 fold). For Viral neutralizing Antibody (VNA) - based on 284 volunteers (213 from the vaccine arm and 71 from the placebo arm), indicates that by day 42 (3 week after the second shot), 81.1% of volunteers in vaccine arm achieved seroconversion (with a geometric mean titre of 88.5 fold). Further, on day 28 (1 week after the second dose) vaccinated arm reported significant proliferation of CD4 lymphocytes compared to CD8 lymphocytes and significant increase in interferon gamma secretion compared to placebo arm. These results indicate the Gam-COVID-Vac vaccine is highly immunogenic in Indian subjects in line with the results of Russia study.

6. PHARMACEUTICAL PARTICULARS

Component I. Frozen solution. It is a dense, hardened, whitish mass. After thawing: homogeneous colorless or yellowish slightly opalescent solution.

Component II. Frozen solution. It is a dense, hardened, whitish mass. After thawing: homogeneous colorless or yellowish slightly opalescent solution.

Characteristics: The vaccine is obtained by biotechnology, which does not use the SARS-CoV-2 virus pathogenic for humans. The product consists of two components: component I and component II. Component I includes a recombinant adenovirus vector based on human adenovirus serotype 26 carrying the gene for the S-protein of the SARS-CoV-2 virus; component II includes a vector based on human adenovirus serotype 5 carrying the protein S gene of the SARS-CoV-2 virus.

6.1 List of Excipients

Component I Excipients: Tris (hydroxymethyl) aminomethane -1.21 mg, sodium chloride - 2.19 mg, sucrose -25.0 mg, magnesium chloride hexahydrate -102.0 μg, EDTA disodium salt dehydrate - 19.0 μg, polysorbate 80 - 250.0 μg, ethanol 95% - 2.50 μl, water for injection Q.s to 0.5 ml.

Component II Excipients: Tris (hydroxymethyl) aminomethane -1.21 mg, sodium chloride - 2.19 mg, sucrose -25.0 mg, magnesium chloride hexahydrate -102.0 μg, EDTA disodium salt dehydrate - 19.0 μg, polysorbate 80 - 250.0 μg, ethanol 95% - 2.50 μl, water for injection Q.s to 0.5 ml.

6.2 Incompatibilities

The product should not be mixed with any other medicinal products or active immunizing agents.

6.3 Shelf-life

Component- I & Component- II – **6 Months**

6.4 Special precautions for storage

Store in a light-proof place at a temperature of -18°C or below.

Store in a thawed state at room temperature (15-25ºC) for no more than 2 hours. Discard any unused contents after this period. Re-freezing is not allowed.

6.5 Nature and contents of container

Primary packaging:

Gam-COVID-Vac is presented as multi dose (3 mL) of Component I and Component II in transparent vial (type I glass) with a rubber stopper and a flip-off plastic cap with aluminium seal. Each vial of multi dose contains 5 doses (3 mL).

6.6 Instructions for use, handling and disposal

Any unused product or waste material should be disposed as per local regulatory requirements.

7. MARKETING AUTHORIZATION

Authorized Indian Agent
M/s Dr. Reddy's Laboratories Ltd., Global Distribution Centre, Survey No. 41, Bachupally (V), Bachupally (M), Medchal - Malkajgiri(Dist.), Hyderabad – 500090, Telangana, INDIA
™ Trademark under registration

8. MARKETING AUTHORISATION NUMBER (S)

Import licence number: RC/BIO-000193-001

9. DATE OF FIRST AUTHORISATION/ RENEWAL OF THE AUTHORISATION

13th April 2021

Online RTI Status Form

Enter Registration Number	CDSCO/R/T/21/00670
Name	Rushil Tamboli
Date of filing	27/07/2021
Public Authority	CENTRAL DRUGS STANDARD CONTROL ORGANISATION
Status	REQUEST DISPOSED OF
Date of action	17/09/2021

Reply :- Point No. 11, 13: The brief of interim clinical trial results containing safety, immunogenicity and efficacy results along with side-effects, contraindications, precautions of approved COVID-19 vaccines are available in Summary of Product Characteristics (SmPC) & factsheet which are publically available on CDSCO website i.e. www.cdsco.gov.in.

Point No. 12: The Subject Expert Commi†ee (SEC) comprises of experts from Microbiology, Pulmonology, Immunology, Paediatrics, Internal medicine etc. from Government Institutes/Medical Colleges. The recommendations of SEC commi†ee for COVID-19 vaccines are available on CDSCO website i.e. www.cdsco.gov.in.

Point No. 15: The brief of interim clinical trial results containing safety, immunogenicity and efficacy results along with side-effects, contraindications, precautions of approved COVID-19 vaccines are available in Summary of Product Characteristics (SmPC) & factsheet which are publically available on CDSCO website i.e.
www.cdsco.gov.in.

CDSCO has not granted permission to conduct clinical trials on pregnant women and breast feeding women.

Point No. 16: CDSCO has granted the following permission to conduct clinical trial on children age group:

1. **Phase II/III clinical trial of Nanoparticle Vaccine (Liquid) (COVOVAX) manufactured by M/s Serum Institute of India Pvt. Ltd. in 920 subjects of 2 to 17 years age group.**
2. **Phase II/III clinical trial of Whole-Virion Inactivated SARS-CoV-2 Vaccine manufactured by M/s Bharat Biotech in 525 subjects 2 to 18 years age group.**
3. **Phase II/III clinical trial of RBD of SARS-CoV-2 gene (New Formulation CpG1018-750 mcg) manufactured by M/s Biological E Limited in 624 subjects ≥5 to <18 years age group.**

In light of urgent need due to COVID pandemic in the country, as per the provisions of New Drugs and Clinical Trials Rules, 2019 under Drugs and Cosmetics Act, 1940 and based on the recommendations of Subject Expert Commi†ee (SEC), CDSCO has granted permission to manufacture DNA-based COVID-19 Vaccine (2 mcg, 3 dose regimen) to M/s Cadila Healthcare for restricted use in emergency situation for prevention of COVID-19 in ≥ 12 years of age.

Further, the details of number of subjects, age group are also available publically and may be seen through CTRI

website i.e. www.ctri.gov.in.

CPIO Details :-	**Sunil Kulshrestha** **Phone: 011-23216367** **rti[dot]cell[at]cdsco[dot]nic[dot]in**
First Appellate Authority Details :-	**A[dot] K[dot] Pradhan** **Phone: 011-23216367** **rti[dot]cell[at]cdsco[dot]nic[dot]in**
Telephone Number	**011-23236973**
Email Id	**jayantwz[at]gmail[dot]com**

Helpline Number : +91-11-23978046 **Toll Free :** 1075 **Helpline Email ID :** ncov2019@gov.in **Covid-19 facilities in States & Union Territories**

Type to search...

VACCINE REGISTRATION

Where should I register for the vaccination?

Where can I get the vaccine from?

How do I pre-register myself online for an appointment for vaccination?

If I cannot pre-register myself online, how do I register on the spot and get vaccinated?

Can a person get the COVID-19 vaccine without registration with Health Department?

What documents are required for registration of eligible beneficiary?

Will a Photo ID be required at the time of registration?

If a person is not able to produce Photo ID at the session site, whether s/he be vaccinated or not?

How will the beneficiary receive information about due date of vaccination?

Will vaccinated beneficiaries receive information on the status of their vaccination after completion?

Will I get any certificate that I am vaccinated?

ABOUT THE VACCINE

Frequently Asked Questions

Get answers to your queries here

UPDATED AS ON 25 MARCH 2021

Which COVID-19 vaccines are licensed in India?

What is Emergency Use Authorization (EUA)/ Permission for restricted use?

Is the EUA a new process introduced for COVID-19 Vaccine?

Have the vaccines undergone the needed clinical trials before EUA?

What is Phase I, II and III of clinical trial for a vaccine?

Why vaccination is not provided to children who are usual target?

What technology has been used in development of the currently available two vaccines in India?

What is the composition of both the vaccines?

Composition of Covishield includes inactivated adenovirus with segments of Coronavirus, Aluminium Hydroxide Gel, L-Histidine, L-Histidine Hydrochloride Monohydrate, Magnesium Chloride Hexahydrate, Polysorbate 80, Ethanol, Sucrose, Sodium Chloride, and Disodium Edetate Dihydrate (EDTA). Composition of Covaxin includes inactivated Coronavirus, Aluminum Hydroxide Gel, TLR 7/8 Agonist, 2-Phenoxyethanol and Phosphate Buffered Saline [NKA1].

Both vaccines require cold chain temperature. How is the cold chain been maintained during storage and transportation of vaccine?

Is COVISHIELD® same as the vaccine been given in UK by Astrazeneca?

What is the dose schedule of both the vaccines?

Do I have a choice of vaccine I will receive?

Developing a vaccine takes years. But this time our scientists have developed a vaccine against the novel coronavirus in such a short time. How was this possible?

Is a COVID-19 vaccine scheduled anytime soon for me?

Is it mandatory to take the vaccine?

Will the vaccine be safe as it is being tested and introduced in a short span of time?

Out of the multiple vaccines available, how is one or more vaccine chosen for administration?

Will the vaccine introduced in India be as effective as the ones introduced in other countries?

Indian regulators have given authorization to Covaxin even before its Phase 3 trial results were out. How do we explain this?

WHO WILL GET THE VACCINE?

Will COVID-19 vaccine be given to everyone simultaneously?

Can a person presently having COVID-19 (confirmed or suspected) infection be vaccinated?

Is it necessary for a COVID-19 recovered person to take the vaccine? And if I had COVID-19 infection and was treated, why should I receive the vaccine?

How will I know if I am eligible for vaccination?

What are the contraindications for this vaccine?

The Health Ministry has advised caution in vaccinating persons with a history of bleeding or coagulation disorder. How does a person know if he/she has a coagulation disorder? What tests can be conducted?

The health advisory also states that those with immunity issues should be cautious about taking the vaccine. What are the markers of 'Immunity issues'?

HOW WILL WE BE VACCINATED?

Out of the multiple vaccines available, how is one or more vaccine chosen for administration?

Does India have the capacity to store the COVID-19 vaccine at temperature of +2 to +8 degree Celsius and transport them at required temperature?

Are there any preventive measures and precautions that one needs to follow at the session site?

WHAT TO EXPECT BEFORE VACCINATION?

What does trial mode mean for a vaccine recipient?

What is the safety and efficacy of the vaccines used in the country?

Which vaccine is better between Covisheild and Covaxin?

What medications should be avoided before taking COVID-19 vaccine and for how long?

Is the vaccine contraindicated in person with chronic diseases?

If one is taking medicines for illnesses like Cancer, Diabetes, Hypertension etc, can s/he take the COVID-19 vaccine and/or If I suffer from HTN/DM/CKD/heart disease/lipid disorders etc., can I safely take this vaccine?

WHAT TO EXPECT AFTER VACCINATION?

Do I need to use the mask/other COVID-19 appropriate precautions after receiving the vaccine?

How long I will remain protected after vaccination?

Does vaccination protect me against newer strains / mutated virus of SARS-CoV 2?

In how many days will the vaccination create an adequate immune response and protection?

Should you avoid alcohol after receiving the COVID-19 vaccine?

What precautions I need to take after receiving the vaccine?

Is it important for me to receive the same vaccine during second dose?

Does this vaccine provide herd immunity?

Toxicology Reports 8 (2021) 1665–1684

ANNEXURE P-10

Contents lists available at ScienceDirect.com by Elsevier

Toxicology Reports

The full issue of the article can be found at: https://doi.org/10.1016/j.toxrep.2021.08.010

journal homepage: https://www.elsevier.com/locate/toxrep

Why are we vaccinating children against COVID-19?

Ronald N. Kostoff , Daniela Calina, Darja Kanduc, Michael B. Briggs, Panayiotis Vlachoyiannopoulos , Andrey A. Svistunov, Aristidis Tsatsakis

A B S T R A C T

This article examines issues related to COVID-19 inoculations for children. The bulk of the official COVID-19- attributed deaths per capita occur in the elderly with high comorbidities, and the COVID-19 attributed deaths per capita are negligible in children. The bulk of the normalized post-inoculation deaths also occur in the elderly with high comorbidities, while the normalized post-inoculation deaths are small, but not negligible, in children. Clinical trials for these inoculations were very short-term (a few months), had samples not representative of the total population, and for adolescents/children, had poor predictive power because of their small size. Further, the clinical trials did not address changes in biomarkers that could serve as early warning indicators of elevated predisposition to serious diseases.

Most importantly, the clinical trials did not address long-term effects that, if serious, would be borne by children/adolescents for potentially decades. A novel *best-case scenario* cost-benefit analysis showed *very conservatively* that there are five times the number of deaths attributable to each inoculation vs those attributable to COVID-19 in the most vulnerable 65+ de- mographic. The risk of death from COVID-19 decreases drastically as age decreases, and the longer-term effects of the inoculations on lower age groups will increase their risk-benefit ratio, perhaps substantially.

Toxicology Reports 8 (2021) 1665–1684

1. Introduction

Currently, we are in the fifteenth month of the WHO-declared global COVID-19 pandemic. Restrictions of different severity are still in effect throughout the world.[1] The global COVID-19 mass inoculation is in its eighth month. As of this writing in mid-June 2021, over 800,000,000 people globally have received at least one dose of the inoculation and roughly half that number have been fully inoculated.[2] In the USA, about 170,000,000 people have received at least one dose and roughly 80 % of that number have been fully inoculated.

Also, in the USA, nearly 600,000 deaths have been officially attributed to COVID-19. Almost 5,000 deaths following inoculation have been reported to VAERS by late May 2021; specifically, "Over 285 million doses of COVID-19 vaccines were administered in the United States from December 14, 2020, through May 24, 2021. During this time, VAERS received 4,863 reports of death (0.0017 %) among people who received a COVID-19 vaccine."[3] (The Vaccine Adverse Events Reporting System (VAERS) is a passive surveillance system managed jointly by the CDC and FDA. Historically, VAERS has been shown to report about 1% of actual vaccine/inoculation adverse events.[4] See Appendix 1 for a first-principles confirmation of that result). By mid-June, deaths following COVID-19 inoculations had reached the 6000 levels.

A vaccine is legally defined as any substance designed to be administered to a human being for the prevention of one or more diseases[5]. For example, a January 2000 patent application that defined vaccines as "compositions or mixtures that when introduced into the circulatory system of an animal will evoke a protective response to a pathogen." was rejected by the U.S. Patent Office because "The immune response produced by a vaccine must be more than merely some immune response but must be protective. As noted in the previous Office Action, the art recognizes the term "vaccine" to be a compound which prevents infection".[6] In the remainder of this article, we use the term 'inoculated' rather than vaccinated, because the injected material in the present COVID-19 inoculations prevents

[1] D. Calina, T. Hartung, I. Mardare, M. Mitroi, K. Poulas, A. Tsatsakis, I. Rogoveanu, A.O. Docea, COVID-19 pandemic and alcohol consumption: impacts and interconnections, Toxicol. Rep. 8 (2021) 529–535.
[2] Coronavirus (COVID-19) Vaccinations. https://ourworldindata.org/covid-vaccinations [Accessed 2021].
[3] CDC, Vaccine Adverse Event Reporting System (VAERS) [Online]. Available: Vaccine Adverse Event Reporting System (VAERS) [Accessed 2021], 2021.
[4] R.N. Kostoff, D. Kanduc, A.L. Porter, Y. Shoenfeld, D. Calina, M.B. Briggs, D.A.Spandidos, A. Tsatsakis, Vaccine- and natural infection-induced mechanisms that could modulate vaccine safety, Toxicol. Rep. 7 (2020) 1448–1458.
[5]CORNELL, Definitions Relating to Taxable Vaccines [Online].
Available: https://www.law.cornell.edu/uscode/text/26/4132#a_2 [Accessed 4.06.2021], 2021.
[6] D.E. Martin, The Fauci/COVID-19 Dossier [Online]
Available:https://f.hubspotusercontent10.net/hubfs/8079569/The%20FauciCOVID-19%20Dossier.pdf

Toxicology Reports 8 (2021) 1665–1684

neither viral infection nor transmission. Since its main function in practice appears to be symptom suppression, it is operationally a “treatment”.

In the USA, inoculations were administered on a priority basis. Initially, first responders and frontline health workers, as well as the frailest elderly, had the highest priority. Then the campaign became more inclusive of lower age groups. Currently, approval has been granted for inoculation administration to the 12–17 years demographic, and the target for this demographic is to achieve the largest number of inoculations possible by the start of school in the fall. The schedule for inoculation administration to the 5–11 years demographic has been accelerated to start somewhere in the second half of 2021, and there is the possibility that infants as young as six months may begin to get inoculated before the end of 2021[7].

The remainder of this article will focus on the USA situation, and address mainly the pros and cons of inoculating children under eighteen. The article is structured as follows:

Section 1 (the present section) introduces the problem.

Section 2 (Background):

1) provides the background for the declared COVID-19 “pandemic” that led to the present inoculations;

2) describes the clinical trials that provided the justification for obtaining Emergency Use Authorization (EUA) from the FDA to administer the inoculations to the larger population;

3) shows why the clinical trials did not predict either the seriousness of adverse events that have occurred so far (as reported in VAERS) or the potential extent of the underlying pre-symptomatic damage that has occurred as a result of the inoculations.

Section 3 (Mass Inoculation) summarizes the adverse events that have occurred already (through reporting in VAERS) from the mass inoculation and will present biological evidence to support the potential occurrence of many more adverse effects from these inoculations in the mid-and long-term.

Section 4 (Discussion) addresses these effects further

Section 5 (Summary and Conclusions) presents the conclusions of this study.

[7]H. Levine, When Will Babies and Children Get the COVID-19 Vaccine? [Online]. Available: https://www.whattoexpect.com/news/first-year/covid19-vaccine-babies-children [Accessed 12 June 2021], 2021.

There are four appendices to this paper.

Appendix A provides some idea of the level of under-reporting of post-inoculation adverse events to VAERS and presents estimations of the actual number of post-inoculation deaths based on extrapolating the VAERS results to real-world experiences.

Appendix B provides a detailed analysis of the major clinical trials that were used to justify EUA for the inoculants presently being administered in the USA.

Appendix C summarizes potential adverse effects shown to have resulted from past vaccines, all of which could potentially occur as a result of the present inoculations.

Appendix D presents a novel *best-case scenario* cost-benefit analysis of the COVID-19 inoculations that have been administered in the USA.

2. Background

2.1. Pandemic history

In December 2019, a viral outbreak was reported in Wuhan, China, and the responsible coronavirus was termed Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2).[8,9] The associated disease was called Coronavirus Disease 2019, or COVID-2019. The virus spread worldwide, and a global pandemic was declared by the WHO in March 2020. [10,11] Restrictive measures of differing severity were imple- mented by countries globally, and included social distancing, quaran- tining, face

[8] A.O. Docea, A. Tsatsakis, D. Albulescu, O. Cristea, O. Zlatian, M. Vinceti, S.A. Moschos, D. Tsoukalas, M. Goumenou, N. Drakoulis, J.M. Dumanov, V.A. Tutelyan, G.G. Onischenko, M. Aschner, D.A. Spandidos, D. Calina, A new threat from an old enemy: Re-emergence of coronavirus (Review), Int. J. Mol. Med. 45 (2020) 1631–1643

[9] A.L. Arsene, I.B. Dumitrescu, C.M. Dragoi, D.I. Udeanu, D. Lupuliasa, V. Jinga, D. Draganescu, C.E. Dinu-Pirvu, G. Dragomiroiu, I.E. Blejan, R.E. Moisi, A.C. Nicolae, H. Moldovan, D.E. Popa, B.S. Velescu, S. Ruta, A new era for the therapeutic management of the ongoing COVID-19 pandemic, Farmacia 68 (2020) 185–196.

[10] M. Goumenou, D. Sarigiannis, A. Tsatsakis, O. Anesti, A.O. Docea, D. Petrakis, D. Tsoukalas, R. Kostoff, V.Rakitskii, D.A. Spandidos, M. Aschner, D. Calina,COVID-19 in Northern Italy: an integrative overview of factors possiblyinfluencing the sharp increase of the outbreak (Review), Mol. Med. Rep. 22 (2020) 20–32

[11] M.T. Islam, M. Hossen, Z. Kamaz, A. Zali, M. Kumar, A.O. Docea, A.L. Arsene, D. Calina, J. Sharifi-Rad, The role of HMGB1 in the immune response to SARSCOV- 2 infection: From pathogenesis towards A new potential therapeutic target, Farmacia 69 (2021) 621–634.

masks, frequent hand sanitation, etc.[12,13] In the USA, these measures were taken as well, differing from state-to-state.[14] At the same time, vaccine development was initiated to control COVID-19.[15] In the USA, non-vaccine treatments were not encouraged at the Federal level, but different treatment regimens were pursued by some healthcare practitioners on an individual level[16,17].

By the end of May 2021, the official CDC death count attributed to COVID-19 was approaching 600,000, as stated previously. This number has been disputed for many reasons. First, before COVID-19 testing began, or in the absence of testing, after it was available, the diagnosis of COVID-19 (in the USA) could be made by the presumption of the healthcare practitioner that COVID-19 existed.[18] Second, after testing began, the main diagnostic used was the RT-PCR test. This test was done at very high amplification cycles, ranging up to 45. [19,20,21] In this range, very high numbers of false positives are possible.

---

[12] P. Sidiropoulou, A.O. Docea, V. Nikolaou, M.S. Katsarou, D.A. Spandidos, A. Tsatsakis, D. Calina, N. Drakoulis, Unraveling the roles of vitamin D status and melanin during COVID-19 (Review), Int. J. Mol. Med. 47 (2021) 92–100.

[13] K. Farsalinos, K. Poulas, D. Kouretas, A. Vantarakis, M. Leotsinidis, D. Kouvelas, A.O. Docea, R. Kostoff, G.T. Gerotziafas, M.N. Antoniou, R. Polosa, A. Barbouni, V. Yiakoumaki, T.V. Giannouchos, P.G. Bagos, G. Lazopoulos, B.N. Izotov, V.A. Tutelyan, M. Aschner, T. Hartung, H.M. Wallace, F. Carvalho, J.L. Domingo, A. Tsatsakis, Improved strategies to counter the COVID-19 pandemic: lockdownsvs. Primary and community healthcare, Toxicol. Rep. 8 (2021) 1–9.

[14] A. Tsatsakis, D. Petrakis, T.K. Nikolouzakis, A.O. Docea, D. Calina, M. Vinceti, M. Goumenou, R.N. Kostoff, C. Mamoulakis, M. Aschner, A.F. Hern´andez, COVID- 19, an opportunity to reevaluate the correlation between long-term effects of anthropogenic pollutants on viral epidemic/pandemic events and prevalence, Food Chem. Toxicol. 141 (2020) 111418.

[15] D. Calina, C. Sarkar, A.L. Arsene, B. Salehi, A.O. Docea, M. Mondal, M.T. Islam, A. Zali, J. Sharifi-Rad, Recent advances, approaches and challenges in targeting pathways for potential COVID-19 vaccines development, Immunol. Res. 68 (2020) 315–324.

[16] M.T. Islam, C. Quispe, M. Martorell, A.O. Docea, B. Salehi, D. Calina, ˇZ. Reiner, J. Sharifi-Rad, Dietary supplements, vitamins and minerals as potential interventions against viruses: perspectives for COVID-19, Int. J. Vitam. Nutr. Res. (2021) 1–18.

[17] J. Sharifi-Rad, C.F. Rodrigues, Z. Stojanovic-Radic, M. Dimitrijevic, A. Aleksic, K. Neffe-Skocinska, D. Zielinska, D. Kolozyn-Krajewska, B. Salehi, S.M. Prabu, F. Schutz, A.O. Docea, N. Martins, D. Calina, Probiotics: versatile bioactive components in promoting human health, Medicina-Lithuania 56 (2020) 30.

[18] CDC, COVID-19 Vaccine Breakthrough Case Investigation and Reporting [Online]. Available: https://www.cdc.gov/vaccines/covid-19/health-departments/breakthrough-cases.html [Accessed 2021], 2021.

[19] M. Neagu, D. Calina, A.O. Docea, C. Constantin, T. Filippini, M. Vinceti, N. Drakoulis, K. Poulas, T.K. Nikolouzakis, D.A. Spandidos, A. Tsatsakis, Back to basics in COVID-19: antigens and antibodies-completing the puzzle, J. Cell. Mol. Med. 25 (2021) 4523–4533.

[20] A. Mandavilli, Your Coronavirus Test Is Positive. Maybe It Shouldn't Be [Online]. Available: https://www.nytimes.com/2020/08/29/health/coronavirus-testing.html.

[21] J. Mercola, Asymptomatic 'Casedemic' Is a Perpetuation of Needless Fear [Online]. Available: https://articles.mercola.com/sites/articles/archive/2020/ 11/19/covid-testing-fraud-fuels-casedemic.aspx?eType=EmailBlastContent&eId=0b802463-f128-49db-83f8-ecb922534dc4

Third, most deaths attributed to COVID-19 were elderly with high comorbidities.[22] As we showed in a previous study, attribution of death to one of many possible comorbidities or especially toxic exposures in combinations[23] is highly arbitrary and can be viewed as a political decision more than a medical decision. For over 5 % of these deaths, COVID-19 was the only cause mentioned on the death certifi- cate. For deaths with conditions or causes in addition to COVID-19, on average, there were 4.0 additional conditions or causes per death.[24] These deaths with comorbidities could equally have been ascribed to any of the comorbidities. Thus, the actual number of COVID-19-based deaths in the USA may have been on the order of 35, 000 or less, characteristic of a mild flu season.

Even the 35,000 deaths may be an overestimate. Comorbidities were based on the clinical definition of specific diseases, using threshold biomarker levels and relevant symptoms for the disease(s) of interest[25,26] But many people have what are known as pre-clinical condi- tions. The biomarkers have not reached the threshold level for official disease diagnosis, but their abnormality reflects some degree of under- lying dysfunction. The immune system response (including pre-clinical conditions) to the COVID-19 viral trigger should not be expected to be the same as the response of a healthy immune system.[27] If pre-clinical conditions had been taken into account and coupled with the false positives as well, the CDC estimate of 94% misdiagnosis would be substantially higher.

2.2. Clinical trials

2.2.1. Clinical trials to gain FDA Emergency Use Authorization (EUA) approval

[22] R.N. Kostoff, M.B. Briggs, A.L. Porter, A.F. Hern´andez, M. Abdollahi, M. Aschner, A. Tsatsakis, The under-reported role of toxic substance exposures in the COVID-19 pandemic, Food Chem. Toxicol. 145 (2020) 111687.
[23] R.N. Kostoff, M. Goumenou, A. Tsatsakis, The role of toxic stimuli combinations in determining safe exposure limits, Toxicol. Rep. 5 (2018) 1169–1172.
[24] Weekly Updates by Select Demographic and Geographic Characteristics https://www.cdc.gov/nchs/nvss/vsrr/covid_weekly/index.htm?fbclid=IwAR3wrg3tTKK59tOHPGAHWFVO3DfslkJ0KsDEPQpWmPbKtp6EsoVV2Qs1Q.
[25] M. Torequl Islam, M. Nasiruddin, I.N. Khan, S.K. Mishra, E.Z.M. Kudrat, T. Alam Riaz, E.S. Ali, M.S. Rahman, M.S. Mubarak, M. Martorell, W.C. Cho, D. Calina, A. O. Docea, J. Sharifi-Rad, A perspective on emerging therapeutic interventions for COVID-19, Front. Public Health 8 (2020) 281.
[26] H. Pott-Junior, M.M.B. Paoliello, A.D.Q.C. Miguel, A.F. Da Cunha, C.C. De Melo Freire, F.F. Neves, L.R. Da Silva De Av´o, M.G. Roscani, S.D.S. Dos Santos, S.G. F. Chach´a, Use of ivermectin in the treatment of Covid-19: a pilot trial, Toxicol. Rep. 8 (2021) 505–510.
[27] D. Calina, A.O. Docea, D. Petrakis, A.M. Egorov, A.A. Ishmukhametov, A.G. Gabibov, M.I. Shtilman, R. Kostoff, F. Carvalho, M. Vinceti, D.A. Spandidos, A. Tsatsakis, Towards effective COVID-19 vaccines: updates, perspectives and challenges (Review), Int. J. Mol. Med. 46 (2020) 3–16.

The unprecedented accelerated development of COVID-19 vaccines in the USA, dubbed Operation Warp Speed, resulted in a handful of substances available for clinical trials by mid-2020[28]. These clinical trials were conducted to predict the safety and efficacy of the potential vaccines (which have turned out to be treatments/inoculations as stated previously), and thereby gain approval for inoculating the public at large.[29] An overview of the Pfizer clinical trials is presented in this section, and a more detailed description of the main clinical trials is shown in Appendix B.

Two types of inoculants have gained FDA EUA in the US: mRNA- based inoculants and viral vector-based inoculants, with the mRNA in- oculants having the widest distribution so far. Comirnaty is the brand name of the mRNA-based inoculant developed by Pfizer/BioNTech, and Moderna COVID-19 Vaccine is the brand name of the mRNA-based inoculant developed by Moderna.[30] Both inoculants contain the ge- netic information needed for the production of the viral protein S (spike), which stimulates the development of a protective immune response against COVID-19.[31] Janssen COVID-19 Vaccine is the brand name of the viral vector-based inoculant developed by Johnson and Johnson. Janssen COVID-19 vaccine uses an adenovirus to transport a gene from the coronavirus into human cells, which then produce the coronavirus spike protein. This spike protein primes the immune system to fight off potential coronavirus infection.[32]

The results of these trials that allowed granting of EUA by the FDA can be found in the inserts to the inoculation materials. For example, the Pfizer inoculation trial results are contained in the fact sheet for healthcare providers administering vaccine (vaccination providers).

[28] C. Sarkar, M. Mondal, M. Torequl Islam, M. Martorell, A.O. Docea, A. Maroyi, J. Sharifi-Rad, D. Calina, Potential therapeutic options for COVID-19: current status, challenges, and future perspectives, Front. Pharmacol. 11 (2020) 572870.

[29] D. Calina, T. Hartung, A.O. Docea, D.A. Spandidos, A.M. Egorov, M.I. Shtilman, F. Carvalho, A. Tsatsakis, COVID-19 vaccines: ethical framework concerning human challenge studies, Daru 28 (2020) 807–812.

[30] D. Calina, A.F. Hern´andez, T. Hartung, A.M. Egorov, B.N. Izotov, T. K. Nikolouzakis, A. Tsatsakis, P.G. Vlachoyiannopoulos, A.O. Docea, Challenges and scientific prospects of the newest generation of mRNA-Based vaccines against SARS-CoV-2, Life 11 (2021) 907.

[31] A.F. Hern´andez, D. Calina, K. Poulas, A.O. Docea, A.M. Tsatsakis, Safety of COVID-19 vaccines administered in the EU: Should we be concerned? Toxicol. Rep. 8 (2021) 871–879.

[32] C. Wang, X. Zhou, M. Wang, X. Chen, The impact of SARS-CoV-2 on the human immune system and microbiome, Infect. Microbes Dis. 3 (2020) 14–21.

Toxicology Reports 8 (2021) 1665–1684

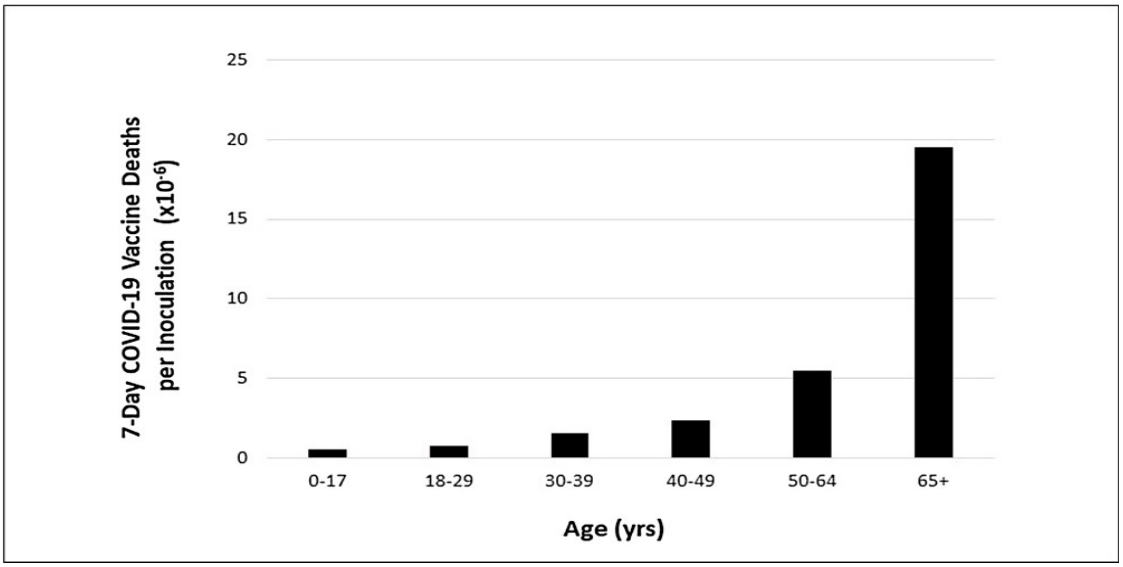


Fig. Post-inoculation deaths per dose of inoculant. 7-day COVID-19 vaccine deaths per inoculation by age in the United States (as of 5/28/2021). Data shown includes the total number of all deaths up to 7 days after receiving the vaccine for both those administered 1 dose and the complete series of doses by age in the United States as of 5/28/2021 reported in VAERS (updated on 5/28/ 2021). COVID-19 Vaccinations (Inoculations) based on CDC data provided by ISSInfo up thru 5/28/2021. Data obtained from https://data.cdc.gov/Vaccinations/COVID-19-Vaccination-Demographics-in-the-United-St/km4m-vcsb on 6/ 10/2021. COVID-19 Vaccinations Deaths based on CDC WONDER VAERS Database as of 5/28/2021, obtained from https://wonder.cdc.gov/controller/datarequest/D8;jsessionid=4B5522C8D1DA68F1A364646B0DA5 on 6/ 9/2021.

……Credible safety science applied to this experiment would have required a much more expansive approach to determining effects on a wide variety of state and flux metrics that could serve as early warning indicators of potentially serious symptoms/disease, and might occur with much higher frequencies at this early stage than the rare serious symptoms. The only mention of these other metrics in the above proposal is in the Phase I trial description: “Percentage of Phase 1 participants with abnormal haematology and chemistry laboratory values”, to be generated seven days after dose 1 and dose 2.

A paper published in NEJM in December 2020[33] summarized the Phase 1 results. The focus was on local and systemic adverse events and efficacy metrics (antibody responses). The only metrics other than these reported were transiently decreased lymphocyte counts.

We view this level of reporting as poor safety science for the following reasons. Before the clinical trials had started, many published articles were reporting serious effects associated with the presence of the SARS-CoV-2 virus such as hyperinflammation, hypercoagulation, hypoxia, etc. SARS-CoV-2 includes the S1 Subunit (spike protein), and it was not known how much of the damage was associated with the spike protein component of SARS-CoV-2. A credible high-quality safety science experiment would have required state measurements of specific biomarkers associated with each of these abnormal general biomarkers before and after the inoculations, such as d-dimers for evidence of enhanced coagulation/clotting; CRP for evidence of enhanced inflammation; troponins for evidence of cardiac damage; occludin and claudin for evidence of enhanced barrier permeability; blood oxygen levels for evidence of enhanced hypoxia; amyloid-beta and phosphorylated tau for evidence of increased predisposition to Alzheimer's disease; Serum HMGB1, CXCL13, Dickkopf-1 for evidence of an increased disposition to autoimmune disease, etc. A credible high-quality safety science experiment would have required flux measurements of products resulting from the mRNA interactions, from the LNP shell interactions, from dormant viruses that might have been stimulated by the mRNA-generated spike protein, etc., emitted through the sweat glands, faeces, saliva, exhalation, etc.

Most importantly, these types of measurements would have shown changes in the host that did not reach the symptom level of expression but raised the general level of host abnormality that could predispose the host to a higher probability of serious symptoms and diseases at some point in the future. Instead, in the absence of high-quality safety science reflected in these experiments, all that could be determined were short-term adverse effects and deaths. This focus on symptoms masked the true costs of the mRNA intervention, which would probably include much larger numbers of people whose health could have been degraded by the intervention as evidenced by increased abnormal values of these biomarkers. For example, the trials and VAERS reported clots that resulted in serious symptoms and deaths but gave no indication of the enhanced predisposition to forming serious clots in the future with a higher base of micro-clots formed because of the mRNA intervention. The latter is particularly relevant to children,

[33] E.E. Walsh, R.W. Frenck Jr., A.R. Falsey, N. Kitchin, J. Absalon, A. Gurtman, S. Lockhart, K. Neuzil, M.J. Mulligan, R. Bailey, K.A. Swanson, P. Li, K. Koury, W. Kalina, D. Cooper, C. Fontes-Garfias, P.Y. Shi, ¨O. Türeci, K.R. Tompkins, K. E. Lyke, V. Raabe, P.R. Dormitzer, K.U. Jansen, U. S¸ahin, W.C. Gruber, Safety and immunogenicity of two RNA-Based Covid-19 vaccine candidates, N. Engl. J. Med. 383 (2020) 2439–2450.

Toxicology Reports 8 (2021) 1665–1684

who have a long future that could be seriously affected by having an increased predisposition to multiple clot-based (and other) serious diseases resulting from these inoculations.

3. Mass inoculation

3.1. Adverse events reported for adults

This section describes the adverse effects that followed COVID-19 mass inoculation in the USA. The main source of adverse effects data used was VAERS. Because VAERS is used to estimate adverse event in- formation by many other countries as well, a short overview of VAERS and its intrinsic problems is summarized in Appendix 1.

The period in the present study covered by the reported inoculations is mid-December 2020 to the end of May 2021. The population inoculated during this period is mainly adults. Child inoculations did not begin until mid-May. Because the different age groups were inoculated starting at different times based on priority, the elapsed times after inoculation will be different, and any adverse event comparisons across age groups will require some type of elapsed post-inoculation time normalization.

We examined VAERS-reported deaths by age group, normalized to:

1) the number of inoculations given

2) the period within seven days after inoculation.

This allows a credible comparison of very short-term adverse effects post-inoculation for all age groups. During this period, which is eight days post-inoculation (where day zero is the day of inoculation), sixty percent of all post-inoculation deaths are reported in VAERS.

Fig. 2 below shows the results circa late May 2021. The age band ranges are different from those in Fig. 1 because the CDC provides inoculation after-effect age bands differently from COVID-19 death age bands. In general, the inoculation deaths by age per inoculant roughly parallel the COVID-19 deaths by age per capita (the curve structures are very similar), with one exception: the 0–17 demographic. In the normalized COVID-19 death graph (Fig. 1), the deaths per capita in the 0–17 demographic are negligible, while in the normalized inoculant death graphs (Fig. 2) the normalized deaths are small, but not negligible. The members of the 65 demographic, where the bulk of deaths are occurring in Figs. 1 and 2, have been receiving inoculations for five months, whereas the members of the youngest demographic have been receiving inoculations only for a few weeks. More time needs to

pass before more definitive conclusions can be drawn about the youngest demographic, and how its members are impacted adversely following the inoculations.

The high death rates from both COVID-19 and the inoculations in the 65+ demographic should not be surprising. In both cases, the immune system is challenged, and in both cases, a dysfunctional immune system characteristic of many elderly people with multiple comorbidities cannot respond adequately to the challenge.

3.1.1. Specific short-term adverse events reported in VAERS

The most comprehensive single evaluation of VAERS-reported adverse events (mainly for adult recipients of the COVID-19 "vaccines") we have seen is a non-peer-reviewed collection of possible side effects by Dr. Ray Sahelian. We recommend reading this short data-rich summary of the broad types of events reported already, in the context that these events are very short-term. Dr. Sahelian identifies five mechanisms he believes are responsible for most of these events, with research potentially uncovering other mechanisms. These five mechanisms include:

1 "An overreacting inflammatory response is known as systemic inflammatory response syndrome (SIRS). This SIRS reaction, perhaps a cytokine storm, can range from very mild to very severe. It can begin the very first day of the shot or begin days or weeks later as a delayed reaction."

2 "Interaction of the spike proteins with ACE2 receptors on cell membranes. Such cells are found widely in the body including the skin, lungs, blood vessels, heart, mouth, gastrointestinal tract, kidneys, and brain."

3 "Interaction of spike proteins with platelets and/or endothelial cells that line the inside of blood vessels. This can lead to clotting or bleeding (low number of circulating platelets in the bloodstream). Some of the clots, even if tiny, cause certain neurological symptoms if the blood supply to nerves is compromised."

4 "Immediate or delayed release of histamine from mast cells and basophils (mast cell activation syndrome, MCAS)."

5 "Swelling of lymph nodes in various areas of the body could interfere with blood flow, put pressure on nerves causing pain, or compromise their proper function."

