U.S. FOOD & DRUG ADMINISTRATION

June 17, 2022

Jianqing Wu, Ph.D., J.D.
[redacted]

Sent via email to: [redacted]

Re: Docket No. FDA-2022-P-0122

Dear Dr. Wu,

This letter responds to the citizen petition dated "January 27, 2022, updated February 3, 2022," and received by FDA on February 4, 2022, that you (Petitioner) submitted to the Food and Drug Administration (FDA, the Agency, we) relating to Emergency Use Authorization and licensure of Coronavirus Disease 2019 (COVID-19) vaccines (the Petition), among other topics.

In the Petition, Petitioner lists the following as "actions requested":

> 1. Investigate medical science information laundering by monopolistic medical publishers and how they have suppressed new discoveries that would have thrown out the reductionist research and treatment model, knowingly produce flawed and fraudulent knowledge for their revenue in the name of science, pursuant to the implied power under 21 U.S. § 355(b)-(c), 42 U.S. § 262(a)(2), 21 U.S. § 564(g)(2), 21 U.S. § 379dd, and 21 C.F.R. §§ 1.21.
>
> 2. Evaluate a true life model and reject the reductionist research and treatment model, and evaluate safety and effectiveness of the mRNA vaccines, pursuant to 21 U.S. § 355(b)-(c), 42 U.S. § 262(a)(2), 21 U.S. § 564(g)(2), and 21 U.S. § 379dd.
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> 3. Suspend all outstanding mRNA vaccine use authorizations and revoke same, pursuant to 21 U.S. § 564(g)(2). All dangers and potential risks are present in all mRNA vaccines and all flaws in the research model, data analysis, and conclusions have impacted the approval of all mRNA vaccines.
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> 4. Urge FDA to initiate investigation with DOJ, FTC, FCC, etc. to understand the extent of criminal violations by information launders, particularly, antitrust violation, wire fraud violation, and wastes of massive federal research funds attributable to the conduct of monopolistic medical publishers. The authority is implied by FDA statutory mission to protect public health.

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5. Request FDA to overhaul its approval framework: rejecting the drugs-for-health hypothesis, adopting a holistic analysis approach, avoiding trade art and junk science, restructuring advisory committee structure and member compositions, pursuant to implied power provided in 21 U.S. § 379dd. Since this will take time, FDA does not need to address this request within 180 days, I will follow up by filing my continuous petitions.

6. The outcome of this petition will affect the health and lives of the U.S. population and potentially billions of people globally. However, federal government, state governments, foundations, etc. generally do not provide funding for researches for finding vaccines risks. Due to such funding biases and suppression of vital researches, Petitioner has to rely on observations, "misinformation", and "underground" data (per the characterization of information-launders) in this petition. FDA should bear responsibility to validate the accuracy of information from such sources. However, even if FDA rejects all "misinformation' and "underground" data, this petition still invalidates research conclusions that FDA has relied upon in granting mRNA vaccines use authorizations.

7. Petitioner started peerless researches as early as the start of the COVID-19 pandemic, but do not get any support from any peers, any funding agencies, and any media. Moreover, this petition is based on a different life model which is backed up by an extremely large amount of factual findings by independent researchers. In the eyes of people who have gotten used to the reductionist "science", the petition may appear to contain inaccuracies, inconsistent data, non-conventional expressions, etc. Those problems cannot be addressed until readers fully understand the new life model. If Petitioner spends years to address those problems, all damages to the U.S. population and humankind will be quickly realized. Petitioner therefore has a need to file this petition without any peer comment and review. The extraordinary circumstance justifies this decision. I hope that public readers of this petition will provide constructive feedback during the review period. Therefore, Petitioner requests FDA to grant a permission to file one to more updated petitions to clarify all difficulties that may inherently arise from evaluating two different science frameworks.

Petition at 1-2.

This letter responds to the Petition in full. We have carefully reviewed the Petition and other information available to the Agency. Based on our review of these materials, and for the reasons described below, we conclude that the Petition does not contain facts demonstrating any reasonable grounds for the requested actions. In accordance with Title 21 CFR (Code of Federal Regulations)10.30(e)(3), and for the reasons stated below, FDA is denying the Petition.

Here is an outline of our response:

I. BACKGROUND

There is currently a pandemic of respiratory disease, COVID-19, caused by a novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The COVID-19 pandemic presents an extraordinary challenge to global health. On January 31, 2020, the Department of Health and Human Services (HHS) issued a declaration of a public health emergency related to COVID-19.[1] On February 4, 2020, pursuant to section 564 of the Federal Food, Drug, and Cosmetic Act (FD&C Act), the Secretary of HHS determined that there is a public health emergency that has a significant potential to affect national security or the health and security of United States (U.S.) citizens living abroad, and that involves the virus that causes COVID-19.[2] On the basis of such determination, on March 27, 2020, the Secretary then declared that circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic ("COVID-19 EUA Declaration"), pursuant to section

[1] Secretary of HHS Alex M. Azar, Determination that a Public Health Emergency Exists (Originally issued on Jan. 31, 2020, and subsequently renewed), https://www.phe.gov/emergency/news/healthactions/phe/Pages/default.aspx.
[2] HHS, Determination of Public Health Emergency, 85 FR 7316, February 7, 2020, https://www.federalregister.gov/documents/2020/02/07/2020-02496/determination-of-public-health-emergency.

564(b)(1) of the FD&C Act.[3] In addition, on March 13, 2020, the President declared a national emergency in response to COVID-19.[4]

Commercial vaccine manufacturers and other entities have developed COVID-19 vaccines, and clinical studies of these vaccines are underway and/or have been publicly reported. Between December 11, 2020, and February 27, 2021, FDA issued EUAs for three vaccines to prevent COVID-19 ("the Authorized COVID-19 Vaccines"), including vaccines sponsored by Pfizer Inc. (Pfizer),[5] ModernaTX, Inc. (Moderna), and Janssen Biotech, Inc. (Janssen). The EUAs have been amended since initial issuance.

On August 23, 2021, the Agency approved Comirnaty (COVID-19 Vaccine, mRNA) ("Comirnaty") and the approval was granted to BioNTech Manufacturing GmbH.[6] Comirnaty is approved for the prevention of COVID-19 caused by SARS-CoV-2 in individuals 16 years of age and older. On January 31, 2022, the Agency approved Spikevax (COVID-19 Vaccine, mRNA) ("Spikevax") and the approval was granted to ModernaTX, Inc. Spikevax is approved for the prevention of COVID-19 caused by SARS-CoV-2 in individuals 18 years of age and older.

II. VACCINES THAT ARE FDA-LICENSED OR RECEIVE AN EMERGENCY USE AUTHORIZATION MEET RELEVANT STATUTORY REQUIREMENTS

A. Investigational New Drugs

Before a vaccine is licensed (approved) by FDA for use by the public, FDA requires that it undergo a rigorous and extensive development program to determine the vaccine's safety and effectiveness. This development program encompasses preclinical research (laboratory research, animal studies[7]) and clinical studies. At the preclinical stage, the sponsor focuses on collecting the data and information necessary to establish that the product will not expose humans to unreasonable risks when used in limited, early-stage clinical studies. Clinical studies, in humans, are conducted under well-defined conditions and with careful safety monitoring through all the phases of the investigational new drug process. FDA's regulations governing the conduct of clinical investigations are set out at 21 CFR part 312.

Before conducting a clinical investigation in the U.S. in which a new drug or biological product is administered to humans, a sponsor must submit an investigational new drug application (IND)

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[3] HHS, Emergency Use Authorization Declaration, 85 FR 18250, April 1, 2020, https://www.federalregister.gov/documents/2020/04/01/2020-06905/emergency-use-authorization-declaration.

[4] Proclamation on Declaring a National Emergency Concerning the Novel Coronavirus Disease (COVID-19) Outbreak, issued March 13, 2020, https://trumpwhitehouse.archives.gov/presidential-actions/proclamation-declaring-national-emergency-concerning-novel-coronavirus-disease-covid-19-outbreak/.

[5] Hereinafter "Pfizer-BioNTech COVID-19 Vaccine".

[6] BioNTech Manufacturing GmbH is the biologics license holder for this vaccine, which is manufactured by Pfizer for BioNTech Manufacturing GmbH (hereinafter "BioNTech").

[7] We support the principles of the "3Rs," to reduce, refine, and replace animal use in testing when feasible. We encourage sponsors to consult with us if they wish to use a non-animal testing method they believe is suitable, adequate, validated, and feasible. We will consider if such an alternative method could be assessed for equivalency to an animal test method.

to FDA.[8] The IND describes the proposed clinical study in detail and, among other things, helps protect the safety and rights of human subjects.[9] In addition to other information, an IND must contain information on clinical protocols and clinical investigators. Detailed protocols for proposed clinical studies permit FDA to assess whether the initial-phase trials will expose subjects to unnecessary risks. Information on the qualifications of clinical investigators (professionals, generally physicians, who oversee the administration of the investigational drug) permits FDA to assess whether they are qualified to fulfill their clinical trial duties. The IND includes commitments to obtain informed consent from the research subjects, to obtain review of the study by an institutional review board (IRB),[10] and to adhere to the IND regulations.

