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OPINION OF THE UNITED STATES COURT OF APPEALS FOR THE SIXTH CIRCUIT (JULY 12, 2022)

UNITED STATES COURT OF APPEALS
FOR THE SIXTH CIRCUIT

CHILDREN'S HEALTH DEFENSE; AMY MILLER,

Plaintiffs-Appellants,

v.

UNITED STATES FOOD AND DRUG ADMINISTRATION; JANET WOODCOCK, MD,

Defendants-Appellees.

Case No. 21-6203

Not Recommended for Publication
File Name: 22a0276n.06

On Appeal from the United States District Court
for the Eastern District of Tennessee

Before: GIBBONS, ROGERS,
and MURPHY, Circuit Judges.

JULIA SMITH GIBBONS, Circuit Judge.

Children's Health Defense ("CHD")[1] and Amy Miller, collectively "plaintiffs," sued the Food & Drug

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[1] CHD is a nonprofit organization that seeks to end "childhood health epidemics by working aggressively to eliminate harmful

Administration and its acting commissioner Dr. Janet Woodcock, collectively "FDA," for "failing to carry out its mission." DE 19, Am. Compl., Page ID 857. Plaintiffs, attempting to represent adult military servicemembers, sought a "stay" of FDA's licensure of Pfizer's Comirnaty COVID-19 vaccine and FDA's reauthorization of the Pfizer-BioNTech emergency use authorization. The district court denied plaintiffs' motion and dismissed the case for lack of subject matter jurisdiction. We affirm because plaintiffs lack standing.

I

The Public Health Service Act requires an approved biologics license application from FDA before companies introduce biological products, like vaccines, into interstate commerce. *See* 42 U.S.C. § 262(a)(1)(A), (i)(1). Separately, the Federal Food, Drug, and Cosmetic Act allows FDA to authorize biological products that are "intended for use in an actual or potential emergency," "[n]otwithstanding" the Public Health Service Act's licensing provisions. 21 U.S.C. § 360bbb-3(a)(1). The Secretary of Health and Human Services may issue such emergency use authorizations ("EUAs") under limited circumstances, which permit the immediate use of a vaccine without first obtaining a biologics license. *Id*. § 360bbb-3(c). FDA's licensing authority under 21 U.S.C. § 262 and its EUA authority under 21 U.S.C. § 360bbb-3 are independent of each other; FDA's licensing authority does not affect its

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exposures, hold those responsible accountable, and establish safeguards so this never happens again." DE 26, Decl., Page ID 1057.

EUA authority and vice versa. *Compare* 21 U.S.C. § 360bbb-3(a)(1), (*l*), (k), *with* 42 U.S.C. § 262(g).

In January 2020, the Secretary of Health and Human Services declared a public emergency in response to the COVID-19 pandemic. Pharmaceutical companies, including Pfizer, Moderna, and Johnson & Johnson, began researching and developing potential vaccines. In December 2020, FDA issued an EUA for the Pfizer-BioNTech vaccine for the prevention of COVID-19 in individuals age sixteen and older. FDA has since reissued the EUA several times to update the vaccine's labeling with additional safety information and to incorporate amendments to the EUA that have, for example, expanded the age groups eligible to receive the vaccine.

In May 2021, CHD filed a Citizen Petition with FDA requesting that it refrain from licensing COVID-19 vaccines and revoke the prior EUAs for COVID-19 vaccines. Then, on August 9, 2021, the Secretary of Defense advised all Department of Defense ("DOD") employees that "he would 'seek the President's approval to make the [COVID-19] vaccines mandatory no later than mid-September, or immediately upon the [FDA's] licensure, whichever comes first.'" *Child.'s Health Def. v. FDA*, ___ F.Supp.3d ___, 2021 WL 5756085, at *1 (E.D. Tenn. Nov. 30, 2021) (citation omitted).

On August 23, 2021, FDA licensed Pfizer's Comirnaty vaccine for use in individuals age sixteen and older and simultaneously reissued an EUA for the Pfizer-BioNTech vaccine. FDA described Comirnaty as "interchangeable" with Pfizer-BioNTech but still "legally distinct" because the two are subject to separate statutory regimes. FDA explained it maintained the Pfizer-BioNTech EUA, despite Comirnaty's licensure,

because there was "no adequate, approved, available alternative" to the EUA product with enough doses "available for distribution" to all individuals over age sixteen and the licensed vaccine had not been approved for children under sixteen or for booster doses. DE 19-1, Pfizer EUA, Page ID 900, n.9.

CHD, "on behalf of its members who have been affected by [FDA's] actions," and Miller sued, asking the district court to enjoin FDA from licensing Comirnaty and extending the Pfizer BioNTech EUA. DE 19, Am. Compl., Page ID 857. Plaintiffs claim that FDA's licensure of Pfizer's Comirnaty and simultaneous extension of the Pfizer-BioNTech EUA violates federal law because EUA designations can only occur when the Secretary finds "that there is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating such disease or condition." 21 U.S.C. § 360bbb-3(c)(3). They allege FDA failed to articulate a satisfactory explanation for its decision to extend the Pfizer-BioNTech EUA once Comirnaty was licensed, thereby making an arbitrary and capricious decision in violation of the Administrative Procedure Act. As a remedy, plaintiffs seek to have FDA's decisions to license Comirnaty and reauthorize the Pfizer-BioNTech EUA "vacate[d] and remand[ed]." DE 19, Am. Compl., Page ID 867.

In support of their claims, plaintiffs attach the declarations of fifteen CHD members who were or are serving in the United States military. These individuals generally allege that unvaccinated servicemembers who refuse to comply with the military's vaccine requirements are facing or will face adverse consequences. As the district court explained, the declarants identify "various objections to receiving the vaccine, including

religious based objections and concerns regarding the effect the vaccine might have on their ability to have children," and many express fears that "they are in jeopardy of being discharged from the military and losing retirement benefits and their future careers" if they remain unvaccinated. *Child.'s Health Def.*, 2021 WL 5756085, at *2. "Plaintiffs also include an affidavit from CHD's general counsel, Mary S. Holland, who states that the interests of the declarants who 'CHD protects are clearly related to CHD's mission and overarching goals as an organization.'" *Id*. (citation omitted).

Plaintiffs moved to stay FDA's licensure of the Comirnaty vaccine and FDA moved to dismiss CHD's complaint for lack of jurisdiction. The district court found that plaintiffs lacked standing and granted FDA's motion to dismiss and denied plaintiffs' motion to stay.

II

The district court dismissed plaintiffs' complaint for lack of subject matter jurisdiction under Federal Rule of Civil Procedure 12(b)(1), a decision we review de novo. *Ass'n of Am. Physicians & Surgeons v. FDA (AAPS)*, 13 F.4th 531, 535 (6th Cir. 2021).

A

An organization can satisfy Article III's standing requirements by suing on its own behalf, called "organizational standing," or by suing on behalf of its members, called "associational" or "representative" standing. *See Online Merchants Guild v. Cameron*, 995 F.3d 540, 547 (6th Cir. 2021); *AAPS*, 13 F.4th at 537. The district court correctly found that CHD lacks both organizational and associational standing.

"To establish direct standing to sue in its own right, an organizational plaintiff" like CHD "must demonstrate that the 'purportedly illegal action increases the resources the group must devote to programs independent of its suit challenging the action.'" *Online Merchants*, 995 F.3d at 547 (citation omitted). On appeal, plaintiffs claim "the amended complaint sufficiently pleads that challenging the FDA's conduct drained substantial CHD resources." CA6 R. 13, Appellant Br., at 20 (formatting altered). Plaintiffs base this argument on the resources CHD allegedly expended in filing the Citizen Petition with FDA. But these allegations are not sufficiently pled in the amended complaint. The amended complaint's only reference to CHD's Citizen Petition is in paragraph seventeen, which states—in its entirety—that "CHD filed a Citizen Petition with the FDA (Exh. 1) on May 16, 2021, asking the FDA to refrain from licensing COVID vaccines and to revoke EUAs for the three existing COVID vaccines. Individuals have submitted over 30,000 comments on this petition." DE 19, Am. Compl., Page ID 859. This is not an assertion that CHD was injured by having to divert resources to oppose FDA's actions. The only mention of diverting resources appears in plaintiffs' district court reply brief. But under a Rule 12(b)(1) motion to dismiss for lack of subject matter jurisdiction that, as here, is a facial attack, courts are limited to assessing the sufficiency of plaintiffs' complaint. *Cartwright v. Garner*, 751 F.3d 752, 759-60 (6th Cir. 2014). Plaintiffs failed to sufficiently plead that CHD has organizational standing.

B

"Even where an organizational plaintiff lacks standing to sue in its own right, it may sue on behalf of its members if 'its members would otherwise have standing to sue in their own right, the interests at stake are germane to the organization's purpose, and neither the claim asserted nor the relief requested requires the participation of individual members in the lawsuit.'" *Online Merchants*, 995 F.3d at 549 (citation omitted). CHD fails to satisfy the first two elements of associational standing.[2]

First, CHD cannot show "the interests it seeks to protect are germane" to its "purpose" as an organization. *See Hunt v. Wash. State Apple Advert. Comm'n*, 432 U.S. 333, 343 (1977); *AAPS*, 13 F.4th at 537. In *Hunt*, the Supreme Court found the Washington State Apple Advertising Commission's "purpose is the protection and promotion of the Washington apple industry," which encompasses litigation to benefit this "specialized segment of the [Washington] economic community." 432 U.S. at 344. Similarly, in *Online Merchants*, we found the Online Merchants Guild's suit "addressing price gouging as it relates to eCommerce falls within the scope of the Guild's mission, 'to advocate for a free and fairly-regulated online marketplace.'" 885 F.3d at 549 (citation omitted).

Here, CHD's purpose is detached from the interests at stake in the complaint. Plaintiffs' appellate brief claims the "protection of military service member's [sic] rights to refuse or consent to COVID vaccines . . . is

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[2] The Supreme Court has explained that "individual participation" is usually unnecessary "when an association seeks prospective or injunctive relief for its members."

a core thrust of the CHD's organizational purpose." CA6 R. 13, Appellant Br., at 34. But CHD's stated mission is to end "childhood health epidemics by working aggressively to eliminate harmful exposures, hold those responsible accountable, and establish safeguards so this never happens again." DE 26, Decl., Page ID 1057. The connection between a suit concerning the vaccination of adult military members and an organization committed to protecting children's health is too attenuated to establish CHD's "stake in the resolution of the *United Food & Com. Workers Union Local 751 v. Brown Grp., Inc.*, 517 U.S. 544, 546 (1996). Because CHD seeks a "stay" of FDA's actions, a form of injunctive relief, this suit likely does not require participation by individual CHD members. dispute" and "position to serve as [FDA's] natural adversary." *United Food & Com. Workers Union Local 751 v. Brown Grp., Inc.*, 517 U.S. 544, 555-56 (1996).

Second, CHD cannot show that its members have standing in their own right. To establish associational standing based on members' standing, an organization must identify a member who has suffered, or imminently will suffer, an injury in fact that is fairly traceable to the challenged conduct and redressable by the relief sought. *See AAPS*, 13 F.4th at 543. Even if CHD could identify a member who has suffered or imminently will suffer an injury in fact, it cannot show the requisite causation or redressability.

Causation. Plaintiffs fail to show causation. Causation requires a causal connection between the alleged injuries and the conduct complained of. *Lujan v. Defs. of Wildlife*, 504 U.S. 555, 560 (1992). The injuries must be "fairly . . . trace[able] to the challenged action

of the defendant, and not . . . th[e] result [of] the independent action of some third party not before the court." *Id.* (citation omitted). Here, plaintiffs' alleged injuries are not fairly traceable to FDA's actions. The military's vaccination requirements, and the alleged possible consequences from failing to comply, stem from DOD decisionmakers. FDA has not imposed any kind of mandate affecting the declarants, and DOD is a third party not before this court.

When a third party causes plaintiffs' alleged harm, the plaintiffs must show the third party's "choices have been or will be made in such manner as to produce causation and permit redressability of injury." *Parsons v. DOJ*, 801 F.3d 701, 713 (6th Cir. 2015) (quoting *Lujan*, 504 U.S. at 562). Plaintiffs claim this requirement is satisfied because FDA and DOD are not independent; rather, they act jointly under a single executive branch. But even when two executive agencies are implicated, traditional third-party causation principles apply. *See Bennett v. Spear*, 520 U.S. 154, 168-71 (1997).

Plaintiffs fail to explain how their alleged injuries are the direct result of the specific FDA action challenged. FDA has not required the general public to be vaccinated, FDA has not required military servicemembers to be vaccinated, and FDA does not control the military. Plaintiffs challenge FDA's licensure and reauthorization of Pfizer's vaccines; this is in no way tied to military leadership's implementation of the vaccination requirements that caused plaintiffs' alleged injuries. Plaintiffs cite no authority requiring that we construe the action of one agency as tantamount to another's, even when both agencies fall within the same branch of government. Further, plaintiffs cite no authority that connects DOD's decision to implement

a vaccine requirement to FDA's decisions about licensure and reauthorization.

Redressability. Besides failing to show causation, plaintiffs fail to show redressability. "[I]t must be 'likely,' as opposed to merely 'speculative,' that the injury will be 'redressed by a favorable decision.'" *Lujan*, 504 U.S. at 561 (citation omitted). Here, plaintiffs must show that ordering FDA to revoke its licensure of Comirnaty and its reauthorization of the Pfizer-BioNTech EUA would redress their alleged injuries from DOD's vaccination requirements. Plaintiffs have failed to do so. On appeal, plaintiffs argue their injuries are redressable because DOD relied on FDA's "misleading representations regarding the 'interchangeability'" between Pfizer's licensed Comirnaty vaccine and reauthorized Pfizer-BioNTech EUA. CA6 R. 13, Appellant Br., at 40. But this does not explain how a "stay" would redress plaintiffs' alleged injuries.

As the district court recognized, if the Comirnaty license is revoked, the Pfizer-BioNTech EUA remains in place and that vaccine is available for administration. DOD, a third party, can continue requiring vaccination of servicemembers as a condition of employment, and it can require vaccination regardless of whether the vaccine is distributed pursuant to a license or EUA. *See* 10 U.S.C. § 1107a. Moreover, DOD could administer COVID-19 vaccines manufactured by other companies with licenses and EUAs not challenged here. Because DOD's vaccine mandate is not tied to FDA's actions, plaintiffs' requested relief will not redress their alleged injuries.

Because CHD's members would not otherwise have standing to sue in their own right and the interests at

stake are not germane to the organization's purpose, CHD lacks associational standing.

C

Miller, a member of CHD and the only individual plaintiff, likewise lacks standing. Her only allegation of harm is that she "is at imminent risk of immediate harm from FDA's actions to both license and contemporaneously authorize Pfizer vaccines against COVID." DE 19, Am. Compl., Page ID 857. She fails to explain what specific harm she faces and how it can be fairly traced to FDA's conduct. She does not claim she is subject to any vaccine mandate or that she will face penalties for failing to get vaccinated. Her allegation that she is at "imminent risk" of unspecified harm is insufficient to establish injury in fact because it is neither concrete nor particularized.

III

The district court dismissed plaintiffs' amended complaint. On appeal, plaintiffs claim this is reversible error because leave to amend a pleading should be freely granted. A district court does not abuse its discretion by dismissing a complaint without leave to amend when no leave was sought. *See Total Benefits Planning Agency, Inc. v. Anthem Blue Cross & Blue Shield*, 552 F.3d 430, 438 (6th Cir. 2008). As this court has explained, "it is not the district court's role to initiate amendments." *Id.* "The argument that the district court should have rescued Plaintiffs by *sua sponte* offering leave to amend the complaint is simply misplaced." *Id.* Plaintiffs never moved for leave to file a second amended complaint nor did they file a proposed second amended complaint. *See Crosby v. Twitter, Inc.*, 921 F.3d 617,

628 (6th Cir. 2019). Moreover, plaintiffs received ample notice that their original complaint failed to sufficiently allege harm when the district court denied their motion for a temporary restraining order. Plaintiffs have had "ample opportunities to present their case." *Stewart v. IHT Ins. Agency Grp., LLC*, 990 F.3d 455, 457 n.* (6th Cir. 2021). We affirm the district court's decision to dismiss plaintiffs' complaint without *sua sponte* offering leave to amend.

IV

We affirm the district court's judgment dismissing plaintiffs' amended complaint because neither CHD nor Miller has standing.

JUDGMENT OF THE UNITED STATES COURT OF APPEALS FOR THE SIXTH CIRCUIT (JULY 12, 2022)

UNITED STATES COURT OF APPEALS
FOR THE SIXTH CIRCUIT

CHILDREN'S HEALTH DEFENSE; AMY MILLER,

Plaintiffs-Appellants,

v.

UNITED STATES FOOD AND DRUG ADMINISTRATION; JANET WOODCOCK, MD,

Defendants-Appellees.

Case No. 21-6203

On Appeal from the United States District Court for the Eastern District of Tennessee at Chattanooga

Before: GIBBONS, ROGERS, and MURPHY, Circuit Judges.

THIS CAUSE was heard on the record from the district court and was submitted on the briefs without oral argument.

IN CONSIDERATION THEREOF, it is ORDERED that the judgment of the district court is AFFIRMED.

ENTERED BY ORDER OF THE COURT

/s/ Deborah S. Hunt
Clerk

MEMORANDUM OPINION AND ORDER OF THE UNITED STATES DISTRICT COURT FOR THE EASTERN DISTRICT OF TENNESSEE (NOVEMBER 30, 2021)

UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF TENNESSEE
CHATTANOOGA DIVISION

CHILDREN'S HEALTH DEF., ET AL.,

Plaintiffs,

v.

FOOD AND DRUG ADMIN., ET AL.,

Defendants.

1:21-CV-00200-DCLC-CHS

Before: Clifton L. CORKER,
United States District Judge.

MEMORANDUM OPINION AND ORDER

This matter is before the Court to consider Plaintiff Children's Health Defense's ("CHD") and Amy Miller's motions for a "stay" [Docs. 9, 14] of Defendant Food and Drug Administration's ("FDA") licensure of the Pfizer Comirnaty COVID-19 vaccine and reauthorization of the Pfizer-BioNTech vaccine's emergency use authorization ("EUA"). Defendants FDA and FDA Acting Commissioner Janet Woodcock oppose Plaintiffs' motion

and have moved to dismiss the case for lack of subject matter jurisdiction [Doc. 22]. The matter has been fully briefed.

I. Background

This case concerns the FDA's licensure of Pfizer's Comirnaty vaccine and its decision to extend, simultaneously, the Pfizer-BioNTech vaccine's EUA [Doc. 19, ¶ 1]. Federal law authorizes the Secretary of Health and Human Services to issue EUAs for vaccines under limited circumstances.[1] This permits the immediate use of a vaccine without having to follow the normal review process. *See* 21 U.S.C. § 360bbb-3. In January 2020, the Secretary of Health and Human Services declared a public health emergency. (https://www.phe.gov/emergency/news/healthactions/phe/Pages/2019-nCoV.aspx). Since that moment, COVID-19 has wreaked havoc on the country, taking the lives of hundreds of thousands of people. In response, Pfizer, Moderna, and Johnson & Johnson began to research and develop potential vaccines. On December 11, 2020, the FDA issued an EUA for the Pfizer-BioNTech COVID-19 vaccine for individuals 16 years of age or older pursuant to 21 U.S.C. § 360bbb-3 [Doc. 19, ¶ 15]. On December 19, 2020, it issued an EUA for Moderna's

[1] The Secretary of Health and Human Services must find that: (1) the investigational drug, in this case the Pfizer-BioNTech vaccine, is intended to treat "a serious or immediately life-threatening disease"; (2) there is no satisfactory alternative therapy available to treat the disease; (3) the investigational drug is undergoing clinical trials; (4) the sponsor of the clinical trial is seeking marketing approval; and (5) there is sufficient evidence of its safety and effectiveness. 21 U.S.C. § 360bbb(c)(1)-(7).

vaccine, and, on February 27, 2021, it issued an EUA for the Johnson & Johnson vaccine.

In May 2021, CHD filed a Citizen Petition with the FDA requesting it refrain from licensing COVID-19 vaccines and revoke the prior EUAs for the three existing vaccines [*Id.*, ¶ 17]. On August 9, 2021, Secretary of Defense Lloyd Austin advised all Department of Defense employees that he would "seek the President's approval to make the [COVID-19] vaccines mandatory no later than mid-September, or immediately upon the [FDA's] licensure, whichever comes first." Memorandum from Sec'y of Def. Lloyd Austin to Dep't of Def. employees (Aug. 9, 2021) (available online). Two weeks later on August 23, 2021, the FDA granted a license to Pfizer's Comirnaty vaccine but not the Pfizer-BioNTech vaccine [*Id.*, ¶ 20]. Although the FDA noted that they were "interchangeable," it still described them as "legally distinct." [*Id.*, ¶ 20]. On that same date, the FDA denied CHD's Citizen Petition.

On August 31, 2021, Plaintiffs CHD, "on behalf of its members who have been affected by the Defendants' actions," and Miller filed their initial complaint and later amended their complaint [Docs. 1; 19, ¶ 4]. Plaintiffs asked the Court to enjoin the FDA from both licensing the Pfizer Comirnaty vaccine and extending the EUA for the Pfizer-BioNTech vaccine. Plaintiffs claim that the FDA's decision to license Pfizer's Comirnaty vaccine while simultaneously extending the EUA for the Pfizer-BioNTech vaccine violates federal law as EUA designations can only occur when, under 21 U.S.C. § 360bbb-3-(3), the Secretary finds "that there is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating such disease or condition." 21 U.S.C. § 360bbb-3-(3)(c)(3).

Plaintiffs reason that, once the FDA licensed Pfizer's Comirnaty vaccine, it had no legal basis to retain EUA status for any of the other vaccines [Doc. 19, ¶¶ 29-30].