These reactions can be classified as Hyperinflammation, Hyper- coagulation, Allergy, and Neurological, and can contribute too many symptoms and diseases, as VAERS is showing. An

excellent review of acute and potential long-term pathologies resulting from the COVID-19 inoculations showed potential relationships to blood disorders, neurodegenerative diseases and autoimmune diseases. This review discussed the relevance of prion-protein-related amino acid sequences within the spike protein.

3.1.2 *Potential mid- and long-term events and serious illnesses for adults and children from past vaccines*

A detailed description of potential mid- and long-term events and serious illnesses for adults and children from past vaccines is presented in Appendix C. Most of these events and illnesses are not predictable, and most, if not all, would be possible for the COVID-19 inoculations in the mid- and long-term for adults and children.

3.1.3 *Potential short-, mid-, and long-term risks of mass COVID-19 inoculation for children*

3.1.3.1. *Intrinsic inoculant toxicity*. Children are unique relative to COVID-19. They have negligible risks of serious effects from the disease, as shown in Fig. 1. Given that the COVID-19 inoculants were only tested for a few months, and mid-or long-term adverse effects are unknown, any mid- or long-term adverse events that emerge could impact children adversely for decades.

We believe that mid-or long-term adverse effects are possible based on the recent emergence of evidence that would support the probability of mid-and long-term adverse effects from the COVID-19 inoculants, such as:

1) The spike protein itself can be a toxin/pathogenic protein:

2) S protein alone can damage vascular endothelial cells (ECs) by downregulating ACE2 and consequently inhibiting mitochondrial function

3) it is concluded that ACE2 and endothelial damage is a central part of SARS-CoV2 pathology and may be induced by the spike protein alone

4) the spike protein of SARS-CoV-1 (without the rest of the virus) reduces ACE2 expression, increases angiotensin II levels, exacerbates lung injury, and triggers cell signaling events that may promote pulmonary vascular remodeling and Pulmonary Arterial Hypertension (PAH) as well as possibly other cardiovascular complications[34]

[34] Y.J. Suzuki, S.G. Gychka, SARS-CoV-2 spike protein elicits cell signaling in human host cells: implications for possible consequences of COVID-19 vaccines, Vaccines 9 (2021) 36.

Toxicology Reports 8 (2021) 1665–1684

5) The recombinant S protein alone elicits functional alterations in cardiac vascular pericytes (PCs).[35] This was documented as:

6) increased migration

7) reduced ability to support EC network formation on Matrigel

8) secretion of pro-inflammatory molecules typically involved in the cytokine storm

9) Production of pro-apoptotic factors responsible for EC death. Furthermore, the S protein stimulates the phosphorylation/activation of the extracellular signal-regulated kinase 1/2 (ERK1/2) through the CD147 receptor, but not ACE2, in cardiac PCs, the S protein may elicit vascular cell dysfunction, potentially amplifying, or perpetuating, the damage caused by the whole corona virus.

10) "Even in the absence of the angiotensin-converting enzyme 2 receptors, the S1 subunit from SARS-CoV-2 spike protein binding to neutral phospholipid membranes leads to their mechanical destabilization and permeabilization. A similar cytotoxic effect of the protein was seen in human lung epithelial cells."

11) The LNP layer encapsulating the mRNA of the inoculant is highly inflammatory in both intradermal and intranasal inoculation[36] and "Polyethylene glycol (PEG) is a cause of anaphylaxis to the Pfizer/BioNTech mRNA COVID-19 vaccine". "Humans are likely developing PEG antibodies because of exposure to everyday products containing PEG. Therefore, some of the immediate allergic responses observed with the first shot of mRNA-LNP vaccines might be related to pre-existing PEG antibodies. Since these vaccines often require a booster shot, anti-PEG antibody formation is expected after the first shot. Thus, the allergic events are likely to increase upon re-vaccination"[37].

There is also the possibility that the components of the LNP shell could induce the ASIA Syndrome (auto- immune/inflammatory syndrome induced by adjuvants), as shown by studies on post-inoculation thyroid hyperactivity and post-inoculation subacute thyroiditis.

---

[35] E. Avolio, M. Gamez, K. Gupta, R. Foster, I. Berger, M. Caputo, A. Davidson, D. Hill, P. Madeddu, The SARS-CoV-2 Spike Protein Disrupts the Cooperative Function of Human Cardiac Pericytes - Endothelial Cells Through CD147 Receptor-mediated Signalling: a Potential Non-infective Mechanism of COVID-19 Microvascular Disease, bioRxiv, 2020.12.21.423721, 2020.

[36] S. Ndeupen, Z. Qin, S. Jacobsen, H. Estanbouli, A. Bouteau, B.Z. Igy´art´o, The mRNA LNP Platform's Lipid Nanoparticle Component Used in Preclinical Vaccine Studies Is Highly Inflammatory, bioRxiv, 2021.

[37] P. Sellaturay, S. Nasser, S. Islam, P. Gurugama, P.W. Ewan, Polyethylene glycol (PEG) is a cause of anaphylaxis to the Pfizer/BioNTech mRNA COVID-19 vaccine, Clin. Exp. Allergy 51 (2021) 861–863.

Toxicology Reports 8 (2021) 1665–1684

12 The spike protein has been found in the plasma of post- inoculation individuals, implying that it could circulate to, and impact adversely, any part of the body.

13 The spike protein of SARS-CoV-2 crosses the blood-brain barrier in mice, and "the SARS-CoV-2 spike proteins trigger a pro-inflammatory response on brain endothelial cells that may contribute to an altered state of BBB function".

14 The spike proteins manufactured in vivo by the present COVID-19 inoculations could potentially "precipitate the onset of autoimmunity in susceptible subgroups, and potentially exacerbate autoimmunity in subjects that have pre-existing autoimmune diseases", based on the finding that anti-SARS-CoV-2 protein antibodies cross-reacted with 28 of 55 diverse human tissue antigens.

15 "The biodistribution of ChaAdOx1 [Astra Zeneca's recombinant adenovirus vaccine candidate against SARS-CoV-2] in mice confirmed the delivery of vaccine into the brain tissues. The vaccine may therefore spur the brain cells to produce CoViD spike proteins that may lead to an immune response against brain cells, or it may spark a spike protein-induced thrombosis. This may explain the peculiar incidences of the fatal cerebral venous sinus thrombosis (CVST) observed with viral vector-based CoViD-19 vaccines"[38]

A complementary perspective to explain adenovirus-based vaccine-induced thrombocytopenia is that "transcription of wildtype and codon-optimized Spike open reading frames enables alternative splice events that lead to C-terminal truncated, soluble Spike protein variants. These soluble Spike variants may initiate severe side effects when binding to ACE2-expressing endothelial cells in blood vessels."

16 A Pfizer Confidential study performed in Japan showed that "modRNA encoding luciferase formulated in LNP comparable to BNT162b2″ injected intramuscularly concentrated in many organs/tissues in addition to the injection site. The main organs/sites identified were adrenal glands, liver, spleen, bone marrow, and ovaries. While damage to any of these organs/sites could be serious (if real for humans), adverse effects on the ovaries could be potentially catastrophic for women of child- bearing or pre-childbearing age.

[38] H.A. Merchant, CoViD vaccines and thrombotic events: EMA issued warning to patients and healthcare professionals, J. Pharm. Policy Pract. 14 (2021) 32.

The main objective of credible biodistribution studies (of inoculants for eventual human use) is to identify the spatio-temporal distribution of the actual inoculant in humans; i.e., how much of the final desired product (in this case, expressed protein antigen/spike protein) is produced in different human tissues and organs as a function of time. That's not what was reported in the Pfizer Confidential study.

Rats were used for the in vivo studies; the relationship of their bio- distribution to that of humans is unclear. They were injected in different locations (hind paw/intramuscular); the relationship to human injections in the deltoid muscle is unclear. They were injected with "modRNA encoding luciferase formulated in LNP comparable to BNT162b2″; it is unclear why they weren't injected with BNT162b2, it is unclear why spike protein expression wasn't evaluated rather than LNP concentration, and it is unclear how well the bio distribution from the actual inoculant used in the experiments compares to the biodistribution from BNT162b2.

They were injected once per rat. Given that a second injection would not be in the same exact location as the first, and that the circulatory system might have changed due to clotting effects from the first injection and other potential vascular complications, it is unclear how the bio- distribution change with the second injection would compare with the first. If a booster injection is given to counter variants, it is unclear how its biodistribution would be altered as a consequence of the preceding two injections.

Clotting will occur with the highest probability where the blood flow is reduced (and more time is available for LNP-endothelial cell inter- action). It is unclear whether the clotting process would show positive feedback behaviour where the initial inoculation constricts the flow in low-velocity regions even further by enhanced clotting, and subsequent inoculations further amplify this reduced flow-enhanced clotting cycle.

The rats were injected under pristine conditions; how that compares with humans, who have been, are being, and will continue to be exposed to multiple toxic substances in combination, is open to question. We know these combinations can act synergistically to adversely impact myriad organs and tissues throughout the body. We don't know how these toxic exposures in humans affect the permeability of the blood/tissue barriers, and especially the ability of the injected material to diffuse into the bloodstream (and also the ability of the manufactured spike proteins to diffuse from the bloodstream into the surrounding tissue).

Higher-level primates should have been used for these short-term experiments, to obtain a more realistic picture of the biodistribution of inoculant in human organs and tissues. In other words, these

laboratory experiments may be just the tip of the iceberg of estimating the amount of inoculant that concentrates in critical organs and tissues of human beings.

The many studies referenced above indicate collectively that the mRNA-based COVID-19 inoculations (the most prolific inoculations used in the USA for COVID-19 so far) consist of (at least) two major toxins: the instructions for the spike protein (mRNA) and the mRNA- encapsulating synthetic fat LNP. The vaccine is injected into the deltoid muscle, at which time it contributes to inflammation at the injection site due in part to the LNP and potentially to anaphylaxis from the LNP PEG-2000 component. Some of the injected material stays at the injection site, where it combines with cells through endocytosis to express spike protein on the cell surface, stimulating the adaptive immune system to eventually produce antibodies to the spike protein.

The remainder of the injected material enters the lymphatic system and the bloodstream, and is distributed to tissues and organs throughout the body: e.g., "Drugs administered by the intramuscular (IM) route are deposited into vascular muscle tissue, which allows for rapid absorption into the circulation". The basis of this process is that the bulky muscles have good vascularity, and therefore the injected drug quickly reaches the systemic circulation and thereafter into the specific region of action, bypassing the first-pass metabolism. The widespread distribution is greatly enhanced by the LNP PEG-2000 coating as follows: building from the success of PEGylating proteins to improve systemic circulation time and decrease immunogenicity. PEG coatings on nanoparticles shield the surface from aggregation, opsonization, and phagocytosis, prolonging systemic circulation time. PEG coatings on nanoparticles have also been utilized for overcoming various bio- logical barriers to efficient drug and gene delivery associated with other modes of administration.[39]

In the bloodstream, one possible outcome is that the LNPs coalesce with the endothelial cells on the inner lining of the blood vessels and transfer the mRNA to the cells through endocytosis. The endothelial cells would then express the spike protein on their surface. Platelets flowing by the spike protein express ACE2 receptors on their surface; therefore, one possible outcome would be activation of the platelets by the spike protein and initiation of clotting. Another possible outcome would be the modified endothelial cells being recognized by innate immune system cells as foreign. These immune killer cells would then destroy parts of the endothelium and weaken the blood-organ barriers. The LNPs would inflame the endothelium as well, both increasing barrier permeability and increasing the blood vessel diameter. This weakening of the blood-organ barriers would be superimposed on any

[39] J.S. Suk, Q. Xu, N. Kim, J. Hanes, L.M. Ensign, PEGylation as a strategy for improving nanoparticle-based drug and gene delivery, Adv. Drug Deliv. Rev. 99 (2016) 28–51.

Toxicology Reports 8 (2021) 1665–1684

inflammation due to the myriad toxic contributing factors operable. The newly-formed cells with spike proteins would penetrate the blood-organ barriers and bind to tissue with expressed ACE2 receptors. Any LNPs that did not coalesce with the endothelial cells, but remained intact, could also pass through the permeable blood-organ barrier, and coalesce directly with the organ cells. This could lead to an attack by innate immune system cells, and be a precursor to autoimmunity.

In the preceding discussion of the Pfizer biodistribution studies, the issue of multiple inoculations on changes in biodistribution was raised. Similarly, the alteration of effects as described above by multiple inoculations must be considered. Each inoculation will have positive aspects and negative aspects. The positive aspects are the formation of antibodies in the muscle cells and lymphatic system. The negative aspects include, but are not limited to, the potential clotting effects and permeability increases for that fraction of the inoculant that enters the bloodstream. The first inoculant dose can be viewed as priming the immune system. The immune response will be relatively modest. The second inoculant dose can be expected to elicit a more vigorous immune response. This will enhance the desired antibody production in the muscle cells and lymphatic system, but may also enhance the immune response to both the blood vessel-lining endothelial cells displaying the spike protein and the platelets, causing more severe damage. If a booster (s) inoculation is also required, this may further enhance both the positive and negative immune responses resulting from the second inoculation. While the positive effects are reversible (antibody levels decrease with time), adverse effects may be cumulative and irreversible, and therefore injury and death rates may increase with every additional inoculation.

….In addition, there were large numbers of different vision and breathing problems reported.

All the major systems of the body are impacted, and many of the major organs as well. Given the lag times in entering data into VAERS and the fact that inoculations of children started fairly recently, we would expect the emphasis to be immediate symptomatic and biomarker reactions. More time is required for organ and system damage to develop and emerge. Cardiovascular problems dominate, as our model for spike protein/LNP circulation and damage predicts, and it is unknown how reversible such problems are. Many of the VAERS symptoms listed above were also found in COVID-19 adult patients.

Consider the example of Multisystem Inflammatory Syndrome in Children (MIS-C). It has emerged in VAERS with modest frequency so far, and it also occurred about a month after COVID-19 infection. In both cases, the presence of the spike protein was a common feature. Many of its characteristic symptoms are those listed above from VAERS. MIS-C has similarities with known disease entities like Kawasaki Disease (KD), toxic shock syndrome (TSS) and macrophage activation syndrome (MAS)/secondary hemophagocytic lymphohistiocytosis (HLH). One presentation of MIS-C is in adolescents with a high

disease burden as evidenced by more organ systems involved, almost universally including cardiac and gastrointestinal systems, and with a higher incidence of shock, lymphopenia, and elevated cardiac biomarkers indicating myocarditis. Since the first reports of children developing MIS-C, it was evident that others presented with some of the classic symptoms of the well-recognized childhood illness KD. Further, despite KD being ordinarily incredibly rare in adults, patients with MIS-A have also been reported with KD-like features. Thus, an examination of the adverse effects from COVID-19 as evidenced through these diseases might shed some light on what can be expected further down the line from the inoculations.

The following section addresses Kawasaki disease (KD) and Multi- system Inflammatory Syndrome in Children (MIS-C).

KD is an acute vasculitis and inflammation that predominantly affects the coronary arteries and can cause coronary artery aneurysms. Other KD manifestations include systemic inflammation of arteries, organs, and tissues, with consequent hepatitis and abdominal pain; lung interstitial pneumonitis, aseptic meningitis due to brain membrane in- flammations; myocarditis, pericarditis, and valvulitis; urinary tract py- uria, pancreatitis; and lymph-node enlargement. In general, although almost all children fully recover, some of them later develop coronary artery dilation or aneurysm. Etiologically and pathologically, numerous studies indicate that KD is triggered by an abnormal autoimmune response caused by an infection. The infection hypothesis is supported by epidemiology data showing that an infectious disease is involved at least as a starting point. Previously proposed infectious agents include Herpesviridae, retroviruses, Parvovirus B19, bocavirus, and bacterial infections such as staphylococci, streptococci, Bartonella, and Yersinia infections [40].

SARS-CoV-2 adds to these infectious agents by eliciting autoantibodies likely via molecular mimicry and cross-reactivity with auto- antigens.

Then, the formation of antigen–antibody immune complexes can lead to KD symptoms via activation of the receptors of mast cells, neutrophils, and macrophages with consequent release of pro-inflammatory cytokines and increase of blood vessel permeability; activation of the complement system, stimulation of neutrophils and macrophages to secrete proteases and more proinflammatory cytokines, thus merging into the “cytokine storm” that characterizes MIS-C. Indeed, features of KD are raised levels of Interleukin (IL)-6, IL-8, IL-15, and IL-17, with the cytokine level predicting coronary aneurysm formation in KD patients.

[40] M.D. Hicar, Antibodies and immunity during Kawasaki disease, Front. Cardiovasc. Med. 7 (2020) 94.

3.1.3.2.2. Potential long-term adverse health effects. In the long-term, SARS-CoV-2-induced KD vasculitis can lead to severe pathologies. Vasculitis has a predilection for coronary arteries with a high compli- cation rate across the lifespan for those with medium to large coronary artery aneurysms. The cytokine-induced inflammation produces endothelial dysfunction and damage to the vascular wall, leading to aneurysmal dilatation. Successively, vascular remodeling can also occur, but this does not imply resolution of the disease or reduction of risk for future complications. A rigorous follow-up to detect progressive stenosis, thrombosis and luminal occlusion that may lead to myocardial ischemia and infarction becomes mandatory. Of equal importance, among other long-term outcomes, children with KD may have increased risks not only for ischemic heart disease, but also for autoimmune dis- orders, cancer as well as an increased all-cause mortality.

Additional questions regarding mass inoculation of children and adolescents include:

a) Do children, being asymptomatic carriers of SARS-CoV-2, transmit the virus?

b) Do recently vaccinated people, infected with SARS-CoV-2, transmit the virus?

There is evidence of children transmitting SARS-CoV-2 in community settings, but the existing literature is heterogeneous with regards to the relative rate at which they do so compared to adults.

Studies from South Korea and Thailand found a very limited number of secondary cases. On the contrary, a large contact tracing study from India concluded that the highest probability of transmission was between case-contact pairs of similar age and that this pattern of enhanced transmission risk was highest among children 0–4 years of age as well as adults 65 years of age and older.

With regard to the second question, it was shown that household members of healthcare workers inoculated with a single dose of either Pfizer or Astra Zeneca COVID-19 inoculant were at significantly reduced risk of PCR-confirmed SARS-CoV-2 infection but at non-statistically significant reduced risk of hospitalization, compared to household members of uninoculated healthcare workers, fourteen days after inoculation. This finding again underlines the association of severe disease to the characteristics of the infected person and not directly to the transmission, implying that the elderly should be inoculated and not the children.

3.2. Novel best-case scenario cost-benefit analysis of COVID-19 inoculations for most vulnerable

Traditional cost-benefit analyses are typically financial tools used to estimate the potential value of a proposed project. They involve generating cost streams over time, benefit streams over time, and then comparing the net present value of these two streams (including risk) to see whether the risk-adjusted

discounted benefits outweigh the risk- adjusted discounted costs. Appendix D presents a detailed non-traditional *best-case scenario* pseudo-cost-benefit analysis of inoculating people in the 65 demographic in the USA. In this incarnation of a cost-benefit analysis, the costs are the number of deaths resulting from the inoculations, and the benefits are the lives saved by the inoculations. The time range used was from December 2019 to end-of-May 2021. No discounting was done; an inoculation-based death occurring immediately post-inoculation was given the same importance/weighting as an inoculation-based death months after inoculation.

Why was this non-traditional approach selected for a cost-benefit analysis? In a traditional non-financial cost-benefit analysis relative to inoculations, the adverse events prevented by the inoculations would be compared with the adverse events resulting from the inoculations. Presently, in the USA, definitions, test criteria, and reporting incentives for COVID-19 and its inoculants have shifted over time, and we believe a standard approach could not be performed credibly. Appendix Da presents some of the problems with the COVID-19 diagnostic criteria on which the above statements are based.

In contrast to the pandemic buildup phase, where many who died *with* COVID-19 were assumed to have died *from* COVID-19 by the medical community and the CDC, the post-inoculation deaths reported in VAERS are assumed by the CDC to be mostly from causes other than the inoculations. We wanted to use a modified cost-benefit analysis that would have less dependence on arbitrary criteria and subjective judgments.

The approach selected can be viewed as a *best-case scenario* pseudo-cost-benefit analysis. We assume the inoculations prevent ***all*** the deaths ***truly*** attributable to COVID-19 (these are the total deaths attributed to COVID-19 officially minus 1) the number of false positives resulting from the PCR tests run at very high amplification cycles and 2) the number of deaths that could have been attributed to one of the many comorbidities that were typical of those who succumbed, as shown in our results section) over the period December 2019 to end-of-May 2021, and relate that number to the deaths ***truly*** attributable to the inoculation (from January 2021 to end-of-May 2021) based on our computations in the results section. The results show ***conservatively*** that there are five times the number of deaths ***truly*** attributable to each inoculation vs those ***truly*** attributable to COVID-19 in the 65+ demographic. As age decreases, and the risk for COVID-19 decreases, the cost-benefit increases. Thus, if the best-case scenario looks ***poor*** for benefits from the inoculations, any realistic scenario will look ***very poor***. For children the chances of death from COVID-19 are negligible, but the chances of serious damage over their lifetime from the toxic inoculations are not negligible.

5. Overall conclusions

Toxicology Reports 8 (2021) 1665–1684

The people with myriad comorbidities in the age range where most deaths with COVID-19 occurred were in very poor health. Their deaths did not seem to increase all-cause mortality as shown in several studies. If they hadn't died with COVID-19, they probably would have died from the flu or many of the other comorbidities they had. We can't say for sure that many/most died from COVID-19 because of: 1) how the PCR tests were manipulated to give copious false positives and 2) how deaths were arbitrarily attributed to COVID-19 in the presence of myriad comorbidities.

The graphs presented in this paper indicate that the frail injection recipients receive minimal benefit from the inoculation. Their basic problem is a dysfunctional immune system, resulting in part or in whole from a lifetime of toxic exposures and toxic behaviors. They are susceptible to either the wild virus triggering the dysfunctional immune system into over-reacting or under-reacting, leading to poor outcomes or the injection doing the same.

This can be illustrated by the following analogy. A person stands in a bare metal enclosure. What happens when the person lights a match and drops it on the floor depends on what is on the floor. If the floor remains bare metal, the match burns for a few seconds until extinguished. If there is a sheet of paper on the floor under the match, the match and the paper will burn for a short time until both are extinguished. If, however, the floor is covered with ammonium nitrate and similar combustible/ explosive materials, a major explosion will result! For COVID-19, the wild virus is the match. The combustible materials are the toxic exposures and toxic behaviors. If there are no biomarker 'footprints' from toxic exposures and toxic behaviors, nothing happens. If there are significant biomarker 'footprints' from toxic exposures and toxic behaviors, bad outcomes result.

Adequate safety testing of the COVID-19 inoculations would have provided a distribution of the outcomes to be expected from 'lighting the match'. Since adequate testing was not performed, we have no idea how many combustible materials are on the floor, and what the expected outcomes will be from 'lighting the match'.

The injection goes two steps further than the wild virus because 1) it contains the instructions for making the spike protein, which several experiments are showing can cause vascular and other forms of damage, and 2) it bypasses many front-line defenses of the innate immune system to enter the bloodstream directly in part. Unlike the virus example, the injection ensures there will always be some combustible materials on the floor, even if there are no other toxic exposures or behaviors. In other words, the spike protein and the surrounding LNP are toxins with the potential to cause myriad short-, mid-, and long-term adverse health effects even in the absence of other contributing factors! Where and when these effects occur will depend on the biodistribution of the injected material. Pfizer's own biodistribution

studies have shown the injected material can be found in myriad critical organs throughout the body, leading to the possibility of multi-organ failure. And these studies were from a single injection. Multiple injections and booster shots may have cumulative effects on organ distributions of inoculant!

The COVID-19 reported deaths are people who died **with** COVID-19, not necessarily **from** COVID-19. Likewise, the VAERS deaths are people who have died **following** inoculation, not necessarily **from** inoculation. As stated before, CDC showed that 94 % of the reported deaths had multiple comorbidities, thereby reducing the CDC's numbers attributed strictly to COVID-19 to about 35,000 for all age groups. Given the number of high false positives from the high amplification cycle PCR tests, and the willingness of healthcare professionals to attribute death to COVID-19 in the absence of tests or sometimes even with negative PCR tests, this 35,000 number is probably highly inflated as well.

On the latter issue, both Virginia Stoner[41] and Jessica Rose[42] have shown independently that the deaths **following** inoculation are not coincidental and are **strongly related to** inoculation through strong clustering around the time of injection. Our independent analyses of the VAERS database reported in Appendix 1 confirmed these clustering findings.

Additionally, VAERS historically has under-reported adverse events by about two orders-of-magnitude, so COVID-19 inoculation deaths ***in the short-term*** could be in the hundreds of thousands for the USA for the period mid-December 2020 to the end of May 2021, potentially swamping the *real* COVID-19 deaths. Finally, the VAERS deaths reported so far are for the very short term. We have no idea what the death numbers will be in the intermediate and long-term; the clinical trials did not test for those.

The clinical trials used a non-representative younger and healthier sample to get EUA for the injection. Following EUA, the mass in- oculations were administered to the very sick (and first responders) initially, and many died quite rapidly. However, because the elderly who died following COVID-19 inoculation were very frail with multiple comorbidities, their deaths could easily be attributed to causes other than the injection (as should have been the case for COVID-19 deaths as well).

Now the objective is the inoculation of the total USA population. Since many of these potential serious adverse effects have built-in lag times of at least six months or more, we won't know what they are until most of the population has been inoculated, and corrective action may be too late.

---

[41] V. Stoner, The Deadly COVID-19 Vaccine Coverup [Online].
Available: https:// www.virginiastoner.com/writing/2021/5/4/the-deadly-covid-19-vaccinecoverup

[42] J. Rose, A report on the US Vaccine Adverse Events Reporting System (VAERS) of the COVID-19 messenger ribonucleic acid (mRNA) biologicals, Sci. Publ. Health Pol. Law 2 (2021) 59–80.

Dr Mike Yeadon
Oast House, The Street,
Wickhambreaux,
Canterbury, Kent
CT3 1RT, United Kingdom

Concerning information in relation to covid-19 vaccination & fertility

TO WHOM IT MAY CONCERN:

Dr. Michael Yeadon, PhD, is an independent life sciences researcher. His first degree was in biochemistry & toxicology, followed by his research-based PhD in respiratory pharmacology. His early work was in appointments to secret government facilities at Porton Down (Chemical Defence Establishment) and at Aldermaston (Forensic Science Service HQ). His subsequent career in the biopharmaceutical industry spanned almost 30 years leading project teams seeking new pharmacological treatments for asthma and COPD. He held positions of increasing responsibility and was, until 2011, Chief Scientific Officer, responsible for allergy & respiratory research worldwide within Pfizer, UK until that facility was closed.

Dr. Yeadon then spent the next decade as an independent consultant, assisting 30 biotechnology companies in the fields of new medicines discovery for inflammatory and immunological diseases of lung and skin. largely during their start-up phase. During that time he also founded and led as CEO his own biotech (Ziarco) which was acquired by Novartis in 2017.

Signed:

Michael Yeadon, PhD

Concerning information in relation to covid-19 vaccination and fertility

Covid-19 vaccines are unlike any previous vaccine & have been inadequately studied:

The medicinal agents which are being called vaccines against covid-19 all utilise new technology. Traditional vaccines comprise a small amount of the pathogen (disease-causing agent) mixed with a material called an adjuvant, which is a substance which induces mild inflammation and thereby alerts the immune system to the presence of a foreign protein. The small amount of pathogen is traditionally 'killed' by heating or by chemical treatment so that it cannot cause the disease against which immunity it sought. Alternatively, the pathogen is grown on by repeatedly infecting one cell culture after another, during which process the lethality of the virus reduces. This is called attenuation and some vaccines use so-called 'live attenuated' material to bring about immunisation. Vaccines of these basic designs cover almost every vaccine ever developed and in use in the population today.

A gross failure of medicines safety regulation has occurred secondary to product misclassification:

The covid-19 vaccines work in an entirely different way and what that means is that it is wholly inappropriate to treat them like other vaccines. However, that is exactly what has happened. The manufacturers have been asked only to comply with the requirements set out in the regulatory standard worldwide. These standards are not to be thought of as low in any way. They are just suited to the type of medical entity with which we have decades of experience.

Traditional vaccines, like any product, can occasionally malfunction and recognising this, regulatory authorities around the world usually maintain a public record of adverse events noted after vaccination, without necessarily attributing causation to the noted adverse event. However, the collection of event types and their frequency, coupled with a description of the alleged injured party, taken together with the relationship in time after vaccination that the adverse event is alleged to have occurred does permit linkages sometimes to be made.

For example, the swine flu vaccine marketed in 2009-10 was eventually withdrawn because the Swedish regulatory authorities noted a striking incidence in young people of a neurological condition, narcolepsy, which was reported in almost 1000 citizens.

As a result of the new-technology products called covid-19 vaccines working quite differently from prior products, appropriately termed vaccines, it is my considered opinion that the regulatory standard has fallen woefully short of the tests required to adequately assess and assure safety.

Recognising that there was an ongoing failure of the regulatory standard, given the technical novelty of the covid-19 vaccines, a petition of concern was drawn up by the present author and one other and lodged with the European Medicines Regulator (EMA) on December 1, 2020 (https://dryburgh.com/wp-content/uploads/2020/12/Wodarg_Yeadon_EMA_Petition_Pfizer_Trial_FINAL_01DEC2020_signed_with_Exhibits_geschwarzt.pdf).

The covid-19 vaccines work entirely differently to conventional vaccines and therefore have a radically different set of potential safety concerns:

The covid-19 vaccines currently subject to emergency use authorisations all share a common and novel feature: they are gene-based products. Instead of containing a small amount of killed or live-attenuated pathogen, they instead comprise genetic code, instructions as it were to manufacture in our own cells a part of the pathogen. In some products, the genetic code is of DNA & use a weakened respiratory virus to ensure delivery to our cells, or of messenger RNA (the intermediate between the DNA of our genes and the protein product thereby manufactured).

There is a further commonality: they cause the recipients cells to manufacture a portion of the SARS-CoV-2 virus called the spike protein. This is literally the spike projecting outwards from the spherical object that contains the virus itself. As detailed elsewhere in this packet of information, coronavirus spike proteins are biologically active and they initiate the blood coagulation cascade among other properties. It is alleged that it is the induction of blood coagulation in various locations in the body which is responsible for a high proportion of the serious adverse events including deaths which are being reported to the Vaccine Adverse Event Reporting System (VAERS) in the USA and in analogous databases elsewhere. The rate of fatal outcomes following covid-19 vaccination, usually from clotting or bleeding disorders, is extraordinary and exceeds that from any previous vaccine by a very large amount, which this reviewer estimates is of the order of 60-fold.

That this astonishingly high rate of adverse events after vaccination is a consequence of two factors: 1. The manufacturers were simply not required to study the way the product moves around the body after injection and 2. They were not required to study the functional effects of the genetic code within the product after administration.

There are no products on the mass market which operate in this way. It is my expert opinion that **this is the greatest failure of medicinal product regulation in relation to reproductive health since thalidomide** and is very much greater in terms of societal impact. It is imperative that all these products be suspended until improved safety testing can determine whether there are any groups in whom the benefits outweigh the risks.

The shadow of thalidomide and changes to drug safety regulation in pregnancy:

The drug name ‘Thalidomide’ is, particularly in Europe, indelibly associated in the public mind with birth defects. Intended to treat nausea associated with early pregnancy, it was prescribed in 46 countries, but not the USA, between 1957 and 1962, when it was withdrawn, having been identified as the causative agent in 10,000 birth malformations involving reduced or absent limbs. Thalidomide is one of the most infamous case of failed drug safety evaluation.

By contrast with regulators in dozens of other countries, the US drug regulatory agency, the Food & Drug Administration, did not approve thalidomide because the reviewer was not satisfied by the available information. Drug safety was substantially reformed worldwide in the aftermath of this event, notably to require manufacturers to conduct what is broadly termed ‘reproductive toxicology’ and also almost always to include rabbits as a test species, because it was later discovered that thalidomide did cause birth defects in rabbits but far less obviously in rodents.

There was a realisation the concept that the fetus was somehow protected from harm by being in the womb was completely mistaken. On the contrary, the intricacies of embryofetal development started to be recognised as a period of extreme vulnerability. Perhaps the most striking cultural change was that women became extremely wary of taking any pharmaceutical during pregnancy.

Covid-19 vaccines have not been taken through reproductive toxicology tests:

It is essential to lay out the backdrop to the current position with clinical use of covid-19 vaccines, for one reason: we have NEVER, since thalidomide, exposed women of childbearing potential (WOCBP) and ESPECIALLY NEVER pregnant women to ANY novel, experimental pharmaceutical product without that product first having completed a full battery of reproductive toxicology tests. Even after this crucial step, pilot studies are always conducted in a small number of pregnant women to minimise risk to the developing fetus. Neither of these essential steps have been undertaken.

No justification for taking risks with the health of unborn children:

Coming to the present, this expert reviewer is astonished at the current position. It is the height of recklessness to allow WOCBP to receive covid-19 vaccines, which are of an entirely novel, gene-based technology for which there is no prior human safety experience in a large population. Worse, the active recommendation that these experimental agents should be administered to pregnant women is, in my opinion, criminally negligent. Furthermore, it is completely incomprehensible that these novel vaccines are recommended for use in pregnancy, most of which happen in women aged 40y or younger, since the dominant risk factor for poor outcomes from infection by SARS-CoV-2 is age.

The Pfizer / BioNTech covid-19 vaccine builds up in the ovaries of rodents:

A distributional study was undertaken for Pfizer in which various formulations of dummy versions of their vaccine candidate was administered to rodents and various tissues sampled over time. The tests did not include the mRNA 'payload' but as this is simply a study of where the container for the mRNA goes, that is irrelevant from a safety perspective. Note that this study does not classify as a reproductive toxicology test as the animals were not pregnant. Instead, the study might best be classified as a pharmacokinetic study, the discipline of understanding how drugs move around the body after administration and the means and timing of its elimination. This study was not released by Pfizer into the public domain, even though this reviewer regards the findings as highly concerning. The information only came to light after a freedom of information enquiry was submitted to the Japanese medicines regulator.

What this study shows is that the lipid nanoparticle shell of the Pfizer vaccine concentrates in spleen and ovaries of rodents. It is not appropriate that this has happened. The intended induction of immunity definitely does NOT require the presence of vaccine components in reproductive tissue. Most commonly, the concentrations of drugs in any tissue in the body peaks quickly after administration, after which they fall away gradually over time. In light of this, it is more troubling still that, instead of falling away gradually over time as expected, the tissue levels RISE over time, suggestive of an active process. The study was aborted 48 hours after administration of the test material, not unreasonably. After that much time, it would be normal to be expecting the peak of tissue concentrations to have passed. However, the highest concentrations were seen at the last time point, 48 hours post-dose, meaning it is not known when the peak time after administration actually is or whether concentrations in the ovaries and spleen rise even higher at extended times (see part of the relevant data table overleaf. The entire document is also attached).

I recently also discovered that this problem of nanoparticle formulations for novel medicines like RNA is well known, with the pharmaceutical formulation experts. In this paper (Schadliuch, A, et al

2012), a relevant quote: ***"Studies in different mouse species and Wistar rats were conducted and a high local concentration of nanoparticles, nanocapsules and nanoemulsions in specific locations of the ovaries were found in all animals…… Nanocarrier accumulation in the ovaries may also comprise an important toxicity issue in humans…."*** It is impossible to evade the conclusion that subject matter experts in the covid-19 vaccine manufacturers MUST have known this, yet they did nothing to explore it in humans or to disclose it to medicines regulators (with the exception of the Japanese regulator). This deduction is inescapable and a major liability issue.

Any experienced reviewer would call for a halt of use of this vaccine in non-menopausal women:

As a toxicologist, I say this: in the absence of evidence that says this is not a predictor for humans, this is what I expect is happening to every female administered this agent. It is to be expected that the consequences of this concentration in reproductive will be adverse. based on observations elsewhere in the body, where blood clots and bleeding have separately been reported. In my opinion, any reasonable reviewer would agree that these vaccines should not be administered to any female below menopause.

2.6.5.5B. PHARMACOKINETICS: ORGAN DISTRIBUTION CONTINUED **Test Article: [3 H]-Labelled LN**

Sample	Total Lipid concentration (µg lipid equivalent / g [or mL]) (males and females combined)							% of Administered Dose		
	0.25 h	1 h	2 h	4 h	8 h	24 h	48 h	0.25 h	1 h	2 h
Lymph node (mandibular)	0.064	0.189	0.290	0.408	0.534	0.554	0.727	-	-	-
Lymph node (mesenteric)	0.050	0.146	0.530	0.489	0.689	0.985	1.37	-	-	-
Muscle	0.021	0.061	0.084	0.103	0.096	0.095	0.192	-	-	-
Ovaries (females)	0.104	1.34	1.64	2.34	3.09	5.24	12.3	0.001	0.009	0.008
Pancreas	0.081	0.207	0.414	0.380	0.294	0.358	0.599	0.003	0.007	0.014
Pituitary gland	0.339	0.645	0.868	0.854	0.405	0.478	0.694	0.000	0.001	0.001
Prostate (males)	0.061	0.091	0.128	0.157	0.150	0.183	0.170	0.001	0.001	0.002
Salivary	0.084	0.193	0.255	0.220	0.135	0.170	0.264	0.003	0.007	0.008

Women generate an autoimmune response to their placenta after vaccination:

As mentioned previously, all of the covid-19 vaccines currently subject to emergency use authorisations utilise novel, gene-based technology for which there are no mass marketed products. What this means is immediately obvious to anyone experienced in the development of medical products: it is unsafe to make any assumptions at all about the safety profile, short or long, after administration to humans. We did not know, prior to the tragic lessons arising from thalidomide, that early in gestation the developing embryo is exquisitely vulnerable to the adverse effects of environmental agents, including pharmaceuticals. It is unreasonable to assume that, because conventional vaccines are not generally considered to represent a safety issue in relation to fertility and pregnancy, that these novel, gene-based products will be safe in pregnancy.

On December 1, 2020, this expert reviewer together with experienced public health medical doctor Dr Wolfgang Wodarg filed a petition of concern with the European Medicines Agency. The principal

grounds of concern were the excessive speed of clinical development, together with a limited series of specific concerns (which were not claimed to be exhaustive):

1. Determination of covid-19 'cases' relied on inadequately controlled PCR testing (it is very widely held by independent experts that the PCR tests used grossly over-estimate prevalence of truly infected 'cases' – in relation to which it is noteworthy that FDA has just announced that it is withdrawing approval from all PCR tests for detection of SARS-CoV-2 infection).

2. The potential for antibody dependent enhancement, which process has caused the termination of all other prior vaccines against coronaviruses (it is being speculated that the high incidence of heart inflammation, called myocarditis, occurring with high frequency especially in young males).

3. The potential for precipitating acute allergic reactions upon administration of the lipid-encapsulated vaccines (Pfizer/BioNTech and Moderna products), which in fact did happen on the very first day of massed vaccination in UK & the label was soon changed to avoid administration to persons suspected of having had allergic responses to injected products in the past).

4. The potential for cross-over immune responses to a protein essential to successful pregnancy. It is this latter concern that the remainder of this note refers.

As a comment, it is to be regretted that it appears the co-petitioners were correct in every particular in relation to their concerns, and deeply troubling for public confidence in drug safety regulation & trust in governments and the pharmaceutical industry that the reward for the public spirit in which they wrote was to be viciously smeared by major media organisations including Reuters and the BBC.

Women administered the Pfizer/BioNTech vaccine rapidly develop antibodies to their placenta

I have previously outlined how these gene-based vaccines are expected to work. The part of the SARS-CoV-2 virus called the spike protein is coded into these new technology products, such that they all induce the body of the recipient to manufacture that spike protein or a portion thereof.

It is conventional good practise to review the scientific literature around chosen targets for use in vaccines, in this case spike protein, to ensure the potential for unwanted effects, when humans are caused to develop immune responses to it, is understood. Two outstanding findings were identified from this scientific literature search. First, spike proteins are able to initiate blood platelet aggregation and this to trigger blood coagulation, which calls into serious doubt the wisdom of having selected spike protein in all the vaccines to date. Second, there is a weak, but obvious (to expert reviewers) similarity of the coronavirus spike protein and a family of human proteins called syncytins. It is wrong to decide the level of similarity solely by reference to the primary amino acid sequence of two proteins and important also to consider the similarity of their 3-dimensional structure.

The Syncytin family of proteins are considered critical for the formation and successful maintenance of the placenta. Therefore, no matter how weak the homology between spike protein and syncytins, the concern arose that, upon making a strong immune response to spike protein, some women might generate an immune response to their own placental proteins. This concern would, in this reviewer's experience of over 30 years in the pharmaceutical industry, be met technically with a small series of studies to examine, hopefully to rule out, this concern. There are a number of ways in which this could be done. It is not difficult to devise a clinical study to evaluate whether or not

women administered a covid-19 vaccine develop circulating antibodies to syncytin-1. Such a study has just been reported as a pre-print:
(https://www.medrxiv.org/content/10.1101/2021.05.23.21257686v1.full.pdf)

15 healthy young women were recruited to the study and were administered the Pfizer / BioNTech covid-19 vaccine. Blood was drawn at various times afterward and the relative amount of antibodies to the SARS-CoV-2 spike protein and to syncytin-1 was measured.