Once the IND is submitted, the sponsor must wait 30 calendar days before initiating any clinical trials, unless FDA informs the sponsor that the trial may begin earlier. During this time, FDA reviews the IND. FDA's primary objectives in reviewing an IND are, in all phases of the investigation, to assure the safety and rights of subjects, and, in Phase 2 and Phase 3, to help assure that the quality of the scientific evaluation of drugs is adequate to permit an evaluation of the drug's effectiveness and safety.[11]

FDA's regulations provide that, once an IND is in effect, the sponsor may conduct a clinical investigation of the product, with the investigation generally being divided into three phases. With respect to vaccines, the initial human studies, referred to as Phase 1 studies, are generally safety and immunogenicity studies performed in a small number of closely monitored subjects. Phase 2 studies may include up to several hundred individuals and are designed to provide information regarding the incidence of common short-term side effects such as redness and swelling at the injection site or fever and to further describe the immune response to the investigational vaccine. If an investigational new vaccine progresses past Phase 1 and Phase 2 studies, it may progress to Phase 3 studies. For Phase 3 studies, the sample size is often determined by the number of subjects required to establish the effectiveness of the new vaccine, which may be in the thousands or tens of thousands of subjects. Phase 3 studies provide the critical documentation of effectiveness and important additional safety data required for licensing.

Additionally, FDA regulations require that an IRB must review clinical investigations involving children as subjects covered by 21 CFR part 50, subpart D and only approve those clinical investigations involving children as subjects that satisfy the criteria in 21 CFR part 50, subpart

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[8] See 21 CFR 312.20(a).

[9] For additional information regarding the IND review process and general responsibilities of sponsor-investigators related to clinical investigations see Investigational New Drug Applications Prepared and Submitted by Sponsor-Investigators; Draft Guidance for Industry, May 2015, https://www.fda.gov/media/92604/download. When final, this guidance will represent FDA's current thinking on this topic.

[10] The IRB is a panel of scientists and non-scientists in hospitals and research institutions that oversees clinical research. IRBs approve clinical study protocols, which describe the type of people who may participate in the clinical study; the schedule of tests and procedures; the medications and dosages to be studied; the length of the study; the study's objectives; and other details. IRBs make sure that the study is acceptable, that participants have given consent and are fully informed of the risks, and that researchers take appropriate steps to protect patients from harm. See The FDA's Drug Review Process: Ensuring Drugs Are Safe and Effective web page, last updated November 2017, https://www.fda.gov/drugs/drug-information-consumers/fdas-drug-review-process-ensuring-drugs-are-safe-and-effective.

[11] 21 CFR 312.22(a).

D, Additional Safeguards for Children in Clinical Investigations. As explained in the preamble to the final rule, "[t]hese safeguards are intended to ensure that the rights and welfare of children who participate in clinical investigations are adequately protected."[12]

At any stage of development, if data raise significant concerns about either safety or effectiveness, FDA may request additional information or studies; FDA may also halt ongoing clinical studies. The FD&C Act provides a specific mechanism, called a "clinical hold," for prohibiting sponsors of clinical investigations from conducting the investigation (section 505(i)(3) of the FD&C Act), and FDA's IND regulations in 21 CFR 312.42 identify the circumstances that may justify a clinical hold. Generally, a clinical hold is an order issued by FDA to the sponsor of an IND to delay a proposed clinical investigation or to suspend an ongoing investigation.[13]

B. Licensed Vaccines Are Safe, Pure, and Potent

FDA has a stringent regulatory process for licensing vaccines.[14,15] The Public Health Service Act (PHS Act) authorizes FDA to license biological products, including vaccines, if they have been demonstrated to be "safe, pure, and potent."[16] Prior to approval by FDA, vaccines are extensively tested in non-clinical studies and in humans. FDA's regulations describe some of the extensive data and information that each sponsor of a BLA for a vaccine must submit to FDA in order to demonstrate the product's safety before FDA will consider licensing the vaccine. FDA requires that the sponsor's application include, among other things, data derived from nonclinical and clinical studies showing the product's safety, purity, and potency; a full description of manufacturing methods for the product; data establishing the product's stability through the dating period; and a representative sample of the product and summaries of results of tests performed on the lot(s) represented by the sample.[17]

As is evident from the language of the PHS Act and FDA's regulations, the licensure process for a vaccine requires the sponsor to establish, through carefully controlled laboratory and clinical studies, as well as through other data, that the product is safe and effective for its proposed indication(s) and use. FDA's multidisciplinary review teams then rigorously evaluate the sponsor's laboratory and clinical data, as well as other information, to help assess whether the safety, purity, and potency of a vaccine have been demonstrated.[18] Only when FDA's standards are met is a vaccine licensed.

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[12] Preamble to final rule, "Additional Safeguards for Children in Clinical Investigations of Food and Drug Administration-Regulated Products" (78 FR 12937 at 12938, February 26, 2013), https://www.federalregister.gov/documents/2013/02/26/2013-04387/additional-safeguards-for-children-in-clinical-investigations-of-food-and-drug.

[13] 21 CFR 312.42(a).

[14] CDC, Ensuring the Safety of Vaccines in the United States, February 2013, https://www.cdc.gov/vaccines/hcp/patient-ed/conversations/downloads/vacsafe-ensuring-bw-office.pdf.

[15] Vaccine Safety Questions and Answers, last updated March 2018, https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/vaccine-safety-questions-and-answers.

[16] Section 351(a)(2)(C)(i)(I) of the PHS Act.

[17] 21 CFR 601.2(a).

[18] FDA, Vaccines, last updated January 2021, https://www.fda.gov/vaccines-blood-biologics/vaccines.

FDA regulations explicitly state that "[a]pproval of a biologics license application or issuance of a biologics license shall constitute a determination that the establishment(s) and the product meet applicable requirements to ensure the continued safety, purity, and potency of such products."[19] Therefore, the manufacturers of vaccines that have been licensed in the U.S. have necessarily demonstrated the safety of the vaccines within the meaning of the applicable statutory and regulatory provisions before the vaccines were licensed and allowed to be marketed.

C. An Emergency Use Authorization for a COVID-19 Preventative Vaccine Is Issued Only If the Relevant Statutory Standards Are Met

Congress established the EUA pathway to ensure that, during public health emergencies, potentially lifesaving medical products could be made available before being approved. The EUA process allows the Secretary of HHS, in appropriate circumstances, to declare that EUAs are justified for products to respond to certain types of threats. When such a declaration is made, FDA may issue an EUA, which is different from the regulatory process for vaccine licensure.

Section 564 of the FD&C Act authorizes FDA to, under certain circumstances, issue an EUA to allow unapproved medical products or unapproved uses of approved medical products to be used in an emergency to diagnose, treat, or prevent serious or life-threatening diseases or conditions caused by chemical, biological, radiological, or nuclear threat agents when there are no adequate, approved, and available alternatives.

On February 4, 2020, pursuant to section 564(b)(1)(C) of the FD&C Act, the Secretary of HHS determined that there is a public health emergency that has a significant potential to affect national security or the health and security of U.S. citizens living abroad, and that involves the virus that causes COVID-19.[20] On the basis of such determination, on March 27, 2020, the Secretary then declared that circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic, pursuant to section 564(b)(1) of the FD&C Act.[21]

Based on this declaration and determination, under section 564(c) of the FD&C Act, FDA may issue an EUA during the COVID-19 pandemic after FDA concludes that the following statutory requirements are met:

- The agent referred to in the COVID-19 EUA Declaration by the Secretary (SARS-CoV-2) can cause a serious or life-threatening disease or condition.

- Based on the totality of scientific evidence available, including data from adequate and well-controlled trials, if available, it is reasonable to believe that the product may be effective in diagnosing, treating, or preventing such serious or life-threatening disease or condition that can be caused by SARS-CoV-2.

[19] 21 CFR 601.2(d).
[20] HHS, Determination of Public Health Emergency, 85 FR 7316, February 7, 2020, https://www.federalregister.gov/documents/2020/02/07/2020-02496/determination-of-public-health-emergency.
[21] HHS, Emergency Use Authorization Declaration, 85 FR 18250, April 1, 2020, https://www.federalregister.gov/documents/2020/04/01/2020-06905/emergency-use-authorization-declaration.

- The known and potential benefits of the product, when used to diagnose, prevent, or treat the identified serious or life-threatening disease or condition, outweigh the known and potential risks of the product.