They allege that the FDA's finding of the unavailability of the Comirnaty vaccine in the United States to support the Pfizer-BioNTech vaccine's continued EUA status is "specious" because, if the vaccines are truly "interchangeable," then Pfizer could simply relabel their BioNTech vaccine as its licensed Comirnaty vaccine [*Id.*, ¶ 46]. They assert the FDA did not articulate a satisfactory explanation for its decision to license the Pfizer Comirnaty vaccine while extending EUA status to the Pfizer-BioNTech vaccine, rendering its decision arbitrary and capricious and in violation of the Administrative Procedures Act ("APA"), 5 U.S.C. § 706(2)(a) [*Id.*, ¶ 32]. Plaintiffs state that "Pfizer cannot unlawfully reap the benefits of a licensure and EUA status simultaneously. . . . " [*Id.*, ¶ 37]. They claim the FDA has given "legal cover for licensed vaccine mandates while gifting Pfizer a bullet-proof liability shield that comes only with an EUA." [*Id.*, ¶ 45]. They describe this as a "bait-and switch" tactic that permits Pfizer to claim licensure of its Comirnaty vaccine but sell off its inventory of BioNTech vaccines "that enjoy blanket liability protection." [*Id.*, ¶ 49]. Plaintiffs also allege that the FDA's licensure of the Comirnaty vaccine has "triggered employer, military, educational and institutional mandates across the country, coercing millions of healthy individuals to take unwarranted, risky medical interventions." [*Id.*, ¶ 50]. Plaintiffs seek to have the FDA's decisions to license the Comirnaty vaccine and reauth-

orize the Pfizer-BioNTech EUA "vacate[d] and remand-[ed]," have attorneys' fees and costs awarded, and "all other appropriate relief as necessary." [*Id.*, pg. 12].

In support of its Complaint, Plaintiffs attached the declarations of 15 CHD members who were, or are, presently serving in the United States military [*Id.*, ¶ 18]. The first declaration is from Pam Long, a member of CHD [Doc. 15, pgs. 1-3]. She is a former Army officer and claims she has "an active network of 18,000 people on social media who have shared concerns about the military vaccine mandate." [*Id.*, pg. 1]. Long alleges that unvaccinated servicemembers, who refuse to comply with the military's vaccine mandate, are denied access to dining facilities and gyms, have been removed from leadership positions in the military, have been ordered to forfeit their leave, and faced physical, emotional, and professional consequences [*Id.*, pgs. 1-3]. She claims that some have retired rather than be vaccinated [*Id.*, ¶ 16]. Long does not identify any of these servicemembers as members of CHD specifically, and she does not allege that she has suffered such penalties herself [*Id.*, pgs. 1-3].

The remaining 14 declarations are from current servicemembers across all branches of the United States military [*Id.*, pgs. 7-197]. Each declaration details various objections to receiving the vaccine, including religious based objections and concerns regarding the effect the vaccine might have on their ability to have children. They express fear that if they fail to comply with the military's mandatory vaccination policy, they are in jeopardy of being discharged from the military and losing retirement benefits and their future careers. Many also claim they have filed for religious exemptions from the vaccine mandate but have yet to have

their requests addressed. Plaintiffs also include an affidavit from CHD's general counsel, Mary S. Holland, who states that the interests of the declarants who "CHD protects are clearly related to CHD's mission and overarching goals as an organization." [Doc. 26, pg. 1]. The only individual Plaintiff is Amy Miller who alleges she is at "imminent risk of immediate harm from [the] FDA's actions to both license and contemporaneously authorize Pfizer vaccines against COVID." [Doc. 19, ¶ 5].

The FDA and its Commissioner have filed a motion to dismiss, claiming Plaintiffs lack Article III standing [Doc. 23, pg. 6]. They assert that Plaintiff CHD does not claim an injury to itself and that Plaintiff Miller only alleges that she is at imminent risk of immediate harm, without describing how she will be harmed [*Id.*, pg. 6]. They contend that CHD relies on associational standing but fails to plead facts to show that its members would have standing to sue in their own right or that the present suit is related to CHD's organizational mission [*Id.*, pg. 7]. They argue none of the declarants state they have: (1) suffered a present, or impending, injury-in-fact; (2) shown that the purported harm they face is traceable to Defendants' conduct; or (3) established that a "stay" would remedy the purported harm. [*Id.*, pgs. 8-12]. They also argue that the present suit is unrelated to CHD's organizational purpose because the declarants are adult service members interested in evading a vaccine mandate and do not represent the interests of children [*Id.*, pgs. 13-14].[2]

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[2] Defendants also make several arguments addressing the merits of Plaintiffs' claim. [Doc. 23, pgs. 14-23]. Because the Court

CHD argues it has associational standing to bring the present suit on behalf of its members [Doc. 25, pgs. 12-17]. Plaintiffs contend that the declarants who are members of CHD have Article III standing to sue in their own right [*Id.*, pgs. 14-15]. They next assert that the present suit is germane to CHD's purpose because its mission is to "end the childhood health epidemics by working aggressively to eliminate harmful exposures, hold those responsible accountable, and establish safeguards so this never happens again." [*Id.*, pg. 16]. They further explain that CHD "fights to protect all citizens from various forms of public health harm." [*Id.*]. Plaintiffs contend that the relief sought does not require the participation of individual members [*Id.*, pg. 17]. Plaintiffs also argue that CHD has organizational standing because it must divert resources "due to the threat the FDA's bait-and-switch imposes on millions of Americans." [*Id.*]. Plaintiffs next contend that Miller has standing to sue because of the FDA's denial of CHD's citizen petition [*Id.*, pg. 18].

II. Analysis

Defendants ask the Court to dismiss Plaintiffs Amended Complaint on the grounds that the Court lacks subject matter jurisdiction under Fed. R. Civ. P 12(b)(1). "A Rule 12(b)(1) motion for lack of subject matter jurisdiction can challenge the sufficiency of the pleading itself (facial attack) or the factual existence of the subject matter jurisdiction (factual attack)." *Cartwright v. Garner*, 751 F.3d 752, 759-60 (6th Cir. 2014) (citing *United States v. Ritchie*, 15 F.3d 592, 598 (6th Cir. 1994)). "A facial attack goes to the question

finds that Plaintiffs lack standing, it declines to consider Defendants' merits arguments.

of whether the plaintiff has alleged a basis for subject matter jurisdiction, and the court takes the allegations of the complaint as true for purposes of Rule 12(b)(1) analysis," while "[a] factual attack challenges the factual existence of subject matter jurisdiction." *Id.* Defendants mount a facial attack on Plaintiffs' complaint for lack of subject matter jurisdiction under Fed. R. Civ. P. 12(b)(1) because they assume the truth of Plaintiffs' factual allegations. Thus, the Court's analysis will focus on determining the sufficiency of Plaintiffs' pleadings to establish subject matter jurisdiction. *Id.*

Courts "do not have a standalone power to evaluate the constitutionality of every law passed by Congress or every initiative implemented by the President." *Ass'n of Am. Physicians & Surgeons v. Food & Drug Admin, et al.*, 13 F.4th 531, 536 (6th Cir. 2021). "A court may engage in such judicial review and issue a remedy regulating the political branches only when necessary in the execution of its duty to decide a case." *Id.* (internal quotations and citations omitted). "It may not issue an advisory interpretation of the Constitution or an advisory injunction regulating those branches whenever a concerned citizen thinks they have acted unlawfully." *Id.* Nor should courts "entertain citizen suits to vindicate the public's nonconcrete interest in the proper administration of the laws." *Lujan v. Def. of Wildlife*, 504 U.S. 555, 581 (1992) (Kennedy, J., concurring); *United States v. Richardson*, 418 U.S. 166, 192 (1974) (Powell, J., concurring) (reasoning that a court may not take on "ideological disputes about the performance of government").

"The party invoking federal jurisdiction bears the burden of establishing [standing]." *Lujan*, 504 U.S. at 561. Before the Court are both CHD, an organizational

plaintiff, and Miller, an individual plaintiff. CHD, as an association, may "sue over injuries suffered by its members even when (as here) the entity itself alleges no personal injury." *Ass'n of Am. Physicians & Surgeons*, 13 F.4th at 537. For a group to assert associational standing, it must show that: "(1) its members would otherwise have standing to sue in their own right; (2) the interests that the suit seeks to protect are germane to the organization's purpose; and (3) neither the claim asserted nor the relief requested requires the participation of individual members in the lawsuit." *Id.* (internal quotations and citations omitted).

The first element of associational standing requires an organization to show "that its members have Article III standing in their own right." *Id.* at 543. "Standing has three elements: injury, causation, and redressability." *WCI, Inc. v. Ohio Dep't of Pub. Safety*, No. 20-3930, 2021 WL 5351864, at *3 (6th Cir. Nov. 17, 2021) (citing *Lujan*, 504 U.S. at 560-61). "An injury is an invasion of a legally protected interest that is concrete and particularized and actual or imminent, not conjectural or hypothetical." *Id.* (citations and internal quotations omitted). A threatened injury must be "certainly impending" to constitute an injury for standing purposes. *Clapper v. Amnesty Int'l USA*, 568 U.S. 398, 401-02 (2013). "[T]he mere possibility that the injury will arise in the future does not suffice." *Ass'n of Am. Physicians & Surgeons*, 13 F.4th at 545 (internal quotations omitted). Generalized grievances do not support Article III standing. "A litigant raising only a generally available grievance" by "claiming only harm to his and every citizen's interest . . . and seeking relief that no more directly and tangibly benefits him than it does the public at large[,] does not" satisfy Article III standing.

In re FirstEnergy Sols. Corp., 828 F. App'x 321, 323 (6th Cir. 2020) (quoting *Hollingsworth v. Perry*, 570 U.S. 693, 707 (2013)). "Article III standing is not to be placed in the hands of 'concerned bystanders,' who will use it simply as a vehicle for the vindication of value interests." *Id.*

The injury CHD and Miller allege relates to the procedures followed by the FDA. They claim that "the FDA is failing to carry out its mission." [Doc. 19, ¶ 3]. They seek "to put the FDA back on the path to lawful protection of the public in these precarious times." [*Id.*, ¶ 3]. CHD claims the FDA has "flagrantly violated federal law" and this Court should step in and "vacate . . . the FDA's decision to license Pfizer's Comirnaty vaccine and to extend its Pfizer BioNTech" EUA. [*Id.*, pg. 12]. But CHD must have an injury that "affect[s] [it] in a personal and individual way." *Spokeo, Inc. v. Robins*, 578 U.S. 330, 339 (2016) (quoting *Lujan*, 504 U.S. at 560 n.1). That injury must be unique and individualized; the alleged injury cannot be a "collective[] harm" that impacts society generally. *In re Carter*, 554 F.3d 979, 989 (6th Cir. 2009). An "abstract generalized grievance" against illegal behavior that is "suffered by all citizens" does not create standing. *Carney v. Adams*, 141 S. Ct. 493, 499 (2020). Putting the FDA "back on the path to lawful protection of the public" is such a generalized grievance and not the type of particularized interest or personalized injury necessary to establish Article III standing.

Similarly, members of CHD also do not have standing in their own right. Those members claim that adverse action likely will occur if the military leadership fails to grant their requests for religious

accommodation.[3] They allege they face court martial, less than an honorable discharge, and exclusion from dining halls and gyms. But all of that is speculative and is not "certainly impending" to constitute an injury for standing purposes. *Clapper*, 568 U.S. at 401-02. Indeed, a majority of the declarants applied for religious exemptions from the mandate but have yet to have their requests denied. None have alleged injuries that have already occurred, only what they believe might occur in the future. But "the mere possibility that the injury will arise in the future does not suffice." *Ass'n of Am. Physicians & Surgeons*, 13 F.4th at 545 (internal quotations omitted).

The same is true for Plaintiff Miller. She has not alleged a concrete and particularized injury and has not shown that any such injury is fairly traceable to Defendants' conduct. Miller alleges she faces an "imminent risk of immediate harm" from the FDA's licensure of the Comirnaty vaccine and reauthorization of the Pfizer-BioNTech EUA. [Doc. 19, ¶ 5]. But she fails to explain what specific harm she faces or whether it is "certainly impending." *Clapper*, 568 U.S. at 401-02. She does not claim she is subject to a vaccine mandate or that she will face penalties for failing to get vaccinated.

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[3] Declarants Craymer, Eschmann, Hastriter, Hollowell, Mason, Meacham, Nuss, Raethel, Santos, Sweger, and Zito state that they have applied for vaccine exemptions and have not yet had their exemptions denied. [Docs. 15, pgs. 7, 19, 28, 38-40, 44-45, 52, 85, 125, 130, 174, 183; 20, pgs. 2-3]. Declarants Shour and Stanzione do not state that they are required to take the Pfizer-BioNTech vaccine, and Declarant Perez asserts that his commanders ignored his religious exemption but fails to state whether he complied with the commanders' instruction to bring documentation of his exemption. [Doc. 15, pgs. 89-92, 133-38, 154-55].

Her allegation that she faces a still-to-be-defined harm is not enough to constitute an injury for Article III standing. *Lujan*, 504 U.S. at 560.

Similarly, her allegation that she has standing through the Citizen Petition fails. The FDA's denial of the Citizen Petition does not confer standing on Miller because, according to Plaintiffs, Miller did not file a Citizen Petition. [Doc. 19, ¶ 17]. Further, it is unclear how the denial of CHD's Citizen Petition injures Miller such that it gives her Article III standing, particularly when Plaintiffs do not explain what repercussions Miller faces because of that denial.

Even assuming they have shown an injury, CHD and Miller still fail to satisfy the causation requirement for standing. For causation to exist, the injuries "ha[ve] to be 'fairly . . . trace[able] to the challenged action of the defendant, and not . . . th[e] result [of] the independent action of some third party not before the court.'" *Lujan*, 504 U.S. at 560-61 (quoting *Simon v. Eastern Ky. Welfare Rights Org.*, 426 U.S. 26, 41-42 (1976)). In this case, the conduct of the FDA "must have a 'casual connection' to the plaintiff's injury." *Gerber v. Herskovitz*, 14 F.4th 500, 505 (6th Cir. 2021) (quoting *Lujan*, 504 U.S. at 560).[4] The vaccine

[4] To be sure, "[i]n the nebulous land of 'fairly traceable,' where causation means more than speculative but less than but-for, the allegation that a defendant's conduct was a motivating factor in the third party's injurious actions satisfies the requisite standard." *Parsons v. United States Dep't of Justice*, 801 F.3d 701, 714 (6th Cir. 2015) (holding plaintiffs established standing when the FBI designated their group as a gang because that designation motivated state authorities to violate their constitutional rights). But here, Plaintiffs have not sufficiently alleged that the FDA's decisions to license the Comirnaty vaccine or give EUA status to

mandates, and the potential consequences for refusing those mandates, are not fairly traceable to the specific actions of the FDA. Instead, the various branches of the United States military are imposing the vaccine mandates—not the FDA. [*See, e.g.*, Doc. 15, pgs. 7-16]. Neither the FDA nor Acting Commissioner Woodcock have imposed mandates that impact the declarants. The only actions that Defendants have taken are to license the Comirnaty vaccine and reauthorize the Pfizer-BioNTech EUA. [Doc. 19, ¶¶ 26-52].

The harms the declarants identify—being subject to vaccine mandates by various branches of the military and the consequences of refusing to comply with those mandates—are tied to the actions of the military leadership and not the FDA.

Moreover, the line of causation between the FDA's actions and the imposition of vaccine mandates is simply too attenuated to satisfy the causation requirement. Where causation is too attenuated, there is no standing. An example of this is found in *Allen v. Wright*, where the Internal Revenue Service (IRS) refused to deny tax-exempt status to racially discriminatory private schools. *Allen v. Wright*, 468 U.S. 737, 739-40 (1984), *abrogated on other grounds by Lexmark Int'l, Inc. v. Static Control Components, Inc.*, 572 U.S. 118 (2014). The parents of African-American children filed suit claiming that the IRS's failure to act harmed them and prevented their children from receiving an education in desegregated public schools. *Id.* at 740. The Court found the parents lacked standing because

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Pfizer-BioNTech's vaccine was the motivating factor in the military's decision to impose vaccine mandates.

they could not show that their injury was fairly traceable to the IRS. *Id.* at 756-57. The "line of causation between [the IRS's conduct] and desegregation of [the plaintiff's] schools [was] attenuated at best." *Id.* at 757. The Court explained that the "injury to [plaintiffs] [was] highly indirect and result[ed] from the independent action of some third party not before the court." *Id.* (internal quotations omitted). The Court noted that it was "entirely speculative . . . whether withdrawal of a tax exemption from any particular school would lead the school to change its policies." *Id.* at 758.

The same is true here. The declarant's purported injury "results from the independent action of some third party not before the court," thereby making the "line of causation between [Defendants' conduct] and [the declarant's injury] attenuated at best." *Allen*, 468 U.S. at 757. And, even if the FDA's actions may have influenced the decision of the military, *see Parsons,* 801 F.3d at 714, the Plaintiffs have not alleged the FDA's actions were a "motivating factor" in the military's decision to impose vaccine mandates.

Even assuming Plaintiff could show injury and causation, they still fail to show their injuries are redressable by a favorable court decision. "[I]t must be 'likely, as opposed to merely speculative, that the injury will be redressed by a favorable decision.'" *Gerber*, 14 F.3d at 505 (quoting *Lujan*, 504 U.S. at 560). In this case, Plaintiffs must show that granting the relief sought would actually redress their alleged injuries. Assuming that the Court enjoins Defendants and requires them to revoke the Comirnaty vaccine license, Plaintiffs injuries are still not redressed. The Pfizer-BioNTech EUA remains in place, and the third parties instituting the vaccine mandates, here the various

branches of the military, can continue requiring servicemembers to get vaccinated as a condition of employment. Indeed, Secretary Austin's memorandum notifying servicemembers of the impending vaccine mandate clearly states that he would seek to impose a vaccine mandate "no later than mid-September, or immediately upon [the FDA's] licensure, *whichever comes first*." Memorandum from Sec'y of Def. Lloyd Austin to Dep't of Def. employees (Aug. 9, 2021) (available online) (emphasis added). The vaccine mandate is not tied to actions of the FDA. Thus, neither Plaintiff can show their purported injuries would be redressable by a favorable ruling.[5]

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[5] Additionally, as to CHD's alleged organizational standing, Plaintiffs' amended complaint does not assert that CHD was injured by having to divert resources to oppose Defendants' actions, which is required to show organizational standing. *Online Merchants Guild v. Cameron*, 995 F.3d 540, 547 (6th Cir. 2021). The amended complaint's failure to state that CHD diverted resources to oppose Defendants' actions is fatal because, under a Rule 12(b)(1) facial attack, the Court is limited to addressing the sufficiency of Plaintiffs' complaint. *Cartwright*, 751 F.3d at 759-60. Indeed, Plaintiffs only reference a diversion of resources in their Reply brief [Doc. 25, pg. 17]. Thus, Plaintiffs have not shown that CHD has organizational standing to bring the present suit.

III. Conclusion

Plaintiffs lack Article III standing to bring suit against Defendants, and the Court lacks subject matter jurisdiction to address the merits of Plaintiffs' claims. Accordingly, Plaintiffs' motions for a "stay" [Docs. 9, 14] are DENIED, and Defendants' motion to dismiss [Doc. 22] is GRANTED, and Plaintiffs' complaint is DISMISSED. A separate judgment shall enter.

SO ORDERED:

/s/ Clifton L. Corker
United States District Judge

JUDGMENT OF THE UNITED STATES DISTRICT COURT FOR THE EASTERN DISTRICT OF TENNESSEE (NOVEMBER 30, 2021)

UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF TENNESSEE
CHATTANOOGA DIVISION

CHILDREN'S HEALTH DEF., ET AL.,

Plaintiffs,

v.

FOOD AND DRUG ADMIN., ET AL.,

Defendants.

1:21-CV-00200-DCLC-CHS

Before: Clifton L. CORKER,
United States District Judge.

JUDGMENT

This case came before the Court on Defendants' Motion to Dismiss [Doc. 22]. For the reasons stated in the accompanying Memorandum Opinion and Order, Defendants' Motion to Dismiss [Doc. 22] is GRANTED. Accordingly, Plaintiffs' motions to stay [Docs. 9, 14] are DENIED, and their amended complaint [Doc. 19] against Defendants is DISMISSED. The Clerk is DIRECTED to close this case.

SO ORDERED:

/s/ Clifton L. Corker
United States District Judge

ENTERED AS A JUDGMENT:

/s/ LeAnna Wilson
Clerk of Court

ORDER OF THE UNITED STATES COURT OF APPEALS FOR THE SIXTH CIRCUIT DENYING PETITION FOR REHEARING (SEPTEMBER 22, 2022)

UNITED STATES COURT OF APPEALS
FOR THE SIXTH CIRCUIT

CHILDREN'S HEALTH DEFENSE; AMY MILLER,

Plaintiffs-Appellants,

v.

UNITED STATES FOOD AND DRUG ADMINISTRATION; JANET WOODCOCK, MD,

Defendants-Appellees.

Case No. 21-6203

Before: GIBBONS, ROGERS, and MURPHY, Circuit Judges.

ORDER

The court received a petition for rehearing en banc. The original panel has reviewed the petition for rehearing and concludes that the issues raised in the petition were fully considered upon the original submission and decision of the case. The petition then was circulated to the full court. No judge has requested a vote on the suggestion for rehearing en banc.

Therefore, the petition is denied.

ENTERED BY ORDER OF THE COURT

/s/Deborah S. Hunt
Clerk

PETITION FOR PANEL REHEARING AND REHEARING EN BANC (AUGUST 26, 2022)

No. 21-6203
Unpublished Opinion issued July 12, 2022
Before: GIBBONS, ROGERS, and MURPHY, Circuit Judges

IN THE UNITED STATES COURT OF APPEALS
FOR THE SIXTH CIRCUIT

CHILDREN'S HEALTH DEFENSE; AMY MILLER,

Plaintiffs-Appellants,

v.

UNITED STATES FOOD AND DRUG ADMINISTRATION; JANET WOODCOCK,

Defendants-Appellees.

On Appeal from the United States District Court for the Eastern District of Tennessee No. 1:21-cv-00200
Hon. Clifton L. Corker, District Judge

PETITION FOR PANEL REHEARING AND REHEARING *EN BANC*

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{ TOC & TOA Omitted }

On July 12, 2022, the Honorable Julia Smith Gibbons, John M. Rogers and Eric E. Murphy, Circuit Judges (the "Panel"), entered an unpublished opinion affirming the dismissal of the case for lack of subject matter jurisdiction (the "Opinion"). Docket Entry No. 25.[1] The grounds for the Opinion's holding was that the District Court had properly ruled that it lacked subject matter jurisdiction to hear the case, because the pleadings of Plaintiffs/Appellants Children's Health Defense and Amy Miller ("Appellants"), failed to adequately allege that they had Article III standing. Opinion, pg. 10.