In the first 1-4 days after vaccination, there was no measurable increase in antibodies to the spike protein. However, there was a striking (2 to 3-fold; marked by a vertical, red arrow) increase in antibody binding to syncytin-1. It is the judgement of this reviewer that the increase in antibodies to syncytin-1 at that time is 'statistically significant', that is, it is very unlikely to have occurred by chance. It is not possible to state what this extent of increase means, but it is consistent with an increased risk of first trimester pregnancy loss. That the elevation of anti-syncytin-1 antibodies was absent by 4 weeks doesn't diminish the potential for harm at early times after vaccination.

It is unaccountable that the authors state that there was "no humoral response to syncytin-1". A figure in the paper is reproduced below. The authors have scribed a horizontal line perpendicular to the Y-axis, which they labelled "positive". There is no information in the paper or in the literature which underwrites the positioning of this line. Absent that information, it is scientifically invalid to claim that the clear-cut increase in binding to syncytin-1 on days 1-4 is functionally irrelevant.

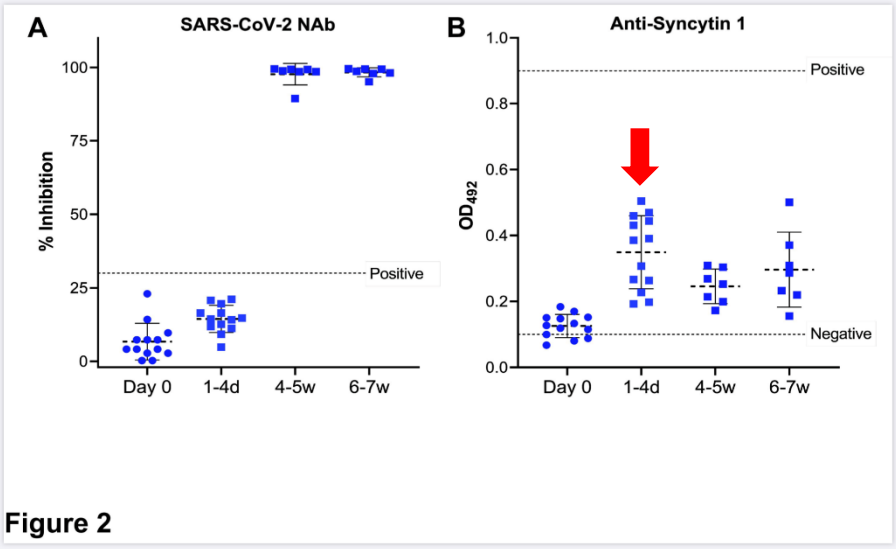


Figure 2

It is sobering to recall again the lessons from thalidomide. It turns out that if the mother, early in pregnancy, took her first dose of thalidomide on day 20 after conception, their baby was likely to be born with brain damage; If on day 21, blind; if on day 24, limbs were often shortened or missing; no damage occurred if taken after day 42 since conception.

The authors of this paper have no basis to claim that the amount of antibodies to syncytin-1 is too small to matter. They appear to be unaware of the thalidomide lessons, which show that periods of exquisite sensitivity exist during early development where the presence of a toxin for periods of as little as two days can terminate development processes which are then never repaired.

This new data, which shows that women do raise antibodies to a component of their placenta after vaccination with the Pfizer/BioTech product, raises serious concerns for fetal safety. It is not safe to assume that this will not have adverse consequences on successful pregnancy. It is not safe to assume that the other vaccines will not have similar effects.

Again, as with the distributional study, a presumption of risk, potentially severe, arises from these clinical observations, and there isn't an aware person who wouldn't call a halt at this point.

Schadlich, A, et al (2012). Accumulation of nanocarriers in the ovary: a neglected toxicity risk? J. Controlled Release, **160**, 105-112.

https://www.sciencedirect.com/science/article/abs/pii/S0168365912000892?via%3Dihub

PETITIONER:
Dr. med. Wolfgang Wodarg

Germany

CO-PETITIONER:
Dr. Michael Yeadon

England, CT3 1RT

December 1, 2020

TO:
European Medicines Agency
Committee for human medicinal products (CHMP)
COVID-19 EMA pandemic Task Force (COVID-ETF)
Domenico Scarlattilaan 6
1083 HS Amsterdam
The Netherlands

info@ema.europa.eu
press@ema.europa.eu

!! URGENT !!

PETITION/MOTION FOR ADMINISTRATIVE/REGULATORY ACTION REGARDING CONFIRMATION OF EFFICACY END POINTS AND USE OF DATA IN CONNECTION WITH THE FOLLOWING CLINICAL TRIAL(S):

PHASE III - EUDRACT NUMBER: 2020-002641-42

SPONSOR PROTOCOL NUMBER: C4591001

SPONSOR:
BIONTECH SE (SOCIETAS EUROPAEA), AN DER GOLDGRUBE 12, 55131 MAINZ, GERMANY

AND ANY OTHER ONGOING CLINICAL TRIALS OF VACCINE CANDIDATES DESIGNED TO STOP TRANSMISSION OF THE VIRUS FROM THE VACCINE RECIPIENT TO OTHERS AND/OR TO PREVENT COVID-19 OR MITIGATE SYMPTOMS OF COVID-19 FOR WHICH PCR RESULTS ARE THE PRIMARY EVIDENCE OF INFECTION WITH SARS-COV-2

ADMINISTRATIVE/REGULATORY STAY OF ACTION

This petition for a stay of action is submitted by the undersigned ("**Petitioner**" or "**Lead Petitioner**") to request the EMA a) stay the Phase III clinical trial(s) of BNT162b (EudraCT Number 2020-002641-42) in the EU (current protocol country: Germany) until study design is amended to conform with the requests in the "Action Requested" section (**B.**) below; and b) stay all other clinical trials of vaccine candidates designed to stop transmission of the virus from the

vaccine recipient to others and/or prevent or mitigate symptoms of COVID-19 for which PCR results are the primary evidence of infection.

Because of the compelling need to ensure the safety and efficacy of any COVID-19 vaccine licensed by the EMA (and/or the German Paul-Ehrlich-Institut), and to allow Petitioner the opportunity to seek appropriate emergency judicial relief should the EMA deny its Petition, **Petitioner respectfully requests that EMA act on the instant Petition immediately.**

A. DECISIONS INVOLVED

I. Approval of trial design and/or decision to not challenge trial design for Phase III trial of BNT162 (EudraCT Number 2020-002641-42)

II. Approval of trial design and/or decision to not challenge trial design of all other clinical trials of vaccine candidates designed to stop transmission of the virus from the vaccine recipient to others and/or to prevent or mitigate symptoms of COVID-19 for which PCR results are the primary evidence of infection.

B. ACTION REQUESTED

I. Stay the Phase III trial of BNT162 in the protocol country Germany and in any other EU protocol countries (as applicable) until study design is amended to provide that:

Before an Emergency Authorization/Conditional Approval and/or Unrestricted Authorization is issued for the Pfizer/BioNTech vaccine, all "endpoints" or COVID-19 cases used to determine vaccine efficacy in the Phase 3 or 2/3 trials should have their infection status confirmed by appropriate Sanger sequencing (as described in section C. III. below), given a) the high cycle thresholds used in some trials; and b) design flaws of certain RT-qPCR tests identical to or modeled after what is sometimes called the "Drosten-Test".

II. Stay the clinical trials of all vaccine candidates designed to stop transmission of the virus from the vaccine recipient to others and/or to prevent or mitigate symptoms of COVID-19 for which PCR results are the primary evidence of infection until study design is amended to provide that:

Before an Emergency Authorization/Conditional Approval and/or Unrestricted Authorization is issued for vaccine designed to stop transmission of the virus from the vaccine recipient to others and/or to prevent or mitigate symptoms of COVID-19, all "endpoints" or COVID-19 cases used to determine vaccine efficacy should have their infection status confirmed by appropriate Sanger sequencing (as described in section B. III. below), given a) the high cycle thresholds used in some trials; and b) design flaws of certain RT-qPCR tests identical to or modeled after what is sometimes called the "Drosten-Test".

III. High cycle thresholds, or Ct values, in RT-qPCR test results have been widely acknowledged to lead to false positives. Also, a group of scientists and researchers have recently called for a retraction of the paper that describes the so called “Drosten-Test” (sometimes also being referred to as the “Corman-Drosten protocol” - a specific RT-qPCR assay described by Corman,Victor M., Drosten, Christian and others in “Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR.” Euro Surveillance 2020;25(3):pii=2000045. https://doi.org/10.2807/1560-7917.ES.2020.25.3.2000045).

All RT-qPCR-positive test results used to categorize patient as “COVID-19 cases” in the trials and used to qualify the trial’s endpoints should be verified by Sanger sequencing to confirm that the tested samples in fact contain a unique SARS-CoV-2 genomic RNA. Congruent with FDA and EMA requirements for a confirmed diagnosis of human papillomavirus (HPV) using PCR, the sequencing electropherogram must show a minimum of 100 contiguous bases matching the reference sequence with an Expected Value (E Value) <10-30 for the specific SARS-CoV-2 gene sequence based on a BLAST search of the GenBank database (aka NCBI Nucleotide database).

C. STATEMENT OF GROUNDS

I. As detailed herein, (i) without the requested stay, the Petitioner and many EU residents/citizens will suffer irreparable harm, (ii) the request is not frivolous and is being pursued in good faith, (iii) the request demonstrates sound public policy, and (iv) the public interest favors granting a stay.

II. Petitioner deems the current study designs for the Phase II/III trials of BNT162b (“the Pfizer/BioNTech trial”) to be inadequate to accurately assess efficacy. Petitioner also deems the designs of clinical trials of vaccine candidates designed to stop transmission of the virus from the vaccine recipient to others and/or to prevent or mitigate symptoms of COVID-19 for which PCR results are the primary evidence of infection to be inadequate to accurately assess efficacy.

III. Petitioner and the public will suffer irreparable harm if the actions requested herein are not granted, because once the EMA (and other appropriate bodies in the various EU member states) approves the COVID-19 vaccines in question, both governments of EU member states and employers in the EU are most likely going to recommend them for widespread use. If the assignment of cases and non-cases during the course of the trials is not accurate, the vaccines will not have been properly tested. If the vaccines are not properly tested, important public policy decisions regarding its use will be based on misleading evidence. The medical and economic consequences to EU member states and their residents/citizens could hardly be higher.

IV. Furthermore, if the vaccines are approved without an appropriate and accurate review of efficacy, then any potential acceptance or mandate of these vaccines is likely to be based on inaccurate evidence regarding the vaccine, namely that it will stop transmission of the virus from the vaccine recipient to others and/or that it will reduce COVID-19 disease and deaths. The Pfizer/BioNTech trial protocol and other trial protocols are currently not designed to determine whether either of those objectives can be met; and even if it was, if cases cannot be

reliably identified, neither objective could be reliably met.

V. The public interest also weighs strongly in favor of the requested relief because improving the accurate determination of primary endpoints (i) will comport with the best scientific practices, (ii) increase public confidence in the efficacy of a product likely to be mandated or intended for widespread use, and (iii) not doing so will have the opposite result and create uncertainties regarding the efficacy of and need for the COVID-19 vaccines.

VI. Petitioner hereby incorporates the grounds, facts, arguments and opinions stated in the "PETITION FOR ADMINISTRATIVE ACTION REGARDING CONFIRMATION OF EFFICACY END POINTS OF THE PHASE III CLINICAL TRIALS OF COVID-19 VACCINES" which has been submitted to the FDA by Dr. Sin Hang Lee via electronic filing on November 25, 2020 (Exhibit A - Docket No. FDA-2020-P-2225). Exhibit A attached hereto shall be incorporated herein and shall be understood to be a part hereof as though included in the body of this petition.

VII. Petitioner hereby also incorporates the grounds, facts, arguments and opinions stated in the external peer review of the "Drosten-Test" (Exhibit B). Design flaws of certain RT-qPCR tests that are identical to or modeled after what is sometimes called the "Drosten-Test" can lead to false-positive results in trials designed such that PCR results are the primary evidence of infection. Exhibit B attached hereto shall be incorporated herein and shall be understood to be a part hereof as though included in the body of this petition.

VIII. For a vaccine to work, our immune system needs to be stimulated to produce a neutralizing antibody, as opposed to a non-neutralizing antibody. A neutralizing antibody is one that can recognize and bind to some region ('epitope') of the virus, and that subsequently results in the virus either not entering or replicating in your cells. A non-neutralizing antibody is one that can bind to the virus, but for some reason, the antibody fails to neutralize the infectivity of the virus. In some viruses, if a person harbors a non-neutralizing antibody to the virus, a subsequent infection by the virus can cause that person to elicit a more severe reaction to the virus due to the presence of the non-neutralizing antibody. This is not true for all viruses, only particular ones. This is called Antibody Dependent Enhancement (ADE), and is a common problem with Dengue Virus, Ebola Virus, HIV, RSV, and the family of coronaviruses. In fact, this problem of ADE is a major reason why many previous vaccine trials for other coronaviruses failed. Major safety concerns were observed in animal models. If ADE occurs in an individual, their response to the virus can be worse than their response if they had never developed an antibody in the first place. This can cause a hyperinflammatory response, a cytokine storm, and a generally dysregulation of the immune system that allows the virus to cause more damage to our lungs and other organs of our body. In addition, new cell types throughout our body are now susceptible to viral infection due to the additional viral entry pathway. There are many studies that demonstrate that ADE is a persistent problem with coronaviruses in general, and in particular, with SARS-related viruses. ADE has proven to be a serious challenge with coronavirus vaccines, and this is the primary reason many of such vaccines have failed in early in-vitro or animal trials. For example, rhesus macaques who were vaccinated with the Spike protein of the SARS-CoV virus demonstrated severe acute lung injury when challenged with SARS-CoV, while monkeys who were not vaccinated did not. Similarly, mice who were immunized with one of four different SARS-CoV vaccines showed histopathological changes in the lungs with eosinophil infiltration after being challenged with

SARS-CoV virus.

IX. There are some concerning issues with the trial designs, spelled out by Dr. Peter Doshi in the British Medical Journal. Dr. Doshi focuses on the two biggest issues. First, none of the leading vaccine candidate trials is designed to test if the vaccine can reduce severe COVID-19 symptoms, defined as: hospital admissions, ICU or death. And, second, the trials are not designed to test if the vaccine can interrupt transmission (https://www.bmj.com/content/bmj/371/bmj.m4037.full.pdf). If neither of these conditions is met, the vaccine in essence performs like a therapeutic drug, except a vaccine would be taken prophylactically, even by the perfectly healthy, and more than likely carries a higher risk of injury than a therapeutic drug. If this were to be true, then therapeutic drugs would be superior to any COVID vaccine.

X. In the Pfizer/BioNTech mRNA vaccine candidate, polyethylene glycol (PEG) is found in the fatty lipid nanoparticle coating around the mRNA. Seventy percent of people make antibodies to PEG and most do not know it, creating a concerning situation where many could have allergic, potentially deadly, reactions to a PEG-containing vaccine. PEG antibodies may also reduce vaccine effectiveness. Pfizer/BioNTech is also inserting an ingredient derived from a marine invertebrate, mNeonGreen, into its vaccine. The ingredient has bioluminescent qualities, making it attractive for medical imaging purposes, but it is unclear why an injected vaccine would need to have that quality. mNeonGreen has unknown antigenicity.

XI. Several vaccine candidates are expected to induce the formation of humoral antibodies against spike proteins of SARS-CoV-2. Syncytin-1 (see Gallaher, B., "Response to nCoV2019 Against Backdrop of Endogenous Retroviruses" - http://virological.org/t/response-to-ncov2019-against-backdrop-of-endogenous-retroviruses/396), which is derived from human endogenous retroviruses (HERV) and is responsible for the development of a placenta in mammals and humans and is therefore an essential prerequisite for a successful pregnancy, is also found in homologous form in the spike proteins of SARS viruses. There is no indication whether antibodies against spike proteins of SARS viruses would also act like anti-Syncytin-1 antibodies. However, if this were to be the case this would then also prevent the formation of a placenta which would result in vaccinated women essentially becoming infertile. To my knowledge, Pfizer/BioNTech has yet to release any samples of written materials provided to patients, so it is unclear what, if any, information regarding (potential) fertility-specific risks caused by antibodies is included.

According to section 10.4.2 of the Pfizer/BioNTech trial protocol, a woman of childbearing potential (WOCBP) is eligible to participate if she is not pregnant or breastfeeding, and is using an acceptable contraceptive method as described in the trial protocol during the intervention period (for a minimum of 28 days after the last dose of study intervention).

This means that it could take a relatively long time before a noticeable number of cases of post-vaccination infertility could be observed.

XII. It appears that Pfizer/BioNTech have not yet released any samples of written materials provided to patients, so it is unclear what, if any, instructions/information patients/subjects were given regarding ADE and PEG-related issues and (potential) fertility- or pregnancy-specific issues.

D. STAY URGENTLY REQUIRED

I. Petitioner any many EU residents/citizens will suffer irreparable harm because once the EMA approves the COVID- 19 vaccine(s) in question, both governments of EU member states and employers in the EU are most likely going to recommend them for widespread use, and hence without the EMA assuring proper safety trials of the vaccines *now*, the Petitioner and others will not have the opportunity to object to receiving the vaccine based on deficient clinical trials *later*.

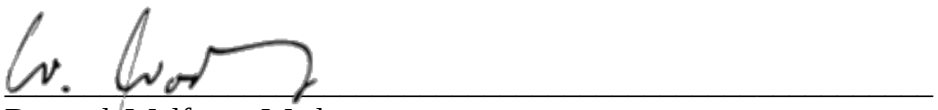
II. Furthermore, if the vaccines are licensed without an appropriate efficacy review and without improving the accurate determination of primary endpoints, then any potential acceptance or mandate of these vaccines are likely to be based on inaccurate beliefs and data about the vaccines, namely that they will or might stop transmission of the virus from the vaccine recipient to others and/or that it will reduce severe COVID-19 disease and deaths. The trial protocols in question are not currently properly designed to determine whether either of those objectives can be met.

III. This petition is also not frivolous and is being pursued in good faith as it seeks to increase the scientific integrity and reliability of the trials of the COVID-19 vaccines.

IV. Finally, the public interest also weighs strongly in favor of the requested relief because improving the accurate determination of primary endpoints (i) will comport with the best scientific practices, (ii) increase public confidence in the efficacy of a vaccine expected to be mandated or strongly recommended for widespread use, and (iii) not doing so will have the opposite result in that it will create uncertainties regarding the efficacy of and need for the COVID-19 vaccines.

V. The Petitioner therefore respectfully urges that this request be granted forthwith.

Respectfully submitted on my behalf and on behalf of Co-Petitioner Dr. Michael Yeadon:



Dr. med. Wolfgang Wodarg

Exhibit A
Exhibit B

Exhibit A

VIA ELECTRONIC FILING

November 25, 2020

Division of Dockets Management
Department of Health and Human Services
Food and Drug Administration
Commissioner Stephen M. Hahn, M.D.
5630 Fishers Lane
Rm. 1061
Rockville, MD 20852

UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES AND THE FOOD AND DRUG ADMINISTRATION

PETITION FOR ADMINISTRATIVE ACTION REGARDING CONFIRMATION OF EFFICACY END POINTS OF THE PHASE III CLINICAL TRIALS OF COVID-19 VACCINES	**:**	**Docket No. FDA-2020-P-2225**

ADMINISTRATIVE STAY OF ACTION

This petition for a stay of action is submitted on behalf of Dr. Sin Hang Lee ("**Petitioner**") pursuant to 21 C.F.R. § 10.35 and related and relevant provisions of the Federal Food, Drug, and Cosmetic Act or the Public Health Service Act to request the Commissioner of Food and Drugs (the "**Commissioner**") stay the Phase III trials of BNT162b (NCT04368728) to conform with the requests in the "Action Requested" section below.

Because of the compelling need to ensure the safety and efficacy of any COVID-19 vaccine licensed by the FDA, and to allow Petitioner the opportunity to seek emergency judicial relief should the Commissioner deny its Petition, **Petitioner respectfully requests that FDA act on the instant Petition by December 11, 2020.**

A. DECISION INVOLVED

1. Approval of trial design for Phase III trial of BNT162 (NCT04368728)[1]

[1] NCT04368728 available at https://www.clinicaltrials.gov/ct2/show/NCT04368728 (last visited November 3, 2020).

B. ACTION REQUESTED

2. Stay the Phase III trial of BNT162 (NCT04368728) until its study design is amended to provide that:

> Before an EUA or unrestricted license is issued for the Pfizer vaccine, or for other vaccines for which PCR results are the primary evidence of infection, all "endpoints" or COVID-19 cases used to determine vaccine efficacy in the Phase 3 or 2/3 trials should have their infection status confirmed by Sanger sequencing, given the high cycle thresholds used in some trials. High cycle thresholds, or Ct values, in RT-qPCR test results have been widely acknowledged to lead to false positives.[2]
>
> All RT-qPCR-positive test results used to categorize patient as "COVID-19 cases" and used to qualify the trial's endpoints should be verified by Sanger sequencing to confirm that the tested samples in fact contain a unique SARS-CoV-2 genomic RNA. Congruent with FDA requirements for a confirmed diagnosis of human papillomavirus (HPV) using PCR, the sequencing electropherogram must show a minimum of 100 contiguous bases matching the reference sequence with an Expected Value (E Value) $<10^{-30}$ for the specific SARS-CoV-2 gene sequence based on a BLAST search of the GenBank database (aka NCBI Nucleotide database).

C. STATEMENT OF GROUNDS

3. As detailed herein, (i) without the requested stay, the Petitioner will suffer irreparable harm, (ii) the request is not frivolous and is being pursued in good faith, (iii) the request demonstrates sound public policy, and (iv) the public interest favors granting a stay. [3]

4. The current study designs for the Phase II/III trials of BNT162b ("**the Pfizer Vaccine**") are inadequate to accurately assess efficacy.

5. Petitioner and the public will suffer irreparable harm if the actions requested herein are not granted, because once the FDA licenses this COVID-19 vaccine, both governments and employers may make this product mandatory (in general, or for airline or international travel) or may recommend it for widespread use. If the assignment of cases and non-cases during the course of the trial is not accurate, the vaccine will not have been properly tested. If the vaccine is not

[2] *See* New York Times. Your Coronavirus Test Is Positive. Maybe It Shouldn't Be. By Apoorva Mandavilli. Published Aug. 29, 2020 and updated Sept. 17, 2020, available at https://www.nytimes.com/2020/08/29/health/coronavirus-testing.html.

[3] The Petitioner hereby incorporates by reference as if fully set forth herein the Statement of Grounds from its Citizen's Petition, dated November 23, 2020, available at, https://beta.regulations.gov/document/FDA-2020-P-2225 (last visited November 25, 2020).

properly tested, important public policy decisions regarding its use will be based on misleading evidence. The medical and economic consequences to the nation could hardly be higher.

6. The New York State Bar Association has already issued a report on COVID-19 recommending that, "a vaccine subject to scientific evidence of safety and efficacy be made widely available, and widely encouraged, and if the public health authorities conclude necessary, required…"[4] Thus, it is reasonable to suspect that COVID-19 vaccines, including the Pfizer vaccine, could become mandatory. Without the FDA assuring proper efficacy trials of the vaccine now, the Petitioner and the public may not have the opportunity to object to receiving the vaccine, which was approved based on currently deficient and unreliable clinical trial data.

7. Furthermore, if the vaccine is approved without an appropriate and accurate review of efficacy, then any potential acceptance or mandate of these vaccines is likely to be based on inaccurate evidence regarding the vaccine, namely that it will stop transmission of the virus from the vaccine recipient to others and/or that it will reduce severe COVID-19 disease and deaths. The Pfizer trial protocol is currently not designed to determine whether either of those objectives can be met; and even if it was, if cases cannot be reliably identified, neither objective could be reliably met.

8. The public interest also weighs strongly in favor of the requested relief because improving the accurate determination of primary endpoints (i) will comport with the best scientific practices, (ii) increase public confidence in the efficacy of a product likely to be mandated or intended for widespread use, and (iii) not doing so will have the opposite result and create uncertainties regarding the efficacy of and need for the COVID-19 vaccines.

7. According to the trial protocol, "8.1. Efficacy and/or Immunogenicity Assessments," the trial's primary endpoint is prevention of symptomatic disease in vaccine recipients. In order to evaluate that endpoint, the trial will track recorded COVID-19 disease. The definition of confirmed COVID-19 is:

> presence of at least 1 of the following symptoms and SARS-CoV-2 NAAT-positive during, or within 4 days before or after, the symptomatic period, either at the central laboratory or at a local testing facility (using an acceptable test):
>
> • Fever;
> • New or increased cough;
> • New or increased shortness of breath;
> • Chills;
> • New or increased muscle pain;
> • New loss of taste or smell;
> • Sore throat;
> • Diarrhea;
> • Vomiting.

[4] https://nysba.org/app/uploads/2020/06/2b-REV-6-12-20-FINAL-HOD-RESOLUTIONS-1-through-4.pdf.

8. As a result, if a participant has a positive reverse transcription-quantitative polymerase chain reaction ("**RT-qPCR**") test along with a cough or sore throat, that participant would be considered as a "confirmed COVID-19 case" and would be counted as an endpoint. Once a trial reaches a certain number of "endpoints", the trial is closer to seeking FDA approval or licensure by demonstrating that the vaccine is "effective" (in that the vaccine group had lower incidence of endpoints than the control group).

9. This effectively means that the efficacy of the vaccine will be determined based on only symptoms of non-specific disease in conjunction with a PCR positive laboratory test.

10. According to the trial protocol, "8.1 Efficacy and/or Immunogenicity Assessments," efficacy will be assessed throughout a participant's involvement in the study through surveillance for potential cases of COVID-19. If, at any time, a participant develops acute respiratory illness (see Section 8.13), for the purposes of the study he or she will be considered to potentially have COVID-19 illness. In this circumstance, the participant should contact the site, an in-person or telehealth visit should occur, and assessments should be conducted as specified in the SoA. The assessments will include a nasal (midturbinate) swab, which will be tested at a central laboratory using a reverse transcription–polymerase chain reaction (RT-PCR) test (Cepheid; FDA approved under EUA), or other equivalent nucleic acid amplification–based test (ie, NAAT), to detect SARS-CoV-2. In addition, clinical information and results from local standard-of-care tests (as detailed in Section 8.13) will be assessed. The central laboratory NAAT result will be used for the case definition, unless no result is available from the central laboratory, in which case a local NAAT result may be used if it was obtained using 1 of the following assays:

- Cepheid Xpert Xpress SARS-CoV-2
- Roche cobas SARS-CoV-2 real-time RT-PCR test (EUA200009/A001)
- Abbott Molecular/RealTime SARS-CoV-2 assay (EUA200023/A001)

11. These test kits referred to in the trial protocol, namely the Cepheid Xpert Xpress SARS-CoV-2, the Roche cobas SARS-CoV-2 real-time RT-PCR test (EUA200009/A001), and the Abbott Molecular/RealTime SARS-CoV-2 assay (EUA200023/A001), are very unreliable tools when they are used to determine whether the nasal swab sample collected from a symptomatic participant contains SARS-CoV-2 or not. These real-time RT-PCR or RT-quantitative PCR tests should be referred to as rRT-PCR or RT-qPCR tests to be distinguished from conventional RT-PCR. The very short RT-qPCR product (amplicon) cannot be analyzed by automated Sanger sequencing as the products of conventional PCR can. And DNA sequencing for validation of the PCR products is needed to correctly determine if the presumptive RT-qPCR-positive SARS-CoV-2 test result is a true positive or a false positive. The reasoning is further outlined as follows:

a. Nowadays DNA sequencing of the PCR amplicon of the genomic nucleic acid of the pathogen is a universally accepted technology for detection and for confirmation of infectious agents, especially pathogenic viruses, in clinical specimens. On January 10,

2020, the first SARS-CoV-2 genome sequence was released online. On the same day, a group of American scientists, most from the CDC, immediately designed 2 complementary panels of primers to amplify the virus genome for sequencing. The PCR amplicons averaged 550 bp in size in their research.[5]

b. The World Health Organization (WHO) guidance titled "WHO Laboratory testing for coronavirus disease (COVID-19) in suspected human cases-Interim guidance dated 19 March 2020" advised "Routine confirmation of cases of COVID-19 is based on detection of unique sequences of virus RNA by NAAT such as real-time reverse transcription-polymerase chain reaction (rRT-PCR) with confirmation by nucleic acid sequencing when necessary."[6]

c. The FDA also recognizes the inherent inaccuracy of the RT-qPCR tests. In its letter issued on February 4, 2020 authorizing emergency use of the CDC 2019-Novel Coronavirus (2019-nCoV, renamed as SARS-CoV-2) Real-Time Reverse Transcriptase (RT)-PCR Diagnostic Panel, the FDA specifically stated that the test panel is "for the ***presumptive*** qualitative detection of nucleic acid from the 2019-nCoV (sic) in upper and lower respiratory specimens."[7]

d. In addition to false-negative results, these RT-qPCR test kits under EUA also generate false-positive test results. For example, 77 positive SARS-CoV-2 test results on a group of football players all turned out to be false positives on repeat tests.[8]

e. The FDA has officially alerted clinical laboratory staff and health care providers of an increased risk of false-positive results with some of these commercial test kits permitted to be used under EUA.[9]

[5] Paden CR, Tao Y, Queen K, Zhang J, Li Y, Uehara A, Tong S. Rapid, Sensitive, Full-Genome Sequencing of Severe Acute Respiratory Syndrome Coronavirus 2. Emerg Infect Dis. 2020 Oct;26(10):2401-2405. doi: 10.3201/eid2610.201800. Epub 2020 Jul 1. PMID: 32610037; PMCID: PMC7510745.

[6] WHO Laboratory testing for coronavirus disease (COVID-19) in suspected human cases-Interim guidance 19 March 2020. Available from: https://www.who.int/publications/i/item/10665-331501.

[7] FDA letter dated February 4, 2020 authorizing emergency use of the CDC 2019-Novel Coronavirus (2019-nCoV, renamed as SARS-CoV-2) Real-Time Reverse Transcriptase (RT)-PCR Diagnostic Panel. See Open letter from FDA to Robert R. Redfield, MD, Director, Centers for Disease Control and Prevention. March 15, 2020. https://www.fda.gov/media/134919/download.

[8] Kevin Patra. Around the NFL- All 77 false-positive COVID-19 tests come back negative upon reruns. Aug 24, 2020. Available from: https://www.nfl.com/news/all-77-false-positive-covid-19-tests-come-back-negative-upon-reruns.

[9] FDA. False Positive Results with BD SARS-CoV-2 Reagents for the BD Max System - Letter to Clinical Laboratory Staff and Health Care Providers. Available from: https://www.fda.gov/medical-devices/letters-health-care-providers/false-positive-results-bd-sars-cov-2-reagents-bd-max-system-letter-clinical-laboratory-staff-and Accessed November 2, 2020; *see also* FDA. Risk of Inaccurate Results with Thermo Fisher Scientific TaqPath COVID-19 Combo Kit - Letter to Clinical Laboratory Staff and Health Care Providers. Available from: https://www.fda.gov/medical-devices/letters-health-care-providers/risk-inaccurate-results-thermo-fisher-scientific-taqpath-covid-19-combo-kit-letter-clinical?utm_campaign=2020-08-17%20Risk%20of%20Inaccurate%20Results%20with%20Thermo%20Fisher%20Scientific%20TaqPath&utm_medium=email&utm_source=Eloqua.

f. To resolve the problems caused by these inherently inaccurate tests, the FDA's position is that false results can be investigated using an additional EUA RT-qPCR assay, and/or Sanger sequencing.[10] Since an additional EUA RT-qPCR test result may also generate a false result, Sanger sequencing is the *de facto* gold standard for confirmation of presumptive qualitative detection of nucleic acid from the SARS-CoV-2 and for excluding false-positive cases.

g. According to the FDA guidance on molecular diagnosis of viral infection caused by human papillomavirus (HPV), a conventional PCR detection of genomic DNA followed by Sanger sequencing on both strands of the PCR amplicon (bi-directional sequencing) that contains a minimum of 100 contiguous bases is acceptable as valid diagnostics for HPV infection provided the sequence matches the reference or consensus sequence, e.g. with an Expected Value (E Value) $<10^{-30}$ for the specific HPV DNA target based on a BLAST search of the GenBank (NCBI Nucleotide) database.[11] Following this FDA guidance, and showing the feasibility of implementing the FDA guidance for accurate diagnosis of COVID-19, a protocol using the nested PCR cDNA amplicon of a 398-base highly conserved SARS-CoV-2 N gene segment as the template for Sanger sequencing was developed for confirmatory detection of SARS-CoV-2 in clinical samples.[12]

h. DNA sequencing verification is necessary for confirmation of the presumptive SARS-CoV-2-positive cases in the Pfizer vaccine's Phase II/III clinical trial because, according to its Protocol, the specimens collected from the symptomatic trial subjects were sent to a central laboratory using a reverse transcription–polymerase chain reaction (RT-PCR) test (Cepheid; FDA approved under EUA), or other equivalent nucleic acid amplification–based test (i.e., NAAT), to detect SARS-CoV-2.

   In order to raise the detection sensitivity, the mean Ct value of the Cepheid system is set as high as 42.9 for the N2 target, and as high as 44.9 for the E target, as shown in Table 4 of Instructions for Users (Cepheid 302-3562, Rev. E September 2020).[13]

[10] FDA. Molecular Diagnostic Template for Laboratories. Policy for Coronavirus Disease-2019 Tests During the Public Health Emergency (Revised) Available from: https://www.fda.gov/media/135659/download .

[11] FDA. Establishing the Performance Characteristics of In Vitro Diagnostic Devices for the Detection or Detection and Differentiation of Human Papillomaviruses. Available from: https://www.fda.gov/media/92930/download.

[12] Lee SH. Testing for SARS-CoV-2 in cellular components by routine nested RT-PCR followed by DNA sequencing. International Journal of Geriatrics and Rehabilitation. 2020; 2:69-96. Available from: http://www.int-soc-clin-geriat.com/info/wpcontent/uploads/2020/03/Dr.-Lees-paper-on-testing-for-SARS-CoV-2.pdf.

[13] Cepheid. GeneXpert. Instructions for Users. XPRSARS-COV2-10. 302-3562, Rev. E September 2020 https://www.cepheid.com/Package%20Insert%20Files/Xpress-SARS-CoV-2/Xpert%20Xpress%20SARS-CoV-2%20Assay%20ENGLISH%20Package%20Insert%20302-3562-GX%20Rev.%20E.pdf.

Table 4. LoD Determination using USA-WA1/2020 Strain

Strain	Concentration (PFU/mL)	Total Valid Results	Hit Rate (%)	Hit Rate (%)	Mean Ct	Mean Ct
			N2 Target	E Target	N2 Target	E Target
SARS-CoV-2 virus (USA_WA1/2020)	0.0200	20	100	95.0	38.3	36.4
	0.0050	22	95.5	68.2	40.5	39.1
	0.0025	22	90.9	36.4	41.5	39.6
	0.0010	22	50.0	18.2	42.0	42.0
	0.0005	22	45.5	18.2	41.7	41.5
	0.0003	22	18.2	4.5	42.1	44.9
	0.0001	22	9.1	0	42.9	N/A
	0	0	0	0	N/A	N/A

At Ct values between 36.0 and 44.9, many RT-qPCR positive test results are false positives.

i. The results of the 3 RT-qPCR test kits used in the trial protocol are not comparable. A sample identified as negative by the Abbott kit can be classified as positive by the Cepheid kit. According to an FDA survey, the limit of detection by the Cepheid Xpert Xpress SARS-CoV-2 test kit and the limit of detection by Abbott RealTime SARS-CoV-2 assay kit are found to be identical, namely both being at 5400 NAAT Detectable Units/ mL, as shown in the comparative data extracted from an FDA reference panel.[14]

5400	Cepheid	Xpert Xpress SARS-CoV-2 test
5400	Abbott Molecular	Abbott RealTime SARS-CoV-2 assay

However, due to the designation of higher cycle threshold test results as positives, the Cepheid Xpert kits have classified many Abbott kit negative cases as positives in a head-to-head comparative study as shown in the following "Table 2" extracted from a report by Basu et al.[15]

[14] FDA. SARS-CoV-2 Reference Panel Comparative Data. https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/sars-cov-2-reference-panel-comparative- data.

[15] *See* bioRxiv preprint doi: https://doi.org/10.1101/2020.05.11.089896; Basu A, Zinger T, Inglima K, Woo KM, Atie O, Yurasits L, See B, Aguero-Rosenfeld ME. Performance of Abbott ID Now COVID-19 Rapid Nucleic Acid Amplification Test Using Nasopharyngeal Swabs Transported in Viral Transport Media and Dry Nasal Swabs in a New York City Academic Institution. J Clin Microbiol. 2020 Jul 23;58(8):e01136-20. doi: 10.1128/JCM.01136-20. PMID: 32471894; PMCID: PMC7383552.

Table 2. Results of sequential nasopharyngeal specimens submitted in VTM from the Emergency Department tested on both Abbot ID NOW and Cepheid GeneXpert for SARS CoV-2 RNA

Sample ID	Abbott IDNOW Result*	Cepheid Result	N2 Ct	E Ct
1	Negative	Positive	43.1	0.0
2	Negative	Positive	40.7	37.0
3	Positive	Positive	32.4	29.0
4	Positive	Positive	32.3	30.3
5	Positive	Positive	18.2	16.2
6	Positive	Positive	31.6	28.5
7	Positive	Positive	35.1	31.3
8	Negative	Positive	44.1	0.0
9	Negative	Positive	44.3	0.0
10	Positive	Positive	29.7	27.1
11	Positive	Positive	27.6	26.2
12	Positive	Positive	19.7	17.5
13	Positive	Positive	18.6	16.2
14	Negative	Positive	36.3	33.3
15	Positive	Positive	23.7	26.5

j. One of the Cepheid Xpert kit users has put out an alert, stating "The instruments are presently set by the manufacturer to interpret a single target positive with very poor amplification efficiency (high Cycle Threshold [Ct] and/or atypical curve) as 'DETECTED.' None of these to date have confirmed positive when tested on other systems using similar targets, and may be a false positive due to background noise."[16]

k. Another group of users also found that some tested samples classified as positives by the Cepheid test kits cannot be confirmed with other test kits. These authors published a report, stating: "We found that the sensitivity of the Xpert Xpress SARS-CoV-2 assay was 100% (20 of 20) and the specificity was 80% (16 of 20). When looking at the cycle threshold (Ct) values from the GeneXpert assay we observed that specimens with no amplification of the *E* gene (ie, Ct=0) and Ct values for the *N2* gene greater than 40 cycles were considered as positives, whereas they were negative using the other RT-PCR system (Da An Gene)."[17]

[16] Diagnostic Laboratory Services Inc. Technical Alert. Cepheid GeneXpert and BD Max Instruments may be Reporting False Positives. https://dlslab.com/documents/bulletins/2020/tech-memo-sars-cov-2-pcr-possible-false-positive-6-19-2020.pdf.

[17] Rakotosamimanana N, Randrianirina F, Randremanana R, Raherison MS, Rasolofo V, Solofomalala GD, Spiegel A, Heraud JM. GeneXpert for the diagnosis of COVID-19 in LMICs. Lancet Glob Health. 2020 Oct 19:S2214-109X(20)30428-9. doi: 10.1016/S2214-109X(20)30428-9. Epub ahead of print. PMID: 33091372; PMCID: PMC7572106.

12. DNA sequencing verification of the RT-qPCR positive test results is absolutely necessary in this placebo-controlled randomized clinical trial because *de facto* unblinding has occurred among the participants. According to the trial protocol Section 8.13. COVID-19 Surveillance (All Participants), "If a participant experiences any of the following (irrespective of perceived etiology or clinical significance), he or she is instructed to contact the site immediately and, if confirmed, participate in an in-person or telehealth visit as soon as possible." This contact would trigger an automatic NAAT test by a Cepheid RT-qPCR assay at the central laboratory or at a local laboratory by any similar acceptable methods.

At the time of enrollment, the participants were informed that each of them would be injected with a vaccine to protect against COVID-19 infection or a saline placebo without disclosing which one of the two was injected into the participant. However, all participants were also informed that the vaccine may cause the following reactions:

- Fever ≥39.0°C (≥102.1°F).
- Redness or swelling at the injection site measuring greater than 10 cm (>20 measuring device units).
- Severe pain at the injection site.
- Any severe systemic event.