- There is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating the disease or condition.

Although EUAs are governed under a different statutory framework than BLAs, FDA has made clear that issuance of an EUA for a COVID-19 vaccine would require that the vaccine demonstrated clear and compelling safety and efficacy in a large, well-designed Phase 3 clinical trial. In the guidance document Emergency Use Authorization for Vaccines to Prevent COVID-19, FDA has provided recommendations that describe key information that would support issuance of an EUA for a vaccine to prevent COVID-19.[22] In the guidance, FDA explained that, in the case of such investigational vaccines, any assessment regarding an EUA will be made on a case-by-case basis considering the target population, the characteristics of the product, the preclinical and human clinical study data on the product, and the totality of the available scientific evidence relevant to the product.[23] FDA has also stated, in this guidance, that for a COVID-19 vaccine for which there is adequate manufacturing information to ensure its quality and consistency, issuance of an EUA would require a determination by FDA that the vaccine's benefits outweigh its risks based on data from at least one well-designed Phase 3 clinical trial that demonstrates the vaccine's safety and efficacy in a clear and compelling manner.[24]

A Phase 3 trial of a vaccine is generally a large clinical trial in which a large number of people are assigned to receive the investigational vaccine or a control. In general, in Phase 3 trials that are designed to show whether a vaccine is effective, neither people receiving the vaccine nor those assessing the outcome know who received the vaccine or the comparator.

In a Phase 3 study of a COVID-19 vaccine, the efficacy of the investigational vaccine to prevent disease will be assessed by comparing the number of cases of disease in each study group. For Phase 3 placebo-controlled efficacy trials, FDA has recommended to manufacturers in guidance that the vaccine should be at least 50% more effective than the comparator, and that the outcome be reliable enough so that it is not likely to have happened by chance.[25] During the entire study, subjects will be monitored for safety events. If the evidence from the clinical trial meets the pre-specified criteria for success for efficacy and the safety profile is acceptable, the results from the trial can potentially be submitted to FDA in support of an EUA request.

During the current public health emergency, manufacturers may, with the requisite data and taking into consideration input from FDA, choose to submit a request for an EUA.

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[22] Emergency Use Authorization for Vaccines to Prevent COVID-19; Guidance for Industry, March 2022, https://www.fda.gov/media/142749/download.
[23] Id. at 4.
[24] Id.
[25] Development and Licensure of Vaccines to Prevent COVID-19; Guidance for Industry, June 2020, https://www.fda.gov/media/139638/download.

It is FDA's expectation that, following submission of an EUA request and issuance of an EUA, a sponsor would continue to evaluate the vaccine and would also work towards submission of a BLA as soon as possible.

III. DISCUSSION

Petitioner makes several requests, including requests relating to EUA and licensure of COVID-19 vaccines. Below, we address each of Petitioner's requested actions and the information provided by Petitioner in support of these requests.

A. Petitioner's Request for Investigation Regarding Medical Publishers

Petition Request No. 1: "Investigate medical science information laundering by monopolistic medical publishers and how they have suppressed new discoveries that would have thrown out the reductionist research and treatment model, knowingly produce flawed and fraudulent knowledge for their revenue in the name of science, pursuant to the implied power under 21 U.S. § 355(b)-(c), 42 U.S. § 262(a)(2), 21 U.S. § 564(g)(2), 21 U.S. § 379dd, and 21 C.F.R. §§ 1.21."

FDA's evaluation of Petition Request No. 1: The Petition's grounds for this requested action seem to be set forth in pages 6-11 of the Petition. In these pages, the Petition asserts that "[t]he drug industry controls the medical industry by controlling commercial medical publishers, financing researches, supporting medical practices, and 'educating' consumers." Petition at 6 [sic]. The Petition further states that "[l]eading medical publishers have a strong interest in maintaining existing revenues from the drug industry and creating entrance barriers to secure their monopoly revenue." Petition at 6-7. As to the assertion of monopolistic business practices, the Petition states: "Due to extremely complex factual patterns and long development history, I can only describe those issues briefly. Some details can be found in my article, more details will be forthcoming, and yet more details can be found by anyone interested in doing research in this subject." Petition at 8. The Petition goes on to assert that science publishers are a "$26 billion industry with 70% scientific articles published by journals owned by five major publishers." This is a problem, according to the Petition, because "[t]hey promote drug-for-health researches by tailoring their article specifications to drugs discoveries and get large amounts of fund by obtaining government trust." Petition at 9 [sic]. "The only possible remedy is to stop information laundering to slowly restore true science" because "[a]fter the medical literature has been filled with junk science, this slow path cannot give human species a realistic hope." Petition at 11.

FDA has carefully considered Request No. 1 and we acknowledge the importance of medical and scientific publications. But as a threshold matter, by its own terms, your Petition does not purport to set forth all relevant factual information. Rather, you call on FDA to initiate an investigation and fact-finding process. You also refer to "forthcoming" information. We are denying your Petition to the extent that it requests, through the citizen petition process, that FDA initiate an investigation. Under 21 CFR 10.30, citizen petitions can request that FDA issue, amend, or revoke a regulation or an order, or take or refrain from taking an administrative action (21 CFR 10.30(b)(3)), and are to be resolved based on information in the administrative record (21 CFR 10.30(j)). An investigation is not an administrative action, and, as your Petition implicitly acknowledges, investigations necessarily require fact finding beyond what is presented

in the current administrative record. By referring to "forthcoming" information, your Petition also acknowledges that it does not address all relevant information. Moreover, FDA is not the federal agency with statutory responsibilities for investigating alleged violations of anti-trust laws. Concerns about anti-trust violations should be directed to the federal agencies with relevant statutory responsibilities. We also do not have statutory responsibility for regulating medical publications. Rather, our statutory responsibilities relate to specific medical products and activities specified by Congress (e.g., the regulation of drugs, biological products, medical devices, tobacco products, foods, and animal drugs).

For all of these reasons, we deny Request No. 1.

B. Petitioner's Request that FDA Evaluate a True Life Model and Reject the Reductionist Research and Treatment Model, and Evaluate the Safety and Effectiveness of mRNA Vaccines

Petition Request No. 2: "Evaluate a true life model and reject the reductionist research and treatment model, and evaluate safety and effectiveness of the mRNA vaccines, pursuant to 21 U.S. § 355(b)-(c), 42 U.S. § 262(a)(2), 21 U.S. § 564(g)(2), and 21 U.S. § 379dd."

FDA's evaluation of Petition Request No. 2: To assess what the Petition means by "true life model" and "reject the reductionist research and treatment model," we look to the Statement of Grounds section of the Petition. The Statement of Grounds describes "a new life model" as follows:

> Each multiple-cellular life being like human is an extremely complex distinctive system controlled by distinctive genome and a large number of personal, environmental, and emotional variables, the optimum performance of which can be achieved only by maintaining balances among a large number of metabolic and disease processes in the life time. Life is maintained by the vascular system which is susceptible to current impacts of life activities, diseases and a large number of other factors. Life can be altered by altering any of the factors in place of other factors. Any of a large number of factors can add current burdens to the vascular system leading to death or reduce burdens on the system to avoid death. Burdens caused by cancer or other diseases could be offset in part or in whole by reducing burdens of other sources. The working order of the life system is maintained by the immune system which is run and influenced by environmental factors, cellular substances/nutrition, emotion/thinking, anger, memory, life activities, life stress, hormones, climate, etc. Good health can be achieved by optimizing some of those factors in place of others. In one aspect, life is like a rechargeable battery which has both energy reserves and vital functional reserves: the person can add more life to the reserves or reduce some of his life from the reserves on a daily basis. In another aspect, life is influenced by cellular memory and CNS memory that affect biochemical and cellular processes and body's structure profile. Hundreds of additional properties could be derived from this life model. The findings of half a century of researches provide irrefutable support to this life model.

Petition at 4 [sic].

Elsewhere in the Statement of Grounds, the Petition describes the "reductionist medical research and treatment model" as "focus[ing] on a single factor in a static manner often by comparing disease outcomes in a binary scale between two groups." Petition at 4. The Petition states that certain "discoveries" have "invalidated" this purported model: that there are a "large number of health influence factors on health;" and that there is "stress role in personal health."