This Petition For Panel Rehearing and Rehearing *En Banc* ("Petition") seeks panel rehearing pursuant to FRAP[2] Rule 40, which provides that a panel hearing will be granted where the petitioner demonstrates that the court has overlooked or misapprehended a point of law.

In addition or alternatively, this Petition seeks rehearing *en banc* pursuant to FRAP Rule 35, which provides that a rehearing *en banc* will be granted where the petitioner either demonstrates that it is necessary to secure or maintain uniformity of the

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[1] All references to "Docket Entry" are to the electronic docket of the U.S. Court of Appeals for the Sixth Circuit, Case No. 21-6203. A true and correct copy of the Opinion is attached herein.

[2] All references to "FRAP" are to the Federal Rules of Appellate Procedure.

court's decisions, or that the proceeding involves a question of exceptional importance.

I. The Opinion's Holding That Appellants Lacked Organizational Standing Merits Granting This Petition

As this Court's Opinion stated: "to establish direct standing to sue in its own right, an organizational plaintiff like [Appellants] must demonstrate that the 'purportedly illegal action increases the resources the group must devote to programs independent of its suit challenging the action.' (citing *Online Merchants*, 995 F.3d 540, 547 (6th Cir. 2021))." Opinion, pg. 5.

The Opinion went on to affirm the District Court's finding that Appellants lacked direct organizational standing, because Appellants' pleading failed to allege facts which, assumed true, adequately pled Article III standing. In so holding, this Court declined to adopt the argument in Appellants' briefing, that a 19-page Citizen Petition researched, drafted and presented to the Appellees prior to the subject lawsuit, constituted an increase in the resources that Appellants had to devote to, independent of its lawsuit against Appellees.[3]

In reviewing a facial attack on a pleading for lack of subject matter jurisdiction, such as Appellee's

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[3] In addition, as discussed more fully in Appellants' briefing, Appellants' pre-suit resources devoted to CHD programs and activities that were drained by Appellees' conduct, in the form of the additional man hours required to review Appellee FDA's 52-page response to Appellants' Citizen Petition. Appellants' Amended Complaint – Attachment #1, Exhibit 4, RE 19-1, page ID #909-962; *see also* Appellants' Opening Brief, at pp. 22-24 and Appellants' Reply Brief, at pp. 3-4.

underlying motion to dismiss here,[4] all factual allegations are presumed true and the pleading is to be construed in favor of the complaining party. *Lujan v. Defenders of Wildlife*, 504 U.S. 555, 561-562 (1992) ("*Lujan*"); *Warth v. Seldin*, 422 U.S. 490, 501-502 (1975); *Gladstone Realtors v. Village of Bellwood*, 441 U.S. 91, 109 (1979) ("*Gladstone*").

The pleadings for purposes of review on a Rule 12(b)(1) motion to dismiss, include supporting materials attached therein such as exhibits and affidavits. In *Carter v. HealthPort Technologies, LLC,* 822 F.3d 47, 56-57 (2nd Cir. 2016) ("*Carter*"), the court held:

> "When the Rule 12(b)(1) motion is facial, *i.e.,* based solely on the allegations of the complaint or the complaint and exhibits attached to it (collectively the 'Pleading'), the plaintiff has no evidentiary burden. [citation]. The task of the district court is to determine whether the Pleading 'allege[s] facts that affirmatively and plausibly suggest that [the plaintiff] has standing to sue.'." *See also: SM Kids, LLC v. Google LLC,* 963 F.3d 206 (2nd Cir. 2020), 210-211 ("*SM Kids*").

Similarly, in *Gladstone, supra,* 441 U.S. at 109, fn 22, the Supreme Court held that the plaintiffs sufficiently pled Article III standing by way of the allegations in their pleadings, which included exhibits:

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[4] Opinion, pg. 5: "But under a Rule 12(b)(1) motion to dismiss for lack of subject matter jurisdiction that, as here, is a facial attack, courts are limited to assessing the sufficiency of plaintiffs' complaint."

> "In addition to the complaints, the records in these cases contain several admissions by respondents, answers to petitioners' interrogatories, and exhibits appended to those answers, including maps of Bellwood. As did the courts below and the parties themselves, we accept as true the facts contained in these discovery materials for the purposes of the standing issue."

The Opinion affirming the District Court's finding that Appellants failed to sufficiently plead Article III standing, held:

> "The amended complaint's only reference to [Appellants'] Citizen Petition is in paragraph seventeen, which states—in its entirety—that 'CHD filed a Citizen Petition with the FDA (Exh. 1) on May 16, 2021, asking the FDA to refrain from licensing COVID vaccines and to revoke EUAs for the three existing COVID vaccines. . . . " Opinion, pg. 5 (emphasis added).

However, as revealed by the emphasized excerpt cited in the Opinion above, the 19-page Citizen Petition researched and drafted by Appellants was in fact attached to the subject pleadings, and thereby duly incorporated within the allegations therein. *Carter, supra,* 822 F.3d at 56-57 ["When the Rule 12(b)(1) motion is facial, *i.e.,* based solely on the allegations of the complaint or the complaint and exhibits attached to it (collectively the 'Pleading') . . . "].

As such, the exhibits combined with the other allegations in Appellants' pleadings, sufficiently pled organizational standing. To hold otherwise would

defeat the purpose of attaching exhibits in support of a pleading in the first instance. Because every plaintiff filing a complaint would be forced to allege *verbatim* any and all relevant text from the contracts and other documents supporting their claims, under penalty of dismissal at the pleadings stage.

The Opinion's affirmance of the District Court's order granting Appellees' motion to dismiss under Rule 12(b)(1), thus overlooked an important point of law and fact that exhibits attached to a plaintiff's complaint are to be considered a part of the plaintiff's pleadings. The Opinion is also inconsistent with Supreme Court and other circuit decisions regarding the issue. *Gladstone, supra*, 441 U.S. at 109, fn 22; *Carter v. HealthPort Technologies, LLC*, 822 F.3d at 56-57; *SM Kids, supra,* 963 F.3d at 210-211.

II. The Opinion's Holding That Appellants Lacked Associational Standing Also Merits Granting This Petition

As set forth in this Court's Opinion, associational standing requires: (a) at least one member has standing, in his or her own right; (b) the interests sought to be protected are germane to the association's purpose; and (c) neither the claim asserted nor the relief requested require the members to participate individually. *Hunt v. Washington State Apple Adv. Comm'n*, 432 U.S. 333, 343 (1977); *compare* Opinion, pp. 5-6. The Opinion's holding that Appellants' pleading failed

to satisfy the first two elements of associational standing, was erroneous and inconsistent with Supreme Court and circuit court precedent.[5]

A. The Interests Sought to Be Protected by Appellants' Pleading Are Germane to Appellant CHD's Purpose

In *Lexmark Int'l, Inc. v. Static Control Components, Inc.,* 572 U.S. 118, 130 (2014) ("*Lexmark*"), the Supreme Court held that in determining Article III standing for plaintiffs bringing claims under the Administrative Procedures Act ("APA"), the "zone-of-interests" standard applied, and further that upon that more fundamentally lax pleading standard: "forecloses suit only when a plaintiff's interests are so marginally related to or inconsistent with the purposes implicit in the statute that it cannot reasonably be assumed that Congress authorized that plaintiff to sue".

The Opinion held that: "The connection between a suit concerning the vaccination of adult military members and an organization committed to protecting children's health is too attenuated", to satisfy the second element of associational standing (that the interests sought to be protected are germane to the association's purpose). Opinion, pg. 6. However, as also set forth in the Opinion: "CHD's stated mission is to end 'childhood health epidemics . . . '." *Id.,* at pg. 6. As such, Appellant CHD's associational purpose is not detached from the interests at stake alleged in the pleadings. This is

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[5] As noted by this Court, CHD's pleading seeks a stay of Appellees' actions, thus not requiring the third element of individual participation per *United Food & Com. Workers Union Local 751 v. Brown Grp., Inc.*, 517 U.S. 544, 546 (1996). Opinion, pg. 6, fn 2.

not a case where CHD's purpose is solely "protecting children's health" (Opinion, pg. 6) on the one hand, and the subject pleadings seeking exclusively to protect against "vaccination of adult military members" (Opinion, pg. 6) on the other. Rather, CHD's mission is to protect its members against "health epidemics", including those that affect children as well as members of the military. To hold an organization like the CHD to such a heightened standard at the pleading stage, would be to conflict with Supreme Court and other circuit court precedent holding that the broader "zone of interests" standard applies to procedural claims under statutory provisions such as the APA. *Lexmark, supra,* 572 U.S. at 130; *Linda R.S. v. Richard D.* 410, U.S. 614, 617 (1973); *Massachusetts v. EPA,* 549 U.S. 497, 517 (2007) ("*Massachusetts*"); *Salmon Spawning & Recovery Alliance v. Gutierrez*, 545 F.3d 1220, 1226 (9th Cir. 2008).

B. The Subject Pleading Sufficiently Alleges the Causation and Redressability Elements for Appellants' Standing in Their Own Right

The Opinion held: "Even if CHD could identify a member who has suffered or imminently will suffer an injury in fact, it cannot show the requisite causation or redressability." Opinion, pg. 7.[6] Associational standing requires the plaintiff to adequately plead that an

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[6] The Opinion did not discuss the "injury in fact" element of associational standing. Opinion, pp. 7-9. This Petition thereby assumes that element was satisfied for purposes of the holding in the Opinion. In any event, the injury in fact element was robustly briefed by Appellants in this appeal. *See* Appellants' Opening Brief, pp. 26-34.

identifiable member has suffered, or imminently will suffer, an injury in fact that is fairly traceable to the challenged conduct and redressable by the relief sought. *Ass'n of Am. Physicians & Surgeon v. FDA*, 13 F.4th 531, 543 (6th Cir. 2021); Opinion, pg. 7. The Supreme Court has interpreted the "fairly traceable" element as one vested in causation. *Lujan, supra,* 504 U.S. at 562.

The Opinion held that Appellants failed to sufficiently allege the fairly traceable element, because the military's vaccination requirements at issue "stem from [third party] DOD decisionmakers.", and further that "FDA has not imposed any kind of mandate affecting the declarants, . . . " Opinion, pg. 7. However federal decisions, including by the Sixth Circuit, consistently hold that third party conduct causing a plaintiff's harm may satisfy the fairly traceable element, where the defendant's conduct was a motivating factor in the third party's injurious actions. For example, as cited in the Opinion itself, the Sixth Circuit held in *Parsons v. U.S. Dep't of Justice*, 801 F.3d 701 (6th Cir. 2015) ("*Parsons*") that: "In the nebulous land of 'fairly traceable,' where causation means more than speculative but less than but-for, the allegation that a defendant's conduct was a motivating factor in the third party's injurious actions satisfies the requisite standard". *Id.,* at 714.

Other federal precedent holds the same. *Booth v. Bowser*, 2022 WL 823068, at *5 (D.C. March 18, 2022) [plaintiff parents adequately pled injury-in-fact despite that the imminent threat of vaccination absent their consent would have been administered by a third party school, and not the Council of the District of Columbia whom they sued for passing the subject vaccination

regulation]; *Scenic America, Inc. v. United States Department of Transportation*, 983 F.Supp.2d 170, 179 (D.D.C. 2013) [plaintiff organization's injury was fairly traceable to the FHA's Guidance document for Article III standing purposes, even though it was the states' individual decisions whether and how to amend their own regulations on digital billboards that caused the organization's harm]; *see also* Appellants' Reply Brief, pp. 8-10.

Similar to the causational component of "fairly traceable", the redressability element of associational standing requires more than mere speculation but appreciably less than but-for. In other words, the claim(s) alleged need not directly reverse the conduct complained of if the requested relief is granted by the court. Rather, the relief granted must slow or reduce the conduct causing the injury. This is particularly so where, as here, the plaintiff alleges violation of a procedurally vested right, such as the APA. *Massachusetts, supra,* 549 U.S. at 517 ["When a litigant is vested with a procedural right, that litigant has standing if there is some possibility that the requested relief will prompt the injury-causing party to reconsider the decision that allegedly harmed the litigant."]; *Lujan, supra,* 504 U.S. at 572, fn 7 ["[a plaintiff] who has been accorded a procedural right to protect his concrete interests can assert that right without meeting all the normal standards for redressiblity and immediacy."].

The findings supporting the Opinion's holding that Appellants' pleadings failed to sufficiently allege the causation and redressability elements of associational standing, substantially exceed the requisite standard for Article III standing:

> "DOD, a third party, can continue requiring vaccination of servicemembers as a condition of employment, and it can require vaccination regardless of whether the vaccine is distributed pursuant to a license or EUA. [citation]. Moreover, DOD could administer COVID-19 vaccines manufactured by other companies with licenses and EUAs not challenged here. Because DOD's vaccine mandate is not tied to FDA's actions, plaintiffs' requested relief will not redress their alleged injuries." Opinion, pp. 8-9 (emphasis added).

The Opinion's findings above, specifically those relying upon the modal terms "can" and "could", describe hypothetical future conduct by the DOD. The fact remains that, as discussed in more detail in Appellants' briefing, DOD supervisors explicitly relied upon the very misrepresentations by Appellees regarding the Comirnaty vaccine and Pfizer EUA alleged in Appellants' pleadings, in mandating vaccination with those products upon military servicemembers. Appellants' Opening Brief, pp. 36-38, 40.

Finally, the allegations in Appellants' pleadings undisputedly allege that Appellees' conduct in misrepresenting that the subject vaccine and EUA were safe and interchangeable, was not just the motivating factor in DOD's vaccination mandates causing injury to Appellants (*Parsons, supra,* 801 F.3d at 714 ["[T]he allegation that a defendant's conduct was a motivating factor in the third party's injurious actions satisfies the requisite standard"]), it was the sole and exclusive factor. *See* Appellants' Opening Brief, pp. 35-39. As such, the portion of the Opinion holding that Appellants' pleadings failed

to adequately plead the fairly traceable and redressability elements of associational standing, was error on an issue of exceptional importance, as well as inconsistent with federal precedent.

CONCLUSION

For the reasons set forth above, panel rehearing and rehearing *en banc* is merited.

Respectfully submitted on August 26, 2022.

BARNES LAW

By: /s/ Robert E. Barnes
Counsel for
Plaintiffs/Appellants
Children's Health Defense and Amy Miller

AMENDED COMPLAINT
(SEPTEMBER 23, 2021)

UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF TENNESSEE

CHILDREN'S HEALTH DEFENSE;
AMY MILLER, an individual,

Plaintiffs,

v.

FOOD & DRUG ADMINISTRATION; and JANET WOODCOCK, acting commissioner of Food & Drugs,

Defendants.

Case No. 1:21-cv-00200
District Judge Clifton L. CORKER,
Mag. Judge Christopher H. STEGER.

AMENDED COMPLAINT
[F.R.C.P. Rule 15(a)(1)(A)]

1. The FDA faced a conundrum: under immense political pressure to rush approval of a COVID-19 vaccine in record time to satiate the mandate fervor of some in the military and corporate America, the FDA acted—without consulting its advisory board, without answering citizen petitions, without addressing scientific concerns, and even without updating its data regarding the Delta coronavirus variant. Knowing that approval and licensure of such a vaccine required revoking all

Emergency Use Authorized vaccines for the same indication, and knowing that revocation would risk liability exposure to vaccine makers, government actors and healthcare workers, the FDA did the impermissible.

2. It answered this conundrum by pretending to "approve" a vaccine that isn't widely available, playing a game of bait-and-switch, and confusing the public into thinking they are getting a vaccine with some legal remedies when in fact they are not because of the bait-and-switch. The FDA purportedly managed to do what the law forbids: "approve" a vaccine but not revoke any Emergency Use Authorized vaccines for the same indication.

3. Plaintiffs Children's Health Defense (CHD) and Amy Miller bring this action because the FDA is failing to carry out its mission. Plaintiffs seek this Court's intervention to put the FDA back on the path to lawful protection of the public in these precarious times.

PARTIES

4. Plaintiff CHD is a not-for-profit membership organization incorporated under the laws of Georgia. Plaintiff sues in its own capacity and on behalf of its members who have been affected by Defendants' actions.

5. Plaintiff Amy Miller is resident of Hamilton County Co., TN, a member of CHD, and is at imminent risk of immediate harm from FDA's actions to both license and contemporaneously authorize Pfizer vaccines against COVID.

6. Defendant FDA is an agency within the U.S. Department of Health and Human Services.

7. Defendant Janet Woodcock, the Acting FDA Commissioner, is sued in her official capacity.

JURISDICTION AND VENUE

8. This action arises out of Defendants' acts under 21 U.S. Code § 360bbb-3, Authorization for medical products for use in emergencies, and the Administrative Procedures Act, 5 U.S.C. § 500 *et seq*.

9. This lawsuit raises federal questions over which this Court has jurisdiction pursuant to 28 U.S.C. §§ 1331, 1361. This Court also has jurisdiction over this matter as complete diversity exists among the parties.

10. Pursuant to 28 U.S.C. § 1391(e), venue is proper in the Eastern District of Tennessee, where Plaintiff Amy Miller resides. Under 5 U.S.C. § 703, venue is proper in any court of competent jurisdiction.

11. An actual and justiciable controversy exists between Plaintiffs and Defendants.

STATEMENT OF FACTS

12. On January 31, 2020, Alex M. Azar, II, the Secretary of Health and Human Services, declared a public health emergency as of January 27, 2020, pursuant to § 319 of the Public Health Service Act, 42 U.S.C. § 247d *et seq*.

13. Section 564 of the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 U.S.C. § 360bbb-3, authorizes the FDA to issue an Emergency Use Authorization (EUA) for a vaccine under certain emergency circumstances, allowing a vaccine to be introduced and administered to the public even when the product has not gone through the review process necessary for approval and licensure.

14. In an emergency, the Secretary of Health and Human Services may issue EUAs if he concludes that the following facts exist: (1) a serious or life-threatening disease; (2) a product "may be effective" in treating or preventing it; (3) "no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating such disease or condition;" (4) a risk-benefit analysis that measures both the known and potential benefits of the product against the known and potential risks of the product is positive; and (5) that the patient's option to accept or decline the product is protected through informed consent. 21 U.S.C. § 360bbb-3(c)(1)-(5).

15. On December 11, 2020, the FDA issued an EUA for use of Pfizer-BioNTech COVID-19 Vaccine to prevent COVID-19 for individuals 16 years of age and older pursuant to Section 564 of the Act.

16. The FDA issued EUAs to Pfizer even though its Phase III clinical trials even now remain incomplete. Pfizer's clinical trial Estimated Primary Completion Date is November 2, 2022, and the Estimated Study Completion Date is May 2, 2023. *See Study to Describe the Safety, Tolerability, Immunogenicity, and Efficacy of RNA Vaccine Candidates Against COVID-19 in Healthy Individuals*, CLINICALTRIALS.GOV, https://clinicaltrials.gov/ct2/show/NCT04368728

17. CHD filed a Citizen Petition with the FDA (Exh. 1) on May 16, 2021, asking the FDA to refrain from licensing COVID vaccines and to revoke EUAs for the three existing COVID vaccines. Individuals have submitted over 30,000 comments on this petition. https://www.regulations.gov/document/FDA-2021-P-0460-0001

18. Pam Long, a former Army officer, Ssgt Samuel Craymer, a current servicemember in the US Air Force, LT John Eschmann, a current servicemember in the US Navy, AE1(AW) Wayne Hastriter, a current servicemember in the US Navy, 2d Lt Cassidy Hollowell, a current servicemember in the US Air Force, TSgt Nathaniel Mason, a current servicemember in the Air National Guard, MSgt Thomas Meacham, a current servicemember in the US Air Force Reserve, Sgt Jake Nuss, a current servicemember in the US Army, CW2 Robert Perez, a current servicemember in the US Army, MSgt Steven Raethel, a current servicemember in the US Air Force, SPC Christopher Santos, a current servicemember in the US Army, LT Jonathan Shour, a current servicemember in the US Navy, Gunnery Sergeant John Stanzione, a current servicemember in the US Marine Corps, CDR Joseph Sweger, a current servicemember in the US Navy, and LCDR Mark Zito, a current servicemember in the US Navy, are active members of CHD as of the filing of this action and have provided declarations on behalf of the organization in this action [Doc. No. 15].

19. Pfizer announced on July 16, 2021 that FDA granted Priority Review designation for the Biologics License Application (BLA) for its mRNA vaccine to prevent COVID-19 in individuals 16 years of age and older. The announcement noted that the FDA had expanded the EUA of the Pfizer-BioNTech COVID-19 vaccine to include individuals 12 years of age and older. (Exh. 2)

20. On August 23, 2021, the FDA granted a license to Pfizer's "Comirnaty" vaccine (Exh. 3) and extended the EUA for its Pfizer-BioNTech vaccine. In its letters to Pfizer and BioNTech, the FDA acknowledged that

Pfizer's vaccines are "interchangeable" yet "legally distinct." (Id. at Ftn. 8) It further stated: "The licensed vaccine has the same formulation as the EUA-authorized vaccine and the products can be used interchangeably . . . The products are legally distinct with certain differences that do not impact safety or effectiveness."

21. The FDA also responded to CHD on August 23, 2021, the same day it granted the license to Pfizer's Comirnaty and extended the EUA for Pfizer-BioNTech vaccine. (Exh. 4)

22. Although Defendant Janet Woodcock is the acting commissioner, the fact that she did not sign the Pfizer's licensure and EUA extension (Exh. 4), she still bears responsibility for the FDA's actions as pled herein.

23. FDA failed to convene its outside expert panel to deliberate on the Pfizer Comirnaty licensure. FDA asserted in its licensure letter to Pfizer: (Exh. 5 Page 2)

> We did not refer your application to the Vaccines and Related Biological Products Advisory Committee because our review of information submitted in you BLA, including the clinical study design and trial results, did not raise concerns or controversial issues that would have benefited from an advisory committee discussion. (emphasis added)

24. FDA deliberately misleads the public by confusing the words approval (implying licensure) and authorization (not licensed). "The EUA will continue to cover adolescents 12 through 15 years of age and the administration of a third dose to certain immuno compromised individuals 12 years of age and older.