It is commonly known to the general public and especially to the informed clinical trial participants that intramuscular injection of a very small amount of sterile normal saline will not cause fever, local redness and swelling, and severe pain, or systemic reactions. The participants receiving placebo would intuitively or reasonably know that they were not injected with a vaccine and were not protected against COVID-19 disease due to the lack of any vaccine reaction after the injection. As a result, more participants receiving placebo than those receiving vaccine would report to the "site" manager when they developed any minor symptoms, such as a sore throat or a new cough for the fear of coming down with COVID-19. The site manager must investigate the symptoms reported, including ordering a RT-qPCR test by Cepheid assay to be performed at the Central Laboratory according to Protocol. The more severe cases might be tested locally by Abbott kits or Roche kits because they might have to be tested in the hospital after admission, and because many hospitals are aware of the high false positive rates generated by the Cepheid kits. The results generated by these test kits are not comparable since the Cepheid test kits using a very high Ct value up to 44.9 for "detection of SARS-CoV-2 genomic RNA" **tend to generate many more false positives than the other test kits**. A higher number of false-positive test results in the participants receiving placebo will artificially raise the efficacy of the vaccine, unless the RT-qPCR test results are verified by nucleotide sequencing to eliminate all false-positive test results.

13. Based on an MPR report published on November 8, 2020, there are only 180 confirmed cases of COVID-19 in this clinical trial series that have been analyzed to support the vaccine efficacy evaluation.[18] If the Sponsor (BioNTech/Pfizer) is unable to perform confirmatory Sanger sequencing tests on these 180 RNA extract residual samples, the Petitioner hereby offers

[18] Diana Ernst, RPh. Final Analysis Reveals COVID-19 Vaccine Candidate BNT162b2 95% Effective. MPR Report. November 18, 2020. https://www.empr.com/home/news/drugs-in-the-pipeline/pfizer-biontech-mrna-based-vaccine-bnt162b2-against-covid19-effective/.

to re-test them immediately with Sanger sequencing[19] and submit the laboratory data to support FDA's evaluation. Therefore, there is no excuse for the Sponsor to refuse using the gold standard Sanger sequencing technology for endpoint validation.

14. In summary, based on the scientific data available in the public domain and the FDA guidance, all RT-qPCR test results for detection of SARS-CoV-2 gene sequence must be considered presumptive. The Cepheid test kits for SARS-CoV-2 are known to generate more false-positive test results than other EUA assay kits.

15. The residues of the tested samples that were classified as positive for SARS-CoV-2 by the Cepheid GeneXpert assay, or equivalent as stated in the Pfizer Clinical Trial Protocol, must be re-tested by a Sanger sequencing method to confirm that the presumptive positive samples in fact contain a unique sequence of SARS-CoV-2 genome. Only then can the positive test results from the Cepheid GeneXpert test kits be accepted as an accurate component of the "endpoint." Only then can one nonspecific symptom plus laboratory positivity be accepted as a valid measure of confirmed COVID-19 cases or "endpoints."

Stay Urgently Required

16. Petitioner will suffer irreparable harm because once the FDA licenses this COVID-19 vaccine, states are expected to make this product mandatory, and hence without the FDA assuring proper safety trials of the vaccine *now*, the Petitioner will not have the opportunity to object to receiving the vaccine based on deficient clinical trials *later*.

17. For example, the New York State Bar Association recently passed a resolution recommending that "[s]hould the level of immunity be deemed insufficient by expert medical and scientific consensus to check the spread of COVID-19 and reduce morbidity and mortality, **a mandate and state action should be considered**."[20] Mandating administration of the vaccine, thereby eliminating the right to informed consent, makes acute the need to assure that the safety and efficacy of any COVID-19 vaccine is robustly studied in an adequate clinical trial monitoring for any potential adverse events.

18. Furthermore, if the vaccine is licensed without an appropriate efficacy review and without improving the accurate determination of primary endpoints, then any potential acceptance or mandate of these vaccines are likely to be based on inaccurate beliefs about the vaccine, namely that it will stop transmission of the virus from the vaccine recipient to others or that it will reduce severe COVID-19 disease and deaths. The trial protocols are not currently designed to determine whether either of those objectives can be met.

[19] Lee SH. Testing for SARS-CoV-2 in cellular components by routine nested RT-PCR followed by DNA sequencing. International Journal of Geriatrics and Rehabilitation. 2020; 2:69-96. Available from: http://www.int-soc-clin-geriat.com/info/wpcontent/uploads/2020/03/Dr.-Lees-paper-on-testing-for-SARS-CoV-2.pdf.

[20] https://nysba.org/app/uploads/2020/11/11.-Health-Law-Section-COVID-19-Report-September-20-2020-with-all-comments.pdf (emphasis added) (last visited November 10, 2020).

19. This request is also not frivolous and is being pursued in good faith as it seeks to increase the scientific integrity and reliability of the trials of the COVID-19 Vaccines.

20. Finally, the public interest also weighs strongly in favor of the requested relief because improving the accurate determination of primary endpoints (i) will comport with the best scientific practices, (ii) increase public confidence in the efficacy of a product expected to be mandated, and (iii) not doing so will have the opposite result in that it will create uncertainties regarding the efficacy of and need for the COVID-19 Vaccines.

21. The Petitioner therefore respectfully urges that this request be granted forthwith.

Respectfully submitted,

Dr. Sin Hang Lee

Review Report by an International Consortium of Scientists in Life Sciences (ICSLS) - Corman-Drosten *et al.*, Eurosurveillance 2020 (Updated: 29.11.2020)

External peer review of the RTPCR test to detect SARS-CoV-2 reveals 10 major scientific flaws at the molecular and methodological level: consequences for false positive results.

Pieter Borger[(1 *)], Bobby Rajesh Malhotra[(2)] , Michael Yeadon[(3)] , Clare Craig[(4)]

Kevin McKernan[(5)] , Klaus Steger[(6)] , Paul McSheehy[(7)] , Lidiya Angelova[(8)]

Fabio Franchi[(9)], Thomas Binder[(10)], Henrik Ullrich[(11)] , Makoto Ohashi[(12)]

Stefano Scoglio[(13)], Marjolein Doesburg-van Kleffens[(14)], Dorothea Gilbert[(15)]

Rainer Klement[(16)], Ruth Schruefer[(17)], Berber W. Pieksma[(18)], Jan Bonte[(19)]

Bruno H. Dalle Carbonare[(20)], Kevin P. Corbett[(21)], Ulrike Kämmerer[(22)]

* Corresponding Author

ABSTRACT

"In the publication entitled “Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR” (Eurosurveillance 25(8) 2020) the authors present a diagnostic workflow and RT-qPCR protocol for detection and diagnostics of 2019-nCoV (now known as SARS-CoV-2), which they claim to be validated, as well as being a robust diagnostic methodology for use in public-health laboratory settings.

In light of all the consequences resulting from this very publication for societies worldwide, a group of independent researchers performed a point-by-point review of the aforesaid publication in which 1) all components of the presented test design were cross checked, 2) the RT-qPCR protocol-recommendations were assessed with respect to good laboratory practice, and 3) parameters examined against relevant scientific literature covering the field.

The published RT-qPCR protocol for detection and diagnostics of 2019-nCoV and the manuscript suffer from numerous technical and scientific errors, including insufficient primer design, a problematic and insufficient RT-qPCR protocol, and the absence of an accurate test validation. Neither the presented test nor the manuscript itself fulfils the requirements for an acceptable scientific publication. Further, serious conflicts of interest of the authors are not mentioned. Finally, the very short timescale between submission and acceptance of the publication (24 hours) signifies that a systematic peer review process was either not performed here, or of problematic poor quality.

We provide compelling evidence of several scientific inadequacies, errors and flaws. Considering the scientific and methodological blemishes presented here, we are confident that the editorial board of Eurosurveillance has no other choice but to retract the publication."

CONCISE REVIEW REPORT

This paper will show numerous serious flaws in the Corman-Drosten paper, the significance of which has led to worldwide misdiagnosis of infections attributed to SARS-CoV-2 and associated with the disease COVID-19. We are confronted with stringent lockdowns which have destroyed many people's lives and livelihoods, limited access to education and these imposed restrictions by governments around the world are a direct attack on people's basic rights and their personal freedoms, resulting in collateral damage for entire economies on a global scale.

There are ten fatal problems with the Corman-Drosten paper which we will outline and explain in greater detail in the following sections.

The first and major issue is that the novel Coronavirus SARS-CoV-2 (in the publication named 2019-nCoV and in February 2020 named SARS-CoV-2 by an international consortium of virus experts) is based on in silico (theoretical) sequences, supplied by a laboratory in China [1], because at the time neither control material of infectious ("live") or inactivated SARS-CoV-2 nor isolated genomic RNA of the virus was available to the authors. To date no validation has been performed by the authorship based on isolated SARS-CoV-2 viruses or full length RNA thereof. According to Corman et al.:

> *"We aimed to develop and deploy robust diagnostic methodology for use in public health laboratory settings without having virus material available."* [1]

The focus here should be placed upon the two stated aims: a) *development* and b) *deployment of a diagnostic test for use in public health laboratory settings*. These aims are not achievable without having any actual virus material available (e.g. for determining the infectious viral load). In any case, only a protocol with maximal accuracy can be the mandatory and primary goal in any scenario-outcome of this magnitude. Critical viral load determination is mandatory information, and it is in Christian Drosten's group responsibility to perform these experiments and provide the crucial data.

Nevertheless these in silico sequences were used to develop a RT-PCR test methodology to identify the aforesaid virus. This model was based on the assumption that the novel virus is very similar to SARS-CoV from 2003 as both are beta-coronaviruses.

The PCR test was therefore designed using the genomic sequence of SARS-CoV as a control material for the Sarbeco component; we know this from our personal email-communication with [2] one of the co-authors of the Corman-Drosten paper. This method to model SARS-CoV-2 was described in the Corman-Drosten paper as follows:

> *"the establishment and validation of a diagnostic workflow for 2019-nCoV screening and specific confirmation, designed in absence of available virus isolates or original*

> *patient specimens. Design and validation were enabled by the close genetic relatedness to the 2003 SARS-CoV, and aided by the use of synthetic nucleic acid technology."*

The Reverse Transcription-Polymerase Chain Reaction (RT-PCR) is an important biomolecular technology to rapidly detect rare RNA fragments, which are known in advance. In the first step, RNA molecules present in the sample are reverse transcribed to yield cDNA. The cDNA is then amplified in the polymerase chain reaction using a specific primer pair and a thermostable DNA polymerase enzyme. The technology is highly sensitive and its detection limit is theoretically 1 molecule of cDNA. The specificity of the PCR is highly influenced by biomolecular design errors.

What is important when designing an RT-PCR Test and the quantitative RT-qPCR test described in the Corman-Drosten publication?

1. The primers and probes:

a) the concentration of primers and probes must be of optimal range (100-200 nM)

b) must be specific to the target-gene you want to amplify

c) must have an optimal percentage of GC content relative to the total nitrogenous bases (minimum 40%, maximum 60%)

d) for virus diagnostics at least 3 primer pairs must detect 3 viral genes (preferably as far apart as possible in the viral genome)

2. The temperature at which all reactions take place:

a) DNA melting temperature (>92°)

b) DNA amplification temperature (TaqPol specific)

c) Tm; the annealing temperature (the temperature at which the primers and probes reach the target binding/detachment, not to exceed 2°C per primer pair). Tm heavily depends on GC content of the primers

3. The number of amplification cycles (less than 35; preferably 25-30 cycles);

In case of virus detection, >35 cycles only detects signals which do not correlate with infectious virus as determined by isolation in cell culture [reviewed in 2]; if someone is tested by PCR as positive when a threshold of 35 cycles or higher is used (as is the case in most laboratories in Europe & the US), the probability that said person is actually infected is less than 3%, the probability that said result is a false positive is 97% [reviewed in 3]

4. Molecular biological validations; amplified PCR products must be validated either by running the products in a gel with a DNA ruler, or by direct DNA sequencing

5. Positive and negative controls should be specified to confirm/refute specific virus detection

6. There should be a Standard Operational Procedure (SOP) available

SOP unequivocally specifies the above parameters, so that all laboratories are able to set up the exact same test conditions. To have a validated universal SOP is essential, because it enables the comparison of data within and between countries.

MINOR CONCERNS WITH THE CORMAN-DROSTEN PAPER

1. In Table 1 of the Corman-Drosten paper, different abbreviations are stated - “nM” is specified, “nm” isn’t. Further in regards to correct nomenclature, nm means “nanometer” therefore nm should read nM here.

2. It is the general consensus to write genetic sequences always in the 5’-3’ direction, including the reverse primers. It is highly unusual to do alignment with reverse complementary writing of the primer sequence as the authors did in figure 2 of the Corman-Drosten paper. Here, in addition, a wobble base is marked as “y” without description of the bases the Y stands for.

3. Two misleading pitfalls in the Corman-Drosten paper are that their Table 1 does not include Tm-values (annealing-temperature values), neither does it show GC-values (number of G and C in the sequences as %-value of total bases).

MAJOR CONCERNS WITH THE CORMAN-DROSTEN PAPER

A) BACKGROUND

The authors introduce the background for their scientific work as: “The ongoing outbreak of the recently emerged novel coronavirus (2019-nCoV) poses a challenge for public health laboratories as virus isolates are unavailable while there is growing evidence that the outbreak is more widespread than initially thought, and international spread through travelers does already occur”.

According to BBC News [4] and Google Statistics [5] there were 6 deaths world-wide on January 21st 2020 - the day when the manuscript was submitted. Why did the authors assume a challenge for public health laboratories while there was no substantial evidence at that time to indicate that the outbreak was more widespread than initially thought?

As an aim the authors declared to develop and deploy robust diagnostic methodology for use in public health laboratory settings without having virus material available. Further, they acknowledge

that "The present study demonstrates the enormous response capacity achieved through coordination of academic and public laboratories in national and European research networks."

B) METHODS AND RESULTS

1. Primer & Probe Design

1a) Erroneous primer concentrations

Reliable and accurate PCR-test protocols are normally designed using between 100 nM and 200 nM per primer [7]. In the Corman-Drosten paper, we observe unusually high and varying primer concentrations for several primers (table 1). For the RdRp_SARSr-F and RdRp_SARSr-R primer pairs, 600 nM and 800 nM are described, respectively. Similarly, for the N_Sarbeco_F and N_Sarbeco_R primer set, they advise 600 nM and 800 nM, respectively [1].

It should be clear that these concentrations are far too high to be optimal for specific amplifications of target genes. **There exists no specified reason to use these extremely high concentrations of primers in this protocol. Rather, these concentrations lead to increased unspecific binding and PCR product amplification.**

Table1: Primers and probes (adapted from Corman-Drosten paper; erroneous primer concentrations are highlighted)

Assay/use	Oligonucleotide	Sequence[a]	Concentration[b]
RdRP gene	RdRp_SARSr-F	GTGARATGGTCATGTGTGGCGG	Use 600 nM per reaction
	RdRp_SARSr-P2	FAM-CAGGTGGAACCTCATCAGGAGATGC-BBQ	Specific for 2019-nCoV, will not detect SARS-CoV. Use 100 nM per reaction and mix with P1
	RdRP_SARSr-P1	FAM-CCAGGTGGWACRTCATCMGGTGATGC-BBQ	Pan Sarbeco-Probe will detect 2019-nCoV, SARS-CoV and bat-SARS-related CoVs. Use 100 nM per reaction and mix with P2
	RdRp_SARSr-R	CARATGTTAAASACACTATTAGCATA	Use 800 nM per reaction
E gene	E_Sarbeco_F	ACAGGTACGTTAATAGTTAATAGCGT	Use 400 nm per reaction
	E_Sarbeco_P1	FAM-ACACTAGCCATCCTTACTGCGCTTCG-BBQ	Use 200 nm per reaction
	E_Sarbeco_R	ATATTGCAGCAGTACGCACACA	Use 400 nm per reaction
N gene	N_Sarbeco_F	CACATTGGCACCCGCAATC	Use 600 nm per reaction
	N_Sarbeco_P	FAM-ACTTCCTCAAGGAACAACATTGCCA-BBQ	Use 200 nm per reaction
	N_Sarbeco_R	GAGGAACGAGAAGAGGCTTG	Use 800 nm per reaction

[a] W is A/T; R is G/A; M is A/C; S is G/C. FAM: 6-carboxyfluorescein; BBQ: blackberry quencher.

[b] Optimised concentrations are given in nanomol per litre (nM) based on the final reaction mix, e.g. 1.5 µL of a 10 µM primer stock solution per 25 µL total reaction volume yields a final concentration of 600 nM as indicated in the table.

1b) Unspecified ("Wobbly") primer and probe sequences

To obtain reproducible and comparable results, it is essential to distinctively define the primer pairs. In the Corman-Drosten paper we observed six unspecified positions, indicated by the letters R, W, M and S (Table 2). The letter W means that at this position there can be

either an A or a T; R signifies there can be either a G or an A; M indicates that the position may either be an A or a C; the letter S indicates there can be either a G or a C on this position. This high number of variants not only is unusual, but it also is highly confusing for laboratories. These six unspecified positions could easily result in the design of several different alternative primer sequences which do not relate to SARS-CoV-2 (2 distinct RdRp_SARSr_F primers + 8 distinct RdRp_SARS_P1 probes + 4 distinct RdRp_SARSr_R). The design variations will inevitably lead to results that are not even SARS CoV-2 related. Therefore, the confusing unspecific description in the Corman-Drosten paper is not suitable as a Standard Operational Protocol. These unspecified positions should have been designed unequivocally.

These wobbly sequences have already created a source of concern in the field and resulted in a Letter to the Editor authored by Pillonel et al. [8] regarding blatant errors in the described sequences. These errors are self-evident in the Corman et al. supplement as well.

Table 2: Primers and probes (adapted from Corman-Drosten paper; unspecified ("Wobbly") nucleotides in the primers are highlighted)

Assay/use	Oligonucleotide	Sequence[a]	Concentration[b]
RdRP gene	RdRp_SARSr-F	GTGARATGGTCATGTGTGGCGG	Use 600 nM per reaction
	RdRp_SARSr-P2	FAM-CAGGTGGAACCTCATCAGGAGATGC-BBQ	Specific for 2019-nCoV, will not detect SARS-CoV. Use 100 nM per reaction and mix with P1
	RdRP_SARSr-P1	FAM-CCAGGTGGWACRTCATCMGGTGATGC-BBQ	Pan Sarbeco-Probe will detect 2019-nCoV, SARS-CoV and bat-SARS-related CoVs. Use 100 nM per reaction and mix with P2
	RdRp_SARSr-R	CARATGTTAAASACACTATTAGCATA	Use 800 nM per reaction
E gene	E_Sarbeco_F	ACAGGTACGTTAATAGTTAATAGCGT	Use 400 nm per reaction
	E_Sarbeco_P1	FAM-ACACTAGCCATCCTTACTGCGCTTCG-BBQ	Use 200 nm per reaction
	E_Sarbeco_R	ATATTGCAGCAGTACGCACACA	Use 400 nm per reaction
N gene	N_Sarbeco_F	CACATTGGCACCCGCAATC	Use 600 nm per reaction
	N_Sarbeco_P	FAM-ACTTCCTCAAGGAACAACATTGCCA-BBQ	Use 200 nm per reaction
	N_Sarbeco_R	GAGGAACGAGAAGAGGCTTG	Use 800 nm per reaction

W is A/T; R is G/A; M is A/C; S is G/C; FAM: 6-carboxyfluorescein; BBQ: blackberry quencher.

[b] Optimised concentrations are given in nanomol per litre (nM) based on the final reaction mix, e.g. 1.5 µL of a 10 µM primer stock solution per 25 µL total reaction volume yields a final concentration of 600 nM as indicated in the table.

The WHO-protocol (Figure 1), which directly derives from the Corman-Drosten paper, concludes that in order to confirm the presence of SARS-CoV-2, two control genes (the E-and the RdRp-genes) must be identified in the assay. It should be noted, that the RdPd-gene has one uncertain position ("wobbly") in the forward-primer (R=G/A), two uncertain positions in the reverse-primer (R=G/A; S=G/C) and it has three uncertain positions in the RdRp-probe (W=A/T; R=G/A; M=A/C). So, two different forward primers,

four different reverse primers, and eight distinct probes can be synthesized for the RdPd-gene. Together, there are 64 possible combinations of primers and probes!

The Corman-Drosten paper further identifies a third gene which, according to the WHO protocol, was not further validated and deemed unnecessary:

"Of note, the N gene assay also performed well but was not subjected to intensive further validation because it was slightly less sensitive."

This was an unfortunate omission as it would be best to use all three gene PCRs as confirmatory assays, and this would have resulted in an almost sufficient virus RNA detection diagnostic tool protocol. Three confirmatory assay-steps would at least minimize-out errors & uncertainties at every fold-step in regards to "Wobbly"-spots. (Nonetheless, the protocol would still fall short of any "good laboratory practice", when factoring in all the other design-errors).

As it stands, the N gene assay is regrettably neither proposed in the WHO-recommendation (Figure 1) as a mandatory and crucial third confirmatory step, nor is it emphasized in the Corman-Drosten paper as important optional reassurance "for a routine workflow" (Table 2).

Consequently, in nearly all test procedures worldwide, merely 2 primer matches were used instead of all three. This oversight renders the entire test-protocol useless with regards to delivering accurate test-results of real significance in an ongoing pandemic.

Figure 1: The N-Gene confirmatory-assay is neither emphasized as necessary third step in the official WHO Drosten-Corman protocol-recommendation below [8] nor is it required as a crucial step for higher test-accuracy in the Eurosurveillance publication.

Background
We used known SARS- and SARS-related coronaviruses (bat viruses from our own studies as well as literature sources) to generate a non-redundant alignment (excerpts shown in Annex). We designed candidate diagnostic RT-PCR assays before release of the first sequence of 2019-nCoV. Upon sequence release, the following assays were selected based on their matching to 2019-nCoV as per inspection of the sequence alignment and initial evaluation (Figures 1 and 2).

All assays can use SARS-CoV genomic RNA as positive control. Synthetic control RNA for 2019-nCoV E gene assay is available via EVAg. Synthetic control for 2019-nCoV RdRp is expected to be available via EVAg from Jan 21st onward.

First line screening assay: E gene assay
Confirmatory assay: RdRp gene assay

1c) Erroneous GC-content (discussed in 2c, together with annealing temperature (Tm))

1d) Detection of viral genes
RT-PCR is not recommended for primary diagnostics of infection. This is why the RT-PCR Test used in clinical routine for detection of COVID-19 is not indicated for COVID-19 diagnosis on a regulatory basis.

"Clinicians need to recognize the enhanced accuracy and speed of the molecular diagnostic techniques for the diagnosis of infections, but also to understand their limitations. Laboratory results should always be interpreted in the context of the clinical presentation of the patient, and appropriate site, quality, and timing of specimen collection are required for reliable test results". [9]

However, it may be used to help the physician's differential diagnosis when he or she has to discriminate between different infections of the lung (Flu, Covid-19 and SARS have very similar symptoms). For a confirmative diagnosis of a specific virus, at least 3 specific primer pairs must be applied to detect 3 virus-specific genes. Preferably, these target genes should be located with the greatest distance possible in the viral genome (opposite ends included).

Although the Corman-Drosten paper describes 3 primers, these primers only cover roughly half of the virus' genome. This is another factor that decreases specificity for detection of intact COVID-19 virus RNA and increases the quote of false positive test results.

Therefore, even if we obtain three positive signals (i.e. the three primer pairs give 3 different amplification products) in a sample, this does not prove the presence of a virus. A better primer design would have terminal primers on both ends of the viral genome. This is

because the whole viral genome would be covered and three positive signals can better discriminate between a complete (and thus potentially infectious) virus and fragmented viral genomes (without infectious potency). In order to infer anything of significance about the infectivity of the virus, the Orf1 gene, which encodes the essential replicase enzyme of SARS-CoV viruses, should have been included as a target (Figure 2). The positioning of the targets in the region of the viral genome that is most heavily and variably transcribed is another weakness of the protocol.

Kim et al. demonstrate a highly variable 3' expression of subgenomic RNA in Sars-CoV-2 [23]. These RNAs are actively monitored as signatures for asymptomatic and non-infectious patients [10]. It is highly questionable to screen a population of asymptomatic people with qPCR primers that have 6 base pairs primer-dimer on the 3 prime end of a primer (Figure 3).

Apparently the WHO recommends these primers. We tested all the wobble derivatives from the Corman-Drosten paper with Thermofisher's primer dimer web tool [11]. The RdRp forward primer has 6bp 3prime homology with Sarbeco E Reverse. At high primer concentrations this is enough to create inaccuracies.

Of note: There is a perfect match of one of the N primers to a clinical pathogen (Pantoea), found in immuno-compromised patients. The reverse primer hits Pantoea as well but not in the same region (Figure 3).

These are severe design errors, since the test cannot discriminate between the whole virus and viral fragments. The test cannot be used as a diagnostic for SARS-viruses.

Figure 2: Relative positions of amplicon targets on the SARS coronavirus and the 2019 novel coronavirus genome. ORF: open reading frame; RdRp: RNA-dependent RNA polymerase. Numbers below amplicon are genome positions according to SARS-CoV, NC_004718 [1];

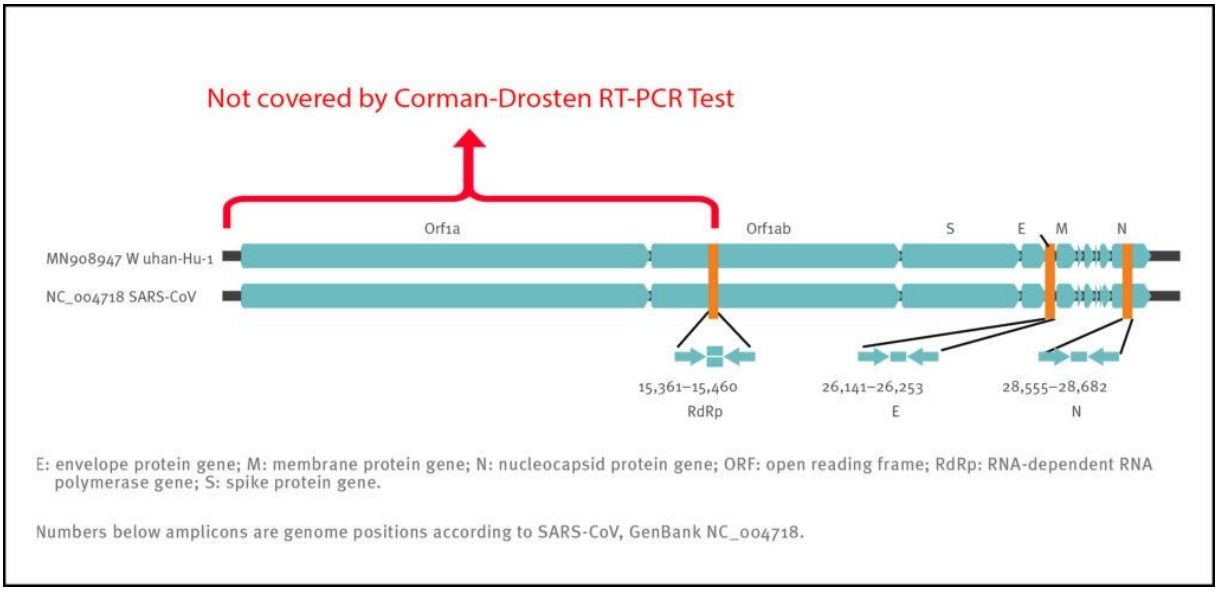
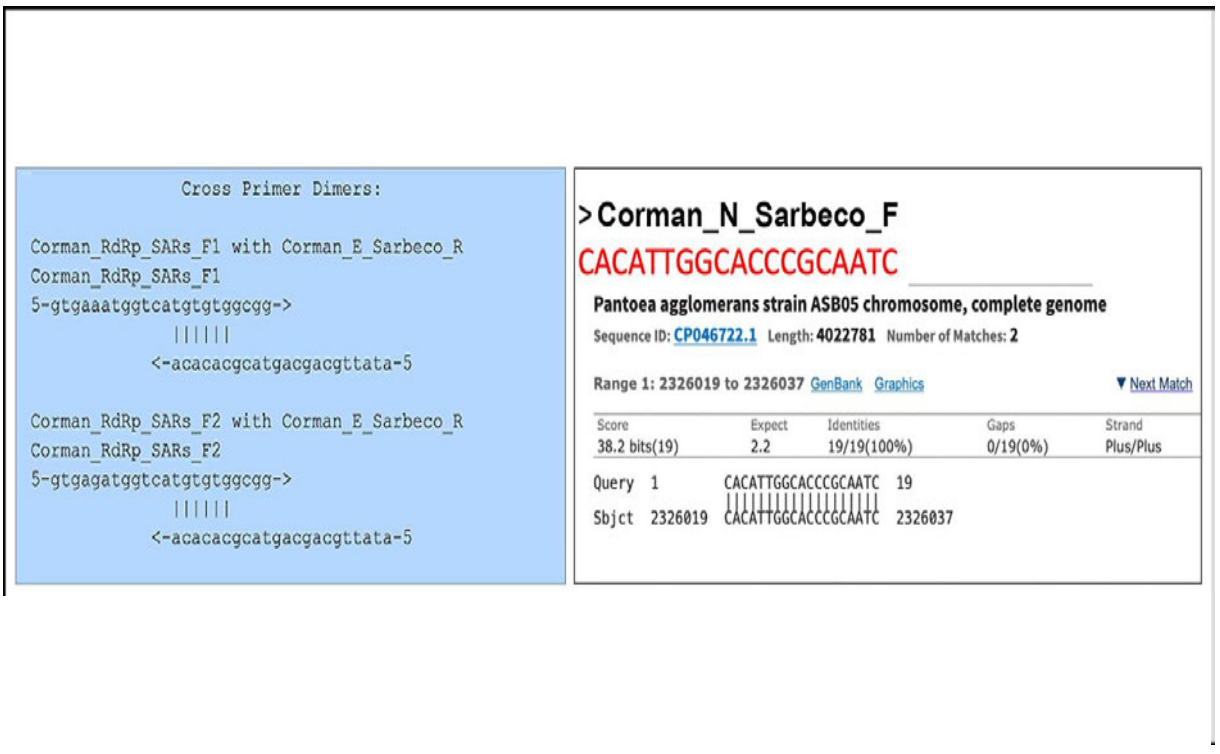


Figure 3: A test with Thermofischer's primer dimer web tool reveals that the RdRp forward primer has a 6bp 3`prime homology with Sarbeco E Reverse (left box). Another test reveals that there is a perfect match for one of the N-primers to a clinical pathogen (Pantoea) found in immuno-compromised patients (right box).



2. Reaction temperature

2a) DNA melting temperature (>92°).
Adequately addressed in the Corman-Drosten paper.

2b) DNA amplification temperature.
Adequately addressed in the Corman-Drosten paper.

2c) Erroneous GC-contents and Tm
The annealing-temperature determines at which temperature the primer attaches/detaches from the target sequence. For an efficient and specific amplification, GC content of primers should meet a minimum of 40% and a maximum of 60% amplification. As indicated in table 3, three of the primers described in the Corman-Drosten paper are not within the normal range for GC-content. Two primers (RdRp_SARSr_F and RdRp_SARSr_R) have unusual and very low GC-values of 28%-31% for all possible variants of wobble bases, whereas primer E_Sarbeco_F has a GC-value of 34.6% (Table 3 and second panel of Table 3).

It should be noted that the GC-content largely determines the binding to its specific target due to its three hydrogen bonds in base pairing. Thus, the lower the GC-content of the primer, the lower its binding-capability to its specific target gene sequence (i.e. the gene to be detected). This means for a target-sequence to be recognized we have to choose a temperature which is as close as possible to the actual annealing-temperature (best practise-value) for the primer not to detach again, while at the same time specifically selecting the target sequence.

If the Tm-value is very low, as observed for all wobbly-variants of the RdRp reverse primers, the primers can bind non-specifically to several targets, decreasing specificity and increasing potential false positive results.

The annealing temperature (Tm) is a crucial factor for the determination of the specificity/accuracy of the qPCR procedure and essential for evaluating the accuracy of qPCR-protocols. Best-practice recommendation: Both primers (forward and reverse) should have an almost similar value, preferably the identical value.

We used the freely available primer design software Primer-BLAST [12, 25] to evaluable the best-practise values for all primers used in the Corman-Drosten paper (Table 3). We attempted to find a Tm-value of 60° C, while similarly seeking the highest possible GC%-value for all primers. A maximal Tm difference of 2° C within primer pairs was considered acceptable. Testing the primer pairs specified in the Corman-Drosten paper, we observed a difference of 10° C with respect to the annealing temperature Tm for primer pair1 (RdRp_SARSr_F and RdRp_SARSr_R). This is a very serious error and makes the protocol useless as a specific diagnostic tool.

Additional testing demonstrated that only the primer pair designed to amplify the N-gene (N_Sarbeco_F and N_Sarbeco_R) reached the adequate standard to operate in a diagnostic test, since it has a sufficient GC-content and the Tm difference between the primers (N_Sarbeco_F and N_Sarbeco_R) is 1.85° C (below the crucial maximum of 2° C difference). Importantly, this is the gene which was neither tested in the virus samples (Table 2) nor emphasized as a confirmatory test. In addition to highly variable melting temperatures and degenerate sequences in these primers, there is another factor impacting specificity of the procedure: the dNTPs (0.4uM) are 2x higher than recommended for a highly specific amplification. There is additional magnesium sulphate added to the reaction as well. This procedure combined with a low annealing temperature can create non-specific amplifications. When additional magnesium is required for qPCR, specificity of the assay should be further scrutinized.

The design errors described here are so severe that it is highly unlikely that specific amplification of SARS-CoV-2 genetic material will occur using the protocol of the Corman-Drosten paper.

Table 3: GC-content of the primers and probes (adapted from Corman-Drosten paper; aberrations from optimized GC-contents are highlighted. Second Panel shows a table-listing of all Primer-BLAST best practices values for all primers and probes used in the Corman-Drosten paper by Prof. Dr. Ulrike Kämmerer & her team.

Normal ranges for GC%: 40 - 60%; normal ranges for TM: 55-65°; Best-practise for qPCR in our case: 60° for both primers (reverse & forward)

Assay/use	Oligonucleotide	Sequence[a]	Concentration[b]
RdRP gene	RdRp_SARSr-F	GTGARATGGTCATGTGTGGCGG	Use 600 nM per reaction
	RdRp_SARSr-P2	FAM-CAGGTGGAACCTCATCAGGAGATGC-BBQ	Specific for 2019-nCoV, will not detect SARS-CoV. Use 100 nM per reaction and mix with P1
	RdRP_SARSr-P1	FAM-CCAGGTGGWACRTCATCMGGTGATGC-BBQ	Pan Sarbeco-Probe will detect 2019-nCoV, SARS-CoV and bat-SARS-related CoVs. Use 100 nM per reaction and mix with P2
	RdRp_SARSr-R	CARATGTTAAASACACTATTAGCATA	Use 800 nM per reaction
E gene	E_Sarbeco_F	ACAGGTACGTTAATAGTTAATAGCGT	Use 400 nm per reaction
	E_Sarbeco_P1	FAM-ACACTAGCCATCCTTACTGCGCTTCG-BBQ	Use 200 nm per reaction
	E_Sarbeco_R	ATATTGCAGCAGTACGCACACA	Use 400 nm per reaction
N gene	N_Sarbeco_F	CACATTGGCACCCGCAATC	Use 600 nm per reaction
	N_Sarbeco_P	FAM-ACTTCCTCAAGGAACAACATTGCCA-BBQ	Use 200 nm per reaction
	N_Sarbeco_R	GAGGAACGAGAAGAGGCTTG	Use 800 nm per reaction

[a] W is A/T; R is G/A; M is A/C; S is G/C. FAM: 6-carboxyfluorescein; BBQ: blackberry quencher.
[b] Optimised concentrations are given in nanomol per litre (nM) based on the final reaction mix, e.g. 1.5 µL of a 10µM primer stock solution per 25 µL total reaction volume yields a final concentration of 600 nM as indicated in the table.

		GC	TM		Search in **MN908947** (first full genome from Wuihan, 12.01.2020)					
Primer pairs	**Sequence (5´-3´)**	**Template strand**	**Length**	**Start**	**Stop**	**Tm**	**GC%**	**Self 5' complementarity**	**Self 3' complementarity**	**Product length (bp)**
E_Sarbeco_F	ACAGGTACGTTAATAGTTAATAGCGT	Plus	26	26269	26294	58.29	34.62	8.00	8.00	**113**
E_Sarbeco_R	ATATTGCAGCAGTACGCACACA	Minus	22	26381	26360	60.93	45.45	7.00	1.00	
N-Sarbeco_F	CACATTGGCACCCGCAATC	Plus	19	28706	28724	60.15	57.89	4.00	0.00	**128**
N-Sarbeco_R	GAGGAACGAGAAGAGGCTTG	Minus	20	28833	28814	58.00	55.00	3.00	1.00	
RdRp_SARSr-F	GTGARATGGTCATGTGTGGCGG		22			63.74	59.09	4.00	to be added in next version	
RdRp_SARSr-R	CARATGTTAAASACACTATTAGCATA		25			53.56	28.00	7.00		
If R= G and S= G	GTGAGATGGTCATGTGTGGCGG		22			63.74	59.09	4.00	1.00	
	CAGATGTTAAAGACACTATTAGCATA		26			55.22	30.77	7.00	5.00	not found in the Sequence
If R= G and S= C	GTGAGATGGTCATGTGTGGCGG		22			63.74	59.09	4.00	1.00	
	CAGATGTTAAACACACTATTAGCATA		26			55.68	30.77	7.00	2.00	
If R= A and S= G	GTGAAATGGTCATGTGTGGCGG		22			62.58	54.55	4.00	1.00	
	CAAATGTTAAAGACACTATTAGCATA		26			54.23	26.92	7.00	5.00	
If R= A and S= C	GTGAAATGGTCATGTGTGGCGG		22			62.58	54.55	4.00	1.00	
	CAAATGTTAAACACACTATTAGCATA		26			54.69	26.92	7.00	2.00	
Probes:										
RdRp-SARSr-P2	CAGGTGGAACCTCATCAGGAGATGC		25			64.89	56.00	6.00	5.00	
RdRp-SARSr-P1	CCAGGTGGWACRTCATCMGGTGATGC									
E-Sarbeco-P1	ACACTAGCCATCCTTACTGCGCTTCG		26			66.78	53.85	4.00	2.00	
N-Sarbeco-P	ACTTCCTCAAGGAACAACATTGCCA		25			63.15	44.00	8.00	3.00	

3. The number of amplification cycles

It should be noted that there is no mention anywhere in the Corman-Drosten paper of a test being positive or negative, or indeed what defines a positive or negative result. These types of virological diagnostic tests must be based on a SOP, including a validated and fixed number of PCR cycles (Ct value) after which a sample is deemed positive or negative. The maximum reasonably reliable Ct value is 30 cycles. Above a Ct of 35 cycles, rapidly increasing numbers of false positives must be expected .

PCR data evaluated as positive after a Ct value of 35 cycles are completely unreliable.

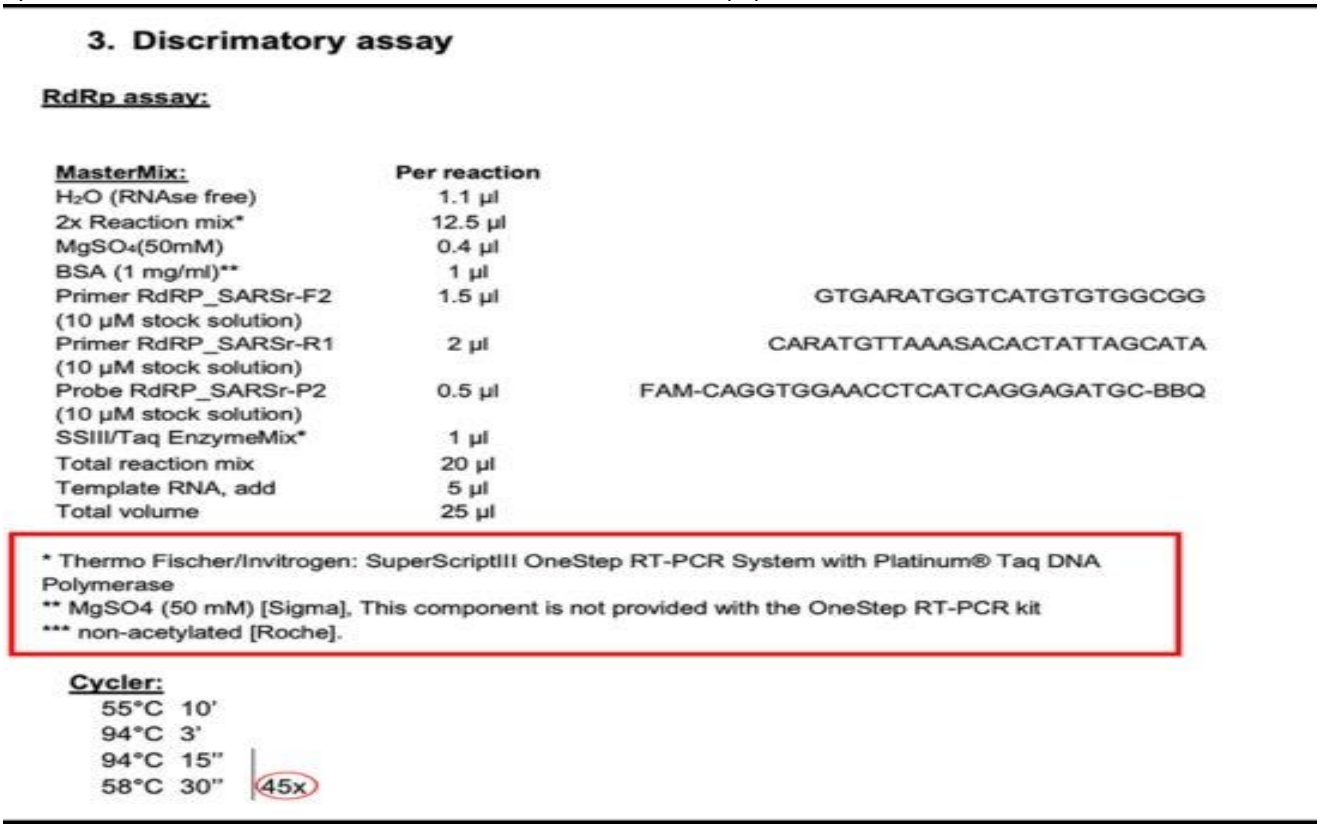
Citing Jaafar et al. 2020 [3]:

"At Ct = 35, the value we used to report a positive result for PCR, <3% of cultures are positive."

