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VIA ELECTRONIC FILING

June 17, 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

Dear Commissioner Hahn,

Enclosed is a Citizen Petition and a Petition for Administrative Stay of Action filed by Del Bigtree and the Informed Consent Action Network ("ICAN") regarding clinical trials of vaccines for SARS-CoV-2 which raise exigent concerns that demand your immediate attention.

ICAN looks forward to receiving a timely decision and we, as counsel to the petitioners, remain available to answer questions and provide any relevant additional information.

Very truly yours,

/s/ Aaron Siri

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UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES
AND THE FOOD AND DRUG ADMINISTRATION

PETITION FOR ADMINISTRATIVE	**:**	
ACTION TO REQUIRE PLACEBO	**:**	
CONTROL GROUP IN CLINICAL	**:**	**Docket No. 2013-S-0610**
TRIALS OF COVID-19 VACCINES	**:**	

CITIZEN PETITION

The undersigned submits this petition pursuant to 21 CFR § 10.30 and related relevant provisions of the Federal Food, Drug, and Cosmetic Act and Public Health Service Act; the Public Health and Welfare at, *inter alia*, 42 U.S.C. § 262(a)(2)(A)-(C) and 42 U.S.C. § 262(j); and 42 U.S.C. § 300aa-10 *et seq.* to request the Commissioner of Food and Drugs (the "**Commissioner**") require that all Phase II and III trials of vaccines against the novel coronavirus, SARS-CoV-2 ("**COVID-19**") include, *inter alia*, a placebo (saline injection) control group (i.e., a comparator group).

A. Action Requested

1. It is hereby requested that the Commissioner:

   a. Require all Phase II and III trials of vaccines against COVID-19 include a placebo control group (i.e., a placebo comparator group).

   b. The placebo shall be a saline injection without anything added. If the vaccine and saline are visually distinguishable, opaque vials should be used.

   c. The placebo control group shall be of at least equivalent size to the experimental group.

   d. All systemic adverse reactions, adverse events, serious adverse events, medically-attended adverse events, new onset medical conditions, and any other health issue arising or exacerbated post-vaccination shall be documented for each subject post-vaccination for a period of at least twelve months for adults, thirty-six months for children and teenagers, and sixty months for infants and toddlers.

B. Statement of Grounds

2. According to the Center for Disease Control and Prevention ("**CDC**") and the Food and Drug Administration ("**FDA**"), randomized placebo-controlled trials are the standard for determining the safety and efficacy of a new drug or biological product, including new vaccines. A "placebo" is defined as "[a] substance or treatment that has no effect on human beings."[1]

[1] https://www.cdc.gov/vaccines/terms/glossary.html (last visited June 2, 2020).

Clinical trials for new pharmaceutical products typically do not use a non-inert substance as a control because, due to its pharmacological effects, a non-inert substance makes it impossible to isolate the effects of just the experimental product being studied.

3. Reflecting the central role of placebos in testing, on May 24, 2020, a member of the FDA's Vaccines and Related Biological Products Advisory Committee ("**VRBPAC**"), Dr. Paul Offit, told CNN News that, in order to determine if a COVID-19 vaccine is safe and effective, "we are waiting for the big trial… the large prospective **placebo controlled trial**, we have 20,000 people who get a vaccine, 10,000 people who get a **placebo**, **then and only then will you know whether a vaccine is safe and effective.**"[2]

4. Likewise, the National Institute of Aging, an institute within the National Institutes of Health, explains as follows regarding designing clinical trials:

> In undertaking a clinical trial, researchers don't want to leave anything to chance. They want to be as certain as possible that the results of the testing show whether or not a treatment is safe and effective. The "gold standard" for testing interventions in people is the "randomized, placebo-controlled" clinical trial. ... A placebo is an inactive substance.[3]

5. Where an effective vaccine already exists for an infection, ethical considerations may require using the existing vaccine, rather than a placebo, as the control (an "**active control**"). The FDA's industry guidance explains that an "active control must be a drug whose effect is well defined," which means "historical placebo-controlled trials are available to define the active control effect."[4] The importance of only using an active control that has already been licensed based on a placebo-controlled trial is explained by the FDA as follows:

> The placebo-controlled trial measures the total pharmacologically mediated effect of treatment. In contrast, an active control trial … measures the effect relative to another treatment. The placebo-controlled trial also allows a distinction between adverse events due to the drug and those due to the underlying disease or background noise.[5]

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[2] https://www.cnn.com/videos/health/2020/05/24/coronavirus-covid-19-vaccine-trials-vaccinologist-concern-ip-vpx.cnn (emphasis added) (last visited June 2, 2020).

[3] https://www.nia.nih.gov/health/why-are-placebos-important (last visited June 2, 2020).

[4] https://www.fda.gov/media/78504/download (last visited June 2, 2020).