Additionally, for logistical reasons, the EUA will continue to cover the use of the Pfizer-BioNTech COVID 19 Vaccine in individuals 16 years of age and older; this use is also now approved." (Exh. 6)

25. The EUA shields manufacturers from liability for both "[a]n unapproved drug, biological product, or device used under an Emergency Use Authorization (EUA) issued by FDA; or [a]n approved drug, biological product, or device used pursuant to Federal law in conditions that are inconsistent with its approval." (Exh. 7)

26. FDA's representation that licensure of its Comirnaty vaccine does not "raise concerns or controversial issues" (Exh. 5 Page 2) is transparently false. Although Janet Woodcock and the FDA have gone to great lengths to obscure its subversion of law, their actions speak for themselves.

ARGUMENT

27. FDA's actions to simultaneously license Pfizer's "Comirnaty" vaccine and to extend Pfizer's EUA for its vaccine that has the "same formulation" and that "can be used interchangeably" violates federal law. (Exh. 3)

28. The law on "Authorization for medical products for use in emergencies" requires that the EUA designation be used only when "there is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating such disease or condition." 21 U.S. Code § 360bbb-3-(3) (emphasis added).

29. Once FDA approved and licensed Pfizer's Comirnaty vaccine, there was no further basis for the

FDA to preserve the EUA status for the Pfizer-BioNTech vaccine that Pfizer acknowledges has the "same formulation" and is "interchangeable."

30. There also is no basis to retain EUA status for other COVID vaccines for the same use and for the same population as Pfizer's Comirnaty vaccine. FDA's decision to evade these requirements is arbitrary and capricious.

31. The FDA has failed to abide by its own criteria for EUA designation; its decision must be vacated and remanded.

32. The Administrative Procedures Act (APA) protects the public from arbitrary and capricious executive branch action by imposing the rule of reason and the rule of law through judicial oversight. An agency is "required to engage in reasoned decision making." *Michigan v. EPA*, 576 U.S. 743, 750 (2015). This requires that the agency "articulate a satisfactory explanation for its action." *Motor Vehicle Mfrs. Ass'n of U.S., Inc. v. State Farm Mut. Auto Ins. Co.*, 463 U.S. 29, 43 (1983).

33. This agency process requires Defendants to articulate clear rationales for decisions, especially when their actions are bound to lead to a medical mandate for millions of people. *Burlington Truck Lines v. United States*, 371 U.S. 156, 158 (1962).

34. When courts abandon this standard of oversight, the public is at grave risk. If pressure from politicians and profiteers rush regulators to license a biologic and violate the law, debacles predictably unfold and tragedies result.

35. A "reasonable time for agency action is typically counted in weeks or months, not years," *In re*

Am. Rivers & Idaho Rivers United, 372 F.3d 413, 419 (D.C. Cir. 2004), and an agency action's exigent context may demand expedited review. *Fund for Animals v. Norton*, 294 F.Supp.2d 92, 114 (D.D.C. 2003) ("pressing human health concerns . . . demand prompt review").

36. Congress requires that courts "shall hold unlawful and set aside" any agency "action," "finding," or "conclusion" whenever the agency failed to follow the necessary process for reasoned decision-making. 5 U.S.C. 706(2)(A).

37. *University of Cincinnati v. Shalala*, 891 F. Supp. 1262, 1269-1270 found that [u]nder this arbitrary and capricious standard, the court must determine "whether the agency decision was based on a consideration of the relevant factors and whether there has been a clear error in judgment." *Motor Vehicle Mfrs. Assn. v. State Farm Mutual Auto, Ins. Co.*, 463 U.S. 29, 43, 77 L.Ed.2d 443, 103 S. Ct. 2856 (1983). This standard of review is narrow; however, notwithstanding, "the agency must examine the relevant data and articulate a satisfactory explanation for its action including a 'rational connection between the facts found and the choice made.'" *Id.* (quoting *Burlington Truck Lines, Inc. v. United States*, 371 U.S. 156, 168, 9 L.Ed.2d 207, 83 S. Ct. 239 (1962)). If the agency's interpretation is reasonable, the court must uphold it even if the court would have reached a different interpretation had that issue first been presented to it. *Tallman*, 380 U.S. at 16. However, the court must reject administrative constructions that are inconsistent with a statutory mandate, frustrate congressional policy, or, otherwise, not supported by "substantial evidence on the record considered as a whole." *Federal Election Com. v. Democratic Senatorial Campaign Committee*, 454 U.S. 27,

29-33, 70 L.Ed.2d 23, 102 S. Ct. 38 (1981); *See also State Farm Mutual Auto. Ins. Co.*, 463 U.S. at 44.

38. By flagrantly violating federal law, the FDA has failed to follow reasoned decision-making. Pfizer cannot unlawfully reap the benefits of licensure and EUA status simultaneously, even if the FDA says it can. This clearly violates Congress' intent regarding emergency medical countermeasures.

39. The FDA has indulged Pfizer to "have it both ways." Pfizer now enjoys the imprimatur of safety, effectiveness and legality from a license while retaining the blanket liability shield of an EUA product.

40. The documents the FDA made public regarding these decisions contain tortured, barely comprehensible language that fails to explain the "legally distinct" differences between the Pfizer vaccines with differing labels and designations. How can vaccines under EUA and license be "interchangeable" yet "legally distinct?" (Exh. 3 Ftn. 8)

41. This linguistic smokescreen almost certainly conceals the fact that the available EUA product, Pfizer-BioNTech, has a priceless PREP Act liability shield (Exh.7) while the unavailable, licensed vaccine, Comirnaty, does not rightfully have that shield.

42. Once the FDA licensed the Comirnaty vaccine for those 16 and older, it was legally obliged to revoke the EUAs for the other COVID vaccines for this age group. Yet it failed to do so.

43. The new Comirnaty vaccine cannot also be authorized for emergency use for the first two doses of vaccines in adults since this is its licensed indication. The Pfizer Comirnaty vaccine should be subject to

ordinary product liability when used for the first two doses of the vaccine for adults.

44. Coverage under the Vaccine Injury Compensation Program, which will eventually afford the Comirnaty vaccine substantial liability protection, only occurs when (1) the vaccine is recommended by the Centers for Disease Control and Prevention for routine administration to children and/or pregnant women; (2) Congress enacts an excise tax on the vaccine; and (3) the Department of Health and Human Services adds the vaccine to the Vaccine Injury Table through publication of a notice of coverage in the *Federal Register*. https://www.hrsa.gov/vaccine-compensation/covered-vaccines/index.html.

45. The FDA is creating legal cover for licensed vaccine mandates while gifting Pfizer a bullet-proof liability shield that comes only with an EUA. It has tried to please two masters: the Executive Branch, which has insisted on licensed vaccines for pervasive mandates, and Pfizer, which demanded indemnification from any vaccine-related injuries and deaths. But the FDA seems to have forgotten its one true client: the American public.

46. While FDA may argue that Pfizer's Comirnaty vaccine is currently unavailable in the United States, and thus it is not in violation of the law as the licensed alternative must be "available," this argument is specious. Pfizer's Comirnaty vaccine is its primary product in Europe; if its two "interchangeable" vaccines are truly so, then Pfizer can relabel its EUA Pfizer-BioNTech vials with Comirnaty labels or vice versa.

47. FDA makes excuses for Comirnaty's lack of availability in its August 23, 2021 letter to Pfizer,

stating that "there is not sufficient approved vaccine available for distribution to this population in its entirety at the time of reissuance of this EUA." (Exh. 3 Ftn. 9)

48. Either Pfizer's vaccine for those 16 and up is licensed or it's not; either it's EUA, or it's not. It clearly contradicts the law for this product to be both licensed and authorized simultaneously. Such trickery undermines the public's confidence in the FDA when it so desperately needs to have that trust. The FDA's actions also undermine the rule of law.

49. The FDA has arbitrarily and capriciously allowed Pfizer to play "bait and switch": to represent that Pfizer vaccines are licensed and available while selling off its inventory of experimental vaccines that enjoy blanket liability protection. These FDA actions are arbitrary, capricious and illegal.

50. The FDA's licensure of the Pfizer Comirnaty vaccine triggered employer, military, educational and institutional mandates across the country, coercing millions of healthy individuals to take unwanted, risky medical interventions.

51. These mandates are creating myriad economic dislocations, including in healthcare, education and law enforcement. Millions will be forced out of jobs and institutions rather than submit to potentially injurious medical interventions.

52. While the finding of "arbitrary and capricious" agency action is a high bar, and courts are appropriately reluctant to second guess administrative action, there are times when justice demands judicial action. Now is such a time.

CAUSE OF ACTION

Failure to Abide by Federal Law as Abuse of Discretion-APA 5 USC 706 (2) (A)

53. Plaintiffs incorporate the foregoing paragraphs as if fully set forth herein.

The FDA's Licensure of Pfizer's Comirnaty Vaccine Is Arbitrary and Capricious

54. An agency's action is "arbitrary and capricious" if it did not articulate any rational connection between the facts it found and the choices it made. *Burlington Truck Lines v. United States*, 371 U.S. 156, 168. The FDA's action failed to articulate a lawful rationale.

55. Defendants authorized the Comirnaty vaccine to give the misleading impression to the public that the vaccine that would be mandated is fully approved, when in fact what is available, according to the FDA's own admission is actually the EUA, liability-free product.

56. Politics and industry pressure should play no role in the approval and authorization process, yet they appear to have been central in the FDA's decision-making process.

57. Defendants acted arbitrarily and capriciously by failing to engage in a pluralistic, critical, open, transparent and scientific dialogue with the public and medical community based on careful, deliberative evaluation of all relevant research before rushing the approval of this vaccine.

58. Defendants' arbitrary and capricious actions warrant vacatur and remand.

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs Amy Miller and Children's Health Defense respectfully ask this Court:

i. To vacate and remand the FDA's decision to license Pfizer's Comirnaty vaccine and to extend its Pfizer-BioNTech Emergency Use Authorization;

ii. To award attorneys' fees and costs, as authorized under 28 U.S.C. 2412; and

iii. To grant all other appropriate relief as necessary.

Respectfully submitted,

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Counsel for Plaintiffs Children's Health Defense and Amy Miller

Dated: September 23, 2021

EXHIBIT 1
MERYL NASS, M.D. CITIZEN PETITION
(MAY 16, 2021)

Division of Dockets Management
Department of Health and Human Services
Food and Drug Administration
Acting Commissioner Janet Woodcock, M.D.
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Dear Acting Commissioner Woodcock:

Enclosed is a Citizen Petition filed on behalf of Children's Health Defense by Meryl Nass, M.D., Scientific Advisory Board member, and Robert F. Kennedy, Jr., Board Chair and Chief Litigation Counsel, requesting that the FDA revoke Emergency Use Authorizations for existing COVID vaccines and refrain from approving and licensing them.

Dr. Nass and Mr. Kennedy look forward to your timely review of this petition. They are available to answer questions and to provide any additional relevant information.

Sincerely yours,

/s/ Mary Holland
President and General Counsel
(845) 445-7807
mary.holland@childrenshealthdefense.org

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

PETITION FOR ADMINISTRATIVE ACTION REGARDING COVID-19 VACCINES BY MERYL NASS, M.D.

DOCKET NO. _____

CITIZEN PETITION

On behalf of Children's Health Defense, the undersigned submit this petition under 21 C.F.R. § 10.20, § 10.30, § 50.23, § 600 – 680, § 601.2; 10 U.S.C. § 1107(f), § 1107a; 21 U.S.C. § 355(i)(4), § 360bbb-3; 42 U.S. Code § 247d; § 564 of the Federal Food, Drug, and Cosmetic Act (FDCA); the Public Readiness and Emergency Preparedness Act; the Public Health Service Act, and § 553(e) of the Administrative Procedures Act.

We request the Acting Commissioner of the Food and Drugs Administration (FDA) to issue, amend, revoke, or refrain from taking the administrative actions listed below regarding emergency use authorizations (EUAs), current and future new drug applications (NDAs), and biologics license applications (BLAs) for all COVID vaccines.

I. Actions Requested

1. FDA should revoke all EUAs and refrain from approving any future EUA, NDA or BLA for any COVID vaccine for all demographic groups because the current risks of serious adverse events or deaths outweigh the benefits, and because existing, approved

drugs provide highly effective prophylaxis and treatment against COVID, mooting the EUAs.

2. Given the extremely low risk of severe COVID illness in children, FDA should immediately refrain from allowing minors to participate in COVID vaccine trials, refrain from amending EUAs to include children, and immediately revoke all EUAs that permit vaccination of children under 16 for the Pfizer vaccine and under 18 for other COVID vaccines.

3. FDA should immediately revoke tacit approval that pregnant women may receive any EUA or licensed COVID vaccines and immediately issue public guidance to that effect.

4. FDA should immediately amend its existing guidance for the use of the chloroquine drugs, ivermectin, and any other drugs demonstrated to be safe and effective against COVID, to comport with current scientific evidence of safety and efficacy at currently used doses and immediately issue notifications to all stakeholders of this change.

5. The FDA should issue guidance to the Secretary of the Defense and the President not to grant an unprecedented Presidential waiver of prior consent regarding COVID vaccines for Servicemembers under 10 U.S.C. § 1107(f) or 10 U.S.C. § 1107a.

6. The FDA should issue guidance to all stakeholders in digital and written formats to affirm that all citizens have the option to accept or refuse administration of investigational COVID vaccines without adverse work, educational or other non-health related consequences, under 21 U.S.C. § 360bbb-3(e)(1)(a)(ii)

(III)[1] and the informed consent requirements of the Nuremberg Code.[2]

7. Pending revocation of COVID vaccine EUAs, FDA should issue guidance that all marketing and promotion of COVID vaccines must refrain from labeling them "safe and effective," as such statements violate 21 U.S.C. § 360bbb-3.

II. Statement of Grounds

A. Safety

8. Vaccine Adverse Event Reporting System (VAERS) data reveal unprecedented levels of deaths and other adverse events since the FDA issued Emergency Use Authorizations (EUAs) for three COVID vaccines. As of May 10, 2021, VAERS reported 4,434 deaths of people who received at least one COVID vaccination.[3]

9. FDA and CDC have not responded to these data by issuing any warnings or restricting the use of these vaccines. Furthermore, the VAERS database is the only safety database to which the public has access. The government withholds extensive safety informa-

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[1] 21 U.S.C. § 360bbb-3, Authorization for medical products for use in emergencies, https://www.govinfo.gov/content/pkg/USCODE-2011-title21/pdf/USCODE-2011-title21-chap9-subchapV-partE-sec360bbb-3.pdf.

[2] Nuremburg Code, BRITISH MEDICAL JOURNAL, No. 7070, Volume 313, p. 1448 (Dec. 7, 1996), https://media.tghn.org/medialibrary/2011/04/BMJ No 7070 Volume 313 The Nuremberg Code.pdf.

[3] VAERS Vaccine Adverse Event Reporting System data, available at https://vaers.hhs.gov/.

tion from the public despite having at least ten additional data sources and expert consultants to analyze these data, according to Nancy Messonier, MD, the Director of the National Center for Immunization and Respiratory Diseases.[4] Examples include databases from the Centers for Medicare and Medicaid, the Veterans Administration, the Defense Department (DMSS), the Vaccine Safety Datalink and the "Genesis" database, which is operated in cooperation with the National Institutes of Health and Brown University and includes 250 long-term care facilities and 35,000 residents.

10. Dr. Messonier told the FDA and its Vaccines and Related Biological Products Advisory Committee (VRBPAC) on December 10, 2020 that it had 11 systems that would evaluate COVID vaccine safety. Five systems would be active at the start of the vaccine program, and an additional six systems would become active over ensuing weeks. She said that the VAERS system was being enhanced for long-term care facilities, and added, "Hopefully you'll understand how robust these systems are." Below is the graphic she presented to the VRBPAC and the public on December 10, 2020.

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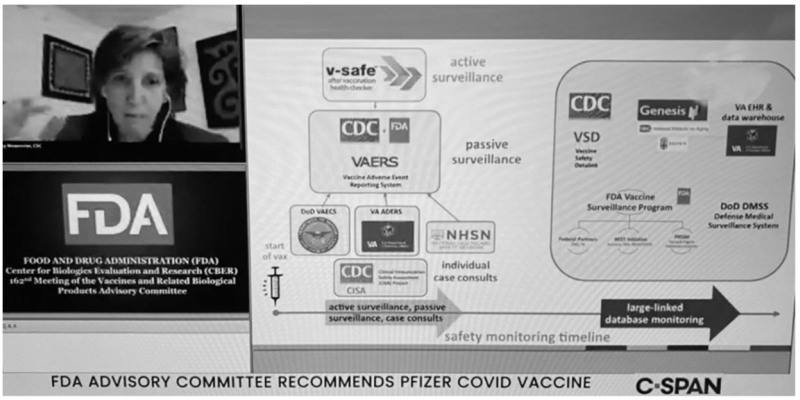
[4] FDA meeting on COVID 19 and Emergency Use Authorization, Part 1 (Video), Dec. 10, 2020, available at https://www.c-span.org/video/?507053-1/fda-meeting-covid-19-vaccine-emergency-authorization-part-1.



11. The CDC website, updated on May 11, 2021 states, "These vaccines have undergone and will continue to undergo the most intensive safety monitoring in U.S. history. This monitoring includes using both established and new safety monitoring systems to make sure that COVID-19 vaccines are safe."[5]

12. The CDC website states that "CDC and FDA physicians review each case report of death as soon as notified and CDC requests medical records to further assess reports."[6] By contrast, a CDC official told a reporter for The Daily Beast that it lacks a "good way to track deaths that occur after vaccination in real time." Furthermore, CDC told the reporter, "there are

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[5] CDC, *Safety of COVID-19 Vaccines* (updated May 11, 2021), https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/safety-of-vaccines.html.

[6] CDC, *Selected Adverse Events Reported after COVID-19 Vaccination* (updated May 11, 2021), https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/adverse-events.html.

no current plans to include vaccination data in the current CDC Covid-19 mortality analysis."[7]

13. Children's Health Defense asked CDC for information on post-vaccination deaths and injuries in early March 2021 and has yet to receive a response.[8]

14. Normally, licensed biologics manufacturers review adverse event reports pursuant to 21 C.F.R. § 600.80, while to date the CDC and the manufacturers appear to dispute most causal links to COVID vaccines. Any COVID vaccine license applicant "assumes responsibility for compliance with the applicable product and establishment standards" according to 21 C.F.R. § 600.3.[9] CDC asserts that a "review of available clinical information, including death certificates, autopsy, and medical records has not established a causal link to COVID-19 vaccines," yet recent assessments acknowledge "a plausible causal relationship between the J&J/Janssen COVID-19 vaccine and a rare and serious adverse event—blood clots with low platelets—which has caused deaths."[10] Denmark, among other nations,

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[7] Erin Banco, *White House asks CDC to study how many have died after COVID vaccine shots*, DAILY BEAST (Jan. 28, 2021), https://www.thedailybeast.com/white-house-asks-cdc-to-study-how-many-have-died-after-covid-vaccine-shots.

[8] Megan Redshaw, *64 Days and Counting — Why Won't the CDC Answer Our Questions?* THE DEFENDER (May 11, 2021), https://childrenshealthdefense.org/defender/64-days-why-wont-cdc-answer-questions/.

[9] Code of Federal Regulations Title 21 § 600.3, https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr=600.3.

[10] CDC, Selected Adverse Events Reported after COVID-19 Vaccination (updated May 11, 2021), https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/adverse-events.html.

has banned the EUA J&J/Janssen COVID vaccine, stating, "the benefits of using the COVID-19 vaccine from J&J do not outweigh the risk of causing possible adverse effect in those who receive the vaccine."[11]

15. CDC calculated rates of adverse effects for anaphylaxis post-vaccination improperly, using VAERS reports as the numerator, even though CDC officials have acknowledged "it is not possible to use VAERS data to calculate how often an adverse event occurs in a population."[12] When Massachusetts General-Brigham hospitals evaluated the rate of anaphylaxis in employees post COVID vaccination, they found anaphylaxis rates approximately 50-100 times greater than the rates CDC calculated using VAERS data. (Pfizer rate 2.7/10,000 vaccinees and Moderna rate 2.3/10,000 vaccinees).[13] Anaphylaxis after vaccination has led to deaths. If this degree of underestimation holds true for other adverse events using the VAERS database, then the safety of COVID vaccines is considerably worse than it currently appears. This rate could be verified by querying the ten databases whose results have been hidden from the public

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[11] Vincent West, *Denmark ditches J&J COVID-19 shots from vaccination programme,* REUTERS (May 3, 2021), https://www.reuters.com/world/europe/denmark-excludes-jj-shot-vaccine-programme-local-media-reports-2021-05-03/.

[12] CDC, Vaccine Adverse Event Reporting System (VAERS), https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/vaers/index.html.

[13] Blumenthal K. G., Robinson L. B., Camargo C. A., et al., *Acute Allergic Reactions to mRNA COVID-19 Vaccines.* JAMA, Vol. 325, No. 15, pp. 1562-1565 (Mar. 8, 2021), https://jamanetwork.com/journals/jama/fullarticle/2777417.

16. Other problems with vaccine safety assessment may exist because of inadequate animal toxicology and pharmacokinetic studies of COVID vaccines. Animal experiments failed to measure the quantity, duration and organ distribution of spike protein production. The animal experiments, incomprehensibly, failed to inject the actual vaccine to be tested during certain pharmacokinetic and toxicology tests. For example, in study 2.6.5.5B, only 2 of the 4 lipid nanoparticle (LNP) components were labeled and injected into rats, and their distribution and persistence in many organs were assessed at animal necropsy, from 15 minutes to 48 hours post-injection. For most organs, at 48 hours the amount of the two LNP components in each organ was still increasing. Thus, the ultimate distribution and persistence of the LNPs are unknown. And we have no information regarding duration and persistence of the mRNA or spike protein production in organs based on this study.[14]

17. A surrogate for mRNA (coding for spike protein) was an entirely different mRNA (coding for luciferase) in LNP injected into mice. In study 2.6.5.5A, bioluminescence was measured in liver through 9 days as a surrogate measure, while no attempt was made to evaluate the presence of spike protein in animal tissues, including in the brains of the experimental animals.[15] These surprising omissions have significant potential safety implications.