In other words, there was no successful virus isolation of SARS-CoV-2 at those high Ct values. Further, scientific studies show that only non-infectious (dead) viruses are detected with Ct values of 35 [22].

Between 30 and 35 there is a grey area, where a positive test cannot be established with certainty. This area should be excluded. Of course, one could perform 45 PCR cycles, as recommended in the Corman-Drosten WHO-protocol (Figure 4), but then you also have to define a reasonable Ct-value (which should not exceed 30). But an analytical result with a Ct value of 45 is scientifically and diagnostically absolutely meaningless (a reasonable Ct-value should not exceed 30). All this should be communicated very clearly. It is a significant mistake that the Corman-Drosten paper does not mention the maximum Ct value at which a sample can be unambiguously considered as a positive or a negative test-result. This important cycle threshold limit is also not specified in any follow-up submissions to date.

Figure 4: RT-PCR Kit recommendation in the official Corman-Drosten WHO-protocol [8]. Only a "Cycler"-value (cycles) is to be found without corresponding and scientifically reasonable Ct (Cutoff-value). This or any other cycles-value is nowhere to be found in the actual Corman-Drosten paper.



3. Discrimatory assay

RdRp assay:

MasterMix:	**Per reaction**	
H_2O (RNAse free)	1.1 µl	
2x Reaction mix*	12.5 µl	
$MgSO_4$(50mM)	0.4 µl	
BSA (1 mg/ml)**	1 µl	
Primer RdRP_SARSr-F2 (10 µM stock solution)	1.5 µl	GTGARATGGTCATGTGTGGCGG
Primer RdRP_SARSr-R1 (10 µM stock solution)	2 µl	CARATGTTAAASACACTATTAGCATA
Probe RdRP_SARSr-P2 (10 µM stock solution)	0.5 µl	FAM-CAGGTGGAACCTCATCAGGAGATGC-BBQ
SSIII/Taq EnzymeMix*	1 µl	
Total reaction mix	20 µl	
Template RNA, add	5 µl	
Total volume	25 µl	

* Thermo Fischer/Invitrogen: SuperScriptIII OneStep RT-PCR System with Platinum® Taq DNA Polymerase
** MgSO4 (50 mM) [Sigma], This component is not provided with the OneStep RT-PCR kit
*** non-acetylated [Roche].

Cycler:

55°C 10'
94°C 3'
94°C 15"
58°C 30" 45x

4. Biomolecular validations

To determine whether the amplified products are indeed SARS-CoV-2 genes, biomolecular validation of amplified PCR products is essential. For a diagnostic test, this validation is an absolute must.

Validation of PCR products should be performed by either running the PCR product in a 1% agarose-EtBr gel together with a size indicator (DNA ruler or DNA ladder) so that the size of the product can be estimated. The size must correspond to the calculated size of the amplification product. But it is even better to sequence the amplification product. The latter will give 100% certainty about the identity of the amplification product. Without molecular validation one can not be sure about the identity of the amplified PCR products. Considering the severe design errors described earlier, the amplified PCR products can be anything.

Also not mentioned in the Corman-Drosten paper is the case of small fragments of qPCR (around 100bp): It could be either 1,5% agarose gel or even an acrylamide gel.

The fact that these PCR products have not been validated at molecular level is another striking error of the protocol, making any test based upon it useless as a specific diagnostic tool to identify the SARS-CoV-2 virus.

5. Positive and negative controls to confirm/refute specific virus detection.

The unconfirmed assumption described in the Corman-Drosten paper is that SARS-CoV-2 is the only virus from the SARS-like beta-coronavirus group that currently causes infections in humans. The sequences on which their PCR method is based are in silico sequences, supplied by a laboratory in China [23], because at the time of development of the PCR test no control material of infectious (“live”) or inactivated SARS-CoV-2 was available to the authors. The PCR test was therefore designed using the sequence of the known SARS-CoV as a control material for the Sarbeco component (Dr. Meijer, co-author Corman-Drosten paper in an email exchange with Dr. Peter Borger) [2].

All individuals testing positive with the RT-PCR test, as described in the Corman-Drosten paper, are assumed to be positive for SARS-CoV-2 infections. There are three severe flaws

in their assumption. First, a positive test for the RNA molecules described in the Corman-Drosten paper cannot be equated to “infection with a virus”. A positive RT-PCR test merely indicates the presence of viral RNA molecules. As demonstrated under point 1d (above), the Corman-Drosten test was not designed to detect the full-length virus, but only a fragment of the virus. We already concluded that this classifies the test as unsuitable as a diagnostic test for SARS-virus infections.

Secondly and of major relevance, the functionality of the published RT-PCR Test was not demonstrated with the use of a positive control (isolated SARS-CoV-2 RNA) which is an essential scientific gold standard.

Third, the Corman-Drosten paper states:

“To show that the assays can detect other bat-associated SARS-related viruses, we used the E gene assay to test six bat-derived faecal samples available from Drexler et al. […] und Muth et al. […]. These virus-positive samples stemmed from European rhinolophid bats. Detection of these phylogenetic outliers within the SARS-related CoV clade suggests that all Asian viruses are likely to be detected. This would, theoretically, ensure broad sensitivity even in case of multiple independent acquisitions of variant viruses from an animal reservoir.”

This statement demonstrates that the E gene used in RT-PCR test, as described in the Corman-Drosten paper, is not specific to SARS-CoV-2.

The E gene primers also detect a broad spectrum of other SARS viruses.

The genome of the coronavirus is the largest of all RNA viruses that infect humans and they all have a very similar molecular structure. Still, SARS-CoV1 and SARS-CoV-2 have two highly specific genetic fingerprints, which set them apart from the other coronaviruses. First, a unique fingerprint-sequence (KTFPPTEPKKDKKKK) is present in the N-protein of SARS-CoV and SARS-CoV-2 [13,14,15]. Second, both SARS-CoV1 and SARS-CoV2 do not contain the HE protein, whereas all other coronaviruses possess this gene [13, 14]. So, in order to specifically detect a SARS-CoV1 and SARS-CoV-2 PCR product the above region in the N gene should have been chosen as the amplification target. A reliable diagnostic test should focus on this specific region in the N gene as a confirmatory test. The PCR for this N gene was not further validated nor recommended as a test gene by the Drosten-Corman paper, because of being “not so sensitive” with the SARS-CoV original probe [1].

Furthermore, the absence of the HE gene in both SARS-CoV1 and SARS-CoV-2 makes this gene the ideal negative control to exclude other coronaviruses. The Corman-Drosten paper does not contain this negative control, nor does it contain any other negative controls. The

PCR test in the Corman-Drosten paper therefore contains neither a unique positive control nor a negative control to exclude the presence of other coronaviruses. This is another major design flaw which classifies the test as unsuitable for diagnosis.

6. Standard Operational Procedure (SOP) is not available

There should be a Standard Operational Procedure (SOP) available, which unequivocally specifies the above parameters, so that all laboratories are able to set up the identical same test conditions. To have a validated universal SOP is essential, because it facilitates data comparison within and between countries. It is very important to specify all primer parameters unequivocally. We note that this has not been done. Further, the Ct value to indicate when a sample should be considered positive or negative is not specified. It is also not specified when a sample is considered infected with SARS-CoV viruses. As shown above, the test cannot discern between virus and virus fragments, so the Ct value indicating positivity is crucially important. This Ct value should have been specified in the Standard Operational Procedure (SOP) and put on-line so that all laboratories carrying out this test have exactly the same boundary conditions. It points to flawed science that such an SOP does not exist. The laboratories are thus free to conduct the test as they consider appropriate, resulting in an enormous amount of variation. Laboratories all over Europe are left with a multitude of questions; which primers to order? which nucleotides to fill in the undefined places? which Tm value to choose? How many PCR cycles to run? At what Ct value is the sample positive? And when is it negative? And how many genes to test? Should all genes be tested, or just the E and RpRd gene as shown in Table 2 of the Corman-Drosten paper? Should the N gene be tested as well? And what is their negative control? What is their positive control?

The protocol as described is unfortunately very vague and erroneous in its design that one can go in dozens of different directions. There does not appear to be any standardization nor an SOP, so it is not clear how this test can be implemented.

7. Consequences of the errors described under 1-5: false positive results.

The RT-PCR test described in the Corman-Drosten paper contains so many molecular biological design errors (see 1-5) that it is not possible to obtain unambiguous results. It is inevitable that this test will generate a tremendous number of so-called “false positives”. The definition of false positives is a negative sample, which initially scores positive, but which is negative after retesting with the same test. False positives are erroneous positive test-results, i.e. negative samples that test positive. And this is indeed what is found in the Corman-Drosten paper. On page 6 of the manuscript PDF the authors demonstrate, that even under well-controlled laboratory conditions, a considerable percentage of false positives is generated with this test:

"In four individual test reactions, weak initial reactivity was seen however they were negative upon retesting with the same assay. These signals were not associated with any particular virus, and for each virus with which initial positive reactivity occurred, there were other samples that contained the same virus at a higher concentration but did not test positive. Given the results from the extensive technical qualification described above, it was concluded that this initial reactivity was not due to chemical instability of real-time PCR probes and most probably to handling issues caused by the rapid introduction of new diagnostic tests and controls during this evaluation study." [1]

The first sentence of this excerpt is clear evidence that the PCR test described in the Corman-Drosten paper generates false positives. Even under the well-controlled conditions of the state-of-the-art Charité-laboratory, 4 out of 310 primary-tests are false positives per definition. Four negative samples initially tested positive, then were negative upon retesting. This is the classical example of a false positive. In this case the authors do not identify them as false positives, which is intellectually dishonest.

Another telltale observation in the excerpt above is that the authors explain the false positives away as "handling issues caused by the rapid introduction of new diagnostic tests". Imagine the laboratories that have to introduce the test without all the necessary information normally described in an SOP.

8. The Corman-Drosten paper was not peer-reviewed

Before formal publication in a scholarly journal, scientific and medical articles are traditionally certified by "peer review." In this process, the journal's editors take advice from various experts ("referees") who have assessed the paper and may identify weaknesses in its assumptions, methods, and conclusions. Typically a journal will only publish an article once the editors are satisfied that the authors have addressed referees' concerns and that the data presented supports the conclusions drawn in the paper." This process is as well described for Eurosurveillance [16].

The Corman-Drosten paper was submitted to Eurosurveillance on January 21st 2020 and accepted for publication on January 22nd 2020. On January 23rd 2020 the paper was online. On January 13th 2020 version 1-0 of the protocol was published at the official WHO website [17], updated on January 17th 2020 as document version 2-1 [18], even before the Corman-Drosten paper was published on January 23rd at Eurosurveillance.

Normally, peer review is a time-consuming process since at least two experts from the field have to critically read and comment on the submitted paper. In our opinion, this paper was not peer-reviewed. Twenty-four hours are simply not enough to carry out a thorough peer review. Our conclusion is supported by the fact that a tremendous number of very serious design flaws were found by us, which make the PCR test completely unsuitable as a diagnostic tool to identify the SARS-CoV-2 virus. Any molecular biologist familiar with RT-PCR

design would have easily observed the grave errors present in the Corman-Drosten paper before the actual review process. We asked Eurosurveillance on October 26th 2020 to send us a copy of the peer review report. To date, we have not received this report and in a letter dated November 18th 2020, the ECDC as host for Eurosurveillance declined to provide access without providing substantial scientific reasons for their decision. On the contrary, they write that "disclosure would undermine the purpose of scientific investigations." [24].

9. Authors as the editors

A final point is one of major concern. It turns out that two authors of the Corman-Drosten paper, Christian Drosten and Chantal Reusken, are also members of the editorial board of this journal [19]. Hence there is a severe conflict of interest which strengthens suspicions that the paper was not peer-reviewed. It has the appearance that the rapid publication was possible simply because the authors were also part of the editorial board at Eurosurveillance. This practice is categorized as compromising scientific integrity.

SUMMARY CATALOGUE OF ERRORS FOUND IN THE PAPER

The Corman-Drosten paper contains the following specific errors:

1. There exists no specified reason to use these extremely high concentrations of primers in this protocol. The described concentrations lead to increased nonspecific bindings and PCR product amplifications, making the test unsuitable as a specific diagnostic tool to identify the SARS-CoV-2 virus.

2. Six unspecified wobbly positions will introduce an enormous variability in the real world laboratory implementations of this test; the confusing nonspecific description in the Corman-Drosten paper is not suitable as a Standard Operational Protocol making the test unsuitable as a specific diagnostic tool to identify the SARS-CoV-2 virus.

3. The test cannot discriminate between the whole virus and viral fragments. Therefore, the test cannot be used as a diagnostic for intact (infectious) viruses, making the test unsuitable as a specific diagnostic tool to identify the SARS-CoV-2 virus and make inferences about the presence of an infection.

4. A difference of 10° C with respect to the annealing temperature Tm for primer pair1 (RdRp_SARSr_F and RdRp_SARSr_R) also makes the test unsuitable as a specific diagnostic tool to identify the SARS-CoV-2 virus.

5. A severe error is the omission of a Ct value at which a sample is considered positive and negative. This Ct value is also not found in follow-up submissions making the test unsuitable as a specific diagnostic tool to identify the SARS-CoV-2 virus.

6. The PCR products have not been validated at the molecular level. This fact makes the protocol useless as a specific diagnostic tool to identify the SARS-CoV-2 virus.

7. The PCR test contains neither a unique positive control to evaluate its specificity for SARS-CoV-2 nor a negative control to exclude the presence of other coronaviruses, making the test unsuitable as a specific diagnostic tool to identify the SARS-CoV-2 virus.

8. The test design in the Corman-Drosten paper is so vague and flawed that one can go in dozens of different directions; nothing is standardized and there is no SOP. This highly questions the scientific validity of the test and makes it unsuitable as a specific diagnostic tool to identify the SARS-CoV-2 virus.

9. Most likely, the Corman-Drosten paper was not peer-reviewed making the test unsuitable as a specific diagnostic tool to identify the SARS-CoV-2 virus.

10. We find severe conflicts of interest for at least four authors, in addition to the fact that two of the authors of the Corman-Drosten paper (Christian Drosten and Chantal Reusken) are members of the editorial board of Eurosurveillance. A conflict of interest was added on July 29 2020 (Olfert Landt is CEO of TIB-Molbiol; Marco Kaiser is senior researcher at GenExpress and serves as scientific advisor for TIB-Molbiol), that was not declared in the original version (and still is missing in the PubMed version); TIB-Molbiol is the company which was “the first” to produce PCR kits (Light Mix) based on the protocol published in the Corman-Drosten manuscript, and according to their own words, they distributed these PCR-test kits before the publication was even submitted [20]; further, Victor Corman & Christian Drosten failed to mention their second affiliation: the commercial test laboratory “Labor Berlin”. Both are responsible for the virus diagnostics there [21] and the company operates in the realm of real time PCR-testing.

In light of our re-examination of the test protocol to identify SARS-CoV-2 described in the Corman-Drosten paper we have identified concerning errors and inherent fallacies which render the SARS-CoV-2 PCR test useless.

CONCLUSION

The decision as to which test protocols are published and made widely available lies squarely in the hands of Eurosurveillance. A decision to recognise the errors apparent in the Corman-Drosten paper has the benefit to greatly minimise human cost and suffering going forward.

Is it not in the best interest of Eurosurveillance to retract this paper? Our conclusion is clear. In the face of all the tremendous PCR-protocol design flaws and errors described here, we conclude: There is not much of a choice left in the framework of scientific integrity and responsibility.

REFERENCES

[1] Corman Victor M, Landt Olfert, Kaiser Marco, Molenkamp Richard, Meijer Adam, Chu Daniel KW, Bleicker Tobias, Brünink Sebastian, Schneider Julia, Schmidt Marie Luisa, Mulders Daphne GJC, Haagmans Bart L, van der Veer Bas, van den Brink Sharon, Wijsman Lisa, Goderski Gabriel, Romette Jean-Louis, Ellis Joanna, Zambon Maria, Peiris Malik, Goossens Herman, Reusken Chantal, Koopmans Marion PG, Drosten Christian. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. Euro Surveill. 2020;25(3):pii=2000045. https://doi.org/10.2807/1560-7917.ES.2020.25.3.2000045

[2] Email communication between Dr. Peter Borger & Dr. Adam Meijer: Supplementary Material

[3] Jafaar et al., Correlation Between 3790 Quantitative Polymerase Chain Reaction–Positives Samples and Positive Cell Cultures, Including 1941 Severe Acute Respiratory Syndrome Coronavirus 2 Isolates. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1491/5912603

[4] BBC, January 21st 2020: https://www.bbc.com/news/world-asia-china-51185836;

Archive: https://archive.is/0qRmZ

[5] Google Analytics - COVID19-deaths worldwide: https://bit.ly/3fndemJ

Archive: https://archive.is/PpqEE

[6] Laboratory testing for COVID-19 Emergency Response Technical Centre, NIVD under

China CDC March 15th, 2020: http://www.chinacdc.cn/en/COVID19/202003/P020200323390321297894.pdf

[7] Real-Time PCR Handbook Life Technologies: https://www.thermofisher.com/content/dam/LifeTech/global/Forms/PDF/real-time-pcr-

handbook.pdf

Nolan T, Huggett J, Sanchez E.Good practice guide for the application of quantitative PCR (qPCR) First Edition 2013

[8] Trestan Pillonel et al, Letter to the editor: SARS-CoV-2 detection by real-time RT-PCR: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7268274/

[9] Kurkela, Satu, and David WG Brown. "Molecular-diagnostic techniques." Medicine 38.10 (2009): 535-540.

[10] Wolfel et al., Virological assessment of hospitalized patients with COVID-2019

https://www.nature.com/articles/s41586-020-2196-x

[11] Thermofischer Primer Dimer Web Tool: https://www.thermofisher.com/us/en/home/brands/thermo-scientific/molecular-biology/molecular-biology-learning-center/molecular-biology-resource-library/thermo-scientific-web-tools/multiple-primer-analyzer.html

Suplementary material by Kevin Mckernan, Corman-Drosten Primer Dimer Results with Thermofischer Primer Dimer Web Tool

[12] Primer-BLAST, NCBI - National Center for Biotechnology Information: https://www.ncbi.nlm.nih.gov/tools/primer-blast/

[13] Marra MA, Steven JMJ, Caroline RA, Robert AH, Angela BW et al. (2003) Science. The

Genome sequence of the SARS-associated coronavirus. Science 300(5624): 1399-1404.

[14] Severe acute respiratory syndrome coronavirus 2 isolate Wuhan-Hu-1, complete genome: https://www.ncbi.nlm.nih.gov/nuccore/MN908947

[15] Borger P. A SARS-like Coronavirus was expected but nothing was done to be prepared. Am J Biomed Sci Res 2020. https://biomedgrid.com/pdf/AJBSR.MS.ID.001312.pdf

https://www.researchgate.net/publication/341120750_A_SARS-like_Coronavirus_was_Expected_but_nothing_was_done_to_be_Prepared;

Archive: https://archive.is/i76Hu

[16] Eurosurveillance paper evaluation / review process: https://www.eurosurveillance.org/evaluation

[17] Official recommendation of the Corman-Drosten protocol & manuscript by the WHO,published on January 13th 2020 as version 1.0 of the document:

https://www.who.int/docs/default-source/coronaviruse/wuhan-virus-assay-v1991527e5122341d99287a1b17c111902.pdf; archive: https://bit.ly/3m3jXVH

[18] Official WHO-recommendation for the Corman / Drosten RT-qPCR-protocol, which directly derives from the Eurosurveillance-publication, document-version 2-1, published on

17th January 2020:
https://www.who.int/docs/default-source/coronaviruse/protocol-v2-1.pdf?sfvrsn=a9ef618c_2

[19] Eurosurveillance Editorial Board, 2020:
https://www.eurosurveillance.org/upload/site-assets/imgs/2020-09-Editorial%20Board%20PDF.pdf;

Archive: https://bit.ly/2TqXBjX

[20] Instructions For Use LightMix SarbecoV E-gene plus EAV Control, TIB-Molbiol & Roche Molecular Solutions, January 11th 2020:
https://www.roche-as.es/lm_pdf/MDx_40-0776_96_Sarbeco-E-gene_V200204_09164154001 (1).pdf

Archive, timestamp - January 11th 2020: https://archive.is/Vulo5;

Archive: https://bit.ly/3fm9bXH

[21] Christian Drosten & Victor Corman, responsible for viral diagnostics at Labor Berlin:
https://www.laborberlin.com/fachbereiche/virologie/

Archive: https://archive.is/CDEUG

[22] Tom Jefferson, Elizabeth Spencer, Jon Brassey, Carl Heneghan Viral cultures for COVID-19 infectivity assessment. Systematic review. Systematic review doi: https://doi.org/10.1101/2020.08.04.20167932
https://www.medrxiv.org/content/10.1101/2020.08.04.20167932v4

[23] Kim et al.,The Architecture of SARS-CoV-2 Transcriptome: https://www.sciencedirect.com/science/article/pii/S0092867420304062

[24] ECDC reply to Dr. Peter Borger, 18th November 2020: Supplementary Material

[25] Prof. Dr. Ulrike Kämmerer & team, survey & Primer-BLAST table: Supplementary Material

Additional literature:

Description RT-PCR RKI Germany, on page 10 of this link: https://www.rki.de/DE/Content/Gesundheitsmonitoring/Gesundheitsberichterstattung/GBEDownloadsJ/JoHM_S5_2020_Studienprotokoll_CORONA_MONITORING_lokal.pdf?__blob=publicationFile

Author's Affiliations:

1) Dr. Pieter Borger (MSc, PhD), Molecular Genetics, W+W Research Associate, Lörrach, Germany

2) Rajesh Kumar Malhotra (Artist Alias: Bobby Rajesh Malhotra), Former 3D Artist / Scientific Visualizations at CeMM - Center for Molecular Medicine of the Austrian Academy of Sciences (2019-2020).

3) University for Applied Arts - Department for Digital Arts Vienna, Austria

4) Dr. Michael Yeadon BSs(Hons) Biochem Tox U Surrey, PhD Pharmacology U Surrey. Managing Director, Yeadon Consulting Ltd former Pfizer Chief Scientist, United Kingdom

Dr. Clare Craig MA, (Cantab) BM, BCh (Oxon), FRCPath, United Kingdom

5) Kevin McKernan, BS Emory University, Chief Scientific Officer, founder Medical Genomics, engineered the sequencing pipeline at WIBR/MIT for the

6) Human Genome Project, Invented and developed the SOLiD sequencer, awarded patents related to PCR, DNA Isolation and Sequencing, USA Prof. Dr. Klaus Steger, Department of Urology, Pediatric Urology and Andrology, Molecular Andrology, Biomedical Research University, Giessen, Germany

7) Dr. Paul McSheehy (BSc, PhD), Biochemist & Industry Pharmacologist, Loerrach, Germany

8) Dr. Lidiya Angelova, MSc in Biology, PhD in Microbiology, Former researcher at the National Institute of Allergy and Infectious Diseases (NIAID), Maryland, USA

9) "Dr. Fabio Franchi, Former Dirigente Medico (M.D) in an Infectious Disease Ward, specialized in "Infectious Diseases" andHygiene and Preventive Medicine", Società Scientifica per il Principio di Precauzione (SSPP), Italy

10) Dr. med. Thomas Binder, Internist and Cardiologist (FMH), Switzerland

11) Prof. Dr. med. Henrik Ullrich, specialist Diagnostic Radiology, Chief Medical Doctor at the Center for Radiology of Collm Oschatz-Hospital, Germany

12) Prof. Dr. Makoto Ohashi, Professor emeritus, PhD in Microbiology and Immunology, Tokushima University, Japan

13) Dr. Stefano Scoglio, B.Sc. Ph.D., Microbiologist, Nutritionist, Italy

14) Dr. Marjolein Doesburg-van Kleffens (MSc, PhD), specialist in Laboratory Medicine (clinical chemistry), Maasziekenhuis Pantein, Beugen, The Netherlands

15) Dr. Dorothea Gilbert (MSc, PhD), PhD Environmental Chemistry and Toxicology. DGI Consulting Services, Oslo, Norway

16) Dr. Rainer J. Klement, PhD. Department of Radiation Oncology, Leopoldina Hospital Schweinfurt, Germany

17) Dr. Ruth Schruefer, PhD, human genetics/ immunology, Munich, Germany,

18) Dra. Berber W. Pieksma, General Practitioner, The Netherlands

19) Dr. med. Jan Bonte (GJ), Consultant Neurologist, The Netherlands

20) Dr. Bruno H. Dalle Carbonare (Molecular biologist), IP specialist, BDC Basel, Switzerland

21) Dr. Kevin P. Corbett, MSc Nursing (Kings College London) PhD (London South Bank) Social Sciences (Science & Technology Studies) London, England, United Kingdom

22) Prof. Dr. Ulrike Kämmerer, specialist in Virology / Immunology / Human Biology / Cell Biology, University Hospital Würzburg, Germany

Author's Contributions:

P.B: Planned and conducted the analyses and research, conceptualising the manuscript. BRM: Planned and conducted the research, conceptualising the figures and manuscript. MY: Conducted the analyses and research.
KMcK: Conducted the analyses and research, conceptualized the manuscript.
KS: Conducted the analyses and research. PMcS: Proofreading the analyses and research.

LA: Proofreading the analyses and research. FF: Proofreading the analyses and research. TB: Proofreading the analyses and research. HU: Proofreading the analyses and research.

MO: Proofreading the analyses and research.
SS: Proofreading the analyses and research.
MDvK: Proofreading the analyses and research.
DG: Proofreading the analyses and research.
RJK: Proofreading the analyses and research.
RS: Proofreading the analyses and research, and the manuscript.
BWK: Proofreading the analyses and research.
RvV: Proofreading the analyses and research.
JB: Proofreading the analyses and research.
KC: Proofreading the analyses and research.
UK: Planned and conducted the analyses and research, conceptualising the manuscript.

Additional Proof-Readers:

Saji N Hameed, Environmental Informatics, University of Aizu, Tsuruga, Ikki-machi, Aizuwakamatsu-shi, Fukushima, Japan Howard R. Steen, MA Chem. Eng. Cantab, Former Research Manager, Germany

Should you get vaccinated?

vaccinetruth
May 25, 2021

354 Comments

Note that views expressed in this opinion article are the writer's personal views and not necessarily those of TrialSite

by Steve Kirsch

I always get vaccinated. I have been fully vaccinated with the Moderna COVID vaccine. My three daughters have all been vaccinated.

I recently learned that these vaccines have likely killed over 25,800 Americans (which I confirmed 3 different ways) and disabled at least 1,000,000 more. And we're only halfway to the finish line. We need to PAUSE these vaccines NOW before more people are killed.

COVID vaccines. The mainstream media isn't asking any questions; they are playing along. YouTube, Facebook, Twitter, and others are all censoring content that goes against the "perfectly safe" narrative so nobody is the wiser. Tony Fauci, the "father of COVID," is still in his job even though all of this is his fault. Cliff Lane, who reports to Tony, is still sandbagging early treatments so that people will falsely believe that the vaccine is the only option. The Democrats are still asleep at the wheel by refusing to request Fauci's unredacted emails from the NIH which will prove he covered up the fact he created the virus in the first place. Biden is clueless urging Americans to vaccinate their kids with a deadly vaccine that has likely killed more than 25,000 Americans so far. Academics in the medical community are nearly all clueless, urging people to get the safe and effective vaccine. When I tried to bring this to the attention of leading academics they told me I was wrong and not to contact them ever again. Sound too hard to believe? I don't blame you. But there is a reason that this article is the most popular article that has ever been on TrialSiteNews with over 1M views so far. It's because everything I've said is true. And nobody will debate me live about it. They all refuse.

Based on what I **now** know about the miniscule vaccine benefits (less than a .5% reduction in absolute risk), side effects (including death), current COVID rates, and the success rate of early treatment protocols, **the answer I would give today to anyone asking me for advice as to whether to take any of the current vaccines would be, "Just say NO."** Waiting for Novavax (and other traditional vaccines) is a much safer option. If you get COVID in the meantime, treating with early treatment protocols that incorporate fluvoxamine and ivermectin is vastly superior to getting the most dangerous vaccine in the last 30 years.

Vaccines are particularly contraindicated if you have already been infected with COVID or are under age 20. For these people, I would say "**NO! NO! NO!**"

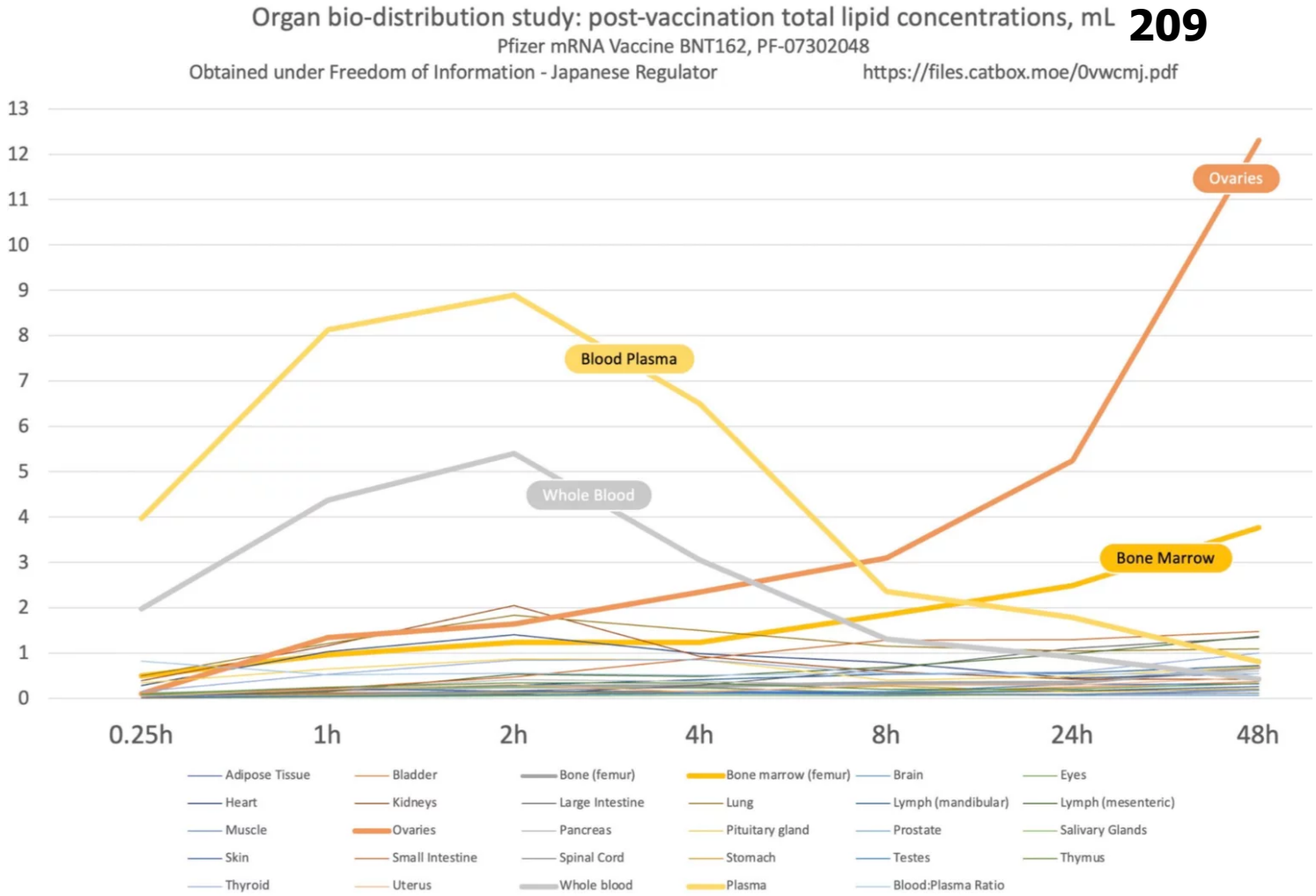
In this article, I will explain **what I have learned since I was vaccinated that totally changed my mind**. You will learn how these vaccines work and the shortcuts that led to the mistakes that were made. You will understand why there are so many side effects and **why these are so varied** and why they usually happen within 30 days of vaccination. You will understand why kids are having heart issues (for which there is no treatment), and temporarily losing their sight, and ability to talk. You will understand why as many as 3% may be severely disabled by the vaccine. You will understand why doctors aren't reporting these as vaccine-related.

In other words, **science says that kids are essentially already vaccinated**. So giving them a dangerous vaccine has virtually no benefit but significant downsides (like death).

But the academics are too vested in the false narrative to let one study take them down. I predict they will ignore the science and try to discredit it. That's exactly what they've done with fluvoxamine and ivermectin even though all those studies were published in peer reviewed journals too. They are good at suppressing science and convincing the masses that the vaccine is needed and safe, regardless of the actual facts. They believe the Phase 3 studies and consider real world events as anecdotal.

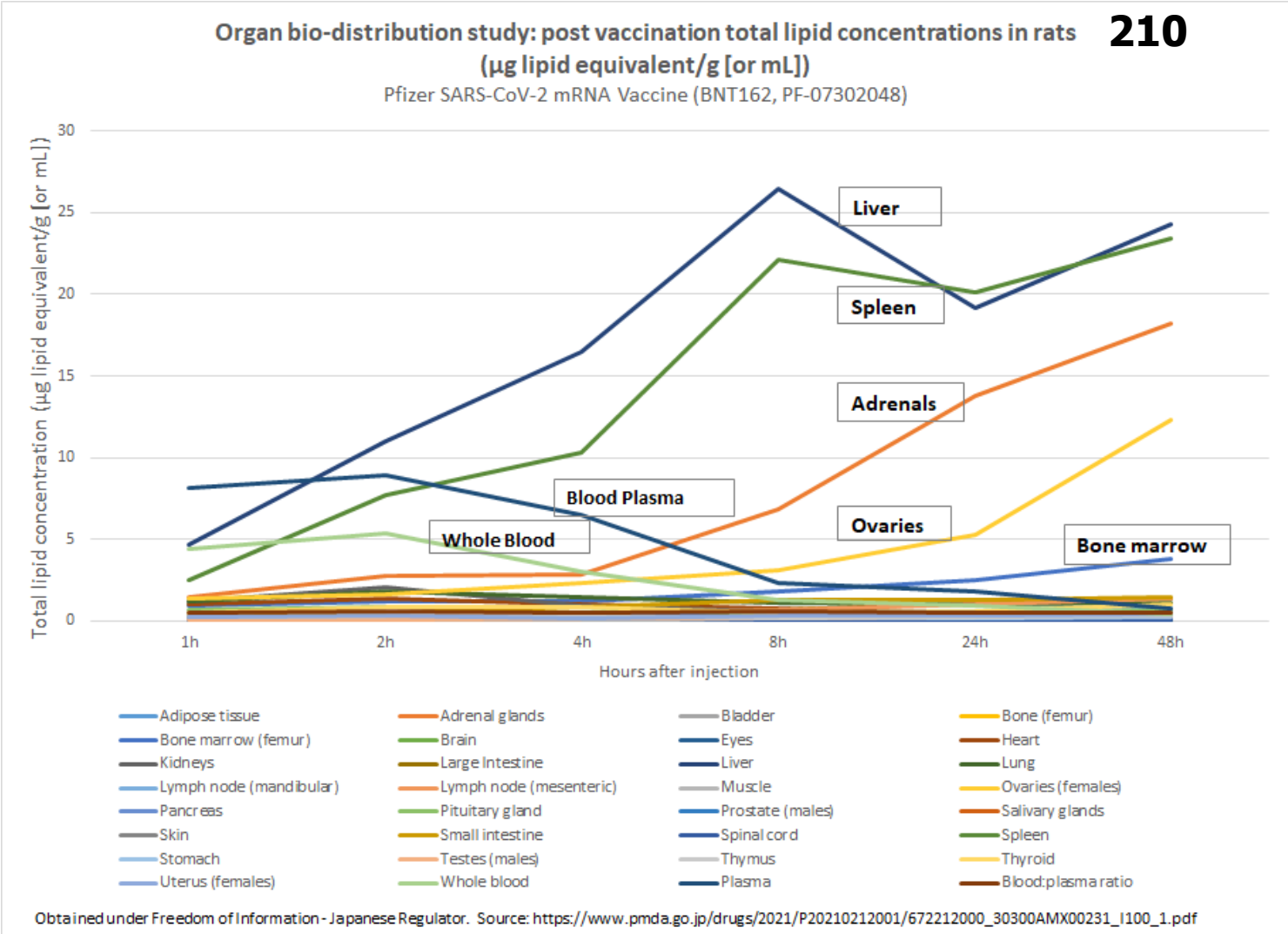
Here's the third item I need you to see. This is the biodistribution graph created from the Pfizer data obtained via Byram Bridle FOIA request to help you visualize where the vaccine is going in your child's body. This shows you the the sites where it cranks out the toxic spike protein; the higher the line, the greater the production of spike protein that can cause damage to blood vessels and cause inflammation.

NOTE: There are areas of the body that are not included here like the injection site (165), liver (24), spleen (23), and adrenals (18). These were not included so you can see more detail. The graph ends at 48 hours because that is the extent of the data provided in the original Pfizer study. The mRNA is basically mostly gone after 48 hours which is why it ends there. I did not commission this slide; it was created by PANDA.



Biodistribution of lipid nanoparticles which carry the mRNA show that the ovaries get the highest concentration. This turns the ovaries into a very large manufacturing plant to turn out toxic spike protein. Accumulation in the bone marrow is likely not good either. What are the long term implications of that?

Here's the chart with all the data (excluding the injection site). As you can see, the ovaries and bone marrow still show up prominently:



Here's what this means. This vaccine seeks out your daughter's ovaries and instructs the cells in the ovaries to turn out a very toxic spike protein. It also goes to your child's brain, heart, and other critical organs. This can cause deafness, blindness, inability to speak, myocarditis, pericarditis, and more at unacceptable rates. It may permanently damage your child's reproductive system. We just don't know. Would you like to volunteer your child for a clinical trial so we can find out? Well if so, and if your child concurs, then get vaccinated and be part of the largest experiment ever done on the human reproductive system.

OK, let's recap what we've learned so far, because there is a lot more to talk about. I am just getting started.

1. The destruction we are doing to our kid's hearts, brains and especially their ovaries. We are harming perfectly healthy young adults. For example, the miscarriage rates are alarming post vaccination: 82% spontaneous abortion rate before 20 weeks.
2. Approximately **2% of people report severe / still annoying side effects** based on the random sampling I've done. This number is extremely high but it totally explains why the "Vaccine Side

Effects" groups in Facebook had over 200,000 members before Facebook deleted them. There are much better options where no healthy person has any added risk of death or disability (since they will not need to be treated at all).

3. The government has been suppressing the fact that repurposed drugs work with virtually 100%success when given early with virtually zero side effects. So the better, safer alternative is considered "unproven" when Cliff Lane (head of the NIH COVID Guidelines who reports to Tony Fauci) knows without a doubt that it works.

Sound like a conspiracy theory? I don't blame you. I don't think there is a conspiracy (except for a select few such as those called out in Chris Martenson's excellent video on the coverup happening after the outbreak). I have no issues with anyone at Moderna or Pfizer or any government agency (**again with the exception of Tony Fauci and Cliff Lane** and a handful of others who were in on it and aren't talking). I think everyone else are all ethical people who started with the best intentions, shit happened, and now people don't want to see the reality because of the cognitive dissonance it would create. So the CDC and FDA ignore all the **subjective** safety signals (like alarming anecdotal reports from doctors) and rely on what I believe (based on info from CDC insiders) is a flawed serious event warning system (combined with pressure not to report that there is anything wrong). Hence everyone is acting like there is nothing wrong because their traditional alarm bells aren't triggering. **A 25X higher event rate** for myocarditis after vaccination… oh, completely normal. They justify that because they think that the vaccine is so helpful (a 10X reduction in cases) that even if there is death caused by the vaccine, society is better off net net. So they support the false narrative that the vaccine is safe. And none of them realize that early treatment of COVID is way better and safer since Fauci and Lane suppress the better option.