In assessing how the Petition requests FDA apply these frameworks, we look to the language in the request. Request No. 2 asks FDA to apply these frameworks pursuant to "21 U.S. § 355(b)-(c), 42 U.S. § 262(a)(2), 21 U.S. § 564(g)(2), and 21 U.S. § 379dd." The first provision, 21 U.S.C. § 355(b)-(c), relates to the new drug approval process. Although vaccines are "drugs" under the FD&C Act,[26] FDA does not authorize or approve vaccines under the new drug approval process. See 42 U.S.C. § 262(j). Therefore, we need not consider the Petition's request as it relates to § 355(b)-(c). The second provision, 42 U.S.C. § 262(a)(2), refers to FDA's approval process for biological products. This provision *is* directly relevant to FDA's vaccine approval (licensure) process; we discuss this further in the next paragraph. The third provision, 21 U.S.C. 564(g)(2), refers to FDA's authority to revise or revoke an emergency use authorization, and this is discussed further in section III.C of this response. The fourth provision, 21 U.S.C. § 379dd, refers to the establishment and functions of the Reagan-Udall Foundation, a nonprofit corporation that Congress established to advance FDA's mission to modernize product development, accelerate innovation, and enhance product safety. While the Petition describes the Reagan-Udall Foundation as providing "a path for incorporating latest scientific advances into FDA approval framework," Petition at 46, none of the Reagan-Udall Foundation's efforts to advance scientific knowledge is directly "incorporated" in any manner into FDA's approval or authorization frameworks. The Reagan-Udall Foundation (and not FDA) determines its scientific priorities. Furthermore, § 379dd is not relevant to FDA's approval or authorization standards for vaccines. The statutory authority to authorize or approve a vaccine rests with the Secretary, as delegated to FDA – not with the Reagan-Udall Foundation. Therefore, for purposes of evaluating the requests in Request No. 2 for FDA's evaluation of mRNA vaccines, § 379dd is not relevant. We evaluate the requests in Request No. 2 only as they relate to 42 U.S.C. § 262(a)(2).

Accordingly, we next consider the requirements in 42 U.S.C. § 262(a)(2). Under § 262(a)(2)(C), FDA shall only approve a biologics license application on the basis of a demonstration that the product is "safe, pure and potent." Evaluating a product's safety, purity, and potency requires consideration of applicable scientific standards. As described elsewhere in this response, the licensure process for a vaccine requires the sponsor to establish, through carefully controlled laboratory and clinical studies, as well as through other data, that the product is safe and effective for its approved indication(s) and use. FDA's multidisciplinary review teams then rigorously evaluate the sponsor's laboratory and clinical data, as well as other information, to help assess whether the safety, purity, and potency of a vaccine has been demonstrated.[27] Only when FDA's standards are met is a vaccine licensed. The Petition does not explain all aspects of how the "true life model" and the "reject[ion of] the reductionist research and treatment model" align

[26] *See* 21 U.S.C. 321(g)(1) (describing a "drug," *inter alia,* as an article used for the prevention of disease).
[27] Vaccines, https://www fda.gov/vaccines-blood-biologics/vaccines.

with FDA's statutory duty to only approve vaccines upon a showing of safety, purity and potency. For example, the Petition does not explain how the "distinctive genome" is relevant to FDA's evaluation of safety, purity, and potency. With respect to the purported ills of the "reductionist medical research and treatment model" for "focus[ing] on a single factor in a static manner often by comparing disease outcomes in a binary scale between two groups," the Petition does not provide any reliable evidence that counters the scientific validity of comparing clinical trial participants who experience symptomatic disease in a control arm versus a vaccine arm. Indeed, FDA's approval of the mRNA vaccines Comirnaty and Spikevax considered FDA's evaluation of clinical trials that were designed with such an endpoint.[28,29] The Petition states that certain "discoveries" have "invalidated" this purported model: that there are a "large number of health influence factors on health;" and that there is "stress role in personal health." However, FDA's evaluation of these mRNA vaccines found that the vaccines are indeed safe and effective,

[28] *See* https://www fda.gov/vaccines-blood-biologics/comirnaty; https://www fda.gov/vaccines-blood-biologics/spikevax.

[29] The Petition states that "I have posed two articles to refuse the validity of clinical trials" on which FDA based its approval of Comirnaty. Petition at 13. The Petition states "[m]y first article showed that statistical analysis cannot produce right results for hypothetical model data under the same assumptions used in research." Petition at 13. We are not sure what this means; for example, it is unclear what the Petition means by "right results" or "hypothetical model data." The Petition also states "[t]he second articles . . has been suppressed by medical journals, they are available as preprint articles." Petition at 13. But neither the Petition nor the self-published articles listed in your References explain how your proposed models satisfy FDA's statutory mandate to base approval decisions on safety, purity, and potency.

and the Petition does not substantiate any error with FDA's findings.[30,31] The Petition thus seems to offer an alternative, supposedly superior scientific method. For example, in reference to § 262(a)(2) the Petition states, "I have shown that effectiveness is computed from data

[30] The Petition is sprinkled with assertions that appear to be included for the purpose of demonstrating supposed flaws with FDA's scientific review of the COVID-19 vaccines. Because these assertions are not adequately substantiated, we reject the suggestion that the assertions cast doubt on the scientific underpinning of FDA's vaccine review program. Furthermore, the Petition does not explain how these supposed flaws demonstrate the superiority of the Petition's proposed approach to reviewing biologics license applications under 42 U.S.C. § 262. Examples of the unsubstantiated assertions include:

- The Petition asserts that there are data from the United Kingdom showing "how vaccination affects the death of COVID-19 infection" and that there is a "dramatically increased death rate among those who have received second shots." Petition at 39. However, this supposed data is in direct conflict with the data from reliable sources. Data available in the United States shows that deaths from COVID-19 are significantly less common among vaccinated individuals. *See* https://www.fda.gov/media/159005/download at 20 (presentation at FDA advisory committee showing that in March 2022, people ages 12 and older had 17x higher COVID-19 associated death rates compared to those with a primary series and booster dose). The links that the Petition provides to support the assertions regarding the UK data do not work, but we are aware of data showing that monthly age-standardized mortality rates (ASMRs) in the United Kingdom for deaths involving COVID-19 have been consistently lower for people who had a third dose or booster at least 21 days earlier compared to unvaccinated people. *See* https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/deathsinvolvingcovid19byvaccinationstatusengland/deathsoccurringbetween1january2021and31march2022. Accordingly, the Petition does not support its claims about data from the United Kingdom.
- The Petition states "I predicted that mRNA vaccines can enter the blood brain barrier cells and thus disrupt the normal protein synthesis for carrier proteins based on several relevant studies." Petition at 19. However, none of the sources you cite for this proposition (i.e., References 238-241) relate to vaccines.
- The Petition states that "some of particles [of the vaccine' can quickly get into the heart by blood return," and that how much this occurs "would depend on how close the needed (sic) is placed to some moderately large veins." Petition at 19. Again, this assertion lacks support. But the point of this discussion seems to be to lead to the Petition's statement that "I predict that mRNA can disrupt the protein synthesis and impair the heart's ability to repair damages." *Id.* FDA does not make approval decisions based on predictions. Rather, FDA makes approval decisions based on data and scientific evidence.
- The Petition states, "Life is like a charged battery; the vaccine can drain some of surviving power and can drain the battery to total death only in those worst circumstances." Petition at 32. The Petition does not explain how this analogy should factor into FDA's review of biologics license applications.
- The Petition also goes on to make such unsupported assertions as "mRNA vaccines promote selection of virulent virus" and "mRNA vaccines increase cancer risk." Petition at 21. Unsupported assertions cannot be a basis for FDA's regulatory decisions. The Petition also cites a publication by Seneff et all for the proposition that various "health risks" associated with mRNA vaccines were "predicted" in that publication. However, we know from our review of clinical trial data and post-authorization safety monitoring that the mRNA vaccines are safe for their approved indication. Furthermore, the Seneff et. al publication does not purport to conduct an independent safety review.

[31] Although not directly relevant to Request No. 2, part of the Petition takes issue with the duration of clinical trials. On pages 17-18, the Petition states that "[m]ost latent side effects would take at least 4 years up to 70 years to materialize," and therefore "clinical trials, particularly with less than a year, can conceal nearly most acute side effects and completely write off all latent side effects." The EUAs for the Pfizer-BioNTech and Moderna COVID-19 Vaccines, as well as the BLA approvals for Comirnaty and Spikevax, were issued based in part on clinical trials in which at least half of vaccine recipients had at least six months of follow-up. This allowed for evaluation of potential adverse events that were not apparent in the immediate post-vaccination period. Adverse events considered plausibly linked to vaccination generally start within six weeks after vaccine receipt. Table VI. National Vaccine Injury Compensation Program. Rockville, MD: Health Resources and Services Administration, 2017 (https://www hrsa.gov/sites/default/files/hrsa/vaccine-compensation/vaccine-injury-table-01-03-2022.pdf). Therefore, the Petition's suggestion that safety assessments can only be made on the basis of 4 to 70 years of follow-up data does not account for this.

reflected small probability and adjusted rate ratio is computed from data involving small probability with massive design biases in addition to wrong life model, wrong research model, and wrong analysis method." Petition at 45. But the evidence of FDA's supposedly inferior scientific method is lacking. The Petition does not explain why FDA's scientific review process fails to ensure that biologics license applications meet the approval standard in § 262(a)(2).