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[14] Study 2.6.5.5.B Pharmacokinetics: Organ Distribution. SARS-CoV-2 mRNA Vaccine (English Portion) (BNT162, PF-07302048), pp. 15-18, https://www.pmda.go.jp/drugs/2021/P20210212001/.

[15] *Id.*

18. Given that only 1 to 13% of adverse reactions have been reported to the FDA and CDC via the VAERS passive reporting system, according to Lazarus et al., the high number of adverse events and deaths following COVID vaccines is alarming.[16] While the Pfizer vaccine has now been used for five months and administered to more than 60 million Americans, FDA has issued no new guidance about the vaccine based on these troubling data, apart from expanding its use in children.

19. The FDA must be aware that the only avenue for an injured party to claim benefits as a result of a COVID vaccine injury is the Countermeasures Injury Compensation Program (CICP).[17] The CICP requires petitioners to prove that the COVID vaccine caused their injuries; the program has an extremely short statute of limitations of one year. If the FDA, working with the vaccine manufacturers, does not compile and publish an accurate list of adverse reactions, which is required for licensing, then these petitioners will have

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16 *See* Lazarus et al., *Electronic Support for Public Health-Vaccine Adverse Event Reporting System*, AGENCY FOR HEALTHCARE RESEARCH AND QUALITY, DEPT. OF HEALTH AND HUMAN SERVICES (Sept. 30, 2010), https://digital.ahrq.gov/ahrq-funded-projects/electronic-support-public-health-vaccine-adverse-event-reporting-system; Shimabukuro et al., *Safety monitoring in the Vaccine Adverse Event Reporting System* (*VAERS*), VACCINE (Nov. 4, 2015), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4632204/; S. Rosenthal and R. Chen, *The reporting sensitivities of two passive surveillance systems for vaccine adverse events,* AM J PUBLIC HEALTH (Dec. 1995), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1615747/.

17 Health and Human Services Administration, *Countermeasures Injury Compensation Program* (*CICP*), https://www.hrsa.gov/cicp.

virtually no opportunity to prove injury or receive compensation.

B. Effectiveness

20. As with safety data on COVID vaccines, effectiveness data continue to evolve. Recently CDC acknowledged "vaccine breakthrough cases" where vaccinated subjects fall ill and potentially transmit the virus. CDC acknowledges that a "small percentage of people who are fully vaccinated against COVID-19 will still get sick and some may be hospitalized or die from COVID-19. It's also possible that some fully vaccinated people might have infections, but not have symptoms (asymptomatic infections)."[18]

21. As of April 26, 2021, CDC reported over 9,000 "breakthrough cases" and 132 COVID-caused deaths among vaccinated people.[19] CDC tracks reports of breakthrough cases via the National Notifiable Diseases Surveillance System (NNDSS)[20] and has recently stopped reporting breakthrough cases absent death or hospitalization.[21] The British government has

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[18] 18 CDC, *What You Should Know About the Possibility of COVID-19 Illness After Vaccination*; (updated April 21, 2021), https://www.cdc.gov/coronavirus/2019-ncov/vaccines/effectiveness/why-measure-effectiveness/breakthrough-cases.html.

[19] CDC, *COVID-19 Breakthrough Case Investigations and Reporting* (updated April 30, 2021), https://www.cdc.gov/vaccines/covid-19/health-departments/breakthrough-cases.html.

[20] CDC, *National Notifiable Diseases Surveillance System (NNDSS)*, https://wwwn.cdc.gov/nndss/.

[21] CDC, *COVID-19 Breakthrough Case Investigations and Reporting* (April 30, 2021), https://www.cdc.gov/vaccines/covid-19/health-departments/breakthrough-cases.html.

also identified efficacy problems stating, "The resurgence in both hospitalisations and deaths is dominated by those that have received two doses of the vaccine, comprising around 60% and 70% of the wave respectively."[22]

22. The U.K. data modelers attribute these rates to the high level of vaccine uptake in the most at-risk elderly age group.[23] Overall, the U.K. believes "evidence shows vaccines are sufficiently effective in reducing hospitalisations and deaths in those vaccinated."[24] The U.K. caveat "sufficiently" is significant compared to the unqualified "effective" label that the FDA currently permits to be communicated to the public.

C. Misbranding as "Safe, Effective and FDA Approved"

23. Recently the FDA sent a warning letter "RE: Unapproved and Misbranded Products Related to Coronavirus Disease 2019 (COVID-19)."[25] FDA

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[22] *SPI-M-O: Summary of further modelling of easing restrictions – Roadmap Step 2*, p. 10 (Mar. 31, 2021), https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/975909/S1182 SPI-M-O Summary of modelling of easing roadmap step 2 restrictions.pdf.

[23] *Id.*

[24] GOV.UK; *COVID-19 Response-Spring 2021 (Summary)* (Feb. 22, 2021), https://www.gov.uk/government/publications/covid-19-response-spring-2021/covid-19-response-spring-2021-summary.

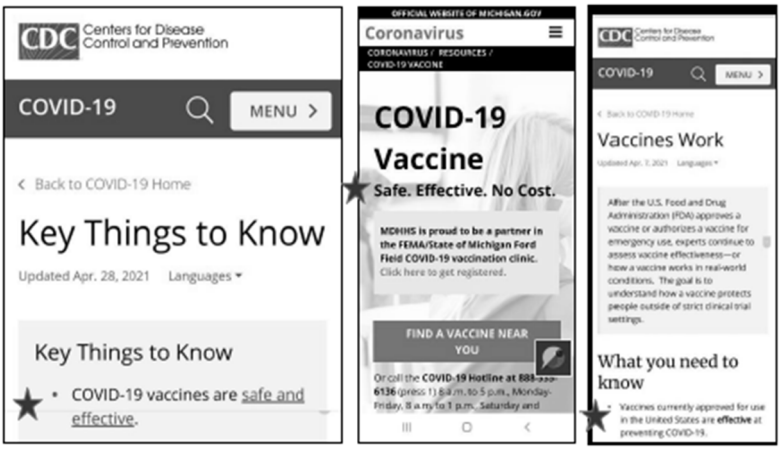
[25] FDA, *Warning Letter to Mercola.com, LLC* (Feb. 18, 2021), https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/warning-letters/mercolacom-llc-607133-02182021.

warned that labeling COVID therapies as Safe, Effective or FDA Approved when they are not proven to be so by FDA standards violates § 505(a) of the FDCA, 21 U.S.C. § 355(a). The same standard should apply to COVID vaccines, as any such products are misbranded drugs and violate § 502 of the FDCA and 21 U.S.C. § 352.

24. The introduction or delivery for introduction of any such product into interstate commerce is prohibited under § 301(a) and (d) of the FDCA and 21 U.S.C. § 331(a) and (d). The FDA specifically warned a vendor: "We advise you to review your websites, product labels, and other labeling and promotional materials to ensure that you are not misleadingly representing your products as safe and effective for a COVID-19-related use for which they have not been approved by FDA and that you do not make claims that misbrand the products in violation of the FD&C Act."

25. FDA must ensure against misrepresenting COVID vaccine products as "safe and effective" when FDA has not so designated them. FDA's description of COVID vaccines pursuant to § 564(d)(3) of the Act states: "based on the totality of scientific evidence available to FDA . . . it is reasonable to believe that Pfizer-BioNTech COVID-19 Vaccine may be effective in preventing COVID-19 when used in accordance with this Scope of Authorization (Section II), pursuant to Section 564(c)(2)(A) of the Act." The FDA language on effectiveness provides a qualification similar to the above-mentioned U.K. regulatory language. FDA's precise technical language to manufacturers does not match its unequivocal "effective" claims on official

government websites, including that of the CDC, as illustrated below.[26]



D. EUA Revocation, Additional EUAs, and Off-Label Use Clarification for COVID Therapies

26. On February 4, 2020 the Secretary of the Department of Health and Human Services (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 citizens living abroad and that involves the virus that causes Coronavirus Disease (COVID-19). Based on this determination, the Secretary on March 27, 2020 declared that circumstances justify emergency use of drugs and

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[26] CDC, Key things to know about COVID-19 vaccines (May 10, 2021), https://www.cdc.gov/coronavirus/2019-ncov/vaccines/keythingstoknow.html; CDC, Safety of COVID-19 vaccines (udated May 11, 2021), https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/safety-of-vaccines.html; FDA, Letter to Pfizer (May 10, 2021), https://www.fda.gov/media/144412/download.

biological products during the COVID-19 pandemic pursuant to § 564 of the FDCA (21 U.S.C. § 360bbb-3).

27. Since December 2020, several manufacturers have received EUAs for COVID vaccines. One of the criteria for these authorizations, beyond the existence of an emergency, is that there are "no adequate, approved, and available alternatives."[27] Many medical professionals and elected officials have objected to the inconsistent handling of EUAs for alternative treatments. Dr. Peter McCullough testified to the Texas Senate on March 10, 2021 that an 85% lower mortality rate from COVID would have been possible if government agencies had publicly recommended early treatments.[28] Now that COVID cases and deaths are decreasing because many if not most Americans are immune, the relative benefit of COVID vaccines has diminished.[29]

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[27] FDA, *Emergency Use Authorization* (updated May 11, 2021), https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization;

FDA, *FAQs on Emergency Use Authorizations (EUAs) for Medical Devices During the COVID-19 Pandemic* (updated April 23, 2021), https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/faqs-emergency-use-authorizations-euas-medical-devices-during-covid-19-pandemic.

[28] Dr. Peter McCullough's testimony to the Texas Senate HHS Committee (Mar. 10, 2021), https://www.youtube.com/watch?v=QAHi3lX3oGM.

[29] Dr. Peter McCullough et al., *SARS-CoV-2 mass vaccination: Urgent questions on vaccine safety 2 that demand answers from international health agencies, regulatory 3 authorities, governments and vaccine developers* (May 8, 2021), https://www.andrewbostom.

28. Three U.S. Senators asked the FDA to clarify why it revoked the previously granted EUAs for hydroxychloroquine (HCQ) and chloroquine (CQ) and under what authority it regulates the practice of medicine. The Senators also asked what authority states have to regulate the prescribing and dispensing of drugs.[30] FDA issued and revoked EUAs for HCQ and CQ donated to the Strategic National Stockpile in a way that confused medical professionals, resulting in their reluctance to prescribe the drugs, including those not under EUA. FDA improperly recommended against the use of chloroquine drugs in outpatients, and against early treatment, which is when these antiviral drugs are likely to be effective. FDA appears to have collaborated with officials in dozens of states and even with certain pharmaceutical and pharmacy companies to restrict the prescribing and dispensing of chloroquine drugs against COVID. These unprecedented actions require explanation. The FDA must immediately revoke its recommendations for the limited use and withholding of these drugs during a life-threatening pandemic and must publicize its revocation widely.

29. Medical professionals also question FDA's approval of Investigational New Drug (IND) human trials performed by the University of Pittsburg

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org/wp-content/uploads/2021/05/Bruno-et-al.-Vaccine-Safety-Urgent-Manuscript-Preprint-May-8-2021.pdf.

[30] Senators Ted Cruz, Mike Lee, Ron Johnson, *Letter to FDA Commissioner Stephen Hahn* (Aug. 18, 2020), https://www.hsgac.senate.gov/imo/media/doc/2020-08-18%20RHJ%20Letter%20to%20FDA%20on%20HCQ%20+%20CQ.pdf.

(REMAP-COVID)[31] and the University of Philadelphia (PATCH)[32] using knowingly borderline lethal doses of HCQ in humans. There were more deaths in the HCQ arm than in the control arm of the REMAP-COVID study and in the other two large multicenter studies, the Solidarity and Recovery studies, that used excessive doses. The PATCH study ended after enrolling only 5 subjects.

30. In other FDA guidance regarding the chloroquine drugs, FDA made the misleading claim that "Hospitalized patients were likely to have greater prospect of benefit (compared to ambulatory patients with mild illness)," and that chloroquine drugs have a "slow onset of action." In its justification for restricting the use of chloroquine drugs, FDA also opined that "it is no longer reasonable to believe that oral formulations of HCQ and CQ may be effective in treating COVID-19, nor is it reasonable to believe that the known and potential benefits of these products outweigh their known and potential risks."[33]

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[31] UNIVERSITY OF PITTSBURG, Department of Critical Care, *UPMC Leads Global Efforts to Fast-track COVID-19 Therapies*, https://www.ccm.pitt.edu/node/1110.

[32] *Penn Launches Trial to Evaluate Hydroxychloroquine to Treat, Prevent COVID-19*, PENN MEDICINE NEWS (April 3, 2020), https://www.pennmedicine.org/news/news-releases/2020/ april/ penn-launches-trial-to-evaluate-hydroxychloroquine-to-treat-prevent-covid19;

The PATCH Trial (Prevention And Treatment of COVID-19 With Hydroxychloroquine) (PATCH), CLINICALTRIALS.GOV (updated Dec. 10, 2020), https://clinicaltrials.gov/ct2/show/NCT04329923.

[33] FDA Letter revoking EUA for Hydroxychloroquine (Jun. 15, 2020), https://www.fda.gov/media/138945/download.

31. These claims fly in the face of substantial evidence of positive effects of the drugs when used early in the disease at usual, approved, therapeutic doses. FDA has chosen to ignore the many trials that were properly conducted. The FDA buttresses its contention of the dangers of these drugs based in part on the FDA-approved trial and other trials that administered excessive, non-therapeutic doses of HCQ and resulted in more deaths in the treated group than the placebo group.

32. Similarly, FDA exhibited bias regarding the effective and safe use of ivermectin for prophylactic use of COVID. In March 2021, the agency stated: "The FDA has not reviewed data to support use of ivermectin in COVID-19 patients to treat or to prevent COVID-19; however, some initial research is underway."[34] Yet already on April 10, 2020, FDA had issued a public warning against the use of ivermectin because, it claimed, Americans were purchasing over the counter (OTC) veterinary ivermectin as a COVID treatment.[35] Research from Australia had been published online a week earlier, on April 3, 2020, supporting use of ivermectin for COVID based on in vitro studies.[36]

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[34] FDA, *Why You Should Not Use Ivermectin to Treat or Prevent COVID-19* (updated May 10, 2021), https://www.fda.gov/consumers/consumer-updates/why-you-should-not-use-ivermectintreat-or-prevent-covid-19.

[35] FDA Letter to Stakeholders, *Do Not Use Ivermectin Intended for Animals as Treatment for COVID-19 in Humans* (April 10 2020), https://www.fda.gov/animal-veterinary/product-safety-information/fda-letter-stakeholders-do-not-use-ivermectin-intended-animals-treatment-covid-19-humans.

[36] Leon Caly, Julian D. Druce, *The FDA-approved drug ivermectin inhibits the replication of SARS-CoV-2 in vitro*,

33. Thus, FDA was aware at least 13 months ago that Americans were using ivermectin to treat and prevent COVID. How could FDA not have reviewed data on ivermectin during an entire year after it was informed about this use? That was a year during which dozens of studies about the drug's use were available as publications or preprints for both prophylaxis and treatment; during which there was a Senate hearing on the drug; and during which half a million Americans died from the disease, who had not been treated with effective medications because of FDA guidance.

34. Furthermore, ivermectin has been used OTC for COVID in many countries and regions with excellent reported treatment success. The drug's safety has been established with at least a billion doses used, and the drug is on the World Health Organization's list of essential drugs.

35. Many medical professionals suspect FDA's feigned ignorance about the drug was a prerequisite to issuing EUAs for COVID vaccines, given the EUA requirement that no approved drug may be available for the same indication. Ivermectin and hydroxychloroquine, both of which have extremely long biological half lives, can be given infrequently as prophylaxis for COVID. Hydroxychloroquine or chloroquine are used weekly to prevent malaria, and they have been used in the same way to prevent COVID. Ivermectin can be used once or twice yearly to prevent river blindness (onchocerciasis), and it has been used weekly or bi-weekly to prevent COVID. Many clinical trials have documented the benefits of both drugs for

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ANTIVIRAL RESEARCH, vol. 178, 104787 (Jun. 2020), https://reader.elsevier.com/reader/sd/pii/S0166354220302011.

COVID prevention. Yet FDA has remained silent about these benefits, even though the efficacy of these preventive treatments probably supercedes that of COVID vaccines.

36. This petition encourages FDA to expeditiously evaluate existing ivermectin research and issue accurate guidance for its use against COVID, *e.g.*, where "18 randomized controlled treatment trials of ivermectin in COVID-19 have found large, statistically significant reductions in mortality, time to clinical recovery, and time to viral clearance."[37] Additional

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[37] P. Kory, G. Meduri et al., *Review of the Emerging Evidence Demonstrating the Efficacy of Ivermectin in the Prophylaxis and Treatment of COVID-19*, AMERICAN JOURNAL OF THERAPEUTICS (May-Jun 2021), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8088823/.

Ahmed, Sabeena et al., *A five-day course of ivermectin for the treatment of COVID-19 may reduce the duration of illness*, INTERNATIONAL JOURNAL OF INFECTIOUS DISEASES, vol. 103, pp. 214-216 (Feb. 2021), https://pubmed.ncbi.nlm.nih.gov/33278625/;

Jans D. A. and Wagstaff K. M., *The broad spectrum host-directed agent ivermectin as an antiviral for SARS-CoV-2*? BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, vol. 538, pp. 163-172 (2021), https://pubmed.ncbi.nlm.nih.gov/33341233/.

Formiga, Fabio Rocha et al., *Ivermectin: an award-winning drug with expected antiviral activity against COVID-19*, JOURNAL OF CONTROLLED RELEASE, vol. 329, pp. 758-761 (Jan. 2021), https://pubmed.ncbi.nlm.nih.gov/33038449/.

Bhowmick, Subhrojyoti et al., *Safety and Efficacy of Ivermectin and Doxycycline Monotherapy and in Combination in the Treatment of COVID-19: A Scoping Review*, DRUG SAFETY, pp. 1-10 (Apr. 16, 2021), https://pubmed.ncbi.nlm.nih.gov/33864232/.

studies have found it highly effective for both pre-and post-exposure prophylaxis of COVID.[38]

37. Finally, reflecting on the FDA's regulatory history is helpful: A proven association between the 1976–1977 swine influenza vaccine and approximately 400 cases of Guillain–Barré syndrome halted that particular national vaccination campaign.[39] The reported deaths following that swine flu vaccination campaign, 30 out of 40-45 million vaccinees,[40] were insignificant compared to the current reported death toll of 4,434 due to COVID vaccines, Today's death rate is more than 50 times higher than that which ended the swine flu vaccine campaign.

38. Regarding the halted swine flu vaccine program, the CDC's *Emerging Infectious Diseases Journal* concluded, "In 1976, the federal government wisely opted to put protection of the public first."[41]

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[38] *Ivermectin for COVID-19: real-time meta analysis of 55 studies*, COVID ANALYSIS (version 81, May 15, 2021), https://ivmmeta.com/.

[39] *See* CDC, H1N1 Flu, FACT SHEET: GUILLAIN-BARRÉ SYNDROME (GBS) (Dec. 15, 2009), https://www.cdc.gov/h1n1flu/vaccination/factsheet_gbs.htm#:~:text=Getting%20GBS%20from%20a%20vaccination,got%20the%20swine%20flu%20vaccine.

[40] Rick Perlstein, *Gerald Ford Rushed Out a Vaccine. It Was a Fiasco*, THE NEW YORK TIMES (Sept. 2, 2020), https://www.nytimes.com/2020/09/02/opinion/coronavirus-vaccine-trump.html; Donald G. McNeil, Jr., *Don't Blame Flu Shots for All Ills, Officials Say*, THE NEW YORK TIMES (Sept 27, 2009), https://www.nytimes.com/2009/09/28/health/policy/28vaccine.html.

[41] Sencer D. J., Millar J., *Reflections on the 1976 Swine Flu Vaccination Program*, EMERGING INFECTIOUS DISEASES,

FDA should learn from this past experience and again put protection of the public first. It is imperative that the FDA swiftly take action to authorize alternative treatments.

E. Children

39. According to the National Center for Health Statistics data as of May 5, 2021, 282 children have died "involving COVID," whereas over 560,000 Americans have died "involving COVID."[42] Three thousand children have been diagnosed with a multi-system inflammatory disorder, of whom about 1%, or approximately 30, have died. Thus the relative risk for children due to COVID is very low.

40. By contrast, recent VAERS reports include the deaths of several children following COVID vaccination.[43] Five of the child death reports footnoted

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Vol. 12, No. 1, pp. 29-33 (Jan. 2006), https://wwwnc.cdc.gov/eid/article/12/1/05-1007_article.

[42] CDC, *Weekly Updates by Select Demographic and Geographic Characteristics*, Provisional Death Counts for Coronavirus Disease 2019 (COVID-19) (updated May 12, 2021), https://www.cdc.gov/nchs/nvss/vsrr/covidweekly/index.htm#SexAndAge.

[43] VAERS reports include:

A 1-year-old, https://medalerts.org/vaersdb/findfield.php?IDNUMBER=1261766&WAYBACKHISTORY=ON; a 2-year-old, https://medalerts.org/vaersdb/findfield.php?IDNUMBER=1255745&WAYBACKHISTORY=ON; two 15-year-olds, https://www.medalerts.org/vaersdb/findfield.php?IDNUMBER=1187918 and https://www.medalerts.org/vaersdb/findfield.php?IDNUMBER=1242573; two 16-year-olds, https://www.medalerts.org/vaersdb/findfield.php?IDNUMBER=1225942; a 17-year old, https://www.openvaers.com/openvaers/1199455; and an infant,

below involve apparent cardiac related deaths, and two were infants. There is one reported death in a 15 year old after receiving the Pfizer BioNTech vaccine, and another reported death of a 15 year old after receiving a Moderna vaccine. Each child must have been enrolled in a clinical trial, since their ages would have precluded them getting the vaccine legally under the EUA. There were only about 1,000 children in the 12-15 year age group in the vaccine arm of Pfizer's trial and probably about the same number in the vaccine arm of Moderna's trial. Thus, the death rate following either vaccination in this age group, assuming these children were trial enrollees, is approximately 2 in 2,000 or 0.1%.