[5] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/e10-choice-control-group-and-related-issues-clinical-trials (last visited June 2, 2020).

Because there is no licensed COVID-19 vaccine, an active control is not appropriate for trials of new COVID-19 vaccines; thus, clinical trials of potential COVID-19 vaccines should include a placebo control group.[6]

6. Without a placebo-controlled trial, cause and effect between a potential adverse effect and the vaccine being studied is very difficult and often impossible to establish.[7] Hence, once licensed, studying claims of injury occurring post-licensure becomes exceedingly difficult. This is because after licensure, it will be considered unethical to conduct a placebo-controlled clinical trial of a licensed COVID-19 vaccine. Having a scientifically valid and robust clinical trial prior to licensure will avoid this quagmire.

7. The need for a robust placebo-controlled clinical trial of any potential COVID-19 vaccine is even more acute since, according to the most recent CDC estimates, COVID-19 rarely injures children and younger healthy adults and, overall, 99.74% of those infected with COVID-19 recover[8]; even without social distancing, it appears only a minority of those in contact with an infected individual become infected; and the vaccine will likely be injected into billions of individuals around the globe. If the vaccine, for example, causes .3% of children to develop a chronic health condition a year after injection, that could cause lifelong health issues for millions of children. Without a randomized placebo-controlled trial of proper size and duration, this potentially catastrophic result will not be identified prior to licensure.

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[6] Moreover, even after a COVID-19 vaccine has been licensed, there are still many considerations that must be taken into account before using a COVID-19 vaccine as a control, rather than a placebo, for any new potential COVID-19 vaccine. *See* https://www.fda.gov/RegulatoryInformation/Guidances/ucm126501.htm ("There are three principal difficulties in interpreting active-control trials. … One problem is that there are numerous ways of conducting a study that can obscure differences between treatments, such as poor diagnostic criteria, poor methods of measurement, poor compliance, medication errors, or poor training of observers. As a general statement, carelessness of all kinds will tend to obscure differences between treatments. Where the objective of a study is to show a difference, investigators have powerful stimuli toward assuring study excellence. *Active-control studies, however, which are intended to show no significant difference between treatments, do not provide the same incentives toward study excellence, and it is difficult to detect or assess the kinds of poor study quality that can arise.* The other problem is that a finding of no difference between a test article and an effective treatment may not be meaningful.") (last visited June 2, 2020).

[7] https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/adverse-reactions.html ("establishing evidence for cause and effect on the basis of case reports and case series alone is usually not possible," rather, researchers need "to compare the incidence of the event among vaccinees with the incidence among unvaccinated persons") (last visited June 2, 2020); https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3505292/ (The entire advantage of a randomized placebo-controlled trial "is the ability to demonstrate causality" i.e., cause-effect relationship.) (last visited June 2, 2020); https://www.cdc.gov/vaccines/pubs/surv-manual/chpt21-surv-adverse-events.html (The Vaccine Adverse Events Reporting System (VAERS) is unable "to determine causation" because "there is a lack of an unvaccinated group for comparison in VAERS.") (last visited June 2, 2020).

[8] https://www.cdc.gov/coronavirus/2019-ncov/hcp/planning-scenarios.html#box (last visited June 2, 2020).

8. Moreover, states in the United States are expected to mandate the vaccine for all their residents. For example, the New York State Bar Association recently issued a report on COVID-19 recommending that "[w]hen the efficacy of a COVID-19 vaccine has been confirmed, enact legislation requiring vaccination of each person unless the person's physician deems vaccination for his or her patient to be clinically inappropriate."[9] Mandating administration of the vaccine, thereby eliminating the right to informed consent, only makes more acute the need to assure that the safety and efficacy of any COVID-19 vaccine is robustly studied in a placebo-controlled trial.

9. Further heightening this need for placebo-controlled studies is the fact that the Secretary of the United States Department of Health & Human Services has already granted those developing and selling any COVID-19 product broad immunity from liability for injuries.[10]

10. Fortunately, most of the FDA-approved Phase II and III study designs for potential COVID-19 candidate vaccines appear to include a saline placebo control group. For example, the leading candidate COVID-19 vaccine in the United States, developed with the National Institute of Allergy and Infectious Disease ("**NIAID**") lists "Placebo: Saline" as the control for its Phase II clinical trial.[11] As another example, the leading COVID-19 vaccines being developed in China both list a placebo control group in their Phase II study designs approved by the FDA.[12]

11. Unfortunately, this is not true for all of the COVID-19 vaccine trials approved by the FDA. For example, the Phase I/II clinical trial of the COVID-19 vaccine ChAdOx1 nCoV-19, currently under development by AstraZeneca, initially provided that the control group would receive a "Saline Placebo."[13] After approving this study design, the FDA inexplicably approved changing the control from a "Placebo Control" to "MenACWY," which is another vaccine for a bacterial infection unrelated to COVID-19. It is ethically and scientifically indefensible to use MenACWY vaccine as a control for a COVID-19 vaccine trial, including because the safety of MenACWY has never been established in a placebo-controlled clinical trial.[14]

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[9] https://nysba.org/app/uploads/2020/05/HealthLawSectionTaskForceCOVID-19Report_5.13.20-1.pdf (last visited June 2, 2020).