For example, why is Monica Gandhi calling for vaccinating kids including her own? Is she evil? Of course not! I asked her for the risk benefit calculation in this tweet. Will she reply? I doubt it. Most of the doctors who swallow the false narrative find it difficult to deal with the facts.

Also, let me point out that in this document I link to a number of sources, some of whom tout conspiracy theories like this is being done deliberately for nefarious purposes. I absolutely don't believe that. If I include a reference to someone else's material I do not endorse any conspiracy theories that are espoused by them. I will make one exception for Chris Martenson. All of his YouTube material I have watched of his work is all top notch, well done, and well supported. Watch this video of Dr. Chris Martenson taking down Fauci's original Senate testimony. It is priceless. Chris mentions my work at 47:30. It's hard to argue with his conspiracy theories.

Biden, CDC, FDA should call a STOP to this now until we know exactly how many people have been killed and/or disabled.

Promoting repurposed drug protocols and educating people to treat as early as possible (even before test results come back) is a safer and more effective approach that can reduce the absolute death toll to a fraction of those killed every year by the flu.

The censorship of patients and doctors is both troubling and unprecedented. Why are doctors threatened with loss of license for raising legitimate concerns? If the vaccine is as safe as they claim, why do we need to muzzzle doctors?

The reason a doctor or scientist isn't writing this article is simple: fear of retribution. You would never get another NIH grant in your career or ever get a drug approved by the FDA.

The lack of transparency is troubling. Nobody will say how many people have been killed by this vaccine. We know it is at least 4,200 in the US alone but is likely much higher. The V-SAFE database is hidden from public view.

How can a vaccine that has killed at least 20,000 people worldwide so far this year be mandatory, yet ivermectin which has killed less than 16 people over the past 30 years (and it's probably zero because the associations are never 100% accurate) is considered **too risky to recommend for COVID** despite 22 published positive studies (for early treatment). That's baffling.

The long term consequences of these vaccines are unknown. We should know these before we inject healthy young adults.

There are viable alternatives with a better risk-reward profile such as early treatment or waiting for the Novavax, Covaxin, or Valneva vaccines. The Valneva vaccine is expected to be variant proof and uses tried and tested vaccine technology.

The most important thing is to educate yourself on the potential benefits and risks of your options, talk with your doctor, and jointly make the decision that is best for you.

If you enjoyed reading this article, please:

1. Follow me on Twitter at @stkirsch
2. Tweet this article on Twitter and other networks
3. Join Vaccine Victims group on Locals (it is free) so when Twitter bans me, we can still talk
4. If you want to know how to treat COVID (acute, long haul, and vaccine syndrome), see Vaccine FAQ
5. If you are looking for a doc to prescribe these drugs, see How to treat COVID
6. If you'd like to read the latest information and reference documents (including videos and slide presentations), see Unsafe vaccines resources which has 40 pages of information and a nice summary at the start. It's also printable.

Steve Kirsch is a high-tech serial entrepreneur based in Silicon Valley. He has been a medical philanthropist for more than 20 years. When the pandemic started, he left his day job at M10 and started the COVID-19 Early Treatment Fund (CETF) which funds researchers from all over the world running outpatient clinical trials on repurposed drugs. CETF funded David Boulware's trials on hydroxychloroquine and the Phase 2 and Phase 3 fluvoxamine trials, among many other research projects. He was recently featured on 60 Minutes which highlighted his work with fluvoxamine. He has no conflicts of interest; his objective is to help save lives. In 2003, Hillary Clinton presented him with a National Caring Award. He wrote this article to share some of what he has learned over the past year about the failure of evidence-based medicine during a pandemic in the hopes that people will realize their mistakes and change their views.

Note that views expressed in this opinion article are the writer's personal views and not necessarily those of TrialSite, Inc. or the COVID-19 Early Treatment Fund.

Related

ANNEXURE P-14

London Times

https://www.londontimes.live/>

DOCTOR ON COVID VAX: “WE SCREWED-UP. WE DIDN’T REALIZE THE SPIKE PROTEIN IS A TOXIN” DOES THIS MEAN EVERYONE VAXINATED IS MANUFACTURING THEIR OWN SPIKE PROTEIN TOXINS IN THEIR OWN BODIES?

<

Doctor on COVID Vax: “We Screwed-Up. We Didn’t Realize the Spike Protein Is a Toxin” Does This Mean Everyone Vaxinated Is Manufacturing Their Own Spike Protein Toxins in Their Own Bodies?

August 10, 2021< https://www.londontimes.live/2021/08/10/>

Doctor on COVID Vax: "We Screwed-Up. We Didn't Realize the Spike Protein Is a Toxin" Does This Mean Everyone Vaxinated Is Manufacturing Their Own Spike Protein Toxins in Their Own Bodies?

By Hal Turner Radio Show

Audio from a radio show has emerged wherein Dr. Byram Bridle reveals the scientists behind the COVID-19 "Vaccine" made a terrible mistake.

According to the Doctor, who cites a brand new, peer-reviewed research study out of Japan **"They made a mistake – they thought the spike protein was a great target antigen, only to discover it is a toxin, that can travel to many organs of the body, causing severe damage."**

WORSE, the spike proteins generated by mRNA vaccines don't stay in the shoulder muscle, but spread to the brain, heart, ovaries, etc.

They also know that **the spike protein is what causes the damage with COVID**—and now it is clear how it is causing so much damage in other parts of the bodies of the vaccinated.

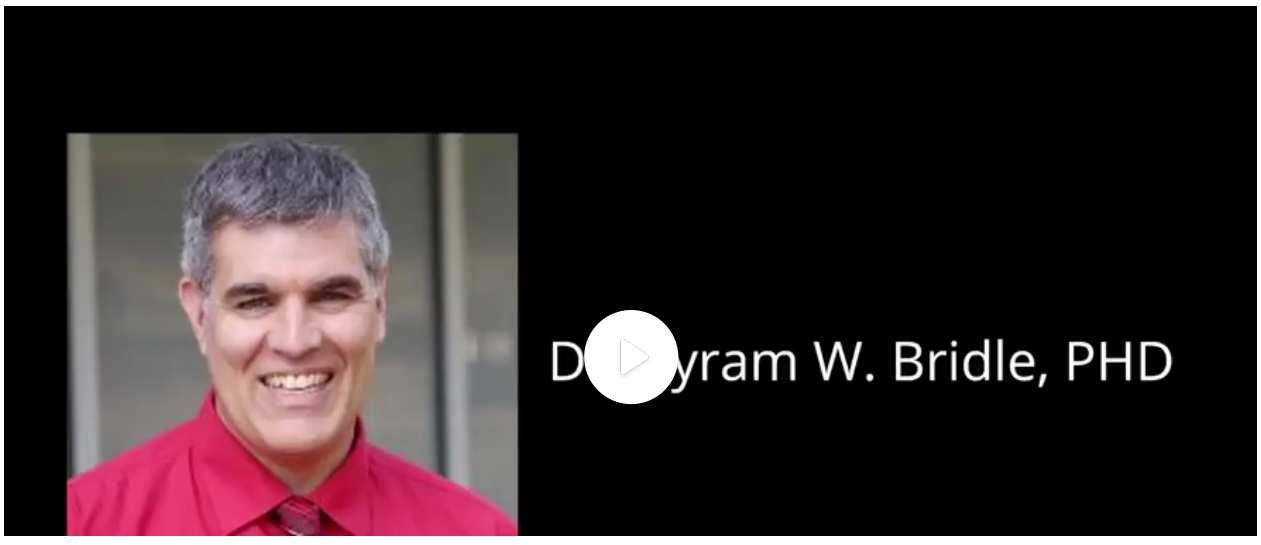
From the video below Dr. Bridle on why the vax injuries are happening:

Spike protein, on its own is the cause of the vascular, neurodegenerative, problems, not the virus.
In the original theory it stay's in deltoid, goes to local draining lymph node, activates immune system.
But a new bio-distribution study from Japan tracked the vax and spike proteins.
It gets into the blood within days of vax, accumulates in spleen, brain, bone marrow, liver, adrenal glands, with high concentrations in ovaries.

Spike protein is a pathogenic toxin that causes damage if in circulation, binds to platelets, epithelial cells of blood vessels, clotting, bleeding, heart problems, brain blood clotting.

Conclusion is "We made a big mistake, and didn't realize it till now." "We thought the spike protein was a great target antigen but never knew the spike protein itself was a pathogenic toxin protein." "By vaccinating people we are inadvertently inoculating them with a toxin."

Give ear to this 8 Minute video. If this Doctor is correct, and if the peer-reviewed report (**HERE < https://www.pmda.go.jp/drugs/2021/P20210212001/672212000_30300AMX00231_I100_1.pdf#page11>**) is accurate, almost everyone who took the vaccine is going to be dead very soon because their own bodies are now manufacturing the very spike protein which is a Toxin that will kill them.



The spike proteins generated by both the mRNA vaccines **don't** stay in the shoulder muscle, **but spread to the brain, heart, ovaries,** etc. They also know that the spike protein is what causes the damage with Covid—and now it is clear how it is causing so much damage in other parts of the bodies of the vaccinated.

< https://www.londontimes.live/global-issues/vax

< https://www.londontimes.live/state-of-affairs/cd

RW Malone MD, MS
Consulting and Analytics for Biopharma
434-979-0090
357 Hebron Valley Rd, Madison, VA 22727

www.rwmalonemd.com
Your World is
Our World

June 19, 2021

From: Robert W. Malone, MD, MS
357 Hebron Valley Rd,
Madison, VA 22727

To: Whom it may Concern

I am writing this letter to support Dr. Bridle's good character and his right to freely express his scientific opinion, which is backed up by the literature and well informed deductive reasoning.

I am a US-based physician and scientist with an extensive record of successful innovation in basic and applied science, pathology, molecular virology, immunology, vaccine development, biodefense, project management, clinical development, regulatory affairs, and bioethics. I have been working in this area since 1984, and have been through multiple outbreaks – usually supporting either pharmaceutical clients or the US Department of Defense. I have been granted "secret" clearance for the DoD. I played a key role in advancing the PHAC rVSV-ZEBOV Ebola vaccine candidate and engaging Merck in development, which resulted in the eventual licensure of this very important product of Canadian PHAC research.

I am also the original inventor of mRNA vaccines and DNA vaccines. This claim is substantiated by academic publications as well a large suite of US and worldwide patents with a filing date of 1989.

I have independently assessed most of the data which serves as the basis for Dr. Bridle's communications regarding safety risks associated with the COVID-19 genetic vaccines, concur with his findings, and have independently raised my concerns with the US FDA including speaking directly with CBER director Peter Marks.

I am particularly alarmed and surprised by the bioethical positions being taken by the government of Canada regarding these experimental – stage vaccines, and very surprised. I have always considered the government and people of Canada to be eminently reasonable, almost to a fault. These policies appear contrary to what I have been trained as the bedrock principles of clinical research/human subjects bioethics.

And then there is the censorship of legitimate academic discourse, which brings us back to the specific case of Dr. Bridle. In short, do his accusers have no shame? I am truly shocked. Again, this is contrary to everything I had ever believed about the people and culture of Canada. I guess I will need to re-think my assumptions about Canadian fundamental reasonableness – ey?

Furthermore, these attacks on him will make him a global martyr and amplify his message. Is that really good public policy?

RW Malone MD, MS
Consulting and Analytics for Biopharma
434-979-0090
357 Hebron Valley Rd, Madison, VA 22727

www.rwmalonemd.com
Your World is
Our World

Please stop. Think about what is going on here. This is not fair. This is not right. This is not proper. Dr. Bridle has examined the data available to him and has drawn reasonable conclusions about the meaning of that data in toto. He is not profiting from this. There are no financial conflicts of interests. He is not someone seeking fame and fortune. He is doing what he can, in good faith, to help protect the people of Canada and the world – and particularly the adolescents and children.

In sum, in regards to COVID-19, I find the general censorship of the government of Canada, the bioethical lapses, and this specific example involving Dr. Bridle to be particularly egregious, and inconsistent with all I had previously believed regarding the fundamental reasonableness and commitment to fairness of Canadian political and social culture.

Please stop politicizing science. The scientific process requires dissent and discussion to arrive at truth. This is a central tenant. Dr. Bridle has spoken truth as he sees it. Others may interpret the data differently. My assessment is very much aligned with that of Dr. Bridle. That does not make it right or wrong. Time will sort this out. But I am quite sure that the attempts to silence Dr. Bridle and damage his career and reputation are fundamentally wrong.

Regardless of your or my individual assessments and opinions, please let science and the scientific process resolve this. These attacks on the credibility of Dr. Bridle and his good faith efforts to provide an alert concerning safety signals associated with these vaccines are highly inappropriate and counterproductive. I suspect that history will not look back on this kindly. Canadians have not always been on the right side of history – witness the indigenous peoples. But in my experience they do try to do the right and proper thing.

So do the right thing here.

Sincerely

Robert W Malone, MD, MS

GlobalResearch
Center for Research on Globalization

Inventor of mRNA Technology: Vaccine Causes Lipid Nanoparticles to Accumulate in 'High Concentrations' in Ovaries

By Megan Redshaw
Global Research, June 18, 2021
Children's Health Defense 17 June 2021

Region: USA
Theme: Science and Medicine

***

On the "Dark Horse Podcast," Dr. Robert Malone, creator of mRNA vaccine technology, said the COVID vaccine lipid nanoparticles — which tell the body to produce the spike protein — leave the injection site and accumulate in organs and tissues.

On June 10, Dr. Robert Malone, creator of mRNA vaccine technology, joined evolutionary biologist Bret Brownstein, Ph.D., for a 3-hour conversation on the "Dark Horse Podcast" to discuss multiple safety concerns related to the Pfizer and Moderna vaccines.

In this short outtake from the full podcast, Malone, Brownstein and tech entrepreneur Steve Kirsch touch on the implications of the controversial Japanese Pfizer biodistribution study. The study was made public earlier this month by Dr. Byram Bridle, a viral immunologist.

They also discuss the lack of proper animal studies for the new mRNA vaccines, and the theory, espoused by virologist Geert Vanden Bossche, Ph.D., that mass vaccination with the mRNA vaccines could produce ever more transmissible and potentially deadly variants.

As The Defender reported June 3, Bridle received a copy of a Japanese biodistribution study — which had been kept from the public — as a result of a freedom of information request made to the Japanese government for Pfizer data.

Prior to the study's disclosure, the public was led to believe by regulators and vaccine developers that the spike protein produced by mRNA COVID vaccines stayed in the shoulder where it was injected and was not biologically active — even though regulators around the world had a copy of the study which showed otherwise.

The biodistribution study obtained by Bridle showed lipid nanoparticles from the vaccine did not stay in the deltoid muscle where they were injected as the vaccine's developers claimed would happen, but circulated throughout the body and accumulated in large concentrations in organs and tissues, including the spleen, bone marrow, liver, adrenal glands and — in

"quite high concentrations" — in the ovaries.

The mRNA — or messenger RNA — is what tells the body to manufacture the spike protein. The lipid nanoparticles are like the "boxes" the mRNA is shipped in, according to Malone. "If you find lipid nanoparticles in an organ or tissue, that tells you the drug got to that location," Malone explained.

According to the data in the Japanese study, lipid nanoparticles were found in the whole blood circulating throughout the body within four hours, and then settled in large concentrations in the ovaries, bone marrow and lymph nodes.

Malone said there needed to be monitoring of vaccine recipients for leukemia and lymphomas as there were concentrations of lipid nanoparticles in the bone marrow and lymph nodes. But those signals often don't show up for six months to three or nine years down the road, he said.

Usually, signals like this are picked up in animal studies and long-term clinical trials, but this didn't happen with mRNA vaccines, Malone said.

Malone said there are two adverse event signals that are becoming apparent to the U.S. Food and Drug Administration (FDA). One of them is thrombocytopenia — not having enough platelets, which are manufactured in the bone marrow. The other is reactivation of latent viruses.

Malone found the ovarian signal perplexing because there is no accumulation in the testes.

Malone said the original data packages contained this biodistribution information. "This data has been out there a long time" within the protected, non-disclosed, purview of the regulators across the world, he said.

According to Malone, the FDA knew the COVID spike protein was biologically active and could travel from the injection site and cause adverse events, and that the spike protein, if biologically active, is very dangerous.

In fact, Malone was one of many scientists to warn the FDA about the dangers of the free spike protein.

Malone suggested autoimmune issues may be related to free-circulating spike protein which developers assured would not happen. To pick up autoimmune issues, a 2- to 3- year follow-up period in phase 3 patients would be required to monitor for potential autoimmune consequences from vaccines — but that monitoring didn't happen with the Pfizer and Moderna vaccines.

Pfizer and Moderna also didn't conduct proper animal studies, Brownstein said. What the animal models give us is a signal that alerts us to what we need to follow up on in humans.

Brownstein said:

> "We've got very alarming short-term stuff. We've got short-term stuff that is alarming on the basis of where we find these lipids, where we find the spike proteins — those things are reasons for concern because it wasn't supposed to be this way. We've also

> got an alarming signal in terms of the hazards and deaths or the harms and the deaths that are reported in the system and there are reasons to think they are dramatic under-reports."

Vaden Bossche got it right

One of the potential harms from the vaccines, Brownstein said, was made famous by Vanden Bossche, a vaccinologist who worked with GSK Biologicals, Novartis Vaccines, Solvay Biologicals, Bill & Melinda Gates Foundation's Global Health Discovery team in Seattle, and Global Alliance for Vaccines and Immunization in Geneva.

Earlier this year, Vanden Bossche put out a call to the World Health Organization, supported by a 12-page document, that described the "uncontrollable monster" that a global mass vaccination campaign could potentially unleash.

Vanden Bossche said a combination of lockdowns, and extreme selection pressure on the virus induced by the intense global mass vaccination program, might diminish the number of cases, hospitalizations and deaths in the short-term, but ultimately, will induce the creation of more mutants of concern. This is what Vanden Bossche calls "immune escape" (i.e. incomplete sterilization of the virus by the human immune system, even following vaccine administration).

Immune escape will in turn trigger vaccine companies to further refine vaccines that will add, not reduce, the selection pressure, producing ever more transmissible and potentially deadly variants.

The selection pressure will cause greater convergence in mutations that affect the critical spike protein of the virus that is responsible for breaking through the mucosal surfaces of our airways, the route used by the virus to enter the human body.

The virus will effectively outsmart the highly specific antigen-based vaccines being used and tweaked, depending on the circulating variants. All of this could lead to a hockey stick-like increase in serious and potentially lethal cases — in effect, an out-of-control pandemic.

Malone said:

> "Vanden Bossche's concern is not theoretical. It is real and we have the data. We're stuck with this virus or its downstream variants pretty much for the rest of our lives and it's going to become more like the flu. We will have continuing evolution and circulation of variants, and that is an escape."

*

Note to readers: Please click the share buttons above or below. Follow us on Instagram, @crg_globalresearch. Forward this article to your email lists. Crosspost on your blog site, internet forums. etc.

Megan Redshaw is a freelance reporter for The Defender. She has a background in political science, a law degree and extensive training in natural health.

Featured image is from Children's Health Defense

ANNEXURE P-17

Title page

Addressing anti-syncytin antibody levels, and fertility and breastfeeding concerns, following BNT162B2 COVID-19 mRNA vaccination

Citra NZ Mattar, PhD,[1,2] Winston Koh, PhD,[3] Yiqi Seow, PhD,[3] Shawn Hoon, PhD,[3] Aparna Venkatesh, PhD,[3] Pradip Dashraath, MRCOG,[4] Li Min Lim, MRCOG,[4] Judith Ong, MRCOG,[4] Rachel Lee, MB,BS,[4] Nuryanti Johana, BSc,[5] Julie SL Yeo, BSc,[5] David Chong, BSc,[1] Lay-Kok Tan, FRANZCOG,[6] Jerry Chan, PhD,[5,7] Mahesh Choolani, PhD,[1,2] Paul Anantharajah Tambyah, MD,[8,9]

[1]Department of Obstetrics and Gynaecology, Yong Loo Lin School of Medicine, National University of Singapore
[2]Department of Obstetrics and Gynaecology, National University Health System, Singapore
[3]Molecular Engineering Laboratory, Institute of Molecular and Cell Biology, Agency for Science Technology and Research, Singapore
[4]Department of Obstetrics and Gynaecology, National University Hospital, Singapore
[5]Department of Reproductive Medicine, KK Women's and Children's Hospital, Singapore
[6]Department of Maternal Fetal Medicine, KK Women's and Children's Hospital, Singapore
[7]Cancer and Stem Cells Program / OBGYN Academic Clinical Program, Duke-NUS Medical School
[8]Department of Medicine, Yong Loo Lin School of Medicine, National University of Singapore
[9]Division of Infectious Diseases, Department of Medicine, National University Health System, Singapore

Correspondence to:

Associate Professor Citra Nurfarah Zaini Mattar, MRANZCOG, Ph.D, Department of Obstetrics & Gynaecology, Yong Loo Lin School of Medicine, National University of Singapore obgcnzm@nus.edu.sg

Professor Paul Anantharajah Tambyah, MD, Division of Infectious Disease, Department of Medicine Yong Loo Lin School of Medicine, National University of Singapore, mdcpat@nus.edu.sg

Address: Yong Loo Lin School of Medicine, NUS, NUHS tower block, 1E Kent Ridge Road, Singapore 119228

Short title: Covid19 vaccine hesitancy and syncytin antibodies

Keywords: SARS-CoV-2; COVID-19; pregnancy; mRNA vaccine; anti-syncytin-1; breast milk; fertility

What are the novel findings of this work?

COVID-19 vaccination with BNT162B2 did not elicit a cross-reacting humoral response to human syncytin-1 despite robust neutralising activity to the SARS-CoV2 spike protein, and while vaccine mRNA was isolated from plasma, it was not found in breast milk.

What are the clinical implications of this work?

Our work directly addresses the fertility and breastfeeding concerns fuelling vaccine hesitancy among reproductive-age women, by suggesting that BNT162B2 vaccination is unlikely to cause adverse effects on the developing trophoblast, via cross-reacting anti-syncytin-1 antibodies, or to the breastfed neonate, via mRNA breast milk transmission.

Abstract

Objective: To determine whether antibodies against the SARS-CoV-2 spike protein following BNT162B2 (Pfizer-BioNTech) COVID-19 mRNA vaccination cross-react with human syncytin-1 protein, and if BNT162B2 mRNA enters breast milk.

Methods: In this observational cohort study of female front-line workers with no history of COVID-19 infection, we amplified BNT162B2 mRNA in plasma and breast milk and assayed anti-SARS-CoV-2 neutralising antibodies and anti-human syncytin-1 binding antibodies in plasma, at early (1-4 days) and late (4-7 weeks) time points following first-dose vaccination.

Results: Fifteen consented participants (mean age 40.4 years, various ethnicities) who received at least one dose of BNT162B2, including five breast-feeding women and two women who were inadvertently vaccinated in early pregnancy, were recruited. BNT162B2 mRNA, detected by amplifying part of the spike-encoding region, was detected in plasma 1-4 days following the first dose (n=13), but not 4-5 weeks later (n=2), nor was the mRNA isolated from aqueous or lipid breast milk fractions collected 0-7 days post-vaccination (n=5). Vaccine recipients demonstrated strong SARS-CoV-2 neutralising activity by at least four weeks after the first dose (n=15), including the two pregnant women. None had placental anti-syncytin-1 binding antibodies at either time-point following vaccination.

Conclusions: BNT162B2-vaccinated women did not transmit vaccine mRNA to breast milk, and did not produce a concurrent humoral response to syncytin-1, suggesting that cross-reactivity to syncytin-

1 on the developing trophoblast, or other adverse effects in the breast-fed infant from vaccine mRNA ingestion, are unlikely.

Introduction

Vaccine hesitancy threatens to compromise global vaccination efforts with lipid nanoparticle-encapsulated mRNA-based COVID-19 vaccines employed under emergency use authorisation to end the pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and its emerging variants. Conspiracy theories propagated through social media cast doubts over the safety of these novel vaccines for fertility and breastfeeding,[1, 2] such that 13% of unvaccinated persons in the USA believe that COVID-19 vaccination may result in infertility.[3] One such claim generating significant traction suggests that vaccine mRNA-translated antibodies – which target the SARS-CoV-2 spike protein – cross-react with human syncytin-1, resulting in infertility and pregnancy loss. Syncytin proteins, which originate from endogenous human retroviruses, are involved in gamete fusion during fertilization and normal placental development,[4-8] and amino acid sequence similarities between syncytin proteins and the SARS-CoV-2 spike protein S2 domain raise the possibility of cross-reacting antibodies following COVID-19 vaccination.[9]

This worrying spectre of disinformation may extend to BNT162B2 mRNA persistence, with the possibility of neonatal transmission via breast milk. Affected women may opt to defer vaccination or temporarily stop breast-feeding due to the lack of data on reproductive or lactational toxicity, even though COVID-19 vaccination is not contraindicated in pregnant or breastfeeding women, or for women planning pregnancy.[10, 11] Given the enduring susceptibility of pregnant and peripartum women to COVID-19 complications, we find these trends worrying as they compound vaccine hesitancy among persons of reproductive age.[12] Although attempts have been made to correct this misinformation by mainstream news outlets and the scientific community,[2, 13] anti-vaccination pundits continue to propagate vaccine scepticism and dampen confidence in vaccine safety, even among female healthcare professionals.[14] To begin to address these issues, we investigated post-vaccination mRNA persistence and anti-syncytin-1 antibodies in plasma and breast milk in female at-risk front-line workers and vaccine recipients.

Methods

Participants

Female front-line workers were approached at the National University Hospital, Singapore, to participate in this institutional review board-approved study (DSRB2012/00917) between February and April 2021. Volunteers were eligible if they were scheduled to receive BNT162B2 and consented to collection of blood and breast milk (where applicable) before and after the first dose. Data is presented according to STROBE guidelines.[15]

Samples

Plasma was collected at Day 0 (pre-vaccination), 1-4 days and 4-7 weeks, while breast milk was collected within 24 hours and daily for the first week, following the first dose. Blood and expressed breast milk were centrifuged at 1500G and 3000G respectively. Plasma, aqueous and lipid factions of breast milk were flash frozen before total RNA extraction with Zymo Research Quick DNA/RNA viral kit (Zymo Research, Irvine, CA). Briefly, samples were treated with DNA/RNA shield, Proteinase K, and viral DNA/RNA buffer to bind DNA and total RNA to the Zymo-Spin™ IIC-XLR Column. DNA was removed with DNase 1, RNA eluted in RNase-free Water, checked for purity and quantified spectrophotometrically.

One-step real time quantitative PCR for detection of vaccine mRNA

TaqMan Primers were designed using the published mRNA sequence of BNT162B2 that was made available to the public,[16] and amplified an 87bp segment of the spike-encoding region to determine the presence of vaccine mRNA in plasma and breast milk (Table 1). Isolated RNA, primers and probe were added to THUNDERBIRD™ Probe One-step (Toyobo, Osaka) qRT-PCR master mix and the real time PCR protocol was run on QuantStudio™ 1 Real-Time PCR System (Applied Biosystems, Foster City, CA). Negative controls were run simultaneously using water and RNA isolated from pre-vaccination plasma. Positive controls were day 1 post-vaccination RNA samples.

Library preparation and whole transcriptome sequencing

First and second strand synthesis was performed with extracted plasma RNA as input (Ovation® RNA-seq system v2 kit, NuGEN Technologies Inc, Redwood City, CA). Illumina Nextera XT DNA Library Preparation kit was used for library production and barcoding. Paired end-sequencing of 300bp read length was performed on the iSeq100 sequencer (Illumina, San Diego, CA).

Sequenced read analyses and assembly

Sequenced reads were aligned to human references using HISAT2 and filtered out. Remaining non-human reads were assembled using SPAdes. Comparative analyses with published Pfizer sequences and MT380725 were performed with MUMMER. Multiple genome alignment and visualization were done using the MUSCLE and R package ggmsa (https://github.com/YuLab-SMU/ggmsa).[17-20]

Anti-syncytin-1 antibody semi-quantitative ELISA

96-well Maxisorp plates (Thermo Fisher Scientific, Massachusetts) were coated with 100ng of human syncytin-1 recombinant protein (MyBioSource, San Diego) overnight (4^{o}C), then washed and blocked with 6% bovine serum albumin (BSA; Sigma, Missouri) in 0.05% Tween:1X PBS (PBST) at 37^{o}C. Pre-vaccination plasma served as the negative control, giving an optical density reading at an absorbance wavelength of 492nm (OD_{492}) of ~0.1.

Positive controls were produced by coating wells with 100ng of human syncytin-1 recombinant protein and incubating with rabbit anti-human syncytin-1 antibody (MyBioSource) at 1:250 dilution, selected after optimization as it gave a consistent OD_{492} of ~0.9. This readout was based on standard ELISAs, as there is no data on clinically-significant thresholds of anti-syncytin-1 antibodies.

Samples and controls were diluted 1:50 with dilution buffer (2% BSA in PBST), incubated in prepared plates at room temperature, then incubated with horseradish peroxidase-conjugated goat anti-rabbit secondary antibody (for positive controls, at 1:1000 dilution; Thermo Fisher Scientific, Massachusetts), or goat anti-rhesus secondary antibody (for all samples, at 1:4000 dilutions; Southern Biotech, Alabama), washing between steps. Plates were loaded with o-phenylenediamine dihydrochloride substrate (Sigma) and colorimetric reactions arrested at 3 minutes with 3M HCl. OD_{492} was analysed in the Sunrise microplate reader (Tecan, Mannedorf, Switzerland). Background absorbance was eliminated with a blank control of dilution buffer.

SARS-COV-2 Neutralising Antibody assay

Neutralizing antibodies (NAb) against SARS-CoV-2 were detected using the SARS-CoV-2 Surrogate Virus Neutralization Test Kit (GenScript, NJ). Samples and controls were pre-incubated with HRP-Receptor Binding Domain (RBD) to allow the binding of circulating NAb to HRP-RBD, and the mixture added to the capture plate (pre-coated with human angiotensin converting enzyme-2 protein).

Circulating NAb HRP-RBD complexes in the supernatant, if any, were removed during washing while unbound HRP-RBD and HRP-RBD bound to non-neutralizing antibodies remained on the capture plate. Colorimetric reactions were elicited and stopped with the addition of TMB and Stop solutions respectively, and colour intensity read at absorbance wavelength of 450nm in the Sunrise microplate reader. Inhibition was calculated based on the OD_{450} absorbance (inversely proportionate to anti-SARS-CoV-2 NAb titers) and inhibition ≥30% was interpreted as a positive result according to manufacturer's instructions.

Post-hoc analysis

Results are expressed as mean±SD and compared by one-way ANOVA using Tukey correction for multiple comparisons.

Results

Participants

Fifteen female at-risk front-line workers who were eligible for the vaccine, including five breast-feeding mothers and two women inadvertently vaccinated in early pregnancy, were recruited for this institutional review board-approved study (DSRB2012/00917) conducted at the National University Hospital of Singapore. No subject was previously diagnosed with COVID-19. Mean age was 40.4±12.2 years. Participants were of Malay, Indian and Chinese ethnicities. All women received two doses of BNT162B2 according to the prescribed schedule, except the two pregnant subjects who each had a single dose before pregnancy confirmation, and subsequently did not receive the second dose (Table 2).

Vaccine mRNA was amplified from post-vaccination plasma and perfectly aligned with the published sequence

Plasma BNT162B2 mRNA was detected within 4 days of vaccination (n=13), including in all breastfeeding women (Ct<30, all samples, Figure 1A,B), but no amplification was observed in either aqueous or lipid breast-milk factions (days 0-7, n=5, Figure 1B). Early plasma samples were not obtained from the two participants with undiagnosed pregnancies at the time of vaccination as they

had not yet been recruited (subjects 101, 102); subsequently these two participants did not amplify plasma BNT162B2 mRNA at week 4, the only single-dose samples at this time point as the other recipients had received their second dose by week 3.

High-quality non-human sequenced reads from whole transcriptome sequencing of plasma- and breast milk-extracted circulating RNA were assembled to obtain draft genomic scaffolds of 4196bp (average coverage of 162X), comparable in size to BNT162B2 mRNA, and we observed perfect alignment from 120-4077bp against the published sequence. No scaffolds greater than 2kb were obtained for pre-vaccination plasma. Multiple sequence alignment performed with GenBank sequence MT380725 (SARS-CoV-2 spike protein) demonstrated agreement at the nucleotide level (Figure 1C).

Anti-syncytin antibodies were not detected in post-vaccination plasma

To determine if recipients mounted the desired immune response to BNT162B2, we first analysed SARS-CoV-2 neutralising antibodies (NAb), finding negative responses at day 0-4 (post-vaccination inhibition at 14.7±4.7%), and strongly positive responses 4-7 weeks post-vaccination (inhibition at 98.7±1.2%, $p<0.001$, Figure 2A), including in the pregnant women (inhibition >89.0% following a single dose). At the same time-points, anti-syncytin-1 binding activities were far below the positive control and were interpreted as negative (Figure 2B).

Discussion

Our study shows that BNT162B2-vaccinated women did not transmit vaccine mRNA to breast milk, and supports the continuation of breastfeeding which may transfer protective antibodies.[21] These data are limited by the lack of surveillance beyond one week post-vaccination. Vaccinated woman should be informed about the current absence of breastfeeding safety data.[10] Our small study is also the first to investigate anti-syncytin antibodies following BNT162B2 vaccination. Our finding that BNT162B2-vaccinated women did not produce a significant antibody response to syncytin-1, despite demonstrating strong neutralising activity against SARS-CoV-2, is important because it suggests that cross-reactivity to syncytin proteins on the developing trophoblast is unlikely. This is in line with computerised basic local alignment search tool (BLAST) comparisons of published nucleotide and protein sequences which have shown very limited amino acid sequence similarity – only two 2-amino acid stretches – between syncytin-1 and the S2 domain of the SARS-CoV-2 spike protein; at least 80

continuous amino acid stretches comprising >35% sequence homology is required for cross-reactivity between proteins to occur.[4] We did not however, examine duration of mRNA persistence or the clinical significance of anti-syncytin-1 antibody levels. As such, we encourage a restrained interpretation of our findings, as post-authorisation surveillance data from the US Vaccine Adverse Event Reporting System (VAERS) highlight spontaneous miscarriage as the most common obstetric outcome after COVID-19 mRNA vaccination.[22] Longitudinal surveillance of larger numbers of reproductive-age women vaccinated pre-conception and in early pregnancy should assist in parsing the role of anti-syncytin antibodies in fertility and pregnancy.

Acknowledgements

This study was funded by National University of Singapore IRB Appointment Research Fund to PAT and National Medical Research Council, Singapore COVID-19 Gap Funding (COVID19FR3-0090) to WK,YS, SH.

References

1. S. Stecklow and A. MacAskill. SPECIAL REPORT The ex-Pfizer scientist who became an anti-vax hero. In *Book SPECIAL REPORT The ex-Pfizer scientist who became an anti-vax hero*, Editor (ed)^(eds). Reuters: City, 2021.
2. V. Male. Are COVID-19 vaccines safe in pregnancy? *Nat Rev Immunol* 2021; **21**: 200-201. DOI 10.1038/s41577-021-00525-y.
3. L. Hamel, A. Kirzinger, L. Lopes, A. Kearney, G. Sparks and M. Brodie. KFF COVID-19 Vaccine Monitor: January 2021. Vaccine Hesitancy. In *Book KFF COVID-19 Vaccine Monitor: January 2021. Vaccine Hesitancy.*, Editor (ed)^(eds). KFF: City, 2021.
4. B. Bjerregaard, J. G. Lemmen, M. R. Petersen, E. Østrup, L. H. Iversen, K. Almstrup, L. I. Larsson and S. Ziebe. Syncytin-1 and its receptor is present in human gametes. *Journal of Assisted Reproduction and Genetics* 2014; **31**: 533-539. DOI 10.1007/s10815-014-0224-1.
5. R. M. Roberts, T. Ezashi, L. C. Schulz, J. Sugimoto, D. J. Schust, T. Khan and J. Zhou. Syncytins expressed in human placental trophoblast. *Placenta* 2021. DOI 10.1016/j.placenta.2021.01.006.
6. B. Soygur and H. Moore. Expression of Syncytin 1 (HERV-W), in the preimplantation human blastocyst, embryonic stem cells and trophoblast cells derived in vitro. *Hum Reprod* 2016; **31**: 1455-1461. DOI 10.1093/humrep/dew097.
7. B. S. Holder, C. L. Tower, V. M. Abrahams and J. D. Aplin. Syncytin 1 in the human placenta. *Placenta* 2012; **33**: 460-466. DOI 10.1016/j.placenta.2012.02.012.
8. B. Soygur, L. Sati and R. Demir. Altered expression of human endogenous retroviruses syncytin-1, syncytin-2 and their receptors in human normal and gestational diabetic placenta. *Histology and histopathology* 2016; **31**: 1037-1047. DOI 10.14670/hh-11-735.
9. M. Kloc, A. Uosef, J. Z. Kubiak and R. M. Ghobrial. Exaptation of Retroviral Syncytin for Development of Syncytialized Placenta, Its Limited Homology to the SARS-CoV-2 Spike Protein and Arguments against Disturbing Narrative in the Context of COVID-19 Vaccination. *Biology (Basel)* 2021; **10**. DOI 10.3390/biology10030238.

10. Centers_for_Disease_Control_and_Prevention. Information about COVID-19 Vaccines for People who Are Pregnant or Breastfeeding. In *Book Information about COVID-19 Vaccines for People who Are Pregnant or Breastfeeding*, Editor (ed)^(eds). CDC: City, 2021.
11. Ministry_of_Health_Singapore. Vaccination Information Sheet (for Vaccination Recipients). In *Book Vaccination Information Sheet (for Vaccination Recipients)*, Editor (ed)^(eds). Ministry of Health, Singapore: City, 2020.
12. S. Kadiwar, J. J. Smith, S. Ledot, M. Johnson, P. Bianchi, N. Singh, C. Montanaro, M. Gatzoulis, N. Shah and E.-F. Ukor. Were pregnant women more affected by COVID-19 in the second wave of the pandemic? *The Lancet* 2021. DOI 10.1016/s0140-6736(21)00716-9.
13. A. Rodriguez. No, the COVID-19 vaccine doesn't cause infertility in women. In *Book No, the COVID-19 vaccine doesn't cause infertility in women*, Editor (ed)^(eds). USA TODAY: City, 2020.
14. Pulse on the Nation's Nurses COVID-19 Survey Series: COVID-19 Vaccine. https://www.nursingworld.org/practice-policy/work-environment/health-safety/disaster-preparedness/coronavirus/what-you-need-to-know/covid-19-vaccine-survey/.
15. E. von Elm, D. G. Altman, M. Egger, S. J. Pocock, P. C. Gøtzsche and J. P. Vandenbroucke. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. *Int J Surg* 2014; **12**: 1495-1499. DOI 10.1016/j.ijsu.2014.07.013.
16. F. P. Polack, S. J. Thomas, N. Kitchin, J. Absalon, A. Gurtman, S. Lockhart, J. L. Perez, G. Pérez Marc, E. D. Moreira, C. Zerbini, R. Bailey, K. A. Swanson, S. Roychoudhury, K. Koury, P. Li, W. V. Kalina, D. Cooper, R. W. Frenck, Jr., L. L. Hammitt, Ö. Türeci, H. Nell, A. Schaefer, S. Ünal, D. B. Tresnan, S. Mather, P. R. Dormitzer, U. Şahin, K. U. Jansen and W. C. Gruber. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. *The New England journal of medicine* 2020; **383**: 2603-2615. DOI 10.1056/NEJMoa2034577.
17. D. Kim, J. M. Paggi, C. Park, C. Bennett and S. L. Salzberg. Graph-based genome alignment and genotyping with HISAT2 and HISAT-genotype. *Nat Biotechnol* 2019; **37**: 907-915. DOI 10.1038/s41587-019-0201-4.
18. R. C. Edgar. MUSCLE: a multiple sequence alignment method with reduced time and space complexity. *BMC Bioinformatics* 2004; **5**: 113. DOI 10.1186/1471-2105-5-113.
19. A. Bankevich, S. Nurk, D. Antipov, A. A. Gurevich, M. Dvorkin, A. S. Kulikov, V. M. Lesin, S. I. Nikolenko, S. Pham, A. D. Prjibelski, A. V. Pyshkin, A. V. Sirotkin, N. Vyahhi, G. Tesler, M. A. Alekseyev and P. A. Pevzner. SPAdes: a new genome assembly algorithm and its applications to single-cell sequencing. *J Comput Biol* 2012; **19**: 455-477. DOI 10.1089/cmb.2012.0021.
20. A. L. Delcher, A. Phillippy, J. Carlton and S. L. Salzberg. Fast algorithms for large-scale genome alignment and comparison. *Nucleic Acids Res* 2002; **30**: 2478-2483. DOI 10.1093/nar/30.11.2478.
21. S. H. Perl, A. Uzan-Yulzari, H. Klainer, L. Asiskovich, M. Youngster, E. Rinott and I. Youngster. SARS-CoV-2–Specific Antibodies in Breast Milk After COVID-19 Vaccination of Breastfeeding Women. *JAMA* 2021. DOI 10.1001/jama.2021.5782.
22. T. T. Shimabukuro, S. Y. Kim, T. R. Myers, P. L. Moro, T. Oduyebo, L. Panagiotakopoulos, P. L. Marquez, C. K. Olson, R. Liu, K. T. Chang, S. R. Ellington, V. K. Burkel, A. N. Smoots, C. J. Green, C. Licata, B. C. Zhang, M. Alimchandani, A. Mba-Jonas, S. W. Martin, J. M. Gee, D. M. Meaney-Delman and C. D. C. v.-s. C.-P. R. Team. Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons. *The New England journal of medicine* 2021. DOI 10.1056/NEJMoa2104983.