41. There are 74 million children in the United States. So far, 282 have died "involving Covid." Two hundred eighty-two in 74 million is a rate of 0.00038%. While many children may not have been exposed to COVID, CDC estimated that 22.2 million children aged 5-17 had had COVID and 127 had died, at the May 12, 2021 meeting of the Advisory Committee on Immunization Practices, or 0.00057%.[44] Available evidence strongly suggests that the vaccine is much more dangerous to children than the disease.

42. A recent opinion piece in the *British Medical Journal* noted that "the likelihood of severe outcomes or death associated with COVID-19 infection is very

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https://www.medalerts.org/vaersdb/findfield.php?IDNUMBER=1166062.

[44] Helen Branswell, *CDC advisory group gives green light to Pfizer's Covid vaccine for adolscents*," STAT (May 12, 2021), https://www.statnews.com/2021/05/12/cdc-advisory-group-gives-green-light-to-pfizers-covid-vaccine-for-adolescents/.

low for children, undermining the appropriateness of an emergency use authorization for child covid-19 vaccines."[45] The authors also suggested child vaccinations could strategically harm vaccination efforts and increase vaccine hesitancy.[46]

F. Servicemembers' Prior Consent

43. Certain citizens and elected officials have recently encouraged the President of the United States to waive U.S. Servicemembers' right to prior consent for COVID vaccines.[47] According to 10 U.S.C. § 1107(f), only the President of the United States may order such a waiver if he determines, in writing, that obtaining consent is not in the national security interest. The intent of any waiver of consent must be related to a member's participation in a "particular military operation," as opposed to the broad sweep some are encouraging.

44. Such a waiver is only permissible when obtaining prior consent is infeasible or contrary to the best interests of the military member. Clearly, prior consent for current servicemembers is feasible for COVID vaccines.[48] Because the President's authority

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[45] W. Pegden, V. Prasad, S. Baral, *Covid vaccines for children should not get emergency use authorization*, BMJ (May 7, 2021), https://blogs.bmj.com/bmj/2021/05/07/covid-vaccines-for-children-should-not-get-emergency-use-authorization/.

[46] *Id.*

[47] Jimmy Panetta, *Letter to President Biden* (Mar. 24, 2021), https://www.documentcloud.org/documents/20521870-panetta dod-covid-vaccine-waiver.

[48] 21 U.S.C. § 50.23: Exception from general requirements, https: //www.ecfr.gov/cgi-bin/text-idx?node=se21.1.50 123&rgn=div8.

is contingent on the standards set forth in § 505(i)(4) of the FDCA and 21 U.S.C. § 355(i)(4), and since the chain of command requires consultation with HHS, the FDA may issue guidance to the President on this matter.[49]

45. The specific law on EUA vaccines was codified in 10 U.S.C. § 1107a.[50] The § 1107a language is similar to § 1107(f) to ensure that troops are granted prior consent and have the "option to accept or refuse administration of a product." National leaders should continue to honor and respect servicemembers' rights. No President has ever waived servicemembers' prior consent under 10 U.S.C. § 1107(f) or 10 U.S.C. § 1107a, and FDA should advise that current circumstances do not warrant such drastic action.

G. Coercion and Compulsion

46. COVID vaccines are optional in accordance with 21 C.F.R. § 360bbb-3(e)(1)(a) as EUA products.[51] Yet throughout the United States, schools, businesses, government and industry are using coercive tactics to encourage, incentivize and compel COVID vaccination as a condition of employment, education and daily living. It is unlikely that most Americans would support such coercion if they were fully informed that COVID vaccines

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[49] *Id.*

[50] 10 U.S.C. § 1107a-Emergency use products, https://www.govinfo.gov/app/details/USCODE-2010-title10/USCODE-2010-title10-subtitleA-partII-chap55-sec1107a/summary.

[51] § 360bbb–3. Authorization for medical products for use in emergencies, https://www.govinfo.gov/content/pkg/USCODE-2011-title21/pdf/USCODE-2011-title21-chap9-subchapV-partE-sec360bbb-3.pdf.

are for emergency use only, investigational, unapproved, and that individuals have the explicit right to refuse by law. Some states are considering or have approved legislation or executive action to bar vaccine mandates.[52] Some professional medical associations also have expressed opposition to these coercive tactics.[53]

47. Coercion and compulsory vaccination are inconsistent with the legal requirements to inform both healthcare workers administering EUA vaccines and vaccine recipients of the significant known and unknown benefits and risks of such use. Most importantly, the FDA must ensure all parties are aware of the "option to accept or refuse" administration of all EUA products and that alternatives are available. These disclosure requirements are entirely inconsistent with coercion, and government agencies should not publish information that violates the law. Information on the government websites of the Equal Employment Opportunity Commission (EEOC)[54] and the Occupational

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[52] Pearson L., Brofsky J., et al., *50-state Update on Pending Legislation Pertaining to Employer-mandated Vaccination*, HUSCH BLACKWELL (updated April 20, 2021), https://www.huschblackwell.com/newsandinsights/50-state-update-on-pending-legislation-pertaining-to-employer-mandated-vaccinations.

[53] Dr. Paul M. Kempen, *Open Letter from Physicians to Universities: Allow Students Back Without COVID Vaccine Mandate*, ASSOCIATION OF AMERICAN PHYSICIANS AND SURGEONS (Apr. 24, 2021), https://aapsonline.org/open-letter-from-physicians-to-universities-reverse-covid-vaccine-mandates/.

[54] EEOC, *What You Should Know About COVID-19 and the ADA, the Rehabilitation Act, and Other EEOC Laws*, §§ K1 & K7 (updated Dec. 16, 2020), https://www.eeoc.gov/wysk/what-you-should-know-about-covid-19-and-ada-rehabilitation-act-and-other-eeo-laws.

Safety and Health Administration (OSHA)[55] in fact ignore these federal disclosure requirements.

48. The armed forces' experience with the very first EUA vaccine mandate against anthrax is instructive.[56] The military now administers the anthrax vaccine on a voluntary basis with informed consent, but only after a federal court halted the mandatory anthrax vaccine program because the FDA had improperly issued a license.[57]

49. The only language in the EUA law, 21 U.S.C. § 360bbb-3(e)(1)(A)(ii)(I-III), that could possibly be construed to imply mandates is the term "consequences" in clause III. Both statutory analysis and legislative history suggest that it is far more likely that this term applies to health-related consequences only, *i.e.*, medical risks and benefits, since that is the topic of that statute section and because it does not refer to punitive

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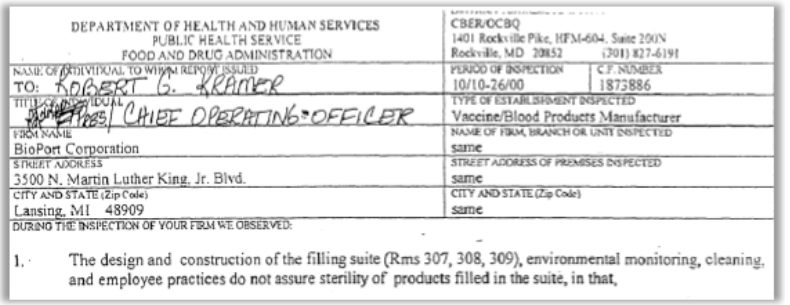
[55] Jeff Yoders, *OSHA Imposes New Guidance For Employer-Required COVID-19 Vaccines*, ENR (May 3, 2021), https://www.enr.com/articles/51691-osha-imposes-new-guidance-for-employer-required-covid-19-vaccines.

[56] FDA, *Anthrax Vaccine Adsorbed (AVA) EUA –ARCHIVED INFORMATION*, https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization-archived-information#anthrax.

[57] *Determination and Declaration Regarding Emergency Use of Anthrax Vaccine Adsorbed for Prevention of Inhalation Anthrax*, FEDERAL REGISTER (Feb. 2, 2005), https://www.federalregister.gov/documents/2005/02/02/05-2027/determination-and-declaration-regarding-emergency-use-of-anthrax-vaccine-adsorbed-for-prevention-of?fbclid=IwAR22J58y3SQ2tVoEUlNgZVU-PmRxoou0P05i9WqS4SUiOcj9HyaiUJ8Dvrg.

measures or consequences, such as termination of employment or education.[58]

50. Another hazard of coercive policies and broad liability for industry is reliance on subpar manufacturers. One of the COVID vaccine manufacturing subcontractors today, Emergent BioSolutions, is the same company, with the same President and Board Chairman, which the FDA cited under its previous name, BioPort, for numerous violations of Good Manufacturing Practices.[59] The image below, taken from an FDA form in 2000, shows the citation to BioPort for deviations from acceptable manufacturing standards for vaccines.



DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

CBER/OCBQ
1401 Rockville Pike, HFM-604, Suite 200N
Rockville, MD 20852 (301) 827-6191

NAME OF INDIVIDUAL TO WHOM REPORT ISSUED
TO: ROBERT G. KRAMER

PERIOD OF INSPECTION: 10/10-26/00
C.F. NUMBER: 1875886

TITLE OF INDIVIDUAL
Mr. Kramer, CHIEF OPERATING OFFICER

TYPE OF ESTABLISHMENT INSPECTED
Vaccine/Blood Products Manufacturer

FIRM NAME
BioPort Corporation

NAME OF FIRM, BRANCH OR UNIT INSPECTED
same

STREET ADDRESS
3500 N. Martin Luther King, Jr. Blvd.

STREET ADDRESS OF PREMISES INSPECTED
same

CITY AND STATE (Zip Code)
Lansing, MI 48909

CITY AND STATE (Zip Code)
same

DURING THE INSPECTION OF YOUR FIRM WE OBSERVED:

1. The design and construction of the filling suite (Rms 307, 308, 309), environmental monitoring, cleaning, and employee practices do not assure sterility of products filled in the suite, in that,

51. Today, Emergent BioSolutions, despite apparent FDA oversight, shipped out unauthorized bulk COVID vaccine ingredients for finishing and

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[58] Parasidis E., Kesselheim A. S., *Assessing The Legality Of Mandates For Vaccines Authorized Via An Emergency Use Authorization*, HEALTH AFFAIRS (Feb. 16, 2021), https://www.healthaffairs.org/do/10.1377/hblog20210212.410237/full/.

[59] Richard Luscombe, *Emergent chief sold $10m in stock before company ruined 15m Covid vaccines*, THE GUARDIAN (Apr. 26, 2021), https://www.theguardian.com/business/2021/apr/26/emergent-biosolutions-robert-kramer-stock-covid-vaccines-error.

filling. Emergent BioSolutions shipped those ingredients to another entity, and the shipments eventually reached buyers in at least four other countries, according to the New York Times.[60] The FDA halted distribution in the U.S. and cited quality deviations[61] that mirrored those that American servicemembers witnessed 20 years ago with the anthrax vaccine.[62] People need to be informed about these manufacturing deviation patterns given the importance and wide use of these products.

52. States may lawfully mandate certain vaccines. But that is not the case for investigational, unapproved EUA medical products. The preemption doctrine,[63] based on the Supremacy Clause of the U.S. Constitution, Article VI., § 2,[64] requires that the federal requirements for informed consent supersede state laws and

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[60] Chris Hamby, *Baltimore Vaccine Plant's Troubles Ripple Across 3 Continents*, THE NEW YORK TIMES (May 6, 2021), https://www.nytimes.com/2021/05/06/world/baltimore-vaccine-countries.html.

[61] FDA, HHS, Form FDA 483, Inspectional Observations (Apr. 20, 2021), https://www.fda.gov/media/147762/download.

[62] Historic FDA Form 483 Deviation Report Documenting that "The manufacturing process for Anthrax Vaccine is not validated." https://nebula.wsimg.com/30662205620a26a4b21274dc49888891?AccessKeyId=0BA19F97E21CB8613CD7&disposition=0&alloworigin=1.

[63] *Preemption*, CORNELL LAW SCHOOL, Legal Information Institute, https://www.law.cornell.edu/wex/preemption.

[64] U.S. Const. art. VI., § 2, "This Constitution, and the Laws of the United States which shall be made in Pursuance thereof; and all Treaties made, or which shall be made, under the Authority of the United States, shall be the supreme Law of the Land; and the Judges in every State shall be bound thereby, any Thing in

regulations that may violate EUA provisions. The FDA should support, defend and enforce federal laws that govern biologics, including EUA products. The option to refuse COVID vaccines is codified in federal law, and President Biden has affirmed this, saying, "I don't think it [vaccination against COVID] should be mandatory. I wouldn't demand it to be mandatory."[65]

H. Conclusion to Statement of Grounds

53. The FDA's mission is "protecting the public health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products."[66] President Roosevelt's signing of the Federal Food, Drug, and Cosmetic Act (FDCA) closed many safety and efficacy loopholes and improved the landscape of consumer protection forever.[67] The 1962 Harris-Kefauver amendment[68] set in motion regulatory standards for biologics licensure that require proven efficacy, and the

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the Constitution or Laws of any State to the Contrary notwithstanding." https://www.archives.gov/founding-docs/constitution-transcript.

[65] Julia Manchester, *Biden: Coronavirus vaccine should not be mandatory*, THE HILL (Apr. 12, 2021), https://thehill.com/homenews/campaign/528834-biden-coronavirus-vaccine-should-not-be-mandatory.

[66] FDA, *What We Do*; https://www.fda.gov/about-fda/what-we-do#mission.

[67] FDA, *80 Years of the Federal Food, Drug, and Cosmetic Act* (Nov. 7, 2018), https://www.fda.gov/about-fda/fda-history-exhibits/80-years-federal-food-drug-and-cosmetic-act.

[68] FDA, *Kefauver-Harris Amendments Revolutionized Drug Development* (Oct. 9, 2012), https://www.fda.gov/consumers/consumer-updates/kefauver-harris-amendments-revolutionized-drug-development.

1972 review sought to ensure proof of efficacy and no misbranding for biologics. These historic advances require reflection. The preamble to the 1972 review stated, "'The importance to the American public of safe and effective vaccines . . . and other biological products cannot be overstated."[69]

54. Biologics, as with all drugs and devices, must have adequate directions for use and be proven safe and effective before FDA approval and licensure. The FDA erred with the anthrax vaccine, and it took a Citizen Petition[70] and federal court decision to make the FDA comply with the FDCA.[71] At other times, the FDA has upheld its mission without prompting to make tough regulatory rulings, as the Supreme Court has acknowledged.[72] With this Petition, we look forward to the FDA's appropriate, tough regulatory action to

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[69] HHS, FDA, *Biological Products March 1936-March 1978*, Preamble, p. 56, 37 Fed. Reg. 16679.

[70] Citizen Petition, FDA Docket 01P-0471/CP1, https://img1.wsimg.com/blobby/go/4fa7f468-a250-4088-926e-3c56a998df1f/downloads/citizen%20petition%20ava%20rempfer%20 dingle.pdf?ver=1620969217312, and Response thereto, https://downloads.regulations.gov/FDA-2001-P-0119-0003/attachment 1.pdf.

[71] *Doe # 1 v. Rumsfeld*, 297 F. Supp. 2d 119, 135; see par. F, reference to Citizen Petition, FDA docket 01p-0471, https://nebula.wsimg.com/2617051f041708e6b5335b6c885478d7?AccessKeyId=0BA19F97E21CB8613CD7&disposition=0&alloworigin=1.

[72] U.S. Reports: *Weinberger v. Hynson, Westcott & Dunning*, 412 U.S. 609 (1972), https://tile.loc.gov/storage-services/service/ll/usrep/usrep412/usrep412609/usrep412609.pdf.

bring its COVID vaccine regulations and guidance into line with federal law.

55. Although EUA law is relatively recent, we ask the FDA to be ever cognizant of its longstanding, statutory mission and duty to protect the public health and to ensure that the American public receives only safe and effective vaccines. Most Americans are not aware of the strict compliance requirements for EUA COVID vaccines nor do they know that these biologics are "investigational" and "unapproved medical products."[73] They do not know that the FDA has not fully approved these vaccines as safe and effective under the FDCA. The reason Americans are unaware is because the FDA has failed to provide and enforce accurate public messaging. Reversing this trend is imperative; the FDA must comply with law.

56. Acting on this Citizen Petition will enhance the FDA's credibility with the public. Given the obvious safety, effectiveness, labeling and branding concerns over COVID vaccines detailed above, along with anticipated comments on this docket, we respectfully appeal to the FDA to implement the actions requested in this Petition.

III. Environmental Impact

57. The undersigned hereby state 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. §§ 25.30 and 25.31.

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[73] FDA, *Emergency Use Authorization for Vaccines explained* (updated Nov. 20, 2020), https://www.fda.gov/vaccines-blood-biologics/vaccines/emergency-use-authorization-vaccines-explained.

IV. Economic Impact

58. Economic impact information will be submitted upon request of the Acting Commissioner.

V. Certification

59. The undersigned certify that, to their best knowledge and belief, this Petition includes all information and views on which the Petition relies, and that it includes representative data and information known to the Petitioners that are unfavorable to the Petition.

Respectfully submitted,

/s/ Meryl Nass, MD
Scientific Advisory Board Member

/s/ Robert F. Kennedy, Jr.
Board Chair and Chief Litigation Counsel

EXHIBIT 2
PFIZER BIONTECH PRESS RELEASE ANNOUNCING FDA PRIORITY REVIEW (JULY 16, 2021)

U.S. FDA GRANTS PRIORITY REVIEW FOR THE BIOLOGICS LICENSE APPLICATION FOR PFIZER-BIONTECH COVID-19 VACCINE

NEW YORK AND MAINZ, GERMANY, JULY 16, 2021—Pfizer Inc. (NYSE: PFE) and BioNTech SE (Nasdaq: BNTX) today announced that the U.S. Food and Drug Administration (FDA) granted Priority Review designation for the Biologics License Application (BLA) for their mRNA vaccine to prevent COVID-19 in individuals 16 years of age and older. The Prescription Drug User Fee Act (PDUFA) goal date for a decision by the FDA is in January 2022.

Pfizer and BioNTech completed the rolling submission of the BLA in May 2021. The application includes clinical data from the pivotal Phase 3 clinical trial of the vaccine, where the vaccine's efficacy and favorable safety profile were observed up to six months after the second dose.

On May 10, 2021, the FDA expanded the Emergency Use Authorization (EUA) of the Pfizer-BioNTech COVID-19 Vaccine to include individuals 12 through 15 years of age. The companies intend to submit a supplemental BLA to support licensure of the vaccine in this age group once the required data six months after the second vaccine dose are available.

The Pfizer-BioNTech COVID-19 Vaccine, which is based on BioNTech proprietary mRNA technology, was developed by both BioNTech and Pfizer. BioNTech is the Marketing Authorization Holder in the European Union, and the holder of emergency use authorizations or equivalent in the United States (jointly with Pfizer), Canada and other countries in advance of a planned application for full marketing authorizations in these countries.

The Pfizer-BioNTech COVID-19 Vaccine has not been approved or licensed by the U.S. Food and Drug Administration (FDA), but has been authorized for emergency use by FDA under an Emergency Use Authorization (EUA) to prevent Coronavirus Disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) for use in individuals 12 years of age and older. The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of the medical product under Section 564 (b) (1) of the FD&C Act unless the declaration is terminated or authorization revoked sooner. Please see Emergency Use Authorization (EUA) Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) and Full EUA Prescribing Information available at www.cvdvaccine-us.com.

Authorized Use in the U.S.:

The Pfizer-BioNTech COVID19 Vaccine is authorized for use under an Emergency Use Authorization (EUA) for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute

respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 12 years of age and older.

Important Safety Information

- Do not administer Pfizer-BioNTech COVID-19 Vaccine to individuals with known history of a severe allergic reaction (eg, anaphylaxis) to any component of the Pfizer-BioNTech COVID-19 Vaccine
- Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of Pfizer-BioNTech COVID-19 Vaccine
- Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of Pfizer-BioNTech COVID-19 Vaccine

  Monitor Pfizer-BioNTech COVID-19 Vaccine recipients for the occurrence of immediate adverse reactions according to the Centers for Disease Control and Prevention guidelines (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/managing-anaphylaxis.html)
- Reports of adverse events following use of the Pfizer-BioNTech COVID-19 Vaccine under EUA suggest increased risks of myocarditis and pericarditis, particularly following the second dose. The decision to administer the Pfizer-BioNTech COVID-19 Vaccine to an individual with a history of myocarditis or pericarditis

should take into account the individual's clinical circumstances

- Syncope (fainting) may occur in association with administration of injectable vaccines, in particular in adolescents. Procedures should be in place to avoid injury from fainting
- Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the Pfizer-BioNTech COVID-19 Vaccine
- The Pfizer-BioNTech COVID-19 Vaccine may not protect all vaccine recipients
- In clinical studies, adverse reactions in participants 16 years of age and older included pain at the injection site (84.1%), fatigue (62.9%), headache (55.1%), muscle pain (38.3%), chills (31.9%), joint pain (23.6%), fever (14.2%), injection site swelling (10.5%), injection site redness (9.5%), nausea (1.1%), malaise (0.5%), and lymphadenopathy (0.3%)
- In a clinical study, adverse reactions in adolescents 12 through 15 years of age included pain at the injection site (90.5%), fatigue (77.5%), headache (75.5%), chills (49.2%), muscle pain (42.2%), fever (24.3%), joint pain (20.2%), injection site swelling (9.2%), injection site redness (8.6%), lymphadenopathy (0.8%), and nausea (0.4%)
- Following administration of the Pfizer-BioNTech COVID-19 Vaccine, the following have been reported outside of clinical trials:
  - severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions,

diarrhea, vomiting, and pain in extremity (arm)

— myocarditis and pericarditis

- Additional adverse reactions, some of which may be serious, may become apparent with more widespread use of the Pfizer-BioNTech COVID-19 Vaccine
- Available data on Pfizer-BioNTech COVID-19 Vaccine administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy
- Data are not available to assess the effects of Pfizer-BioNTech COVID-19 Vaccine on the breastfed infant or on milk production/excretion
- There are no data available on the interchangeability of the Pfizer-BioNTech COVID-19 Vaccine with other COVID-19 vaccines to complete the vaccination series. Individuals who have received one dose of Pfizer-BioNTech COVID-19 Vaccine should receive a second dose of Pfizer-BioNTech COVID-19 Vaccine to complete the vaccination series
- Vaccination providers must report Adverse Events in accordance with the Fact Sheet to VAERS online at https://vaers.hhs.gov/reportevent.html. For further assistance with reporting to VAERS call 1-800-822-7967. The reports should include the words "Pfizer-BioNTech COVID-19 Vaccine EUA" in the description section of the report
- Vaccination providers should review the Fact Sheet for Information to Provide to Vaccine Recipients/Caregivers and Mandatory Requirements

for Pfizer-BioNTech COVID-19 Vaccine Administration Under Emergency Use Authorization

- Before administration of Pfizer-BioNTech COVID-19 Vaccine, please see Emergency Use Authorization (EUA) Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) including Full EUA Prescribing Information available at www.cvdvaccine-us.com

About Pfizer: Breakthroughs That Change Patients' Lives

At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety and value in the discovery, development and manufacture of health care products, including innovative medicines and vaccines. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's premier innovative biopharmaceutical companies, we collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For more than 170 years, we have worked to make a difference for all who rely on us. We routinely post information that may be important to investors on our website at www.Pfizer.com. In addition, to learn more, please visit us on www.Pfizer.com and follow us on Twitter at (CD-Pfizer and (CD-Pfizer News, LinkedIn, YouTube and like us on Facebook at Facebook.com/Pfizer.