Accordingly, we conclude that Request No. 2 does not set forth a basis for FDA to take any action.

C. Petitioner's Request that FDA Suspend All Outstanding mRNA Vaccine Use Authorizations and Revoke Same

Petition Request No. 3: "Suspend all outstanding mRNA vaccine use authorizations and revoke same, pursuant to 21 U.S. § 564(g)(2). All dangers and potential risks are present in all mRNA vaccines and all flaws in the research model, data analysis, and conclusions have impacted the approval of all mRNA vaccines."

FDA's evaluation of Petition Request No. 3: We interpret Petitioner's request as a request to revoke the EUAs for the Pfizer-BioNTech and Moderna COVID-19 Vaccines ("the Authorized mRNA COVID-19 Vaccines"), which are the only mRNA vaccines available under EUA, under the authority in section 564(g)(2) of the FD&C Act. Petitioner has provided no evidence that would provide a basis for FDA to conclude the Authorized mRNA COVID-19 Vaccines do not meet the EUA standard. Indeed, FDA is not aware of any information indicating that the known and potential benefits of the Authorized mRNA COVID-19 Vaccines are outweighed by their known and potential risks, nor has Petitioner provided any such information in the Petition. In this section, we address publications Petitioner has provided in support of his positions, where those publications are of the scientific rigor that FDA would rely on for our regulatory decisions.

Section 564(g)(2) of the FD&C Act provides the standard for revocation of an EUA. Under this statutory authority, FDA may revise or revoke an EUA if:

> (A) the circumstances described under [section 564(b)(1) of the FD&C Act] no longer exist;
> (B) the criteria under [section 564(c) of the FD&C Act] for issuance of such authorization are no longer met; or
> (C) other circumstances make such revision or revocation appropriate to protect the public health or safety.

At the outset, we note that Congress has provided FDA with discretion under section 564 of the FD&C Act and nothing in the statute *requires* FDA to *revoke* existing EUAs in any circumstance. Rather, section 564(g)(2) of the FD&C Act says that, in certain circumstances, "*may* revise or revoke" an EUA.[32] The verb "may" is ordinarily permissive, particularly when

[32] Section 564(g)(2) of the FD&C Act (emphasis added).

the statute elsewhere uses the term "shall" to confer a mandatory duty.[33] Further underscoring FDA's discretion, the EUA statute explicitly provides that all decisions regarding EUAs are "committed to agency discretion."[34]

A permissive reading of "may" also accords with the statutory purpose of giving FDA flexibility to "permit rapid distribution of promising new drugs and antidotes in the most urgent circumstances,"[35] because it allows the Agency to permit continued distribution of EUA products and thereby removes the need for manufacturers to limit supply or delay seeking approval to exhaust supplies of authorized product.

FDA's guidance entitled Emergency Use Authorization of Medical Products and Related Authorities ("EUA Guidance"),[36] notes that once an EUA is issued for a product, in general, that EUA will remain in effect for the duration of the EUA declaration under which it was issued, "unless the EUA is revoked because the criteria for issuance . . . are no longer met or revocation is appropriate to protect public health or safety (section 564(f),(g) [of the FD&C Act])."[37]

In this section, we assess whether any of the statutory conditions under which FDA may revoke an EUA are met with respect to any of the Authorized mRNA COVID-19 Vaccines, namely: (1) whether the circumstances justifying issuance under section 564(b)(1) of the FD&C Act no longer exist, (2) whether the criteria for issuance under section 564(c) of the FD&C Act are no longer met, and (3) whether other circumstances make a revision or revocation appropriate to protect the public health or safety.

i. Circumstances Justifying the Emergency Use Continue to Exist

As explained above in section I, on February 4, 2020, pursuant to section 564(b)(1)(C) of the FD&C Act, the Secretary of HHS determined that there is a public health emergency that has a significant potential to affect national security or the health and security of U.S. citizens living abroad, and that involves the virus that causes COVID-19.[38] On the basis of such determination, on March 27, 2020, the Secretary then made the COVID-19 EUA Declaration, pursuant to section 564(b)(1) of the FD&C Act.[39]

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[33] See *Old Line Life Ins. Co. of Am. v. Garcia*, 411 F.3d 605, 614-15 (6th Cir. 2005); *Goodman v. City Prods. Corp, Ben Franklin Div.*, 425 F.2d 702, 703 (6th Cir. 1970); *Anderson v. Yungkau*, 329 U.S. 482, 485 (1947) ("[W]hen the same Rule uses both 'may' and 'shall,' the normal inference is that each is used in its usual sense—the one act being permissive, the other mandatory."); see also A. Scalia & B.A. Garner, *Reading Law: The Interpretation of Legal Texts* 112 (2012) ("The traditional, commonly repeated rule is that *shall* is mandatory and *may* is permissive. . ."). There is nothing to indicate that section 564(g)(2) of the FD&C Act departs from this ordinary meaning of "may."

[34] See section 564(i) of the FD&C Act. *See also Association of American Physicians & Surgeons v. FDA*, 2020 WL 5745974, at *3 (6th Cir. Sept. 24, 2020) (citing to section 564(i) of the FD&C Act for the proposition that "emergency-use authorizations are exempt from review under the [Administrative Procedure Act].").

[35] *See* 2004 U.S.C.C.A.N. S17, S18 (Statement of President Bush Upon Signing P.L. 108-276, PROJECT BIOSHIELD ACT OF 2004).

[36] Emergency Use Authorization of Medical Products and Related Authorities; Guidance for Industry and Other Stakeholders, January 2017 (EUA Guidance), https://www.fda.gov/media/97321/download.

[37] Id. at 28.

[38] HHS, Determination of Public Health Emergency, 85 FR 7316, February 7, 2020, https://www.federalregister.gov/documents/2020/02/07/2020-02496/determination-of-public-health-emergency.

[39] HHS, Emergency Use Authorization Declaration, 85 FR 18250, April 1, 2020, https://www.federalregister.gov/documents/2020/04/01/2020-06905/emergency-use-authorization-declaration.

The circumstances described under section 564(b)(1) of the FD&C Act continue to exist (i.e., the COVID-19 EUA Declaration remains in effect, and the circumstances supporting the EUA declaration remain in existence). FDA therefore is not revoking the EUAs for the authorized COVID-19 vaccines under the authority in section 564(g)(2)(A) of the FD&C Act.

ii. The Criteria for Issuance of the EUA Continue to be Met

This section describes why the criteria under section 564(c) of the FD&C Act continue to be met with respect to the Authorized mRNA COVID-19 Vaccines and why, therefore, FDA is not revoking these EUAs under the authority in section 564(g)(2)(B) of the FD&C Act at this time.

Criterion 1: The agent referred to in the COVID-19 EUA Declaration by the Secretary (SARS-CoV-2) can cause a serious or life-threatening disease or condition (section 564(c)(1) of the FD&C Act).

FDA has concluded that SARS-CoV-2, which is the subject of the EUA declaration, can cause a serious or life-threatening disease or condition. FDA is not aware of science indicating that there is any change in the ability of the SARS-CoV-2 virus to cause a serious or life-threatening disease or condition, namely COVID-19, nor has Petitioner provided any information about such a change.

The SARS-CoV-2 pandemic continues to present an extraordinary challenge to global health and, as of June 11, 2022, has caused more than 500 million cases of COVID-19 and claimed the lives of more than 6 million people worldwide.[40] In the U.S., as of June 11, 2022 more than 85 million cases and over 1 million deaths have been reported to the CDC.[41] On January 31, 2020, the U.S. Secretary of HHS declared a public health emergency related to COVID-19 and mobilized the Operating Divisions of HHS, and the U.S. President declared a national emergency in response to COVID-19 on March 13, 2020. Additional background information on the SARS-CoV-2 virus and COVID-19 pandemic may be found in the FDA decision memoranda for the Pfizer-BioNTech COVID-19 Vaccine and Moderna COVID-19 Vaccine.[42]

Additionally, with respect to the impact of the SARS-CoV-2 pandemic on the pediatric population, as of June 10, 2022, approximately 5.7 million and 5.1 million COVID-19 cases in individuals 12 through 17 years of age and individuals 5 through 11 years of age, respectively have been reported to the CDC. Some of these cases have resulted in hospitalization and death. The cumulative rate of COVID-19 associated hospitalization was 59.1 per 100,000 for the 5 through 11 population and 125.1 per 100,000 for the 12 through 17 population as of June 4, 2022

[40] Johns Hopkins University School of Medicine, Coronavirus Resource Center (accessed June 11, 2022), https://coronavirus.jhu.edu/map.html.