Conflict of interest

PAT received funding from Johnson&Johnson, Arcturus, Roche, AJ Biologicals, all paid to the institution. The authors declare no other conflicts of interest that may affect the objectivity of this work.

Figure Legends

Figure 1. Detection of BNT162B2 mRNA and Multiple sequence alignment of plasma RNA vaccine assembly, Pfizer sequence and MT380725 spike protein sequence. (A) Amplification at Ct<30 was observed in all plasma samples between 1 and 4 days post-vaccination, but not in 4-week plasma collected from subjects 101 and 102 (undiagnosed pregnancies at the time of the first dose). Negative control (pre-vaccination plasma) and water blanks did not amplify, demonstrating the specificity of the TaqMan primers/probe. (B) Five paired breast milk and plasma samples were analysed for BNT162B2 mRNA, which amplified (Ct<30) in day 1-4 plasma but not in day 0-7 breast milk. Negative control (pre-vaccination plasma) and water blanks did not amplify, demonstrating the specificity of the TaqMan primers/probe. (C) An 87bp region of the spike protein-encoding region of the BNT162B2 mRNA was amplified from RNA extracted from plasma. Whole transcriptome sequencing was performed on extracted RNA. A draft scaffold of 4196 bases with an average coverage of 162X, of comparable size to the vaccine RNA, was obtained only from non-human sequenced reads of post-vaccination samples. No scaffolds >2kb were obtained from pre-vaccination plasma. We observed perfect alignment from bases 120 to 4077 when we compared our assembled sequence to the public Pfizer sequence, and a high degree of agreement at the nucleotide level (other than at the start and end of the sequences) when multiple sequence alignment was performed with GenBank sequence MT380725 of the SARS-CoV-2 spike protein.

Figure 2. Antibodies to SARS-CoV-2 and syncytin-1. A commercial neutralising assay was used to detect SARS-CoV-2 neutralising antibodies, and an ELISA was designed in-house to determine the presence of anti-syncytin-1 antibodies. (A) All subjects were negative for SARS-CoV-2 neutralising antibodies on days 0-4 and strongly positive by at least week 4, and none showed co-existing binding antibodies to human syncytin-1 antigen (B). Dashed line represents mean, error bars represent SD; d-days, w-weeks.

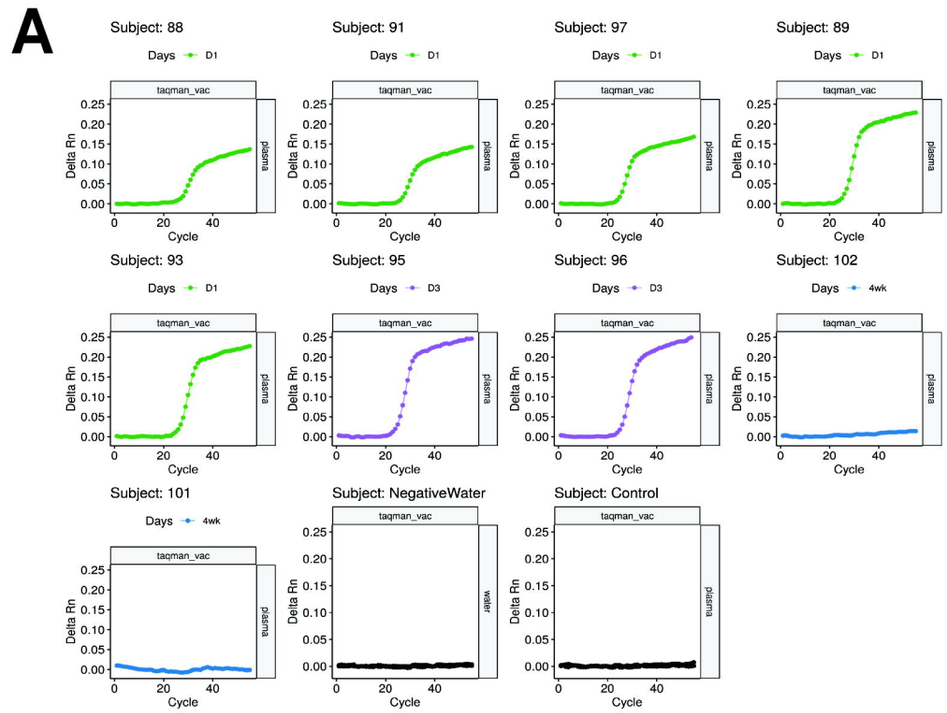
Tables

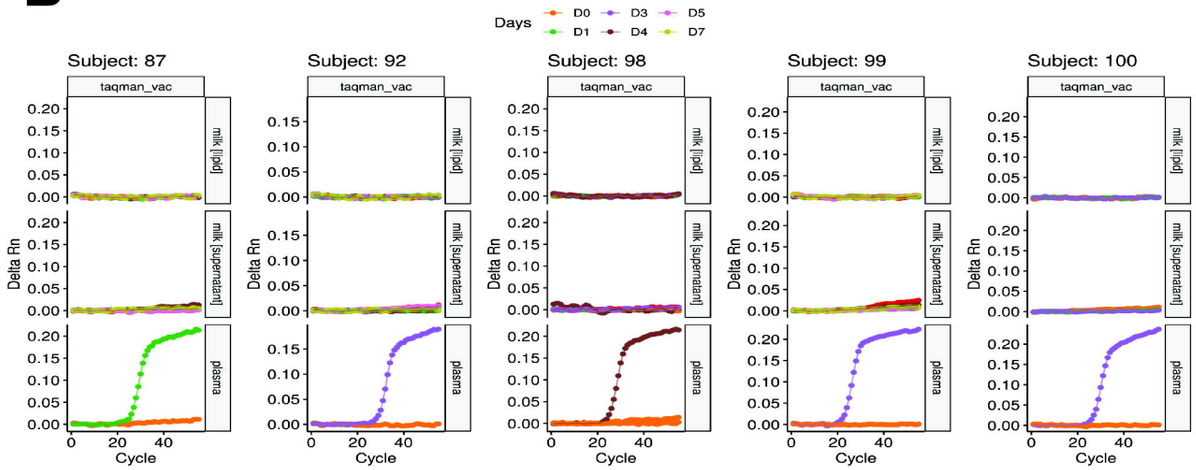
Table 1. Primers used to amplify a region of the spike-encoding region of the BNT162B2 mRNA

Forward	5'-AGAACCACACAAGCCCCGAC-3'
Reverse	5'-GCCGGTCGATCTCTTTCTGG-3'
Probe	/5HEX/CAGCGGAAT/ZEN/CAATGCCAGCG/3IABkFQ/

Table 2. Participant characteristics

	No. (%)
Study participants	
Approached to participate in study	18
Consented, completed study	15 (83.3)
Consented, did not complete study (vaccination deferred)	1 (5.6)
Declined participation	2 (11.1)
Participant features	15 (100.0)
Age, mean (SD), y	40.4 (12.2)
Parous	14 (93.3)
Pregnant at vaccination	2 (13.3)
Received 2 doses	13 (86.7)
Received 1 dose	2 (13.3)
Malay ethnicity	4 (26.7)
Indian ethnicity	4 (26.7)
Chinese ethnicity	7 (46.6)
Samples collected	
Day 0 plasma	13/15 (86.7)
Day 1-4 plasma	13/15 (86.7)
Week 4-5 plasma	8/15 (53.3)
Week 6-7 plasma	6/15 (40.0)
Day 0-7 breast milk	5/5 (100.0)
Incomplete samples	
Unable to return for blood collection (late time-point)	1 (6.7)
Insufficient plasma for analysis (early time-point)	1 (6.7)


A
Subject: 88
Subject: 91
Subject: 97
Subject: 89
Subject: 93
Subject: 95
Subject: 96
Subject: 102
Subject: 101
Subject: NegativeWater
Subject: Control
Days
D1
D3
4wk
taqman_vac
plasma
water
Delta Rn
Cycle


B
Days
D0
D1
D3
D4
D5
D7
Subject: 87
Subject: 92
Subject: 98
Subject: 99
Subject: 100
taqman_vac
milk [lipid]
milk [supernatant]
plasma
Delta Rn
Cycle


C
234

Figure 1

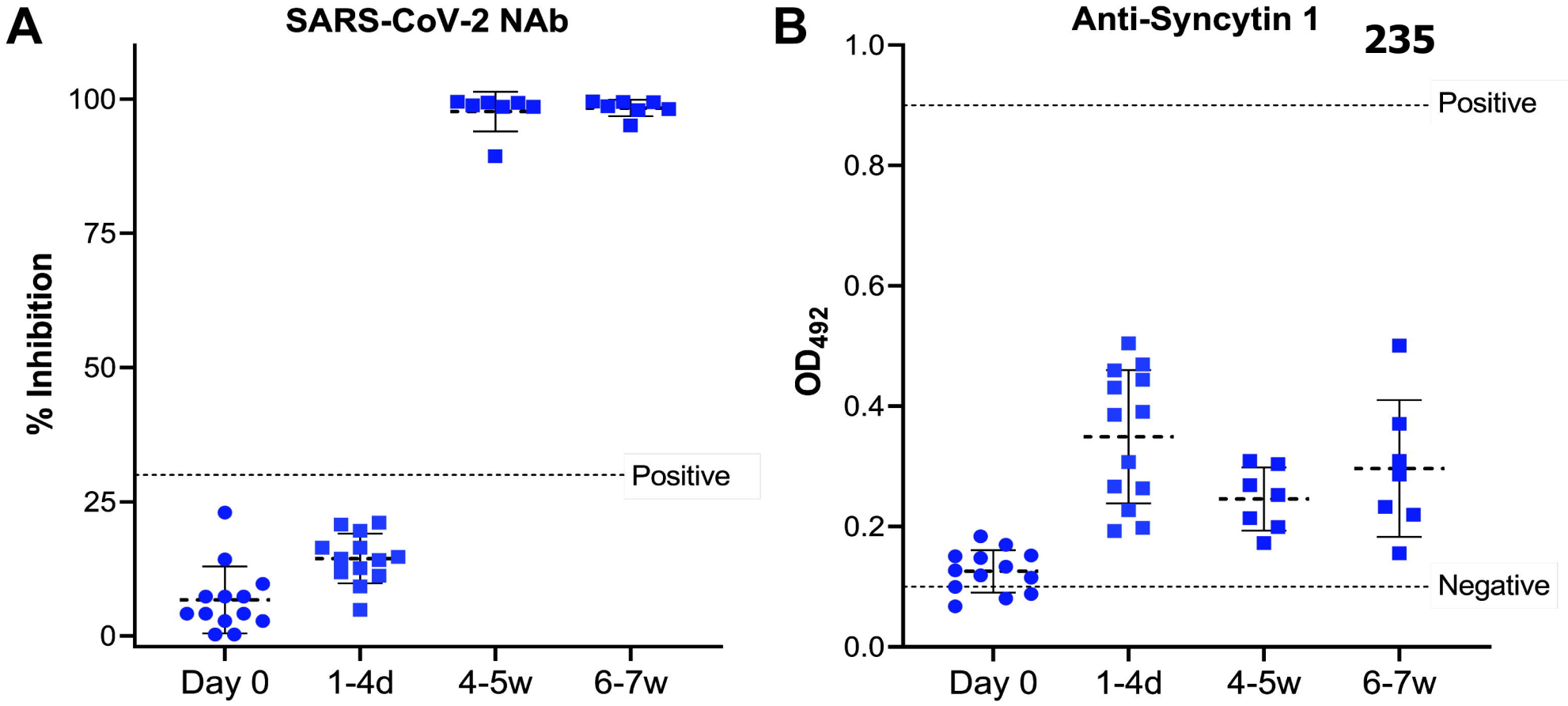

A
SARS-CoV-2 NAb
% Inhibition
100
75
50
25
0
Positive
Day 0
1-4d
4-5w
6-7w
B
Anti-Syncytin 1
235
OD492
1.0
0.8
0.6
0.4
0.2
0.0
Positive
Negative
Day 0
1-4d
4-5w
6-7w

Figure 2

ANNEXURE P-18 236

Home › Conservative Head… › 57 Top Scientists …

in Conservative Headlines, Health & Medicine

57 Top Scientists And Doctors Release Shocking Study On COVID Vaccines And Demand Immediate Stop to ALL Vaccinations

5 months ago

363.2k Views

Share this story:

11.8K
Shares

A group of 57 leading scientists, doctors and policy experts has released a report calling in to question the safety and efficacy of the current COVID-19 vaccines and are now calling for an immediate end to all vaccine programs. We urge you to read and share this damning report.

237

There are two certainties regarding the global distribution of Covid-19 vaccines. The first is that

governments and the vast majority of the mainstream media are pushing with all their might to get these experimental drugs into as many people as possible. The second is that those who are willing to face the scorn that comes with asking serious questions about vaccines are critical players in our ongoing effort to spread the truth.

You can read an advanced copy of this manuscript in preprint below. It has been prepared by nearly five dozen highly respected doctors, scientists, and public policy experts from across the globe to be urgently sent to world leaders as well as all who are associated with the production and distribution of the various Covid-19 vaccines in circulation today.

There are still far too many unanswered questions regarding the Covid-19 vaccines' safety, efficacy, and necessity. This study is a bombshell that should be heard by everyone, regardless of their views on vaccines. There aren't nearly enough citizens who are asking questions. Most people simply follow the orders of world governments, as if they have earned our complete trust. They haven't done so. This manuscript is a step forward in terms of accountability and the free flow of information on this crucial subject. Please take the time to read it and share it widely.

SARS-CoV-2 mass vaccination: Urgent questions on vaccine safety that demand answers from international health agencies, regulatory authorities, governments and vaccine developers

Roxana Bruno[1], Peter McCullough[2], Teresa Forcades i Vila[3], Alexandra Henrion-Caude[4], Teresa García-Gasca[5], Galina P. Zaitzeva[6], Sally Priester[7], María J. Martínez Albarracín[8], Alejandro Sousa-Escandon[9], Fernando López Mirones[10], Bartomeu Payeras Cifre[11], Almudena Zaragoza Velilla[10], Leopoldo M. Borini[1], Mario Mas[1], Ramiro Salazar[1], Edgardo Schinder[1], Eduardo A Yahbes[1], Marcela Witt[1], Mariana Salmeron[1], Patricia Fernández[1], Miriam M. Marchesini[1], Alberto J. Kajihara[1], Marisol V. de la Riva[1], Patricia J. Chimeno[1], Paola A. Grellet[1], Matelda Lisdero[1], Pamela Mas[1], Abelardo J. Gatica Baudo[12], Elisabeth Retamoza[12], Oscar Botta[13], Chinda C. Brandolino[13], Javier Sciuto[14], Mario Cabrera Avivar[14], Mauricio Castillo[15], Patricio Villarroel[15], Emilia P. Poblete Rojas[15], Bárbara Aguayo[15], Dan I. Macías Flores[15], Jose V. Rossell[16], Julio C. Sarmiento[17], Victor Andrade-Sotomayor[17], Wilfredo R. Stokes Baltazar[18], Virna Cedeño Escobar[19], Ulises Arrúa[20], Atilio Farina del Río[21], Tatiana Campos Esquivel[22], Patricia Callisperis[23], María Eugenia Barrientos[24], Karina Acevedo-Whitehouse[5],*

[1]Epidemiólogos Argentinos Metadisciplinarios. República Argentina.

[2]Baylor University Medical Center. Dallas, Texas, USA.

[3]Monestir de Sant Benet de Montserrat, Montserrat, Spain

[4]INSERM U781 Hôpital Necker-Enfants Malades, Université Paris Descartes-Sorbonne Cité, Institut Imagine, Paris, France.

[5]School of Natural Sciences. Autonomous University of Querétaro, Querétaro, Mexico.

[6]Retired Professor of Medical Immunology. Universidad de Guadalajara, Jalisco, Mexico.

[7]Médicos por la Verdad Puerto Rico. Ashford Medical Center. San Juan, Puerto Rico.

[8]Retired Professor of Clinical Diagnostic Processes. University of Murcia, Murcia, Spain

[9]Urologist Hospital Comarcal de Monforte, University of Santiago de Compostela, Spain.

[10]Biólogos por la Verdad, Spain.

[11]Retired Biologist. University of Barcelona. Specialized in Microbiology. Barcelona, Spain.

[12]Center for Integrative Medicine MICAEL (Medicina Integrativa Centro Antroposófico Educando en Libertad). Mendoza, República Argentina.

[13]Médicos por la Verdad Argentina. República Argentina. ´

[14]Médicos por la Verdad Uruguay. República Oriental del Uruguay.

[15]Médicos por la Libertad Chile. República de Chile.

[16]Physician, orthopedic specialist. República de Chile.

[17]Médicos por la Verdad Perú. República del Perú.

[18]Médicos por la Verdad Guatemala. República de Guatemala.

[19]Concepto Azul S.A. Ecuador.

[20]Médicos por la Verdad Brasil. Brasil.

[21]Médicos por la Verdad Paraguay.

[22]Médicos por la Costa Rica.

[23]Médicos por la Verdad Bolivia.

[24]Médicos por la Verdad El Salvador.

* Correspondence: Karina Acevedo-Whitehouse, karina.acevedo.whitehouse@uaq.mx

Abstract

Since the start of the COVID-19 outbreak, the race for testing new platforms designed to confer immunity against SARS-CoV-2, has been rampant and unprecedented, leading to emergency authorization of various vaccines. Despite progress on early multidrug therapy for COVID-19 patients, the current mandate is to immunize the world population as quickly as possible. The lack of thorough testing in animals prior to clinical trials, and authorization based on safety data generated during trials that lasted less than 3.5 months, raise questions regarding the safety of these vaccines. The recently identified role of SARS-CoV-2 glycoprotein Spike for inducing endothelial damage characteristic of COVID-19, even in absence of infection, is extremely relevant given that most of the authorized vaccines induce the production of Spike glycoprotein in the recipients. Given the high rate of occurrence of adverse effects, and the wide range of types of adverse effects that have been reported to date, as well as the potential for vaccine-driven disease enhancement, Th2-immunopathology, autoimmunity, and

immune evasion, there is a need for a better understanding of the benefits and risks of mass vaccination, particularly in the groups that were excluded in the clinical trials. Despite calls for caution, the risks of SARS-CoV-2 vaccination have been minimized or ignored by health organizations and government authorities. We appeal to the need for a pluralistic dialogue in the context of health policies, emphasizing critical questions that require urgent answers if we wish to avoid a global erosion of public confidence in science and public health.

Introduction

Since COVID-19 was declared a pandemic in March 2020, over 150 million cases and 3 million deaths have been reported worldwide. Despite progress on early ambulatory, multidrug-therapy for high-risk patients, resulting in 85% reductions in COVID-19 hospitalization and death [1], the current paradigm for control is mass-vaccination. While we recognize the effort involved in development, production and emergency authorization of SARS-CoV-2 vaccines, we are concerned that risks have been minimized or ignored by health organizations and government authorities, despite calls for caution [2-8].

Vaccines for other coronaviruses have never been approved for humans, and data generated in the development of coronavirus vaccines designed to elicit neutralizing antibodies show that they may worsen COVID-19 disease via antibody-dependent enhancement (ADE) and Th2 immunopathology, regardless of the vaccine platform and delivery method [9-11]. Vaccine-driven disease enhancement in animals vaccinated against SARS-CoV and MERS-CoV is known to occur following viral challenge, and has been attributed to immune complexes and Fc-mediated viral capture by macrophages, which augment T-cell activation and inflammation [11-13].

In March 2020, vaccine immunologists and coronavirus experts assessed SARS-CoV-2 vaccine risks based on SARS-CoV-vaccine trials in animal models. The expert group concluded that ADE and immunopathology were a real concern, but stated that their risk was insufficient to delay clinical trials, although continued monitoring would be necessary [14]. While there is no clear evidence of the occurrence of ADE and vaccine-related immunopathology in volunteers immunized with SARS-CoV-2 vaccines [15], safety trials to date have not specifically addressed these serious adverse effects (SAE). Given that the follow-up of volunteers did not exceed 2-3.5 months after the second dose [16-19], it is unlikely such SAE would have been observed. Despite92 errors in reporting, it cannot be ignored that even accounting for the number of vaccines administered, according to the US Vaccine Adverse Effect Reporting System (VAERS), the number of deaths per million vaccine doses administered has increased more than 10-fold. We believe there is an urgent need for open scientific dialogue on vaccine safety in the context of large-scale immunization. In this paper, we describe some of the risks of mass vaccination in the context of phase 3 trial exclusion criteria and discuss the SAE reported in national

and regional adverse effect registration systems. We highlight unanswered questions and draw attention to the need for a more cautious approach to mass vaccination.

SARS-CoV-2 phase 3 trial exclusion criteria

With few exceptions, SARS-CoV-2 vaccine trials excluded the elderly [16-19], making it impossible to identify the occurrence of post-vaccination eosinophilia and enhanced inflammation in elderly people. Studies of SARS-CoV vaccines showed that immunized elderly mice were at particularly high risk of life-threatening Th2 immunopathology [9,20]. Despite this evidence and the extremely limited data on safety and efficacy of SARS-CoV-2 vaccines in the elderly, mass-vaccination campaigns have focused on this age group from the start. Most trials also excluded pregnant and lactating volunteers, as well as those with chronic and serious conditions such as tuberculosis, hepatitis C, autoimmunity, coagulopathies, cancer, and immune suppression [16-29], although these recipients are now being offered the vaccine under the premise of safety.

Another criterion for exclusion from nearly all trials was prior exposure to SARS-CoV-2. This is unfortunate as it denied the opportunity of obtaining extremely relevant information concerning post-vaccination ADE in people that already have anti-SARS-Cov-2 antibodies. To the best of our knowledge, ADE is not being monitored systematically for any age or medical condition group currently being administered the vaccine. Moreover, despite a substantial proportion of the population already having antibodies [21], tests to determine SARS-CoV-2-antibody status prior to administration of the vaccine are not conducted routinely.

Will serious adverse effects from the SARS-CoV-2 vaccines go unnoticed?

COVID-19 encompasses a wide clinical spectrum, ranging from very mild to severe pulmonary pathology and fatal multi-organ disease with inflammatory, cardiovascular, and blood coagulation dysregulation [22-24]. In this sense, cases of vaccine-related ADE or immunopathology would be clinically-indistinguishable from severe COVID-19 [25]. Furthermore, even in the absence of SARS-CoV-2 virus, Spike glycoprotein alone causes endothelial damage and hypertension in vitro and in vivo in Syrian hamsters by down-regulating angiotensin-converting enzyme 2 (ACE2) and impairing mitochondrial function [26]. Although these findings need to be confirmed in humans, the implications of this finding are staggering, as all vaccines authorized for emergency use are based on the delivery or induction of Spike glycoprotein synthesis. In the case of mRNA vaccines and adenovirus-vectorized vaccines, not a single study has examined the duration of Spike production in humans following vaccination. Under the cautionary principle, it is parsimonious to consider vaccine-induced Spike synthesis could cause clinical signs of severe COVID-19, and erroneously be counted as new cases of SARS-CoV-2 infections. If so, the true adverse effects of the current global vaccination strategy may

never be recognized unless studies specifically examine this question. There is already non-causal evidence of temporary or sustained increases138 in COVID-19 deaths following vaccination in some countries (Fig. 1) and in light of Spike's pathogenicity, these deaths must be studied in depth to determine whether they are related to vaccination.

Unanticipated adverse reactions to SARS-CoV-2 vaccines

Another critical issue to consider given the global scale of SARS-CoV-2 vaccination is autoimmunity. SARS-CoV-2 has numerous immunogenic proteins, and all but one of its immunogenic epitopes have similarities to human proteins [27]. These may act as a source of antigens, leading to autoimmunity [28]. While it is true that the same effects could be observed during natural infection with SARS-CoV-2, vaccination is intended for most of the world population, while it is estimated that only 10% of the world population has been infected by SARS-CoV-2, according to Dr. Michael Ryan, head of emergencies at the World Health Organization. We have been unable to find evidence that any of the currently authorized vaccines screened and excluded homologous immunogenic epitopes to avoid potential autoimmunity due to pathogenic priming.

Some adverse reactions, including blood-clotting disorders, have already been reported in healthy and young vaccinated people. These cases led to the suspension or cancellation of the use of adenoviral vectorized ChAdOx1-nCov-19 and Janssen vaccinesin some countries. It has now been proposed that vaccination with ChAdOx1-nCov-19 can result in immune thrombotic thrombocytopenia (VITT) mediated by platelet-activating antibodies against Platelet factor-4, which clinically mimics autoimmune heparin-induced thrombocytopenia [29]. Unfortunately, the risk was overlooked when authorizing these vaccines, although adenovirus-induced thrombocytopenia has been known for more than a decade, and has been a consistent event with adenoviral vectors [30]. The risk of VITT would presumably be higher in those already at risk of blood clots, including women who use oral contraceptives [31], making it imperative for clinicians to advise their patients accordingly.

At the population level, there could also be vaccine-related impacts. SARS-CoV-2 is a fast-evolving RNA virus that has so far produced more than 40,000 variants [32,33] some of which affect the antigenic domain of Spike glycoprotein [34,35]. Given the high mutation rates, vaccine-induced synthesis of high levels of anti-SARS-CoV-2-Spike antibodies could theoretically lead to suboptimal responses against subsequent infections by other variants in vaccinated individuals [36], a phenomenon known as "original antigenic sin" [37] or antigenic priming [38]. It is unknown to what extent mutations that affect SARS-CoV-2 antigenicity will become fixed during viral evolution [39], but vaccines could plausibly act as selective forces driving variants with higher infectivity or transmissibility. Considering the high similarity between known SARS-CoV-2 variants, this scenario is unlikely [32,34] but if future variants were to differ more in key epitopes, the global vaccination strategy might have helped shape an even

more dangerous virus. This risk has recently been brought to the attention of the WHO as an open letter [40].

Discussion

The risks outlined here are a major obstacle to continuing global SARS-CoV-2 vaccination. Evidence on the safety of all SARS-CoV-2 vaccines is needed before exposing more people to the184 risk of these experiments, since releasing a candidate vaccine without time to fully understand the resulting impact on health could lead to an exacerbation of the current global crisis [41]. Risk-stratification of vaccine recipients is essential. According to the UK government, people below 60 years of age have an extremely low risk of dying from COVID-191 187 . However, according to Eudravigillance, most of the serious adverse effects following SARS-CoV-2 vaccination occur in people aged 18-64. Of particular concern is the planned vaccination schedule for children aged 6 years and older in the United States and the UK. Dr. Anthony Fauci recently anticipated that teenagers across the country will be vaccinated in the autumn and younger children in early 2022, and the UK is awaiting trial results to commence vaccination of 11 million children under 18. There is a lack of scientific justification for subjecting healthy children to experimental vaccines, given that the Centers for Disease Control and Prevention estimates that they have a 99.997% survival rate if infected with SARS-CoV-2. Not only is COVID-19 irrelevant as a threat to this age group, but there is no reliable evidence to support vaccine efficacy or effectiveness in this population or to rule out harmful side effects of these experimental vaccines. In this sense, when physicians advise patients on the elective administration of COVID-19 vaccination, there is a great need to better understand the benefits and risk of administration, particularly in understudied groups.

In conclusion, in the context of the rushed emergency-use-authorization of SARS-CoV-2 vaccines, and the current gaps in our understanding of their safety, the following questions must be raised:

- Is it known whether cross-reactive antibodies from previous coronavirus infections or vaccine 206 induced antibodies may influence the risk of unintended pathogenesis following vaccination with COVID-19?
- Has the specific risk of ADE, immunopathology, autoimmunity, and serious adverse reactions been clearly disclosed to vaccine recipients to meet the medical ethics standard of patient understanding for informed consent? If not, what are the reasons, and how could it be implemented?
- What is the rationale for administering the vaccine to every individual when the risk of dying from COVID-19 is not equal across age groups and clinical conditions and when the phase 3 trials excluded the elderly, children and frequent specific conditions?

- What are the legal rights of patients if they are harmed by a SARS-CoV-2 vaccine? Who will cover the costs of medical treatment? If claims were to be settled with public money, has the public been made aware that the vaccine manufacturers have been granted immunity, and their responsibility to compensate those harmed by the vaccine has been transferred to the tax-payers?

In the context of these concerns, we propose halting mass-vaccination and opening an urgent pluralistic, critical, and scientifically-based dialogue on SARS-CoV-2 vaccination among scientists, medical doctors, international health agencies, regulatory authorities, governments, and vaccine developers. This is the only way to bridge the current gap between scientific evidence and public health policy regarding the SARS-CoV-2 vaccines. We are convinced that humanity deserves a deeper understanding of the risks than what is currently touted as the official position. An open scientific dialogue is urgent and indispensable to avoid erosion of public confidence in science and public health and to ensure that the WHO and national health authorities protect the interests of humanity during the current pandemic. Returning public health policy to evidence-based medicine, relying on a careful evaluation of the relevant scientific research, is urgent. It is imperative to follow the science.

1 https://www.gov.uk/government/publications/covid-19-reported-sars-cov-2-deaths-in-england/covid-19-confirmed-deaths-in-england-report

Conflict of Interest Statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

References

1. McCullough PA, Alexander PE, Armstrong R, et al. Multifaceted highly targeted sequential multidrug treatment of early ambulatory high-risk SARS-CoV-2 infection (COVID-19). Rev Cardiovasc Med (2020) 21:517–530. doi:10.31083/j.rcm.2020.04.264
2. Arvin AM, Fink K, Schmid MA, et al. A perspective on potential antibody- dependent enhancement of SARS-CoV-2. Nature (2020) 484:353–363. doi:10.1038/s41586-020-2538-8
3. Coish JM, MacNeil AJ. Out of the frying pan and into the fire? Due diligence warranted for ADE in COVID-19. Microbes Infect (2020) 22(9):405-406. doi:10.1016/j.micinf.2020.06.006
4. Eroshenko N, Gill T, Keaveney ML, et al. Implications of antibody-dependent enhancement of infection for SARS-CoV-2 countermeasures. Nature Biotechnol (2020) 38:788–797. doi:10.1038/s41587-020-0577-1
5. Poland GA. Tortoises, hares, and vaccines: A cautionary note for SARS-CoV-2 vaccine development. Vaccine (2020) 38:4219–4220. doi:10.1016/j.vaccine.2020.04.073

6. Shibo J. Don't rush to deploy COVID-19 vaccines and drugs without sufficient safety guarantees. Nature (2000) 579,321. doi:10.1038/d41586-020-00751-9
7. Munoz FA, Cramer JP, Dekker CL, et al. Vaccine-associated enhanced disease: Case definition and guidelines for data collection, analysis, and presentation of immunization safety data. Vaccine (2021) https://doi.org/10.1016/j.vaccine.2021.01.055
8. Cardozo T, Veazey R. Informed consent disclosure to vaccine trial subjects of risk of COVID-19 vaccines worsening clinical disease. Int J Clin Pract (2020) 28:e13795. doi: 10.1111/ijcp.13795
9. Bolles D, Long K, Adnihothram S, et al. A double-inactivated severe acute respiratory syndrome coronavirus vaccine provides incomplete protection in mice and induces increased eosinophilic proinflammatory pulmonary response upon challenge. J Virol (2001) 85:12201–12215. doi:10.1128/JVI.06048-11
10. Weingartl H, Czub M, Czub S, et al. Immunization with modified vaccinia virus Ankarabased recombinant vaccine against severe acute respiratory syndrome is associated with enhanced hepatitis in ferrets. J Virol (2004) 78:12672–12676. doi:10.1128/JVI.78.22.12672-12676.2004272
11. Tseng CT, Sbrana E, Iwata-Yoshikawa N, et al. Immunization with SARS coronavirus vaccines leads to pulmonary immunopathology on challenge with the SARS virus. PLoS One (2012) 7(4):e35421. doi: 10.1371/journal.pone.0035421
12. Iwasaki A, Yang Y. The potential danger of suboptimal antibody responses in COVID-19. Nat Rev Immunol (2020) 20:339–341. doi:10.1038/s41577-020-0321-6
13. Vennema H, de Groot RJ, Harbour DA, et al. Early death after feline infectious peritonitis virus challenge due to recombinant vaccinia virus immunization. J Virol (1990) 64:1407-1409
14. Lambert PH, Ambrosino DM, Andersen SR, et al. Consensus summary report for CEPI/BC March 12-13, 2020 meeting: Assessment of risk of disease enhancement with COVID-19 vaccines. Vaccine (2020) 38(31):4783-4791. doi:10.1016/j.vaccine.2020.05.064
15. de Alwis R, Chen S, Gan S, et al. Impact of immune enhancement on Covid-19 polyclonal hyperimmune globulin therapy and vaccine development. EbioMedicine (2020) 55:102768. doi:10.1016/j.ebiom.2020.102768
16. Folegatti PM, Ewer KJ, Aley PK, et al. Safety and immunogenicity of the ChAdOx1 nCoV 287 19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2, single-blind, randomised controlled trial. Lancet (2020) 396:467–783. doi:10.1016/S0140-6736(20)31604-4
17. Polack FP, Thomas SJ, Kitchin N. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. N Engl J Med (2020) 383:2603–2615. doi:10.1056/NEJMoa2034577
18. Ramasamy MN, Minassian AM, Ewer KJ, et al. Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002): a single-blind, randomised, controlled, phase 2/3 trial. Lancet (2021) 396:1979–93. doi: 10.1016/S0140-6736(20)32466-1

19. Chu L, McPhee R, Huang W, et al. mRNA-1273 Study Group. A preliminary report of a randomized controlled phase 2 trial of the safety and immunogenicity of mRNA-1273 SARS-CoV-2 vaccine. Vaccine (2021) S0264-410X(21)00153-5. doi:10.1016/j.vaccine.2021.02.007
20. Liu L, Wei Q, Lin Q, et al. Anti-spike IgG causes severe acute lung injury by skewing macrophage responses during acute SARS-CoV infection. JCI Insight (2019) 4(4):e123158. doi:10.1172/jci.insight.123158.
21. Ioannidis PA. Infection fatality rate of COVID-19 inferred from seroprevalence data. Bull WHO (2021) 99:19–33F. http://dx.doi.org/10.2471/BLT.20.265892
22. Martines RB, Ritter JM, Matkovic E, et al. Pathology and Pathogenesis of SARS-CoV-2 Associated with Fatal Coronavirus Disease, United States Emerg Infect Dis (2020) 26:2005-2015. doi:10.3201/eid2609.202095
23. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. JAMA (2020) 323:1239-1242. doi:10.1001/jama.2020.2648
24. Xu Z, Shi L, Wang Y, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respiratory Med (2020) 8:420-422 doi:10.1016/S2213-2600(20)30076-X
25. Negro F. Is antibody-dependent enhancement playing a role in COVID-19 pathogenesis? Swiss Medical Weekly (2020) 150:w20249. doi:10.4414/smw.2020.20249317
26. Lei Y, Zhang J, Schiavon CR et al., Spike Protein Impairs Endothelial Function via Downregulation of ACE 2. Circulation Res (2021) 128:1323–1326. https://doi.org/10.1161/CIRCRESAHA.121.318902
27. Lyons-Weiler J. Pathogenic priming likely contributes to serious and critical illness and mortality in COVID-19 via autoimmunity, J Translational Autoimmunity (2020) 3:100051. doi:10.1016/j.jtauto.2020.100051
28. An H, Park J. Molecular Mimicry Map (3M) of SARS-CoV-2: Prediction of potentially immunopathogenic SARS-CoV-2 epitopes via a novel immunoinformatic approach. bioRxiv [Preprint]. 12 November 2020 [cited 2020 April 19] https://doi.org/10.1101/2020.11.12.344424
29. Greinacher A, Thiele T, Warkentin TE, Weisser K, Kyrle PA, Eichinger S. Thrombotic Thrombocytopenia after ChAdOx1 nCov-19 Vaccination. N Engl J Med (2021). doi: 10.1056/NEJMoa2104840
30. Othman M, Labelle A, Mazzetti I et al. Adenovirus-induced thrombocytopenia: the role of von Willebrand factor and P-selectin in mediating accelerated platelet clearance. Blood (2007) 109:2832–2839. doi:10.1182/blood-2006-06-032524
31. Ortel TL. Acquired thrombotic risk factors in the critical care setting. Crit Care Med (2010) 38(2 Suppl):S43-50. doi:10.1097/CCM.0b013e3181c9ccc8

32. Grubaugh ND, Petrone ME, Holmes EC. We shouldn't worry when a virus mutates during disease outbreaks. Nat Microbiol (2020) 5:529–530. https://doi.org/10.1038/s41564-020-0690-4
33. Greaney AJ, Starr TN, Gilchuk P, et al. Complete Mapping of Mutations to the SARS-CoV 339 2 Spike Receptor-Binding Domain that Escape Antibody Recognition. Cell Host Microbe (2021) 29:44–57.e9. doi:10.1016/j.chom.2020.11.007.
34. Lauring AS, Hodcroft EB. Genetic Variants of SARS-CoV-2—What Do They Mean? JAMA (2021) 325:529–531. doi:10.1001/jama.2020.27124
35. Zhang L, Jackson CB, Mou H, et al. The D614G mutation in the SARS-CoV-2 spike protein reduces S1 shedding and increases infectivity. bioRxiv [Preprint]. June 12 2020 [cited 2021 Apr 19] https://doi.org/10.1101/2020.06.12.148726
36. Korber B, Fischer WM, Gnanakaran S et al. Sheffield COVID-19 Genomics Group. Tracking changes in SARS-CoV-2 spike: evidence that D614G increases infectivity of the COVID-19 virus. Cell (2020) 182:812-827.e19. doi:10.1016/j.cell.2020.06.043
37. Francis T. On the doctrine of original antigenic sin. Proc Am Philos Soc (1960) 104:572–578.
38. Vibroud C, Epstein SL. First flu is forever. Science (2016) 354:706–707. doi:10.1126/science.aak9816
39. Weisblum Y, Schmidt F, Zhang F, et al. Escape from neutralizing antibodies by SARS 354 CoV-2 spike protein variants. Elife (2020) 9:e61312. doi:10.7554/eLife.61312
40. Vanden Bossche G (March 6, 2021) https://dryburgh.com/wp-356content/uploads/2021/03/Geert_Vanden_Bossche_Open_Letter_WHO_March_6_2021.pdf
41. Coish JM, MacNeil AJ. Out of the frying pan and into the fire? Due diligence warranted for ADE in COVID-19. Microbes Infect (2020) 22(9):405-406. doi:10.1016/j.micinf.2020.06.006

Figure legends

Figure 1. Number of new COVID-19 deaths in relation to number of people that have received at least one vaccine dose for selected countries. Graph shows data from the start of vaccination to May 3rd 365 , 2021. A) India (9.25% of population vaccinated), B) Thailand (1.58% of population vaccinated), C) Colombia (6.79% of population vaccinated), D) Mongolia (31.65% of population vaccinated), E) Israel (62.47% of population vaccinated), F) Entire world (7.81% of population vaccinated). Graphs were built using data from Our World in Data (accessed 4 May 2021) https://github.com/owid/covid-19-data/tree/master/public/data/vaccinations

247

#COVID VACCINE #COVID VACCINE DEATH #COVID VACCINE REACTION #VACCINES

WHAT'S YOUR REACTION?





122	95	123	68	336
YES!	TERRIBLE!	LOVE	FAKE NEWS	YUGE!

COMMENTS

ANNEXURE P-19

NEWS

27 health experts implore FDA 'slow down and get the science right' before approving vaccines

A citizen petition calls on the FDA to withhold full approval of vaccines for COVID-19 until efficacy and safety measures are met.

Shutterstock

Megan Redshaw, J.D.

Tue Jun 8, 2021 - 7:21 pm EDT **249**

June 8, 2021 (Children's Health Defense) – A group of 27 clinicians, researchers and advocates last week filed an urgent Citizen Petition with the U.S. Food and Drug Administration (FDA) urging the agency not to prematurely grant full approval to any COVID vaccine.

"Premature FDA approval of any COVID-19 vaccine could negatively impact the health and safety of U.S. residents, with global ramifications considering the international importance of FDA decisions," the group said.