Pfizer Disclosure Notice

The information contained in this release is as of July 16, 2021. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about Pfizer's efforts to combat COVID-19, the collaboration between BioNTech and Pfizer to develop a COVID-19 vaccine, the BNT162 mRNA vaccine program and the Pfizer-BioNTech COVID-19 Vaccine (BNT-162b2) (including qualitative assessments of available data, potential benefits, expectations for clinical trials, the anticipated timing of regulatory submissions, regulatory approvals or authorizations and anticipated manufacturing, distribution and supply) involving substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, the uncertainties inherent in research and development, including the ability to meet anticipated clinical endpoints, commencement and/or completion dates for clinical trials, regulatory submission dates, regulatory approval dates and/or launch dates, as well as risks associated with preclinical and clinical data (including the Phase 3 data), including the possibility of unfavorable new preclinical, clinical or safety data and further analyses of existing preclinical, clinical or safety data; the ability to produce comparable clinical or other results, including the rate of vaccine effectiveness and safety and tolerability profile observed to date, in additional analyses of the Phase 3 trial and additional studies or in larger, more diverse populations following commercialization;

the ability of BNT162b2 to prevent COVID-19 caused by emerging virus variants; the risk that more widespread use of the vaccine will lead to new information about efficacy, safety, or other developments, including the risk of additional adverse reactions, some of which may be serious; the risk that preclinical and clinical trial data are subject to differing interpretations and assessments, including during the peer review/publication process, in the scientific community generally, and by regulatory authorities; whether and when additional data from the BNT162 mRNA vaccine program will be published in scientific journal publications and, if so, when and with what modifications and interpretations; whether regulatory authorities will be satisfied with the design of and results from these and any future preclinical and clinical studies; whether and when other biologics license and/or emergency use authorization applications or amendments to any such applications may be filed in particular jurisdictions for BNT162b2 or any other potential vaccines that may arise from the BNT162 program, and if obtained, whether or when such emergency use authorization or licenses will expire or terminate; whether and when any applications that may be pending or filed for BNT162b2 (including the Biologics License Application or any requested amendments to the emergency use or conditional marketing authorizations) or other vaccines that may result from the BNT162 program may be approved by particular regulatory authorities, which will depend on myriad factors, including making a determination as to whether the vaccine's benefits outweigh its known risks and determination of the vaccine's efficacy and, if approved, whether it will be commercially successful; decisions

by regulatory authorities impacting labeling or marketing, manufacturing processes, safety and/or other matters that could affect the availability or commercial potential of a vaccine, including development of products or therapies by other companies; disruptions in the relationships between us and our collaboration partners, clinical trial sites or third-party suppliers; the risk that demand for any products may be reduced or no longer exist; risks related to the availability of raw materials to manufacture a vaccine; challenges related to our vaccine's ultra-low temperature formulation, two-dose schedule and attendant storage, distribution and administration requirements, including risks related to storage and handling after delivery by Pfizer; the risk that we may not be able to successfully develop other vaccine formulations, booster doses or new variant-specific vaccines; the risk that we may not be able to create or scale up manufacturing capacity on a timely basis or maintain access to logistics or supply channels commensurate with global demand for our vaccine, which would negatively impact our ability to supply the estimated numbers of doses of our vaccine within the projected time periods as previously indicated; whether and when additional supply agreements will be reached; uncertainties regarding the ability to obtain recommendations from vaccine advisory or technical committees and other public health authorities and uncertainties regarding the commercial impact of any such recommendations; challenges related to public vaccine confidence or awareness; uncertainties regarding the impact of COVID-19 on Pfizer's business, operations and financial results; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2020 and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at www.sec.gov and www.pfizer.com.

About BioNTech

Biopharmaceutical New Technologies is a next generation immunotherapy company pioneering novel therapies for cancer and other serious diseases. The Company exploits a wide array of computational discovery and therapeutic drug platforms for the rapid development of novel biopharmaceuticals. Its broad portfolio of oncology product candidates includes individualized and off-the-shelf mRNA-based therapies, innovative chimeric antigen receptor T cells, bi-specific checkpoint immuno-modulators, targeted cancer antibodies and small molecules. Based on its deep expertise in mRNA vaccine development and in-house manufacturing capabilities, BioNTech and its collaborators are developing multiple mRNA vaccine candidates for a range of infectious diseases alongside its diverse oncology pipeline. BioNTech has established a broad set of relationships with multiple global pharmaceutical collaborators, including Genmab, Sanofi, Bayer Animal Health, Genentech, a member of the Roche Group, Regeneron, Genevant, Fosun Pharma, and Pfizer. For more information, please visit www.BioNTech.de.

BioNTech Forward-looking Statements

This press release contains "forward-looking statements" of BioNTech within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements may include, but may not be limited to, statements concerning: BioNTech's efforts to combat CQVID-19; the collaboration between BioNTech and Pfizer to develop a COVID-19 vaccine (including a potential second booster dose of BNT162b2 and/or a potential booster dose of a variation of BNT162b2 having a modified mRNA sequence); our expectations regarding the potential characteristics of BNT162b2 in our clinical trials and/or in commercial use based on data observations to date; the ability of BNT162b2 to prevent COVID-19 caused by emerging virus variants; the expected time point for additional readouts on efficacy data of BNT162b2 in our clinical trials; the nature of the clinical data, which is subject to ongoing peer review, regulatory review and market interpretation; the timing for submission of data for, or receipt of, any marketing approval or Emergency Use Authorization; our contemplated shipping and storage plan, including our estimated product shelf life at various temperatures; and the ability of BioNTech to supply the quantities of BNT162 to support clinical development and market demand, including our production estimates for 2021. Any forward-looking statements in this press release are based on BioNTech current expectations and beliefs of future events, and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to: the ability to

meet the pre-defined endpoints in clinical trials; competition to create a vaccine for COVID-19; the ability to produce comparable clinical or other results, including our stated rate of vaccine effectiveness and safety and tolerability profile observed to date, in the remainder of the trial or in larger, more diverse populations upon commercialization; the ability to effectively scale our productions capabilities; and other potential difficulties.

For a discussion of these and other risks and uncertainties, see BioNTech's Annual Report as Form 20-F for the Year Ended December 31, 2020, filed with the SEC on March 30, 2021, which is available on the SEC's website at www.sec.gov. All information in this press release is as of the date of the release, and BioNTech undertakes no duty to update this information unless required by law.

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EXHIBIT 3
LETTER FROM DENISE M. HINTON
CHIEF SCIENTIST FOOD AND DRUG
ADMINISTRATION TO PFIZER

August 23, 2021

Pfizer Inc.
Attention: Ms. Elisa Harkins
500 Arcola Road
Collegeville, PA 19426

Dear Ms. Harkins:

On February 4, 2020, pursuant to Section 564 (b)(1)(C) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act or the Act), the Secretary of the Department of Health and Human Services (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 citizens living abroad, and that involves the virus that causes Coronavirus Disease 2019 (COVID-19).[1] On the basis of such determination, the Secretary of HHS on March 27, 2020, declared that circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic, pursuant to Section 564 of the Act (21 U.S.C. 360bbb-3), subject to terms of any authorization issued under that

[1] U.S. Department of Health and Human Services, Determination of a Public Health Emergency and Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3. February 4, 2020.

section.[2, 3, 4, 5]

On December 11, 2020, the Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for emergency use of Pfizer-BioNTech COVID-19

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[2] U.S. Department of Health and Human Services, Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3, 85 FR 18250 (April 1, 2020).

[3] In the May 10, 2021 revision, FDA authorized Pfizer-BioNTech Vaccine for the prevention of COVID-19 in individuals 12 through 15 years of age, as well as for individuals 16 years of age and older. In addition, FDA revised the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) to include the following Warning: "Syncope (fainting) may occur in association with administration of injectable vaccines, in particular in adolescents. Procedures should be in place to avoid injury from fainting." In addition, the Fact Sheet for Recipients and Caregivers was revised to instruct vaccine recipients or their caregivers to tell the vaccination provider about fainting in association with a previous injection.

[4] In the June 25, 2021 revision, FDA clarified terms and conditions that relate to export of Pfizer-BioNTech COVID-19 Vaccine from the United States. In addition, the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) was revised to include a Warning about myocarditis and pericarditis following administration of the Pfizer-BioNTech COVID-19 Vaccine. The Fact Sheet for Recipients and Caregivers was updated to include information about myocarditis and pericarditis following administration of the Pfizer-BioNTech COVID-19 Vaccine.

[5] In the August 12, 2021 revision, FDA authorized a third dose of the Pfizer-BioNTech COVID-19 Vaccine administered at least 28 days following the two dose regimen of this vaccine in individuals 12 years of age or older who have undergone solid organ transplantation, or individuals 12 years of age or older who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

Vaccine for the prevention of COVID-19 for individuals 16 years of age and older pursuant to Section 564 of the Act. FDA reissued the letter of authorization on: December 23, 2020, February 25, 2021, May 10, 2021, June 25, 2021, and August 12, 2021.

On August 23, 2021, FDA approved the biologics license application (BLA) submitted by BioNTech Manufacturing GmbH for COMIRNATY (COVID-19 Vaccine, mRNA) for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 16 years of age and older.

On August 23, 2021, having concluded that revising this EUA is appropriate to protect the public health or safety under section 564(g)(2) of the Act, FDA is reissuing the August 12, 2021 letter of authorization in its entirety with revisions incorporated to clarify that the EUA will remain in place for the Pfizer-BioNTech COVID-19 vaccine for the previously-authorized indication and uses, and to authorize use of COMIRNATY (COVID-19 Vaccine, mRNA) under this EUA for certain uses that are not included in the approved BLA. In addition, the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) was revised to provide updates on expiration dating of the authorized Pfizer-BioNTech COVID-19 Vaccine and to update language regarding warnings and precautions related to myocarditis and pericarditis. The Fact Sheet for Recipients and Caregivers was updated as the Vaccine Information Fact Sheet for Recipients and Caregivers, which comprises the Fact Sheet for the authorized Pfizer-BioNTech COVID-19 Vaccine and information about the FDA-licensed vaccine, COMIRNATY (COVID-19 Vaccine, mRNA).

Pfizer-BioNTech COVID-19 Vaccine contains a nucleoside-modified messenger RNA (modRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2 formulated in lipid particles. COMIRNATY (COVID-19 Vaccine, mRNA) is the same formulation as the Pfizer-BioNTech COVID-19 Vaccine and can be used interchangeably with the Pfizer-BioNTech COVID-19 Vaccine to provide the COVID-19 vaccination series.[6]

For the December 11, 2020 authorization for individuals 16 years of age and older, FDA reviewed safety and efficacy data from an ongoing phase 1/2/3 trial in approximately 44,000 participants randomized 1:1 to receive Pfizer-BioNTech COVID-19 Vaccine or saline control. The trial has enrolled participants 12 years of age and older. FDA's review at that time considered the safety and effectiveness data as they relate to the request for emergency use authorization in individuals 16 years of age and older. FDA's review of the available safety data from 37,586 of the participants 16 years of age and older, who were followed for a median of two months after receiving the second dose, did not identify specific safety concerns that would preclude issuance of an EUA. FDA's analysis of the available efficacy data from 36,523 participants 12 years of age and older without evidence of SARS-CoV-2 infection prior to 7 days after dose 2 confirmed the vaccine was 95% effective (95% credible interval 90.3, 97.6) in preventing COVID-19 occurring at least 7 days after the second dose (with 8 COVID-19 cases in

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[6] The licensed vaccine has the same formulation as the EUA-authorized vaccine and the products can be used interchangeably to provide the vaccination series without presenting any safety or effectiveness concerns. The products are legally distinct with certain differences that do not impact safety or effectiveness.

the vaccine group compared to 162 COVID-19 cases in the placebo group). Based on these data, and review of manufacturing information regarding product quality and consistency, FDA concluded that it is reasonable to believe that Pfizer-BioNTech COVID-19 Vaccine may be effective. Additionally, FDA determined it is reasonable to conclude, based on the totality of the scientific evidence available, that the known and potential benefits of Pfizer-BioNTech COVID-19 Vaccine outweigh the known and potential risks of the vaccine, for the prevention of COVID-19 in individuals 16 years of age and older. Finally, on December 10, 2020, the Vaccines and Related Biological Products Advisory Committee voted in agreement with this conclusion.

For the May 10, 2021 authorization for individuals 12 through 15 years of age, FDA reviewed safety and effectiveness data from the above-referenced, ongoing Phase 1/2/3 trial that has enrolled approximately 46,000 participants, including 2,260 participants 12 through 15 years of age. Trial participants were randomized 1:1 to receive Pfizer-BioNTech COVID-19 Vaccine or saline control. FDA's review of the available safety data from 2,260 participants 12 through 15 years of age, who were followed for a median of 2 months after receiving the second dose, did not identify specific safety concerns that would preclude issuance of an EUA. FDA's analysis of SARS-CoV-2 50% neutralizing antibody titers 1 month after the second dose of PfizerBioNTech COVID-19 Vaccine in a subset of participants who had no serological or virological evidence of past SARS-CoV-2 infection confirm the geometric mean antibody titer in participants 12 through 15 years of age was non-inferior to the geometric mean antibody titer in participants 16 through 25 years of

age. FDA's analysis of available descriptive efficacy data from 1,983 participants 12 through 15 years of age without evidence of SARS-CoV-2 infection prior to 7 days after dose 2 confirm that the vaccine was 100% effective (95% confidence interval 75.3, 100.0) in preventing COVID-19 occurring at least 7 days after the second dose (with no COVID-19 cases in the vaccine group compared to 16 COVID-19 cases in the placebo group). Based on these data, FDA concluded that it is reasonable to believe that PfizerBioNTech COVID-19 Vaccine may be effective in individuals 12 through 15 years of age. Additionally, FDA determined it is reasonable to conclude, based on the totality of the scientific evidence available, that the known and potential benefits of Pfizer-BioNTech COVID-19 Vaccine outweigh the known and potential risks of the vaccine, for the prevention of COVID-19 in individuals 12 through 15 years of age.

For the August 12, 2021 authorization of a third dose of the Pfizer-BioNTech COVID-19 Vaccine in individuals 12 years of age or older who have undergone solid organ transplantation, or individuals 12 years of age or older who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise, FDA reviewed safety and effectiveness data reported in two manuscripts on solid organ transplant recipients. The first study was a single arm study conducted in 101 individuals who had undergone various solid organ transplant procedures (heart, kidney, liver, lung, pancreas) a median of 97±8 months earlier. A third dose of the Pfizer-BioNTech COVID-19 Vaccine was administered to 99 of these individuals approximately 2 months after they had received a second dose. Levels of total SARS-CoV-2 binding

antibodies meeting the pre-specified criteria for success occurred four weeks after the third dose in 26/59 (44.0%) of those who were initially considered to be seronegative and received a third dose of the Pfizer-BioNTech COVID-19 Vaccine; 67/99 (68%) of the entire group receiving a third vaccination were subsequently considered to have levels of antibodies indicative of a significant response. In those who received a third vaccine dose, the adverse event profile was similar to that after the second dose and no grade 3 or grade 4 events were reported. A supportive secondary study describes a double-blind, randomized-controlled study conducted in 120 individuals who had undergone various solid organ transplant procedures (heart, kidney, kidney-pancreas, liver, lung, pancreas) a median of 3.57 years earlier (range 1.99-6.75 years). A third dose of a similar mRNA vaccine (the Moderna COVID-19 vaccine) was administered to 60 individuals approximately 2 months after they had received a second dose (*i.e.*, doses at 0, 1 and 3 months); saline placebo was given to 60 individuals or comparison. The primary outcome was anti-RBD antibody at 4 months greater than 100 U/mL. This titer was selected based on NHP challenge studies as well as a large clinical cohort study to indicate this antibody titer was protective. Secondary outcomes were based on a virus neutralization assay and polyfunctional T cell responses. Baseline characteristics were comparable between the two study arms as were pre-intervention anti-RBD titer and neutralizing antibodies. Levels of total SARS-CoV-2 binding antibodies indicative of a significant response occurred four weeks after the third dose in 33/60 (55.0%) of the Moderna COVID-19 vaccinated group and 10/57 (17.5%) of the placebo individuals. In the 60 individuals who received a third vaccine dose, the

adverse event profile was similar to that after the second dose and no grade 3 or grade 4 adverse events were reported. Despite the moderate enhancement in antibody titers, the totality of data (*i.e.*, supportive paper by Hall et al. demonstrated efficacy of the product in the elderly and persons with co-morbidities) supports the conclusion that a third dose of the Pfizer-BioNTech COVID-19 vaccine may be effective in this population, and that the known and potential benefits of a third dose of Pfizer-BioNTech COVID-19 Vaccine outweigh the known and potential risks of the vaccine for immunocompromised individuals at least 12 years of age who have received two doses of the Pfizer-BioNTech COVID-19 Vaccine and who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

Having concluded that the criteria for issuance of this authorization under Section 564(c) of the Act are met, I am authorizing the emergency use of Pfizer-BioNTech COVID-19 Vaccine for the prevention of COVID-19, as described in the Scope of Authorization section of this letter (Section II) and subject to the terms of this authorization. Additionally, as specified in subsection III.BB, I am authorizing use of COMIRNATY (COVID-19 Vaccine, mRNA) under this EUA when used to provide a two-dose regimen for individuals aged 12 through 15 years, or to provide a third dose to individuals 12 years of age or older who have undergone solid organ transplantation or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of Pfizer-BioNTech COVID-19 Vaccine for the prevention of COVID-19 when administered as described in the Scope of Authorization (Section II) meets the criteria for issuance of an authorization under Section 564(c) of the Act, because:

A. SARS-CoV-2 can cause a serious or life-threatening disease or condition, including severe respiratory illness, to humans infected by this virus;

B. Based on the totality of scientific evidence available to FDA, it is reasonable to believe that Pfizer-BioNTech COVID-19 Vaccine may be effective in preventing COVID-19, and that, when used under the conditions described in this authorization, the known and potential benefits of Pfizer-BioNTech COVID-19 Vaccine when used to prevent COVID-19 outweigh its known and potential risks; and

C. There is no adequate, approved, and available[7] alternative to the emergency use of

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[7] Although COMIRNATY (COVID-19 Vaccine, mRNA) is approved to prevent COVID-19 in individuals 16 years of age and older, there is not sufficient approved vaccine available for distribution to this population in its entirety at the time of reissuance of this EUA. Additionally, there are no products that are approved to prevent COVID-19 in individuals age 12 through 15, or that are approved to provide an additional dose to the immunocompromised population described in this EUA.

Pfizer-BioNTech COVID-19 Vaccine to prevent COVID-19.[8]

II. Scope of Authorization

I have concluded, pursuant to Section 564(d)(1) of the Act, that the scope of this authorization is limited as follows:

- Pfizer Inc. will supply Pfizer-BioNTech COVID-19 Vaccine either directly or through authorized distributor(s),[9] to emergency response stakeholders[10] as directed by the U.S. government,

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[8] No other criteria of issuance have been prescribed by regulation under Section 564(c)(4) of the Act.

[9] "Authorized Distributor(s)" are identified by Pfizer Inc. or, if applicable, by a U.S. government entity, such as the Centers for Disease Control and Prevention (CDC) and/or other designee, as an entity or entities allowed to distribute authorized Pfizer-BioNTech COVID-19 Vaccine.

[10] For purposes of this letter, "emergency response stakeholder" refers to a public health agency and its delegates that have legal responsibility and authority for responding to an incident, based on political or geographical boundary lines (*e.g.*, city, county, tribal, territorial, State, or Federal), or functional (*e.g.*, law enforcement or public health range) or sphere of authority to administer, deliver, or distribute vaccine in an emergency situation. In some cases (*e.g.*, depending on a state or local jurisdiction's COVID-19 vaccination response organization and plans), there might be overlapping roles and responsibilities among "emergency response stakeholders" and "vaccination providers" (*e.g.*, if a local health department is administering COVID-19 vaccines; if a pharmacy is acting in an official capacity under the authority of the state health department to administer COVID-19 vaccines). In such cases, it is expected that the conditions of authorization that apply to emergency response stakeholders and vaccination providers will all be met.

including the Centers for Disease Control and Prevention (CDC) and/or other designee, for use consistent with the terms and conditions of this EUA;

- The Pfizer-BioNTech COVID-19 Vaccine covered by this authorization will be administered by vaccination providers[11] and used only to prevent COVID-19 in individuals ages 12 and older; and
- Pfizer-BioNTech COVID-19 Vaccine may be administered by a vaccination provider without an individual prescription for each vaccine recipient.