[10] https://www.phe.gov/Preparedness/legal/prepact/Pages/default.aspx (last visited June 2, 2020).

[11] https://www.clinicaltrials.gov/ct2/show/NCT04405076 (last visited June 2, 2020).

[12] https://www.clinicaltrials.gov/ct2/show/NCT04341389; (last visited June 2, 2020); https://www.clinicaltrials.gov/ct2/show/NCT04383574 (last visited June 2, 2020).

[13] https://clinicaltrials.gov/ct2/history/NCT04324606 (last visited June 2, 2020).

[14] *Ibid.* The trade name for MenACWY vaccine in the United States is Menveo. This product was licensed for adults based on a clinical trial in which the control group of 1,966 participants received either Menomune (209 participants) or Menactra (1,757 participants). https://www.fda.gov/media/78514/download (last visited June 2, 2020). Menactra was licensed based on a clinical trial in which Menomune

12. Permitting clinical trials of a potential COVID-19 vaccine without a placebo control group is inappropriate, scientifically and ethically, especially given the above. The use of a non-inert substance as a control creates significant uncertainty in confirming, among other things, the safety of a COVID-19 vaccine. There is no reason to create such uncertainty or to compromise the scientific validity and robustness of the clinical trial for any candidate COVID-19 vaccine by having a control that is anything other than a saline placebo.

13. Moreover, as reflected in the FDA's guidance to industry, to assure sufficient power to properly compare the safety profile between the COVID-19 vaccine group and the saline placebo group, the saline placebo group should be at least the size of the group receiving the COVID-19 vaccine.[15]

14. Finally, to assure that the potential adverse events from the candidate COVID-19 vaccine are captured, all systemic adverse reactions, adverse events, serious adverse events, medically-attended adverse events, new onset medical conditions, and any other health issue arising or exacerbated post-vaccination should be documented for each subject post-vaccination for a period of at least twelve months for adults, thirty-six months for children and teenagers, and sixty months for infants and toddlers. These minimal timeframes will increase the confidence that adverse and non-specific health issues that the COVID vaccine may cause are captured. This is why, for example, the drugs Enbrel[16], Lipitor[17], and Botox[18] had safety review periods of 6.6 years, 4.8 years and 51 weeks, respectively, with a placebo control group. The adverse events captured during these time-frames should also not be limited merely to "serious adverse events," since there are many serious autoimmune, neurological and chronic health disorders that have a serious impact on the quality of life but yet are categorized by the FDA as "adverse reactions" and not "serious adverse reactions." And the time frame for the safety review should be longer for minors, and in

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was the active comparator. https://www.fda.gov/media/75619/download (last visited June 2, 2020). Quizzically, the clinical trials section of the package insert for Menomune only lists the clinical trial in which it was used as a comparator against Menactra. https://www.fda.gov/media/83562/download (last visited June 2, 2020). Meaning, the same clinical trial in which Menactra was studied with Menomune as its active control is apparently relied upon by the FDA to support the safety of both of these products. Using any of these products as an active control for a COVID-19 vaccine is unscientific and unacceptable. The control should be a saline placebo.

[15] https://www.fda.gov/media/87621/download (last visited June 2, 2020).

[16] https://www.accessdata.fda.gov/drugsatfda_docs/label/2012/103795s5503lbl.pdf (last visited June 2, 2020).

[17] https://www.accessdata.fda.gov/drugsatfda_docs/label/2009/020702s056lbl.pdf (last visited June 2, 2020).

[18] https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/103000s5302lbl.pdf (last visited June 2, 2020).

particular for babies and toddlers since autoimmune, neurological and developmental disorders will often not be diagnosed until after babies are a few years old.[19]

15. The undersigned therefore respectfully urges that the actions requested above be adopted forthwith.

C. Environmental Impact

16. The undersigned hereby states that the relief requested in this petition will have no environmental impact and, therefore, an environmental assessment is not required under 21 C.F.R. Sections 25.30 and 25.31.

D. Certification

17. I certify that, to the best of my knowledge and belief: (a) this petition includes all information and views upon which the petition relies; (b) this petition includes representative data and/or information known to the petitioner which are unfavorable to the petition; and (c) I have taken reasonable steps to ensure that any representative data and/or information which are unfavorable to the petition were disclosed to me. I further certify that the information upon which I have based the action requested herein first became known to the party on whose behalf this petition is submitted on or about the following date: May 28, 2020. I have not received or expect to receive payments, including cash and other forms of consideration, to file this information or its contents. I verify under penalty of perjury that the foregoing is true and correct as of the date of the submission of this petition.