The FDA citizen petition process, described in Title 21 of the Code of Federal Regulations (21 CFR Part 10), allows individuals and community organizations to request the agency make changes to health policy. At any time, any "interested person" can request the FDA "issue, amend or revoke a regulation or order," or "take or refrain from taking any other form of administrative action."

In their petition, the group outlined many unanswered questions surrounding the efficacy and safety of COVID vaccines, and detailed how data must be collected before the FDA considers granting any vaccine full approval.

"We are concerned that the premature licensure of a COVID-19 vaccine can seriously undermine public confidence in regulatory authorities, particularly if long-term safety issues were to emerge following licensure," petitioners wrote.

In an op-ed published today in The BMJ, four of the petition's signatories, writing on behalf of the group, said:

> "The message of our petition is 'slow down and get the science right — there is no legitimate reason to hurry to grant a license to a coronavirus vaccine.' We believe the existing evidence base — both pre- and post-authorization — is simply not mature enough at this point to adequately judge whether clinical benefits outweigh the risks in all populations."

The petition states a COVID vaccine should be fully approved only when substantial evidence demonstrates the benefits of a specific product outweigh the harms for the indicated, recipient population. The petitioners "respectfully" requested the FDA act on the petition by June 11. They plan to seek judicial relief if the petition is denied.

The FDA granted Emergency Use Authorization (EUA) to three COVID vaccines — Pfizer, Moderna and Johnson & Johnson (J&J) — allowing rapid and widespread vaccine rollout across the U.S. However, the EUAs were granted without a built-in expiration date, which means they can lawfully be distributed even after a "public health emergency" no longer exists.

The 20-page citizen petition and supporting documents are filed under Docket ID FDA-2021-P-0521 on regulations.gov. Anyone can comment on the petition, or read others' comments, including the FDA's official reply once it arrives.

Petitioners ask the FDA to implement eight efficacy and safety measures before granting a COVID vaccine full FDA approval:

1. Complete at least two years of follow-up of participants originally enrolled in pivotal clinical trials, even if the trials were unblinded and now lack a placebo control. All vaccine manufacturer phase 3 trials were already designed with this planned duration.

2. Prior to including in the list of populations for which a vaccine is approved, ensure there is substantial evidence that clinical effectiveness outweighs harms in special populations including: infants, children and adolescents; those with past SARS-CoV-2 infection; immunocompromised; pregnant women; nursing women; frail older adults; and individuals with cancer, autoimmune disorders and hematological conditions.

3. Require thorough safety assessment of spike proteins being produced by body tissues following vaccine administration, and spike proteins' full biodistribution, pharmacokinetics and tissue specific toxicity.

4. Complete vaccine biodistribution studies from administration site and safety implications of mRNA translation in distant tissues.

5. Require data of all severe adverse reactions reported following COVID vaccination, such as deaths, reported in VAERS and other pharmacovigilance systems.

6. Assess safety in individuals receiving more than two doses.

7. Include gene delivery and therapy experts in the Vaccines and Related Biological Products Advisory Committee (VRBPAC), in recognition of the fact that the novel COVID vaccines work on the premise of gene delivery, in contrast to conventional vaccines.

8. Enforce stringent conflict-of-interest requirements to ensure individuals involved in data analysis and BLA-related decision-making processes have no conflict of interests with vaccine manufacturers.

The petitioners provided a rationale for each requested action and a list of what they said were invalid reasons for rushing full approval of COVID vaccines. They explained that approving COVID vaccines for the purpose of ensuring they are accessible after the public health emergency has ended, or in an effort to ensure adequate access to vaccines across the population, are two objectives that can be accomplished with current EUAs.

The group also said giving full approval to a COVID vaccine in an effort to pave the way for vaccine mandates or to bolster public confidence were outside the scope of the FDA's purview.

"Premature FDA approval of any COVID-19 vaccine could negatively impact the health and safety
of U.S. residents, with global ramifications considering the international importance of FDA decisions," the group said.

The petition author and co-authors include:

- Linda Wastila, BSPharm, MSPH, PhD and professor at University of Maryland School of Pharmacy
- Peter Doshi, PhD, associate professor at University of Maryland School of Pharmacy
- Patrick Whelan, MD, PhD associate clinical professor of pediatrics David Geffen School of Medicine at UCLA
- Hamid A. Merchant, BPharm, MPharm, PhD, RPh, CQP, PGCertHE, FHEA, SRPharmS and subject leader department of pharmacy at University of Huddersfield
- Donald W. Light, PhD and professor of comparative health policy and psychiatry at Rowan University School of Osteopathic Medicine
- Florence T. Bourgeois MD and associate professor of pediatrics at Harvard Medical School
- Robert M. Kaplan, PhD and distinguished research professor UCLA Fielding School of Public Health
- Peter A. McCullough, MD and professor at Texas A & M College of Medicine
- Anthony J Brookes, PhD and professor of genetics University of Leicester
- David Healy, MD, FRCPsych and professor of psychiatry McMaster University Ontario, Canada
- Byram Bridle, viral immunologist and associate professor at University of Guelph, Ontario
- Kim Witczak, founder and CEO of Woodymatters and global drug safety advocate
- Christine Stabell Benn, MD, PhD and professor of global health at University of Southern Denmark
- Matthew Herder, JSM, LLM, Director, Health Law Institute at Dalhousie University Nova Scotia, Canada
- Tom Jefferson, MD, MRCGP FFPHM, British epidemiologist who works with the Cochrane Collaboration, advisor to the Italian National Agency for Regional Health Services and is senior associate tutor at University of Oxford

- Peter Collignon, infectious disease physician, microbiologist at Canberra Hospital
  and professor at the Australian National University Medical School
- Peter C. Gøtzsche, Professor, DrMedSci, MD, MSc Director Institute for Scientific Freedom Copenhagen, Denmark
- Peter Aaby, MSc, DMSc, Head of Bandim Health Project, Guinea-Bissau University of Southern Denmark
- Ulrich Keil, MD, MPH, PhD, FRCP professor emeritus University of Münster, Germany
- Juan Erviti, PharmD, PhD Unit of Innovation and Organization Navarre Health Service, Spain
- Iona Heath, CBE FRCGP and past president of the Royal College of General Practitioners London, UK
- Joseph A. Ladapo, MD, PhD associate professor of Medicine David Geffen School of Medicine at UCLA
- Barbara Mintzes, BA, MSc, PhD, associate professor, School of Pharmacy at the University of Sydney, Australia
- Huseyin Naci, MHS, PhD associate professor of Health Policy London School of Economics and Political Science
- Angela Spelsberg, MD, Comprehensive Cancer Center Aachen, Germany
- Erick Turner, MD, associate professor of psychiatry at Oregon Health & Science University
- Allyson M Pollock, MBChB, FRCPH, FRCP, FRCGP, clinical professor of Public Health Institute of Health and Society, Newcastle University and director of the Newcastle University Centre for Excellence in Regulatory Science.

Earlier this month, Children's Health Defense Chairman (CHD) Robert F. Kennedy Jr. and Dr. Meryl Nass, on behalf of CHD, filed a Citizen Petition with the FDA requesting the agency not only refrain from licensing COVID vaccines, but also immediately revoke the vaccines' EUAs.

> We invite parents, healthcare practitioners, military members and others to comment on our petition to the FDA calling on the agency to immediately remove COVID vaccines from the market.https://t.co/qRyByqdAL7
>
> — Robert F. Kennedy Jr (@RobertKennedyJr) June 8, 2021

CHD submitted 72 references supporting the request for revocation and restraint. To read the full **253**

CHD petition text, download it from the FDA website or read the full petition here — then submit your comments using this form.

TOPICS

Freedom Politics - U.S.

TAGGED AS

Covid-19 Emergency Use Authorization Fda Title 21 Vaccines Vaers

Science, Public Health Policy, and The Law
Volume 2:23-33
November 28, 2020
Ethics in Science and Technology

An Institute for Pure and Applied Knowledge (IPAK)
Public Health Policy Initiative (PHPI)

Misapplication of the Precautionary Principle has Misplaced the Burden of Proof of Vaccine Safety

Judy Wilyman*, Principia Scientific International (PSI)&
Citizens for Health Awareness

Abstract
Vaccination is a medical intervention that comes with a risk for some people. In the expression of infectious diseases, it is known that the pathogen alone does not cause disease: it is a combination of the pathogen, environment, and genetic factors that determines expression and severity of the disease in individuals. In 1960 Macfarlane Burnet, Nobel Prize laureate for immunology, stated that genetics, nutrition, psychological and environmental factors may play a more important role in resistance to disease than the assumed benefits of artificial immunity induced by vaccination. He considered that genetic deterioration of the population may be a consequence of universal mass vaccination and he postulated that in the long-term vaccination may be against the best interests of the state. The current belief that much of the burden of infectious diseases can be alleviated if every child, in every geographical location, has access to multiple vaccines, does not consider the influence of genetics and environment on the health of populations. The historical record shows that deaths and illnesses to infectious diseases fell due to public health reforms – and prior to the introduction of most vaccines. Since 1990 there has been a 5-fold increase in chronic illness in children in developed countries and an exponential increase in autism that correlates directly with the expansion of government vaccination programs. Many individuals are genetically predisposed to the chronic illnesses that are increasing in the population and since 1995 governments have not used mortality or morbidity to assess outcomes of vaccination programs. Human health can be protected in government policies if the precautionary principle is used in the correct format that puts the onus of proof of harmlessness on the government and pharmaceutical industry, and not the general public. This has not been done in current vaccination programs and we cannot rule out the possibility that the increased use of vaccines is destroying the genetic fabric of society as MacFarlane Burnet postulated.

Keywords
vaccine safety, comorbidity, fatality, impact, regulation

Contents

* Author contact: judywilyman@protonmail.com

Editor-in-Chief, **James Lyons-Weiler**

1. Introduction

The focus of this paper is to examine the historical evidence for the control of infectious diseases and to describe the changes in health outcomes that have occurred in all populations concurrent with the increased use of vaccines. The decline in health that is being observed is discussed with respect to governments' use of the precautionary principle to show that its use in the correct format is critical to protecting public health.

2. Causality Inference Unsupported

When the World Health Organisation (WHO) and governments claim that vaccines are 'safe and effective' this claim is based on a lack of scientific evidence because they have never performed the empirical causal study that would prove or disprove the direct link that we are observing, in all countries, between the significant increase in chronic illness in children and the expanding vaccination program [1][2][3]. This causal study would use an inert placebo in the unvaccinated group to provide empirical evidence of the effects of the vaccine /combination of vaccines on the human infant, but such a study has never been conducted [4]. This evidence could also be collected from active surveillance systems that monitor adverse health events of all vaccinated individuals for 5-10 years. But these monitoring systems have also never been implemented [4]. Further, the WHO and national governments have never tested vaccines, even the vaccines with a long history of use, in formal controlled clinical trials to demonstrate with empirical evidence that the vaccine can prevent the vaccine-targeted disease [5]. This is significant because governments routinely use the term 'vaccine-preventable diseases' to imply that vaccines can prevent disease.

3. Reliance on Proxy Outcome Measure

Instead of studying the effects of vaccines on detectable infection rates, studies use the surrogate of seroconversion (antibody titre) to claim that vaccines can prevent infectious diseases. Titres are known to not be a reliable indicator of protection from the disease [5][6][7]. This does not suggest that vaccines do not have any benefit in reducing the transmission of the disease in the community, only that it is not accurate to describe these diseases as "vaccine-preventable diseases" when this criteria has not been proven by governments.

Stanley Plotkin described as the 'father of world vaccinology', states that it is not possible to rely on the antibody titre that is considered suitable to confer immunity for measles because it is not known [8]. He also states that antibody titre is not a reliable indicator because we do not know precisely how antibodies work. In other words, without the empirical clinical evidence from controlled clinical trials to demonstrate that *vaccine-induced* (artificial) antibody titre is *protective* against each infection, we cannot claim that vaccines are effective in preventing them.

It is known that antibody sero-conversion is achieved by natural exposure to the infectious agent, with or without clinical symptoms. Cases without symptoms are referred to as asymptomatic infections (sub-clinical infections) and they result in long-term immunity in contrast to the short-term immunity obtained after a vaccine [6][8][9]. Plotkin also admits that some vaccinated individuals are still being diagnosed with vaccine-targeted diseases after they are vaccinated and they can spread these diseases even if asymptomatic - *'The possibility that a subclinical infection or paucisymptomatic infection (a few symptoms) with measles virus occurs in vaccinees must be considered'* [8].

4. Precautionary Principle Misapplied and Burden of Proof

Government vaccination programs are now recommending up to 16 vaccines for children (>52 doses from 0-14 years old). Yet the claims made by the WHO and governments about the safety and efficacy of the program are not evidence-based due to a lack of sufficient empirical evidence. It is incumbent on the proponent of this medical procedure, *the WHO and governments*, to provide the evidence that this program is safe and effective, not the general public upon whom the policies are enforced. This is because governments have a duty of care to promote healthy outcomes in government health policies and this can only be done if a medical procedure is proven not to cause significant harm in the population before it is implemented [10] .

This is implied in the precautionary principle (pp) when it is used in the correct format in decisions for government health policies. The risk to human health that current vaccination programs represent has arisen because the precautionary principle has not been applied in a manner that would protect human health in the design of government vaccination policies. In order to protect human health, the PP should be used in the format that states that the onus of proof of harmlessness of any medical intervention is on vaccine proponents, and *not the general public* [10]. When used in this format the PP will protect human health in government policy. This is because the government is required to provide sufficient evidence to make causal inference on the question of whether the combined schedule of 16+ vaccines is, or is not causing the chronic illness that we are seeing escalate in children *before* they recommend or mandate this program for children. Instead, safety is presumed, out of concern for instilling doubt in the publics' mind about vaccines, and retrospective studies are used to assess safety *after* the vaccines are unleashed upon the public. The reversal of the PP in the design of these programs places the burden of proof of harm, in individual instances, *on the general public*. This is logically equivalent to placing the burden of proof of harmlessness on the public. In this format it allows public health authorities and doctors to ignore the empirical evidence of chronic illness that is *increasing* in children in direct correlation to the increased use of vaccines.

Governments and doctors today claim this association is a 'coincidence' and that vaccines are 'safe and effective' by ignoring evidence supportive of plausibility of a causal relationship between vaccination and chronic illness in children and by not investigating this relationship in controlled clinical trials.

When the precautionary principle is reversed to put the burden of proof of harmlessness on the general public, instead of the pharmaceutical companies and governments, then it can be used to protect the vested interests of industry in government vaccination policies and not the health of the general public.

The current alignment in misuse of the precautionary principle can be expected to lead to the perceived need for enforced policy due to the reliance on uninformed or misinformed regulation of vaccines (Figure 1). An appropriate application of the precautionary principle could be expected to reduce resistance to vaccination due to transparency, informed regulation and respect for informed consent (Figure 1).

Vaccination is a medical intervention that comes with a risk for some people. When adopting a strategy to prevent infectious diseases it is important to choose the preventative measure that best addresses the causal mechanisms for the disease. In the expression of infectious diseases in humans it is a combination of the agent, environment, lifestyle and genetic factors that determines the severity of the disease. There is a wealth of data showing that environmental factors are the primary determinants of health and infectious disease [7][9][11][12].

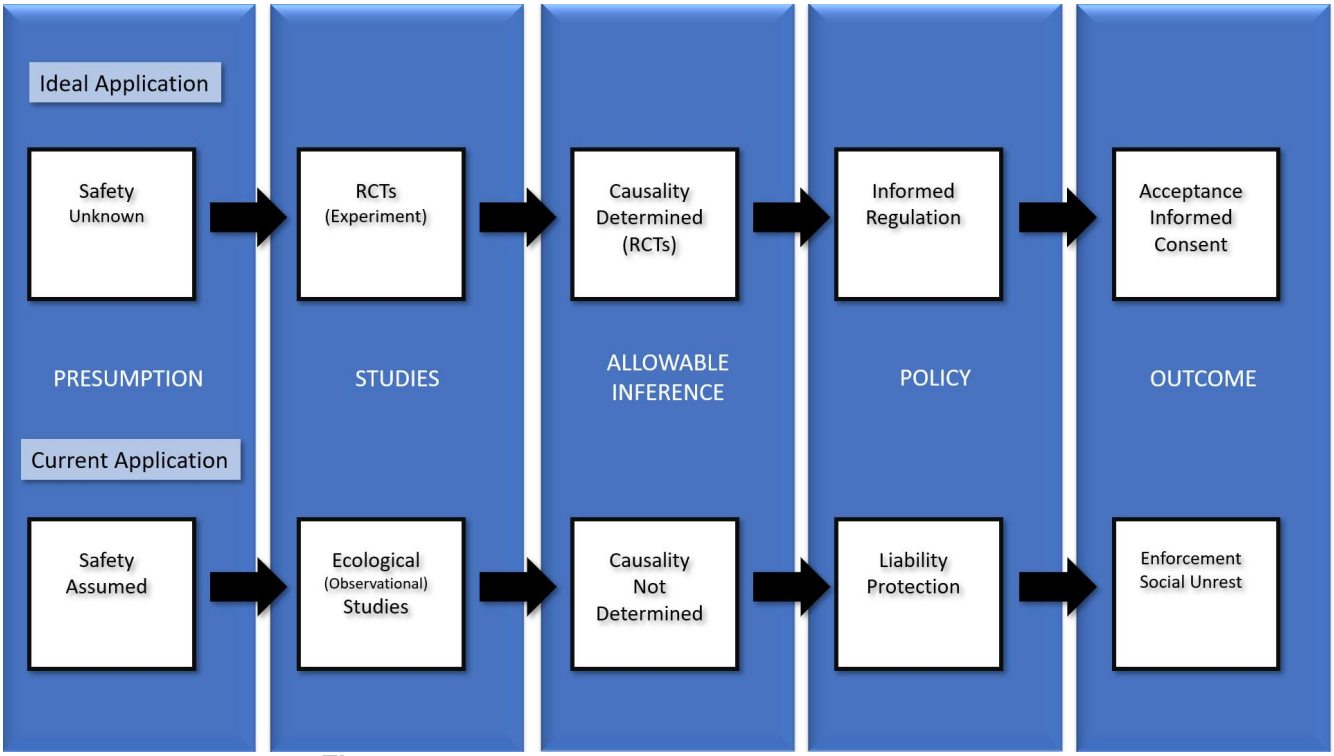


Figure 1. Ideal and Current Regulatory Process Flows

A public health policy that does not include these causal factors in the solution, and relies solely on vaccination that does not address these causal factors, will not produce healthy outcomes in communities.

5. Complex Causality

In 1960 Frank Macfarlane Burnet received the Nobel Prize for immunology. He stated that genetics, nutrition, psychological and environmental factors may play a more important role in resistance to disease than the assumed benefits of artificial immunity induced by vaccination [13]. He considered that genetic deterioration of the population may be a consequence of universal mass vaccination and he postulated that in the long-term vaccination may be against the best interests of the state. The current belief stated by the Global Alliance for Vaccines and Immunisation (GAVI), an alliance that advises the WHO on global vaccination programs, is that much of the burden of infectious diseases can be alleviated if every child, in every geographical location, has access to multiple vaccines [12].

However, this claim does not consider the influence of synergistic toxicity of vaccines, genetics, lifestyle and environment on the health of populations. Since 1990 there has been a 5-fold increase in chronic illness in children/adults in highly vaccinated populations and an exponential increase in autism that correlates directly with the expansion of government vaccination programs [1][2][3][4]. This chronic illness includes childhood cancer, autism, autoimmune diseases, hypersensitivity (allergies), anaphylaxis, seizures, and behavioural and learning difficulties. Is this the genetic deterioration of the population that Macfarlane Burnet predicted in 1952? Vaccines contain foreign DNA from the attenuated/inactivated or genetically engineered pathogens (virus-like particles) plus foreign animal and/or human DNA derived from the manufacturing process. There are two well established pathologies that can potentially develop from injecting children with DNA contaminants such as human foetal cells in the MMR vaccine or animal DNA, such as calf, chicken or monkey, in other vaccines [14]. These mechanisms include insertional mutagenesis in which the human foetal DNA inserts

into the child DNA causing mutations that can lead to cancer and other diseases, and autoimmune diseases that are triggered by the human foetal DNA used in the manufacturing process of vaccines.

Autoimmune diseases cause the child's immune system to attack his or her own body. This leads to diseases such as childhood rheumatoid arthritis, diabetes, hypersensitivity, allergies, anaphylaxis, autism, Crohn's disease etc – all of which are escalating in children in countries with high vaccination rates. These are diseases that are also listed by the pharmaceutical companies as being associated with vaccines for decades [4]. There is also significant research linking vaccines as a plausible cause of this chronic illness [4][14][15][16]. All of these chronic illnesses have escalated in children since the expansion of the vaccination programs in 1990, and even though vaccines are demonstrated to be a plausible cause of this decline in health governments have not investigated this correlation to the childhood vaccination program with causal science.

This is despite the strength of an association, such as, in individual cases, satisfaction of all of Hill's causality conditions possible given the setting and additional strong evidence such as a linear dose-response relationship [9], being consistent with cause and effect. Further, if vaccination policies are to truly protect human health, governments would be promoting vaccination programs on studies that demonstrate an improvement in children's health outcomes. But they cannot do this because children's health has significantly declined with the expansion of this program. How can this be called a 'health policy' when children's health is declining?

6. Inconsistent Evidence on Efficacy

It is also noted that developing countries have had mass vaccination programs for many decades, yet infectious diseases are still predominant [12]. In addition, individuals are not equally susceptible to all diseases or infectious agents [9][13][17] and there is a range of outcomes that can occur after infection. These include no symptoms at all (subclinical infections that are asymptomatic), mild, severe or death. Focusing on the overall incidence of infectious diseases, such as whooping cough and measles, by publicising every case, does not inform the public of the risk of the disease in the community. That is, the deaths and serious illnesses occurring due to these infections. In all developed countries public health reforms, nutrition and smaller family sizes resulted in mostly non-serious cases of measles after 1950 even when measles infection rates were high [13][18][19][20]. Death and serious disease from measles infection were extremely rare after this time. Measles has not been a significant risk to children in Australia since 1950 and this cannot be due to vaccination because a vaccine was not introduced into voluntary vaccination programs in Australia until after 1969 [21] [22]. The Commonwealth of Australia Director General of Health (1913-1945) stated the decline of infectious diseases in Australia occurred at the same time as the period of sanitary reform and prior to the introduction of most vaccines [23]. Another prominent public health authority claimed in 1956 that *'pertussis (whooping cough) was an uncommon cause of death for children and there is a significant decline in mortality if the age of infection increases'* [24][25]. Whooping cough was removed from Australia's national notifiable disease list (with measles and influenza) in 1950 and its decline cannot be due to a vaccine because it was not introduced into voluntary vaccination programs until 1952 in Australia [21]. It is also observed that whooping cough, measles and mumps are common in highly vaccinated populations [22].

Many infections from an agent (virus/bacteria) are subclinical which means they do not produce any signs or symptoms, but they still confer immunity to future infection [9] The vast majority of cases of measles and whooping cough, in infants over the age of one year, in developed countries are non-serious cases of disease. They are self-limiting and the child will receive long-term immunity from this natural infection. This is how herd immunity was originally established [9]. Stewart confirms that notifications are an incomplete indicator of prevalence and they are not an indication of the severity of the disease in the population [26]. Hence, publi-

cising each case of these diseases in the media as if every case is a public health emergency is not informing the public of the lack of severity of *most of these cases* in developed countries. This is the reason that the Australian government took whooping cough, measles and influenza off the national notifiable disease list in 1950 and there was no vaccine for these diseases at this time. These diseases were no longer considered of serious concern in the majority of cases in developed countries after this time even though they were still present.

Burnet stated that the risk of infections such as pertussis (whooping cough) and measles to the community can only be determined by examining the age-incidence of death and illness, not the overall incidence of the disease in the population. This is because these diseases are mainly severe in children less than one year of age [13]. It is also recognised that case-fatality rates will vary greatly in different investigations because of the different criteria that can be used in diagnosing and reporting diseases and death [13]. This information is not made transparent in the statistics that are used by health departments and the media to promote vaccines to the public in 2020.

Currently media reports of cases of whooping cough, measles and other infectious diseases are being used to encourage the *assumption* that a high incidence of these cases results in high mortality and morbidity in the community. This assumption is incorrect. Most cases (99%) of these diseases in developed countries are *non-serious cases* and would otherwise go unnoticed and provide long-term immunity in the individuals if they were not reported. Media articles that report these non-serious cases of disease without reporting the vaccination status (or severity) leave the public to *assume* that the cases are all occurring in unvaccinated people. This assumption is also incorrect. Many vaccinated children/adults are still getting these infectious diseases [7][8]. This contradicts the claim that vaccine-created herd immunity can prevent infectious diseases. Significant outbreaks of infectious diseases in highly vaccinated populations are evidence that vaccine-created herd immunity is not supported by the evidence.

The GAVI alliance that advises the World Health Organization (WHO) on which vaccines to recommend in government programs, has been criticised for focusing on vaccination to control infectious diseases. This focus has been described as a major flaw in public health policy because it is driven by major financial inducements and not the evidence of healthier outcomes in communities [27], This focus by GAVI for public health policy is in contrast to the focus of field workers, European donors and governments of developing countries. These groups do not prioritise vaccines in public health policy because they do not believe that this is the best strategy for achieving healthy outcomes in the developing world [27]. Chronic illness in all countries is increasing with the increased use of vaccines and there are still outbreaks of infectious diseases even in highly vaccinated populations. The risk of death from infectious diseases was reduced in developed countries *before* the vaccines were introduced and therefore it is necessary for governments to provide the annual statistics of the number of these cases that are occurring in vaccinated people to demonstrate the claim that vaccines *can prevent* these diseases in the majority of cases.

7. Herd Immunity

Vaccine manufacturers and governments also do not provide sufficient evidence that vaccines can create herd immunity in the population. Yet they are promoting infectious diseases as ‘vaccine-preventable’ diseases and claiming that the vaccines create ‘herd immunity’. Governments are recommending vaccines in coercive and mandatory programs without providing sufficient empirical evidence [28], a result of the misapplication of the precautionary principle (Figure 1). Mandatory vaccination policies are being promoted to the public based on the concept of creating herd immunity without any evidence to support this theory. The term ‘herd immunity’ was first used with respect to the creation of immunity by natural exposure in communities through asymptomatic and mild infections [9][29][30].Health departments and the GAVI/WHO are only theorising that vaccines can also create herd immunity because

vaccine manufacturers have not provided this evidence.

There are several reasons why vaccines may not be able to achieve herd immunity. Firstly, there can be more than one strain of an organism that causes the disease which may not be included in the vaccine [8][29][31]. These strains also mutate from year to year, or the vaccine may select for strains not adequately targeted by the antigen source in the vaccine. Secondly, humans may not be the only reservoir for the disease. The virus/bacteria may be found in other animals therefore transmission is not always interrupted by vaccination programs [9]. For example, strains of whooping cough (pertussis) are also found in dogs. These criteria contradict the government's claim that all vaccines can create herd immunity. This is significant because the government uses the claim of 'vaccine-created herd immunity' to promote vaccines and to state that it is everyone's responsibility to vaccinate to protect the community. Further, vaccines are not protective for a proportion of the population due to their genetics. Many people are pre-disposed to chronic illnesses due to the influence of vaccine components on their genetic make-up. Hence, vaccines will cause an unknown number of adverse health outcomes in the population because governments are ignoring the science of epigenetics and are not systematically monitoring the health outcomes of vaccination programs to determine the frequency of adverse events to vaccines.

The claim that vaccines can produce herd immunity in populations is only an *assumption* by the GAVI alliance: an alliance that includes the Federation of Pharmaceutical Companies and many other corporations that profit from vaccines [32]. When health needs are determined by outside experts, they do not always fulfill the needs of the community [33]. The targeted vaccination levels of 80-90% that governments are recommending are also assumptions that have been accepted by the community on faith and not empirical evidence [29] (p158). Further the duration of immunity should also be considered in the decision to mandate vaccines in the community. Natural infection with measles and whooping cough produces long-term immunity [8][34] and the risk of death and serious illness from these diseases were reduced in developed countries by 1950/60, before vaccines were introduced. This was a result of the improvements to the environment and lifestyle from political and economic decisions that reduced the virulence of these infectious agents:

8. Risk Due to Population-Wide Vaccination Strategy

It is unnecessary and harmful to vaccinate every individual because not everyone has the same risk of getting these infectious diseases even if they are infected by the agent [34][9]. This is a key factor to consider when the vaccines that are being used to mitigate the risk also carry a serious risk of death or chronic illness for many people due to their genetics. This fact will undermine the genetic fabric of society if all individuals are vaccinated. This is a form of artificial selection on humans with unknown consequences. Further, natural infections in children over one year of age are essential for priming all parts of the immune system to function properly and to provide better community protection through long-term immunity [13][29].

In addition to the foreign animal and human DNA there are many chemicals in the vaccine carrier that the public is not informed about. These chemicals are referred to as 'excipients' because they are not active components of vaccines in inducing immunity. Whilst an excipient is defined as a 'non-active component' the chemicals in the vaccine carrier do react in the human body and they are a plausible cause of the chronic illnesses that we are seeing increase in populations.

Examples of these chemicals are the neurotoxins, aluminium and mercury. Mercury is present in some vaccines in the form of thimerosal and it has not been removed from all childhood vaccines [35][36]. Genetic predisposition alone should prevent any vaccine from being coerced or mandated in genetically diverse populations. When the mitigating preventative measure involves a medical intervention that is associated with serious adverse health outcomes in some people, including death,

it is against the tenets of good medical practice and ethics to provide financial incentives to medicate healthy people with this intervention [37][38]. The guiding principles set by the Australian Medical Association (AMA) state that doctors must put their patient's best interest first and that they will not use their medical knowledge to breach human rights [39]. These principles have been set by the World Medical Association (WMA). Health is not promoted in communities when doctors and health professionals do not have autonomy in the medical advice that they provide to patients [40]. Governments claim current vaccination policies promote 'health' in the community, but they do not evaluate or promote these policies on evidence of *improved health outcomes* in the population. Prior to 1995 the surrogate of age standardised infant mortality rates was used as an indicator of the health status of communities. This was an inadequate way of determining the health of communities as there are many aspects of health that are difficult to measure. This includes disability, pain, chronic illness and mental well-being. However, it was a useful measure of health in the first part of the twentieth century when infectious diseases were prevalent, and children were dying from these infectious diseases. After the risk from infectious diseases had declined by 1950/60, infant mortality rates were no longer the best measure of the health of communities. By the 1990's it was observed that infant mortality rates in countries that use the highest number of doses of vaccines were increasing in a direct dose-response correlation with the expanding vaccination program. For example, the US specified 26 doses of vaccine for infants less than one year of age in 2011 yet 33 developed nations had lower infant mortality rates than the US and they used less doses of vaccine. Linear regression analysis showed a high statistically significant correlation between increasing number of vaccine doses and increasing infant mortality rates, particularly between nations giving 12-14 vaccines (Japan and Sweden) and those like the US and Australia who give 24-26 vaccines in the first year of life [40]. Miller also found a dose-dependent association between the number of vaccines administered simultaneously in one visit and the likelihood of hospitalisation or death from an adverse event (AE): the younger the age the more likely the occurrence of a significant AE [41]. Governments have not used infant mortality rates to assess the outcomes of vaccination programs since 1995 [42] (p11). After this time, vaccines were promoted on the need to raise the vaccination rate to 95% to establish vaccine-created herd immunity. However, governments do not have to provide evidence that a vaccine can create herd immunity to get it listed on the government recommended program [28]. Consequently, many vaccines have been mandated for children in Australia that have never been used by adults and were clearly not responsible for controlling the diseases with a 95% uptake by 1950/60.

9. Back to Evidence (3)

The fact that governments have never used health outcomes of children to evaluate and promote vaccination programs means there is no causal-level evidence to support claims that vaccination programs are promoting health in the community. These programs are not being evaluated or promoted on health outcomes. They are being promoted on the *assumption* that a 95% uptake rate of each vaccine results in healthier communities. There is no scientific justification for this uptake rate or evidence that communities are healthier when it is achieved. The evidence of children's health since 1990 in all countries demonstrates health is declining in direct correlation to the government's expanding vaccination program. A government that does not investigate this direct dose-response correlation, a significant indicator of causality, and other evidence consistent with causality, before claiming the vaccination program is safe is experimenting on the entire population without informed consent, and is committing a crime against the population.

10. Conclusion

The deterioration of the health of populations is not being associated with the increased use of vaccines because governments do not systematically

monitor vaccinated populations with active surveillance systems for 5-10 years. They also do not use: i) inert placebos in the clinical trials for safety ii) acknowledge the mechanisms by which vaccines can cause these chronic illnesses iii) investigate the direct-dose response correlation to chronic illnesses or iv) acknowledge parents' evidence of vaccine injury. Many of these illnesses/deaths have been linked as being associated with vaccines for over six decades, as reported on pharmaceutical package inserts. Government policies that allow unsupported claims of the benefits and risks of vaccines due to a lack of scientific evidence are unfounded. Coercive and mandatory vaccination policies may be a threat to the genetic fabric of human populations due to our genetic diversity. Human health is at serious risk whilst ever governments do not apply the precautionary principle in a manner that renders public health programs capable of protecting human health. The proper application would cause the burden of proof of harmlessness to rest with pharmaceutical companies and governments, not the general public. This will result in the protection of human health in government policy and not the vested interests of pharmaceutical companies and others with a financial interest in promoting vaccines.

References

[1] Australian Institute of Health and Welfare (AIHW). **Australian Government: i) Selected Chronic Diseases Among Australia's Children. ii) Chronic Diseases and Associated Risk Factors. iii) A Picture of Australia's Children** . *Bulletin*, September 2005.

[2] Public Health Agency of Canada. **Thimerosal Updated Statement ACS-6. Canada** . *Communicable Disease Report*, 33, July 2007. LINK .

[3] **Mercury in Medicine Report, US Congressional Record; Findings and Recommendations, Safe Exposure Standard as Reported in Executive Summary** . May 2003. aapsonine.org .

[4] Informed Consent Action Network (ICAN). **Vaccine Safety: Introduction to Vaccine Safety Science & Policy in the United States (Version 1)** . *ICAN website*, 2017. ICAN .

[5] Medical Products Agency (MPA). **Public Assessment Report. Scientific Discussion. Afluria, suspension for injection, Influenza vaccine (split virion, inactivated). Mutual Recognition Procedure** . *SE/H/o485/01/E01* . *Sweden*, June 2007. PDF .

[6] Australian Government (AG). **Immunise Australia Program (IAP)** . *Department of Health and Ageing*, 2006. health.gov.au .

[7] Wilyman J. **A critical analysis of the Australian government's rationale for its vaccination policy, PhD thesis** . *University of Wollongong*, 2015. University of Wollongong .

[8] Plotkin SA. **Is There a Correlate of Protection for Measles Vaccine?** . *The Journal of Infectious Diseases*, 221(10):1571–1572, Nov. 2020.

[9] Friis RH and Sellers TA. **Epidemiology for Public Health Practice (3rd Ed)** . *Massachusetts: Jones and Bartlett Publishers*, 2004.

[10] Science and Environmental Health Network (SEHN). **The Precautionary Principle** . 2011. SEHN .

[11] World Health Organisation Commission on Social Determinants of Health (CSDH). **Action on the Social Determinants of Health: Learning From Previous Experiences** . 2005.

[12] World Health Organisation. **Immunisation Service Delivery (ISD)**. *Expanded Program on Immunisation (EPI)*, October 2013.

[13] Burnet FM. **The Pattern of Disease in Childhood** . *Australasian Annals of Medicine*, 1(2):93–107, 1952.

[14] Deisher TA, Doan NV, and Jarzyna P. **Insertional Mutagenesis and Autoimmunity Induced Disease caused by Human Fetal**

and Retroviral Residual Toxins in Vaccines. 2016.

[15] Arumugham V. **Evidence that Food Proteins in Vaccines cause the Development of Food Allergies and its Implication for Vaccination Policies** . *Journal of Developing Drugs*, 2015. DOI .

[16] Arumugham V and Trushin MV. **Cancer immunology, bioinformatics, and chemokine evidence link vaccines contaminated with animal proteins to autoimmune disease: a detailed look at Crohn's Disease and Vitiligo** . *Journal of Pharmaceutical Sciences and Research*, 10(8):2106–2110, 2018.

[17] Gilbert SG. **A Small Dose of Toxicology: the health effects of common chemicals. Florida** . *: CRC Press*, 2004.

[18] McKeown T. **The role of Medicine: Dream, Mirage or Nemesis?** . *Oxford: Basil Blackwell*, 1979.

[19] Stanley FJ. **Centenary Article: Child Health Since Federation . In Yearbook Australia 2001**. *Canberra: Australian Bureau of Statistics [ABS Catalogue No. 1301.0]*, pages 368–400, 2001.

[20] Illich I. **Medical Nemesis: The Expropriation of Health** . *London: Calder and Boyars L.*, 1976.

[21] Commonwealth of Australia (CoA). **Official Yearbook of the Commonwealth of Australia, No.37-72**. *Commonwealth of Australia*, 1986.

[22] Warfel JM, Zimmerman LI, and Merkel TJ. **Acellular pertussis vaccines protect against disease but fail to prevent infection and transmission in a non-human primate model, Division of Bacterial, Parasitic and Allergenic Products** . *Center for Biologics Evaluation and Research . US Food and Drug Administration (FDA)*, 2013.

[23] Australian Government (AG). Department of Health and Ageing Communicable Diseases Control. **Vaccine Preventable Diseases and Vaccination Coverage in Australia 2003-2005, Appendix 5: Government funding of National Immunisation Programs in Australia** . *Communicable Diseases Intelligence Journal (CDIJ)*, 31=Supplee, June 2007.

[24] Cumpston JHL and Ed. Lewis MJ. **Health and Disease in Australia: A History by JHL Cumpston** . *Canberra: Australian Government Publishing Service*, 1989.

[25] Lancaster HO. **Infant Mortality in Australia** . *The Medical Journal of Australia*, (2):100–108, 1956.

[26] Stewart GT. **Vaccination against Whooping Cough: Efficacy v Risks** . *The Lancet*, pages 234–237, Jan 1977.

[27] Muraskin W. **The Global Alliance of Vaccines and Immunisation: is it a new model for effective public-private cooperation in international public health?** . *American Journal of Public Health*, 94(11):1922–5, Nov 2004.

[28] Nolan T. **The Australian model of immunisation advice and vaccine funding** . *Vaccine*, pages A76–A83, April 2010.

[29] Colgrove J. **State of Immunity: The Politics of Vaccination in Twentieth Century America** . *Berkeley: University of California Press*, 2006.

[30] Habakus LK. **A Human Rights Assessment. In Habakus and Holland M. (Eds). Vaccine Epidemic: how corporate greed, biased science and coercive government threaten our human rights, our health and our children** . *New York: Skyhorse. Chapter 3*, 2011.

[31] Behrman RE and Kliegman RM eds. (Third Ed.). **Nelson Essentials of Pediatrics** . *Philadelphia: WB Saunders Company*, 1998.

[32] McNeill D, Andresen S, and Sandberg K. . **The global politics of health: actors and initiatives** . *In Roalkvam S, McNeill D and Blume S (Eds). Protecting the World's Children Immunisation Policies and Practice. Oxford. Oxford University Press*, pages 59–87, 2013.

[33] Basch PF. **Vaccines and World Health** . *Science, Policy and Practice. New York and Oxford: Oxford University Press*, 1994.

[34] Wendelboe AM, Van Rie A, Salmaso S, and Englund JA. **Duration of Immunity Against Pertussis After Natural Infection or Vaccination** . *The Pediatric Infectious Disease Journal*, 24(5):558–561, 2005.

[35] Exley C. **The Toxicity of Aluminium in Humans** . *Morphologie*, 100(329):51–55, June 2016.

[36] Dorea JG. **to aluminium and mercury in early life (infancy)** . *Environ Research*, 188:109734, Sep 2020.

[37] Medical Board of Australia (MBA). **Good Medical Practice: A Code of Conduct for Doctors in Australia** . 2010. Medicalboard.gov.au .

[38] Seedhouse D. **Ethics: The Heart of Health Care (Third Edition)** . *Chichester UK: Wiley*, 2009.

[39] Australian Medical Association (AMA). **Declaration of Geneva. Guiding principles of a Medical Practitioner** . 2006. AMA .

[40] Miller NZ and Goldman S. **Infant mortality rates regressed against number of vaccine doses routinely given: Is there a biochemical or synergistic toxicity?** . *Human Experimental Toxicology*, 30(9):1420–1428, September 2011.

[41] Miller NZ. **Combining Childhood Vaccines at One Visit is Not Safe** . *Journal of American Physicians and Surgeons*, 21(2):47–49, 2016.

[42] Blume S, Jani J, and Roalkvim S. **Saving children's lives: perspectives on immunization. In Roalkvim S. McNeill D and Blume S (Eds). Protecting the World's Children: Immunisation Policies and Practice** . *Oxford: Oxford University Press*, pages 1–30, 2013.