[41] CDC, COVID Data Tracker (accessed June 11, 2022), https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covidview/index.html.

[42] These decision memoranda are available on FDA's website, at https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/comirnaty-and-pfizer-biontech-covid-19-vaccine ("Pfizer-BioNTech COVID-19 Vaccine EUA Decision Memoranda and Addenda") and https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/spikevax-and-moderna-covid-19-vaccine ("Moderna COVID-19 Vaccine EUA Decision Memoranda and Addenda"), and they are incorporated by reference in this response.

based on COVID-NET data reported to the CDC.[43] As of June 13, 2022, 1056 deaths associated with COVID-19 have been reported among individuals ages 5 through 17.[44] It is difficult to estimate the incidence of COVID-19 among pediatric populations because they are frequently asymptomatic and infrequently tested, and may also be unreported due to the availability of at-home test kits. While it has largely been the case that COVID-19 tends to be less severe in children than adults, the Omicron wave has seen more kids getting sick with the disease and being hospitalized, and children may also experience longer term effects, even following initially mild disease. As with adults, pediatric populations with underlying conditions such as asthma, chronic lung disease, and cancer are at higher risk than their heathier counterparts for COVID-19-related hospitalization and death. Of the children who have developed severe COVID-19, most have had underlying medical conditions. However, recent data have demonstrated the potential for serious illness among children with no underlying health conditions. Multisystem inflammatory syndrome in children (MIS-C) is a rare but serious COVID-19-associated condition that can present with persistent fever, laboratory markers of inflammation and heart damage, and, in severe cases, hypotension and shock. As of May 31, 2022, the CDC received reports of 8,525 cases and 69 deaths that met the definition for MIS-C.[45]

Therefore, the criterion under section 564(c)(1) of the FD&C Act continues to be met with respect to the Authorized mRNA COVID-19 vaccines.

Criterion 2: Based on the totality of scientific evidence available, including data from adequate and well-controlled trials, if available, it is reasonable to believe that the product may be effective in diagnosing, treating, or preventing such serious or life-threatening disease or condition that can be caused by SARS-CoV-2 (section 564(c)(2)(A) of the FD&C Act).

FDA has determined that based on the totality of scientific evidence available, including data from adequate and well-controlled trials, it is reasonable to believe that the Authorized mRNA COVID-19 Vaccines may be effective to prevent, diagnose, or treat such serious or life-threatening disease or condition that can be caused by SARS-CoV-2. The basis for this determination is explained in detail in FDA's decision memoranda regarding the Pfizer-BioNTech COVID-19 Vaccine EUA and the Moderna COVID-19 Vaccine EUA.[46] FDA is not aware of any data that change this conclusion, nor has Petitioner provided any such data in the Petition. The criterion under section 564(c)(2)(A) of the FD&C Act continues to be met with respect to the Authorized mRNA COVID-19 vaccines.

Criterion 3: The known and potential benefits of the product, when used to diagnose, prevent, or treat the identified serious or life-threatening disease or condition, outweigh the known and potential risks of the product (section 564(c)(2)(B) of the FD&C Act).

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[43] CDC, COVID-NET Laboratory-confirmed COVID-19 hospitalizations, https://covid.cdc.gov/covid-data-tracker/#covidnet-hospitalization-network. The current network covers nearly 100 counties and represents approximately 10% of US population (~32 million people).

[44] CDC, Demographic Trends of COVID-19 cases and deaths in the US reported to CDC, https://covid.cdc.gov/covid-data-tracker/#demographics.

[45] CDC, Health Department-Reported Cases of Multisystem Inflammatory Syndrome in Children (MIS-C) in the United States, https://covid.cdc.gov/covid-data-tracker/#mis-national-surveillance.

[46] FDA's Pfizer-BioNTech COVID-19 Vaccine EUA Decision Memoranda and Addenda; FDA's Moderna COVID-19 Vaccine EUA Decision Memoranda and Addenda.

FDA authorized the Authorized mRNA COVID-19 Vaccines after reaching determination that, among other things, the known and potential benefits of these vaccines, when used to prevent COVID-19, outweigh their known and potential risks. The bases for these determinations are explained in detail in FDA's Pfizer-BioNTech COVID-19 Vaccine EUA Decision Memoranda and Addenda and Moderna COVID-19 Vaccine EUA Decision Memoranda and Addenda.

Petitioner points to numerous publications in his argument that there are safety and effectiveness concerns with the Authorized mRNA Vaccines, and that such concerns justify the revocation of the EUAs for the Authorized mRNA Vaccines.

However, Petitioner presents no information that alters FDA's assessment of the known and potential benefits of the Authorized mRNA COVID-19 Vaccines, or whether such known and potential benefits outweigh the known and potential risks. Known and potential benefits, in populations in which the vaccine is authorized for use, include reduction in the risk of symptomatic COVID-19 and associated serious complications.[47]

Petitioner has not provided any data, nor is FDA aware of any data, that changes FDA's conclusion that the known and potential benefits of the Authorized mRNA COVID-19 Vaccines, when used to prevent COVID-19, outweigh their known and potential risks.[48] The criterion under section 564(c)(2)(B) of the FD&C Act continues to be met with respect to the Authorized mRNA COVID-19 Vaccines.

Criterion 4: There is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating the disease or condition (section 564(c)(3) of the FD&C Act).

The only FDA-approved drugs or biological products indicated to prevent COVID-19 in any population are Comirnaty and Spikevax. Spikevax is approved for the prevention of COVID-19 disease in individuals 18 years of age and older, and Comirnaty is approved for the prevention of COVID-19 disease in individuals 16 years of age and older.

Although there are two approved COVID-19 vaccines, that does not mean that there is now an "adequate, approved, and available" alternative such that continuation of the EUAs for these vaccines is no longer justified. Although the two approved vaccines are approved to prevent COVID-19 in certain individuals who fall within the scope of the authorizations for the Authorized mRNA Vaccines, there is not sufficient approved vaccine available for distribution to this population in its entirety. Additionally, there are no COVID-19 vaccines that are approved to provide: COVID-19 vaccination in individuals younger than 16 years of age; a third primary series dose to certain immunocompromised populations; a homologous booster dose; or a heterologous booster dose following completion of primary vaccination with another authorized COVID-19 vaccine.

[47] FDA's Pfizer-BioNTech COVID-19 Vaccine EUA Decision Memoranda and Addenda.

[48] Petitioner has provided citations to a number of sources to support the proposition that there are questions about the benefits and risks. We have reviewed sources that the Petitions cites in support of various propositions related to benefits and risks, and we disagree that the sources support the propositions for which they are cited.

Therefore, there is no adequate, approved, and available alternative to the Authorized mRNA COVID-19 Vaccine for preventing COVID-19. The criterion under section 564(c)(3) of the FD&C Act continues to be met.

iii. No Other Circumstances Make a Revision or Revocation Appropriate to Protect the Public Health or Safety

As noted above, section 564(g)(2)(C) of the FD&C Act provides that FDA may revise or revoke an EUA if circumstances justifying its issuance (under section 564(b)(1)) no longer exist, the criteria for its issuance are no longer met, or other circumstances make a revision or revocation appropriate to protect the public health or safety. The EUA guidance explains that such circumstances may include:

> significant adverse inspectional findings (e.g., when an inspection of the manufacturing site and processes has raised significant questions regarding the purity, potency, or safety of the EUA product that materially affect the risk/benefit assessment upon which the EUA was based); reports of adverse events (number or severity) linked to, or suspected of being caused by, the EUA product; product failure; product ineffectiveness (such as newly emerging data that may contribute to revision of the FDA's initial conclusion that the product "may be effective" against a particular CBRN agent); a request from the sponsor to revoke the EUA; a material change in the risk/benefit assessment based on evolving understanding of the disease or condition and/or availability of authorized MCMs; or as provided in section 564(b)(2), a change in the approval status of the product may make an EUA unnecessary.[49]

As of the date of this writing, FDA has not identified any such circumstances that would make revocation of the EUA of the Authorized mRNA COVID-19 Vaccines appropriate to protect the public health or safety, nor has Petitioner provided any such data. FDA determined the EUA standard is met for the Authorized mRNA COVID-19 Vaccines for the reasons outlined in the memoranda supporting the authorizations.

For the reasons explained in this citizen petition response, the Petition has not demonstrated that other circumstances make revocation of the Authorized mRNA Vaccines appropriate. FDA therefore sees no justifiable basis upon which to take any action based on Petitioner's request with respect to the EUAs of the Authorized mRNA COVID-19 Vaccines. Accordingly, we deny Petitioner's request that FDA "[s]uspend all outstanding mRNA vaccine use authorizations and revoke same, pursuant to 21 U.S. § 564(g)(2)."[50]

D. Petitioner's Request for Investigation Regarding "[C]riminal [V]iolations by [I]nformation [L]aunderers"

[49] EUA Guidance at 29.
[50] Petition at 1-2.