Informed Consent Action Network
Del Bigtree, President
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[19] For example, according to the CDC, even for a common neurological disorder such as ADHD, "5 years of age was the average age of diagnosis for children reported as having severe ADHD." https://www.cdc.gov/ncbddd/adhd/features/key-findings-adhd72013.html (last visited June 2, 2020). As another example, learning disabilities, a group of common developmental issues, are often "identified once a child is in school." https://www.nichd.nih.gov/health/topics/learning/conditioninfo/diagnosed (last visited June 2, 2020). Even for asthma, a very common autoimmune condition, whose symptoms are obvious, diagnosis can be difficult for children under 5 years of age because lung function tests aren't accurate before 5 years of age and "[s]ometimes a diagnosis can't be made until later, after months or even years of observing symptoms." https://www.mayoclinic.org/diseases-conditions/childhood-asthma/diagnosis-treatment/drc-20351513 (last visited June 2, 2020).

UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES
AND THE FOOD AND DRUG ADMINISTRATION

PETITION FOR STAY OF ACTION	**:**	
TO REQUIRE PLACEBO CONTROL	**:**	
GROUP IN CLINICAL TRIALS	**:**	**Docket No. 2013-S-0610**
OF COVID-19 VACCINES	**:**	

ADMINISTRATIVE STAY OF ACTION

The undersigned submits this petition under 21 CFR § 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**") require that all Phase II and III trials vaccines against the novel coronavirus, SARS-CoV-2 ("**COVID-19**") include, *inter alia*, a placebo (saline injection) control group (i.e., a comparator group).

A. Decision Involved

1. Approval of the Investigational New Drug ("**IND**") Application(s) or any other approval by the FDA which approved a Phase II and/or Phase III trial for ChAdOx1 nCoV-19 with a control group that will receive MenACWY instead of a saline placebo, as well as the approval of any other Phase II or Phase IIII trial for any COVID-19 vaccine with a control group that receives anything other than a saline placebo.

B. Action Requested

2. A stay of the approval of the application for any Phase II and III trials of vaccines against COVID-19, including for ChAdOx1 nCoV-19, that do not include a placebo control group (i.e., a placebo comparator group) until:

a. the study design for the trial is amended to include a placebo control group (i.e., a placebo comparator group);

b. the placebo is specified as a saline injection and, if visually distinguishable from the vaccine, both should be packaged in opaque vials; and

c. the placebo control group is of at least equivalent size to the experimental group.

C. Statement of Grounds

3. The undersigned hereby incorporates by reference as if fully set forth herein the Statement of Grounds from its Citizen's Petition submitted simultaneously with this request. These incorporated allegations support that: (i) without the requested stay above, the petitioner will suffer irreparable harm, (ii) the requested stay 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.

4. Petitioner will suffer irreparable harm because once the FDA licenses a 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*. (*Citizen's Petition* ¶¶ 2-8.) Furthermore, if the vaccine is licensed without a placebo control group now, ethical considerations may prevent such a placebo controlled study post-licensure, thereby preventing any such study from ever occurring. (*Citizen's Petition* ¶ 5.) The request for a stay is not frivolous and is being pursued in good faith as it seeks to increase the scientific integrity and reliability of the trials of any potential COVID vaccine. (*Citizen's Petition* ¶¶ 2-12.) Requiring a placebo control group for the trials of a vaccine where no vaccine exists for the target infection is well supported by the sound public policy detailed in the FDA's own guidance documents. (*Citizen's Petition* ¶¶ 2-7.) Finally, the public interest weighs strongly in favor of the requested relief because using a placebo control (i) will comport with the best scientific practices, (ii) increase public confidence in the safety and efficacy of a product expected to be mandated, and (iii) using a non-inert substance as a control will have the opposite result in that it will create uncertainties regarding the safety of the COVID vaccine. (*Citizen's Petition* 2-12.)

5. The undersigned therefore respectfully urges that the actions requested above be adopted forthwith.

D. Certification

6. I certify that, to the best of my knowledge and belief: (a) this petition includes all information and views upon which the petition relies; (b) this petition includes representative data and/or information known to the petitioner which are unfavorable to the petition; and (c) I have taken reasonable steps to ensure that any representative data and/or information which are unfavorable to the petition were disclosed to me. I further certify that the information upon which I have based the action requested herein first became known to the party on whose behalf this petition is submitted on or about the following date: May 28, 2020. I have not received or expect to receive payments, including cash and other forms of consideration, to file this information or its contents. I verify under penalty of perjury that the foregoing is true and correct as of the date of the submission of this petition.

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