Petition Request No. 4: "Urge FDA to initiate investigation with DOJ, FTC, FCC, etc. to understand the extent of criminal violations by information launders, particularly, antitrust violation, wire fraud violation, and wastes of massive federal research funds attributable to the conduct of monopolistic medical publishers. The authority is implied by FDA statutory mission to protect public health."

FDA's evaluation of Request No. 4: As with request No. 1, this request is not amenable to the citizen petition process. Decisions regarding FDA's enforcement activities are made on a case-by-case basis and are within the discretion of FDA. Requests for the Agency to initiate enforcement action and related regulatory activity are expressly excluded from the scope of FDA's citizen petition procedures (*See* 21 CFR 10.30(k)).[51]

E. Petitioner's Request that FDA Overhaul its Approval Framework

Petition Request No. 5: "Request FDA to overhaul its approval framework: rejecting the drugs-for-health hypothesis, adopting a holistic analysis approach, avoiding trade art and junk science, restructuring advisory committee structure and member compositions, pursuant to implied power provided in 21 U.S. § 379dd. Since this will take time, FDA does not need to address this request within 180 days, I will follow up by filing my continuous petitions."[52]

FDA's evaluation of Request No. 5: It is unclear whether Petitioner is requesting that FDA overhaul its approval framework for biological products or for all drugs, including biological products. Accordingly, in this section, we discuss the framework for approval of biological products as well as other drugs. Additionally, as noted earlier in this response, 21 U.S.C. § 379dd refers to the establishment and functions of the Reagan-Udall Foundation, a nonprofit corporation that Congress established to advance FDA's mission to modernize product development, accelerate innovation, and enhance product safety. It is not relevant to FDA's approval standards for drugs and biological products, and the statutory authority to approve drugs and biological products rests with the Secretary (as delegated to FDA), not with the Reagan-Udall Foundation. Therefore, for purposes of evaluating Request No. 5, 21 U.S.C.§ 379dd is not relevant and is not further discussed.

The FD&C Act and FDA regulations require that an applicant seeking to market a new drug submit an application to FDA for review and approval.[53] To be approved, a new drug application (NDA) submitted under section 505(b) of the FD&C Act must, among other things, be supported by investigations showing the drug product to be safe and effective for its intended use(s).[54] Section 505(c)(1)(A) of the FD&C Act states that FDA will "approve the application if [FDA] . . . finds that none of the grounds for denying approval specified in [section 505(d) of the FD&C Act] applies." Section 505(d) of the FD&C Act and FDA's regulation in 21 CFR 314.125(b) include grounds for refusing to approve an application. For example, FDA will refuse to approve an application if adequate tests do not show that the drug is safe for use under

[51] We also note that requests related to statutes administered by other federal agencies should be directed to those agencies. FDA does not have statutory responsibility for administering all federal laws.
[52] Petition at 2.
[53] Section 505(a) of the FD&C Act (21 U.S.C. 355(a)) and 21 CFR part 314.
[54] Section 505(b)(1) of the FD&C Act.

the conditions prescribed, recommended, or suggested in the proposed labeling.[55] FDA will also refuse to approve an application if the applicant fails to provide substantial evidence of effectiveness.[56] As stated in section 505(d) of the FD&C Act, "substantial evidence" means:

> . . . evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof.

The characteristics of adequate and well-controlled clinical investigations are described in FDA's regulation in 21 CFR 314.126.

As explained earlier in this response, the statutory framework for licensure (i.e., approval) of biological products is set forth in the PHS Act. Section 351(a) of the PHS Act authorizes FDA to approve BLAs on the basis of a demonstration that "the biological product that is the subject of the application is safe, pure, and potent"; and "the facility in which the biological product is manufactured, processed, packed, or held meets standards designed to assure that the biological product continues to be safe, pure, and potent."[57] The standard for licensure of a biological product as potent under section 351(a) of the PHS Act has long been interpreted to include effectiveness.[58] Proof of effectiveness generally consists of controlled clinical investigations as defined in the provision for adequate and well-controlled studies for new drugs.[59]

To the extent Petitioner is requesting that FDA revise or deviate from the statutory framework for approval, such a request is outside the scope of FDA's authority and cannot be granted. To the extent Petitioner is requesting that FDA modify its implementation of the statutory framework for approval (in particular by "rejecting the drugs-for-health hypothesis, adopting a holistic analysis approach, avoiding trade art and junk science, [and] restructuring advisory committee structure and member compositions"), we assess this request below.

As noted, Petitioner's request for overhauling the approval framework involves, among other things, "rejecting the drugs-for-health hypothesis" and "adopting a holistic analysis approach."[60] In addition to failing to define either the "drugs-for-health hypothesis" or "holistic analysis approach," Petitioner also fails to explain how acceptance or rejection of such hypothesis or approach relates to the statutory standards that control FDA's approval decisions. Petitioner's vague references to these terms and other similar terms do not provide adequate basis for any

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[55] Section 505(d)(2) of the FD&C Act; 21 CFR 314.125(b)(3).
[56] Section 505(d)(5) of the FD&C Act; 21 CFR 314.125(b)(5).
[57] Section 351(a)(2)(C)(i) of the PHS Act.
[58] See 21 CFR 600.3(s) and the Guidance for Industry, Providing Clinical Evidence of Effectiveness for Human Drug and Biological Products, May 1998, https://www.fda.gov/files/drugs/published/Providing-Clinical-Evidence-of-Effectiveness-for-Human-Drug-and-Biological-Products..pdf?msclkid=1cc0d903cfa511ec8ae8a8aef181ed1d.
[59] See 21 CFR 314.126 and the Guidance for Industry, Providing Clinical Evidence of Effectiveness for Human Drug and Biological Products, May 1998, https://www.fda.gov/files/drugs/published/Providing-Clinical-Evidence-of-Effectiveness-for-Human-Drug-and-Biological-Products..pdf?msclkid=1cc0d903cfa511ec8ae8a8aef181ed1d.
[60] Petition at 2.

FDA action.[61] Additionally, to be clear, we note that FDA's approval of a drug or biological product is based on data and information submitted to the agency, not reliance upon any hypothesis regarding whether a product supports health. FDA reviews and assesses the data and information submitted in a drug or biological product application on a case-by-case basis to determine whether the applicable statutory standards for approval are met. When such standards are satisfied, the application is approved.

Another component of Petitioner's request for overhauling the approval framework is "avoiding trade art and junk science."[62] Petitioner fails to explain what is meant by "trade art" and thus FDA cannot assess whether everything that falls within such category should be categorically rejected for purposes of drug and biological product approval. Petitioner provides the following examples of what Petitioner considers to be "junk science": "[R]eductionist treatment model, clinical trials, statistical models, flawed disease theories, drug-for-health hypothesis, and whatever that can help [medical publishers] to generate revenues."[63]

Although we agree that data and information used to support approval of drugs and biological products should be scientifically sound, we disagree that all categories of data and information that Petitioner considers "junk science" are necessarily without scientific merit and should be categorically rejected for purposes of drug and biological product approval. For example, the scientific quality of a clinical trial (including any associated statistical modeling) would need to be assessed on a case-by-case basis. Clinical trials have played a critical role in evaluating and

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[61] The following examples illustrate how Petitioner refers to the "drugs-for-health hypothesis," "holistic analysis approach," and other similar terms:

- "The partnership between the drug industry and the publishing industry become even more important after 1980. Massive post-1980 research findings ... started showing failure of drugs. Thus, **the drug-for-health hypothesis** is constantly under challenge and the need to use alternative health measures arose. … The drug industry must cling onto flawed research models that can inflate drug benefits and write off drug side effects, and the publishers must do their part to suppress discoveries that could pronounce the end of **drug-for-health** era. Moreover, since the medical publishers share medical trade revenue, they must know that putting more people on more drugs can generate more profits than curing their diseases and they have the same incentive to keep alive the **drug-for-health** medicine." Petition at 7 (emphasis added).
- "[Medical publishers] promote **drug-for-health** researches by tailoring their article specifications to drugs discoveries and get large amounts of fund by obtaining government trust." Petition at 9 (emphasis added).
- "Under the quantitative model, over active immune system might kill more host cells that the body can replenish, resulting in structural damages. Over active immune system and disrupted protein synthesis may collectively weaken the blood vessel structure. When failure point (expressed in systemic peak pressure) in a person's vascular system is reduced from 300 mm Hg to 200 mm Hg, the person may die at more situations. Similarly, protein synthesis pattern may be altered by varying degrees. Damaged bone structure may result in a diminished capacity of generating white blood cells. When the body needs more immune cells, bone marrows could not generate them to meet short term demand. Those problems can be addressed only by using a **holistic balance approach**, the validity of which has been found in the roles of sex hormones and stress hormones. Evolution might have set a sophisticated balance in stress hormone, sex hormone and use of the immune system." Petition at 34 (emphasis added).
- "Any problem in the research model, data analysis and contextual knowledge must be corrected before the effectiveness and safety conclusions can be trusted. The standard is not static, but must be improved continuously with the progress of scientific discoveries. FDA is obligated to find how those findings affect its drug approval. Its current legal standard does not preclude use of additional and better research methods and **holistic risk analysis framework**." Petition at 46 (emphasis added).

[62] Petition at 2.

[63] Petition at 8.

establishing the safety and effectiveness of drugs, and the safety, purity, and potency of biological products, and Petitioner presents no reliable evidence that clinical trials are not appropriate for such purposes. Petitioner asserts that "[a] large number of post-1980 studies have proved that clinical trials cannot provide valid comparison with a controlled group."[64] Petitioner further asserts that "effectiveness and safety cannot be directly measured reliably by using a controlled trial because there are no similar persons for comparison…and the statistical analysis is often misused because there is no statistical distribution."[65] However, the 2019 and 2020 documents authored by Wu and Zha that Petitioner cites in support of these assertions appear to be preprints that have not been published in a scientific journal and that do not provide new data or information to support such assertions that is of the scientific quality that FDA would consider in making regulatory decisions. Additionally, the 2018 publication authored by Krauss that Petitioner references to support these assertions is an assessment of bias in 10 randomized clinical trials. The publication does not conclude that clinical trials cannot provide valid comparison with a control group – rather the author concludes, in part, that randomized clinical trials can be improved by attention to the assumptions, biases and limitations of clinical trials. We discuss additional examples of Petitioner's unsubstantiated assertions regarding clinical trials in section III.B of this response.

Certain of Petitioner's other examples of "junk science" (i.e., the "reductionist treatment model" and "drug-for-health hypothesis") have been addressed in this response and, as explained, do not provide any basis for FDA action. Petitioner's remaining examples of "junk science (i.e., "flawed disease theories" and "whatever that can help [medical publishers] to generate revenues") similarly provide no basis for FDA action. Because Petitioner provides no definition or objective criteria for determining what constitutes a "flawed disease theory," it is not possible to assess whether everything that falls within such category is necessarily without scientific merit such that it should be categorically rejected for purposes of drug and biological product approval. Additionally, whether data and information might help medical publishers generate revenue does not relate to the statutory standards for approval and thus is not a relevant consideration for purposes of determining whether the data and information support approval of a drug or biological product. FDA will continue to evaluate, on a case-by-case basis, the data and information submitted in a drug or biological product application to determine whether the applicable approval standards are satisfied.

The final component of Petitioner's request for overhauling the approval framework is "restructuring advisory committee structure and member compositions."[66] However, the Statement of Grounds in the Petition includes no mention of the advisory committee structure or member composition. Petitioner provides no information on what type of restructuring is requested or why such restructuring is needed. As such, Petitioner provides no basis for any FDA action with respect to advisory committee structure or member composition.

FDA has reviewed the issues raised by the Petitioner relating to the request to "overhaul its approval framework: rejecting the drugs-for-health hypothesis, adopting a holistic analysis approach, avoiding trade art and junk science, restructuring advisory committee structure and

[64] Petition at 46.
[65] *Id*.
[66] Petition at 2.

member compositions, pursuant to implied power provided in 21 U.S. § 379dd." For the reasons outlined above, FDA denies this request.

F. Petitioner's Request Regarding FDA Validation of the Accuracy of Certain Information

Request No. 6: "The outcome of this petition will affect the health and lives of the U.S. population and potentially billions of people globally. However, federal government, state governments, foundations, etc. generally do not provide funding for researches for finding vaccines risks. Due to such funding biases and suppression of vital researches, Petitioner has to rely on observations, 'misinformation', and 'underground' data (per the characterization of information-launders) in this petition. FDA should bear responsibility to validate the accuracy of information from such sources. However, even if FDA rejects all 'misinformation' and 'underground' data, this petition still invalidates research conclusions that FDA has relied upon in granting mRNA vaccines use authorizations."

FDA's evaluation of Request No. 6: This request suggests a misunderstanding of FDA's statutory responsibilities. FDA's responsibility in connection with vaccines is to ensure that the relevant statutory standards are met for the vaccines that the agency regulates, and when such standards are not met FDA's responsibility is to take appropriate action. In the context of reviewing product applications, FDA may review the soundness of scientific information submitted in support of applications and also consider other relevant scientific information as appropriate. However, FDA does not have a statutory mandate to proactively "validate the accuracy" of scientific information, irrespective of the publication's connection to a product application. Your Petition does not explain the legal basis for concluding that FDA should proactively "validate the accuracy" of such scientific information. This request thus lacks legal support. Consequently, you have not provided adequate legal grounds for your requested action. *See* 21 CFR 10.30(b)(3) (requiring citizen petitions to set forth the legal grounds on which the petition relies).

G. Petitioner's Request for FDA Permission to File Updated Petitions

Petition Request No. 7: "Petitioner started peerless researches as early as the start of the COVID-19 pandemic, but do not get any support from any peers, any funding agencies, and any media. Moreover, this petition is based on a different life model which is backed up by an extremely large amount of factual findings by independent researchers. In the eyes of people who have gotten used to the reductionist "science", the petition may appear to contain inaccuracies, inconsistent data, non-conventional expressions, etc. Those problems cannot be addressed until readers fully understand the new life model. If Petitioner spends years to address those problems, all damages to the U.S. population and humankind will be quickly realized. Petitioner therefore has a need to file this petition without any peer comment and review. The extraordinary circumstance justifies this decision. I hope that public readers of this petition will provide constructive feedback during the review period. Therefore, Petitioner requests FDA to grant a permission to file one to more updated petitions to clarify all difficulties that may inherently arise from evaluating two different science frameworks."

FDA's evaluation of Request No. 7: The only specific request included in in this language appears to be for FDA to grant Petitioner "permission to file one to more updated petitions to clarify all difficulties that may inherently arise from evaluating two different science frameworks."

The regulations governing citizen petitions set forth procedures for supplementing or amending a citizen petition. Pursuant to 21 CFR 10.30(g), "[a] petitioner may supplement, amend, or withdraw a petition without Agency approval and without prejudice to resubmission at any time until the Commissioner rules on the petition, unless the petition has been referred for a hearing under parts 12, 13, 14, or 15 of this chapter." To the extent that Request No. 7 asks FDA for permission to file an update to the Petition before such time as FDA may rule on the Petition, we deny the request because there is no need for FDA to grant permission for such supplements or amendments.

To the extent that Request No. 7 asks FDA for permission to update the Petition after FDA rules on the Petition, we note that once FDA has ruled on a citizen petition, the petition "may be supplemented, amended, or withdrawn only with the approval of the Commissioner."[67] A request for FDA to approve, in advance, an unspecified number of supplements and/or amendments to the Petition over an unspecified period of time in the future is overly broad. There is insufficient information at this time for FDA to evaluate whether each such amendment and/or supplement will be justified in the future. Rather, if Petitioner seeks to make a specific update to the Petition in the future, Petitioner may request approval for a supplement or amendment pursuant to 21 CFR 10.30(g), and FDA will consider whether approval of such request is justified based on the information provided.

For these reasons, FDA denies this request.

IV. CONCLUSION

FDA has considered Petitioner's requests. For the reasons given in this letter, FDA denies the requests and therefore denies the Petition in its entirety.

We also note that the Petition states that Petitioner plans to submit "continuous" Petitions. While the citizen petition process in 21 CFR 10.30 is available to all persons, we note that citizen

[67] 21 CFR 10.30(g).

petitions are to be resolved based on information in the administrative record (see 21 CFR 10.30(j)).[68] Accordingly, FDA will not grant a citizen petition that is not supported with an administrative record that provides adequate justification for the requested action.

Sincerely,

Peter Marks, MD, PhD
Director
Center for Biologics Evaluation and Research

cc: Dockets Management Staff

[68] Under 21 CFR 10.30(i), the record consists of: (1) The petition, including all information on which it relies, filed by the Division of Dockets Management; (2) All comments received on the petition, including all information submitted as a part of the comments; (3) If the petition resulted in a proposal to issue, amend, or revoke a regulation, all of the documents specified in § 10.40(g); (4) The record, consisting of any transcripts, minutes of meetings, reports, FEDERAL REGISTER notices, and other documents resulting from certain optional procedures; (5) The Commissioner's decision on the petition, including all information identified or filed by the Commissioner with the Division of Dockets Management as part of the record supporting the decision; and (6) All documents filed with the Division of Dockets Management under § 10.65(h).