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[11] For purposes of this letter, "vaccination provider" refers to the facility, organization, or healthcare provider licensed or otherwise authorized by the emergency response stakeholder (*e.g.*, non-physician healthcare professionals, such as nurses and pharmacists pursuant to state law under a standing order issued by the state health officer) to administer or provide vaccination services in accordance with the applicable emergency response stakeholder's official COVID-19 vaccination and emergency response plan(s) and who is enrolled in the CDC COVID-19 Vaccination Program. If the vaccine is exported from the United States, a "vaccination provider" is a provider that is authorized to administer this vaccine in accordance with the laws of the country in which it is administered. For purposes of this letter, "healthcare provider" also refers to a person authorized by the U.S. Department of Health and Human Services (*e.g.*, under the PREP Act Declaration for Medical Countermeasures against COVID-19) to administer FDA-authorized COVID-19 vaccine (*e.g.*, qualified pharmacy technicians and State-authorized pharmacy interns acting under the supervision of a qualified pharmacist). *See*, *e.g.*, HHS. Fourth Amendment to the Declaration Under the Public Readiness and Emergency Preparedness Act for Medical Countermeasures Against COVID-19 and Republication of the Declaration. 85 FR 79190 (December 9, 2020).

This authorization also covers the use of the licensed COMIRNATY (COVID-19 Vaccine, mRNA) product when used to provide a two-dose regimen for individuals aged 12 through 15 years, or to provide a third dose to individuals 12 years of age or older who have undergone solid organ transplantation or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

Product Description

The Pfizer-BioNTech COVID-19 Vaccine is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. The Pfizer-BioNTech COVID-19 Vaccine does not contain a preservative.

Each 0.3 mL dose of the Pfizer-BioNTech COVID-19 Vaccine contains 30 mcg of a nucleoside-modified messenger RNA (modRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2. Each dose of the Pfizer-BioNTech COVID-19 Vaccine also includes the following ingredients: lipids (0.43 mg (4-hydroxybutyl) azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2[(polyethylene glycol)-2000]-N,N-ditetradecyl-acetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection) contributes an additional 2.16 mg sodium chloride per dose.

The dosing regimen is two doses of 0.3 mL each, 3 weeks apart. A third dose may be administered at least 28 days following the second dose of the two dose

regimen of this vaccine to individuals 12 years of age or older who have undergone solid organ transplantation, or individuals 12 years of age or older who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

The manufacture of the authorized Pfizer-BioNTech COVID-19 Vaccine is limited to those facilities identified and agreed upon in Pfizer's request for authorization.

The Pfizer-BioNTech COVID-19 Vaccine vial label and carton labels are clearly marked for "Emergency Use Authorization." The Pfizer-BioNTech COVID-19 Vaccine is authorized to be distributed, stored, further redistributed, and administered by emergency response stakeholders when packaged in the authorized manufacturer packaging (*i.e.*, vials and cartons), despite the fact that the vial and carton labels may not contain information that otherwise would be required under the FD&C Act.

Pfizer-BioNTech COVID-19 Vaccine is authorized for emergency use with the following product-specific information required to be made available to vaccination providers and recipients, respectively (referred to as "authorized labeling"):

- Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers): Emergency Use Authorization (EUA) of Pfizer-BioNTech COVID-19 Vaccine to Prevent Coronavirus Disease 2019 (COVID-19)
- Vaccine Information Fact Sheet for Recipients and Caregivers About COMIRNATY (COVID-19 Vaccine, mRNA) and Pfizer-BioNTech COVID-19 Vaccine to Prevent Coronavirus Disease (COVID-19).

I have concluded, pursuant to Section 564(d)(2) of the Act, that it is reasonable to believe that the known and potential benefits of Pfizer-BioNTech COVID-19 Vaccine, when used to prevent COVID-19 and used in accordance with this Scope of Authorization (Section II), outweigh its known and potential risks.

I have concluded, pursuant to Section 564(d)(3) of the Act, based on the totality of scientific evidence available to FDA, that it is reasonable to believe that Pfizer-BioNTech COVID-19 Vaccine may be effective in preventing COVID-19 when used in accordance with this Scope of Authorization (Section II), pursuant to Section 564(c)(2)(A) of the Act.

Having reviewed the scientific information available to FDA, including the information supporting the conclusions described in Section I above, I have concluded that Pfizer-BioNTech COVID-19 Vaccine (as described in this Scope of Authorization (Section II)) meets the criteria set forth in Section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of Pfizer-BioNTech COVID-19 Vaccine under this EUA must be consistent with, and may not exceed, the terms of the Authorization, including the Scope of Authorization (Section II) and the Conditions of Authorization (Section III). Subject to the terms of this EUA and under the circumstances set forth in the Secretary of HHS's determination under Section 564(b)(1)(C) described above and the Secretary of HHS's corresponding declaration under Section 564(b)(1), Pfizer-BioNTech COVID-19 Vaccine is authorized to prevent COVID-19 in individuals 12 years of age and older as described in the Scope of Authorization (Section II) under this EUA, despite the

fact that it does not meet certain requirements otherwise required by applicable federal law.

III. Conditions of Authorization

Pursuant to Section 564 of the Act, I am establishing the following conditions on this authorization:
Pfizer Inc. and Authorized Distributor(s)

A. Pfizer Inc. and authorized distributor(s) will ensure that the authorized Pfizer-BioNTech COVID-19 Vaccine is distributed, as directed by the U.S. government, including CDC and/or other designee, and the authorized labeling (*i.e.*, Fact Sheets) will be made available to vaccination providers, recipients, and caregivers consistent with the terms of this letter.

B. Pfizer Inc. and authorized distributor(s) will ensure that appropriate storage and cold chain is maintained until delivered to emergency response stakeholders' receipt sites.

C. Pfizer Inc. will ensure that the terms of this EUA are made available to all relevant stakeholders (*e.g.*, emergency response stakeholders, authorized distributors, and vaccination providers) involved in distributing or receiving authorized PfizerBioNTech COVID-19 Vaccine. Pfizer Inc. will provide to all relevant stakeholders a copy of this letter of authorization and communicate any subsequent amendments that might be made to this letter of authorization and its authorized labeling.

D. Pfizer Inc. may develop and disseminate instructional and educational materials (*e.g.*, video regard-

ing vaccine handling, storage/cold-chain management, preparation, disposal) that are consistent with the authorized emergency use of the vaccine as described in the letter of authorization and authorized labeling, without FDA's review and concurrence, when necessary to meet public health needs during an emergency. Any instructional and educational materials that are inconsistent with the authorized labeling are prohibited.

E. Pfizer Inc. may request changes to this authorization, including to the authorized Fact Sheets for the vaccine. Any request for changes to this EUA must be submitted to Office of Vaccines Research and Review (OVRR)/Center for Biologics Evaluation and Research (CBER). Such changes require appropriate authorization prior to implementation.[12]

F. Pfizer Inc. will report to Vaccine Adverse Event Reporting System (VAERS):

- Serious adverse events (irrespective of attribution to vaccination);

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[12] The following types of revisions may be authorized without reissuing this letter: (1) changes to the authorized labeling; (2) non-substantive editorial corrections to this letter; (3) new types of authorized labeling, including new fact sheets; (4) new carton/container labels; (5) expiration dating extensions; (6) changes to manufacturing processes, including tests or other authorized components of manufacturing; (7) new conditions of authorization to require data collection or study. For changes to the authorization, including the authorized labeling, of the type listed in (3), (6), or (7), review and concurrence is required from the Preparedness and Response Team (PREP)/Office of the Center Director (OD)/CBER and the Office of Counterterrorism and Emerging Threats (OCET)/Office of the Chief Scientist (OCS).

- Cases of Multisystem Inflammatory Syndrome in children and adults; and
- Cases of COVID-19 that result in hospitalization or death, that are reported to Pfizer Inc.

These reports should be submitted to VAERS as soon as possible but no later than 15 calendar days from initial receipt of the information by Pfizer Inc.

G. Pfizer Inc. must submit to Investigational New Drug application (IND) number 19736 periodic safety reports at monthly intervals in accordance with a due date agreed upon with the Office of Biostatistics and Epidemiology (OBE)/CBER beginning after the first full calendar month after authorization. Each periodic safety report is required to contain descriptive information which includes:

- A narrative summary and analysis of adverse events submitted during the reporting interval, including interval and cumulative counts by age groups, special populations (*e.g.*, pregnant women), and adverse events of special interest;
- A narrative summary and analysis of vaccine administration errors, whether or not associated with an adverse event, that were identified since the last reporting interval;
- Newly identified safety concerns in the interval; and
- Actions taken since the last report because of adverse experiences (for example, changes made to Healthcare Providers Administering

Vaccine (Vaccination Providers) Fact Sheet, changes made to studies or studies initiated).

H. No changes will be implemented to the description of the product, manufacturing process, facilities, or equipment without notification to and concurrence by FDA.

I. All manufacturing facilities will comply with Current Good Manufacturing Practice requirements.

J. Pfizer Inc. will submit to the EUA file Certificates of Analysis (CoA) for each drug product lot at least 48 hours prior to vaccine distribution. The CoA will include the established specifications and specific results for each quality control test performed on the final drug product lot.

K. Pfizer Inc. will submit to the EUA file quarterly manufacturing reports, starting in July 2021, that include a listing of all Drug Substance and Drug Product lots produced after issuance of this authorization. This report must include lot number, manufacturing site, date of manufacture, and lot disposition, including those lots that were quarantined for investigation or those lots that were rejected. Information on the reasons for lot quarantine or rejection must be included in the report.

L. Pfizer Inc. and authorized distributor(s) will maintain records regarding release of Pfizer-BioNTech COVID-19 Vaccine for distribution (*i.e.*, lot numbers, quantity, release date).

M. Pfizer Inc. and authorized distributor(s) will make available to FDA upon request any records maintained in connection with this EUA.

N. Pfizer Inc. will conduct post-authorization observational studies to evaluate the association between Pfizer-BioNTech COVID-19 Vaccine and a pre-specified list of adverse events of special interest, along with deaths and hospitalizations, and severe COVID-19. The study population should include individuals administered the authorized Pfizer-BioNTech COVID-19 Vaccine under this EUA in the general U.S. population (12 years of age and older), populations of interest such as healthcare workers, pregnant women, immunocompromised individuals, subpopulations with specific comorbidities. The studies should be conducted in large scale databases with an active comparator. Pfizer Inc. will provide protocols and status update reports to the IND 19736 with agreed-upon study designs and milestone dates.

Emergency Response Stakeholders

O. Emergency response stakeholders will identify vaccination sites to receive authorized Pfizer-BioNTech COVID-19 Vaccine and ensure its distribution and administration, consistent with the terms of this letter and CDC's COVID-19 Vaccination Program.

P. Emergency response stakeholders will ensure that vaccination providers within their jurisdictions are aware of this letter of authorization, and the terms herein and any subsequent amendments that might be made to the letter of authorization, instruct them about the means through which

they are to obtain and administer the vaccine under the EUA, and ensure that the authorized labeling [*i.e.*, Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) and Vaccine Information Fact Sheet for Recipients and Caregivers] is made available to vaccination providers through appropriate means (*e.g.*, e-mail, website).

Q. Emergency response stakeholders receiving authorized Pfizer-BioNTech COVID-19 Vaccine will ensure that appropriate storage and cold chain is maintained.

Vaccination Providers

R. Vaccination providers will administer the vaccine in accordance with the authorization and will participate and comply with the terms and training required by CDC's COVID-19 Vaccination Program.

S. Vaccination providers will provide the Vaccine Information Fact Sheet for Recipients and Caregivers to each individual receiving vaccination and provide the necessary information for receiving their second dose and/or third dose.

T. Vaccination providers administering the vaccine must report the following information associated with the administration of the vaccine of which they become aware to VAERS in accordance with the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers):

- Vaccine administration errors whether or not associated with an adverse event

- Serious adverse events (irrespective of attribution to vaccination)
- Cases of Multisystem Inflammatory Syndrome in children and adults
- Cases of COVID-19 that result in hospitalization or death

Complete and submit reports to VAERS online at https://vaers.hhs.gov/reportevent.html. The VAERS reports should include the words "Pfizer-BioNTech COVID-19 Vaccine EUA" in the description section of the report. More information is available at vaers.hhs.gov or by calling 1-800-822-7967. To the extent feasible, report to Pfizer Inc. by contacting 1-800-438-1985 or by providing a copy of the VAERS form to Pfizer Inc.; Fax: 1-866-635-8337.

U. Vaccination providers will conduct any follow-up requested by the U.S government, including CDC, FDA, or other designee, regarding adverse events to the extent feasible given the emergency circumstances.

V. Vaccination providers will monitor and comply with CDC and/or emergency response stakeholder vaccine management requirements (*e.g.*, requirements concerning obtaining, tracking, and handling vaccine) and with requirements concerning reporting of vaccine administration data to CDC.

W. Vaccination providers will ensure that any records associated with this EUA are maintained until notified by FDA. Such records will be made available to CDC, and FDA for inspection upon request.

Conditions Related to Printed Matter, Advertising, and Promotion

X. All descriptive printed matter, advertising, and promotional material, relating to the use of the Pfizer-BioNTech COVID-19 Vaccine shall be consistent with the authorized labeling, as well as the terms set forth in this EUA, and meet the requirements set forth in section 502(a) and (n) of the FD&C Act and FDA implementing regulations.

Y. All descriptive printed matter, advertising, and promotional material relating to the use of the Pfizer-BioNTech COVID-19 Vaccine clearly and conspicuously shall state that:

- This product has not been approved or licensed by FDA, but has been authorized for emergency use by FDA, under an EUA to prevent Coronavirus Disease 2019 (COVID-19) for use in individuals 12 years of age and older; and
- The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of the medical product under Section 564(b)(1) of the FD&C Act unless the declaration is terminated or authorization revoked sooner.

Condition Related to Export

Z. If the Pfizer-BioNTech COVID-19 Vaccine is exported from the United States, conditions C, D, and O through Y do not apply, but export is permitted only if 1) the regulatory authorities of the

country in which the vaccine will be used are fully informed that this vaccine is subject to an EUA and is not approved or licensed by FDA and 2) the intended use of the vaccine will comply in all respects with the laws of the country in which the product will be used. The requirement in this letter that the authorized labeling (*i.e.*, Fact Sheets) be made available to vaccination providers, recipients, and caregivers in condition A will not apply if the authorized labeling (*i.e.*, Fact Sheets) are made available to the regulatory authorities of the country in which the vaccine will be used.

Conditions With Respect to Use of Licensed Product

AA. COMIRNATY (COVID-19 Vaccine, mRNA) is now licensed for individuals 16 years of age and older. There remains, however, a significant amount of Pfizer-BioNTech COVID-19 vaccine that was manufactured and labeled in accordance with this emergency use authorization. This authorization thus remains in place with respect to that product for the previously-authorized indication and uses (*i.e.*, for use to prevent COVID-19 in individuals 12 years of age and older with a two-dose regimen, and to provide a third dose to individuals 12 years of age or older who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise).

BB. This authorization also covers the use of the licensed COMIRNATY (COVID-19 Vaccine,

mRNA) product when used to provide a two-dose regimen for individuals aged 12 through 15 years, or to provide a third dose to individuals 12 years of age or older who have undergone solid organ transplantation or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise. Conditions A through W in this letter apply when COMIRNATY (COVID-19 Vaccine, mRNA) is provided for the uses described in this subsection III.BB, except that product manufactured and labeled in accordance with the approved BLA is deemed to satisfy the manufacturing, labeling, and distribution requirements of this authorization.

IV. Duration of Authorization

This EUA will be effective until the declaration that circumstances exist justifying the authorization of the emergency use of drugs and biological products during the COVID-19 pandemic is terminated under Section 564(b)(2) of the Act or the EUA is revoked under Section 564(g) of the Act.

Sincerely,

-/s/-

RADM Denise M. Hinton
Chief Scientist
Food and Drug Administration

EXHIBIT 4
FDA LETTER RESPONSE TO CITIZEN PETITION OF MERYL NASS, M.D.

(August 23, 2021)

Meryl Nass, M.D.
Robert F. Kennedy, Jr.
Children's Health Defense
1227 North Peachtree Parkway, Suite 202
Peachtree City, GA 30269

Re: Citizen Petition (Docket Number FDA-2021-P-0460)
Dear Dr. Nass and Mr. Kennedy,

This letter responds to the citizen petition dated May 16, 2021 that you submitted to the Food and Drug Administration (FDA, the Agency, we) on behalf of Children's Health Defense (Petitioner) relating to: clinical trials, Emergency Use Authorization, licensure, and advertising and promotion of vaccines to prevent Coronavirus Disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (the Petition).

In the Petition, Petitioner requests that FDA:

1. "revoke all EUAs and refrain from approving any future EUA, NDA, or BLA for any COVID vaccine for all demographic groups";

2. "immediately refrain from allowing minors to participate in COVID vaccine trials, refrain from amending EUAs to include children, and immediately revoke all EUAs that permit vaccination of children under 16 for the Pfizer vaccine and under 18 for other COVID vaccines";

3. "immediately revoke tacit approval that pregnant women may receive any EUA or licensed COVID vaccines and immediately issue public guidance to that effect";

4. "immediately amend [FDA's] existing guidance for the use of the chloroquine drugs, ivermectin, and any other drugs demonstrated to be safe and effective against COVID. . .and immediately issue notifications to all stakeholders";

5. "issue guidance to the Secretary of the Defense [sic] and the President not to grant an unprecedented Presidential waiver of prior consent regarding COVID vaccines for Servicemembers [sic]";

6. "issue guidance . . . to affirm that all citizens have the option to accept or refuse administration of investigational COVID vaccines without adverse work, educational or other non-health related consequences"; and

7. "[p]ending revocation of COVID vaccine EUAs, FDA should issue guidance that all marketing and promotion of COVID vaccines must refrain from labeling them 'safe and effective.'"

Petition at 1-2.

In this letter, we discuss the safety of licensed and authorized vaccines. We then turn to the requests contained in the Petition. We consider each of your requests in light of the legal standards for FDA action, and provide our conclusions based on the facts, the science, and the law.

This letter responds to the Petition in full. FDA has carefully reviewed the Petition and other relevant

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 action. In accordance with 21 CFR § 10.30 (e)(3), and for the reasons stated below, FDA is denying the Petition.

Here is an outline of our response:

I. Background

II. Vaccines That Are FDA-Licensed or Receive an Emergency Use Authorization Meet Relevant Statutory Requirements

  a. Vaccines that are FDA-Licensed are Safe

    i. Vaccines that are FDA-Licensed are Shown to Be Safe at the Time of Licensure

    ii. Vaccine Safety Continues to Be Monitored Post-Licensure

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

III. Discussion

  a. Investigational New Drugs

  b. The Citizen Petition

    i. Petitioner's Request to Revoke all Emergency Use Authorizations for COVID-19 Vaccines and Refrain from Issuing any Future EUA or Approving any Future NDA, or BLA for any COVID-19 Vaccine for all Demographic Groups because the

Current Risks of Serious Adverse Events or Deaths Outweigh the Benefits, and Because Existing, Approved Drugs Provide Highly Effective Prophylaxis and Treatment against COVID-19, Mooting the EUAs

1. Petitioner's Request to Revoke all Emergency Use Authorizations for COVID-19 Vaccines
2. Petitioner's Request to Refrain from Granting any Future EUA for a COVID-19 Vaccine for any Population
3. Petitioner's Request to Refrain from Approving any Future NDA for any COVID-19 Vaccine for any Population
4. Petitioner's Request to Refrain from Licensing any Future BLA for any COVID-19 Vaccine for any Population

ii. Petitioner's Request Regarding COVID-19 Vaccines in Children

1. Request to Immediately Refrain from Allowing COVID-19 Vaccine Trials to Include Pediatric Subjects
2. Request that FDA Refrain from Issuing EUA Amendments for Authorized COVID-19 Vaccines to Include Indications for Pediatric Populations
3. Request that FDA Immediately Revoke all EUAs for COVID-19 Vaccines with Pediatric Indications

iii. Petitioner's Request that FDA Immediately Revoke Tacit Approval that Pregnant Women may Receive any EUA or Licensed COVID-19 Vaccines and Immediately Issue Public Guidance

1. Covid-19 in Pregnancy
2. Certain Content and Format Requirements for Prescription Drug Labeling for Products Approved Under NDAs or BLAs
3. Inclusion of Contraindications and Pregnancy Information in the Labeling for the Authorized COVID-19 Vaccines
4. Inclusion of Contraindications and Pregnancy Information in the Labeling for Licensed COVID-19 Vaccines

iv. Petitioner's Request that FDA Immediately Amend its Guidance regarding Certain Approved Drugs [chloroquine drugs, ivermectin, "and any other drugs demonstrated to be safe and effective against COVID"]

v. Petitioner's Request that FDA Issue Guidance to the Secretary of Defense and the President

vi. Petitioner's Request that FDA Issue Guidance to Stakeholders Regarding the Option to Refuse or Accept Administration of Investigational COVID-19 Vaccines

vii. Petitioner's Request that FDA Issue Guidance Regarding Marketing and Promotion of COVID-19 Vaccines

c. Conclusion

Appendix I: Aspects of Vaccine Development and Process for Licensure

I. Background

There is currently a pandemic of respiratory disease, COVID-19, caused by a novel coronavirus, 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 FD&C Act (21 U.S.C. § 360bbb-3), 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.[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

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[1] Secretary of Health and Human Services 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.

EUA Declaration"), pursuant to section 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 are developing COVID-19 vaccine candidates, and clinical studies of these vaccines are underway and/or have been completed. Between December 11, 2020 and February 27, 2021, FDA issued emergency use authorizations for three vaccines to prevent COVID-19, including vaccines sponsored by Pfizer Inc. (Pfizer); ModernaTX, Inc. (Moderna); and Janssen Biotech, Inc. (Janssen), a pharmaceutical company of Johnson & Johnson. FDA received a Biologics License Application (BLA) for the COVID-19 vaccine, BNT162b2, intended to prevent COVID-19 in individuals 16 years of age and older. As announced by FDA on August 23, 2021, the Agency is issuing a biologics license for this COVID-19 vaccine (COVID-19 Vaccine, mRNA; Comirnaty) to BioNTech Manufacturing GmbH.[5]

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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] BioNTech Manufacturing GmbH is the biologics license holder for this vaccine, which is manufactured by Pfizer Inc. for BioNTech Manufacturing GmbH (hereinafter "BioNTech"). The basis for FDA's licensure decision is set forth in FDA's Summary

II. Vaccines That Are FDA-Licensed or Receive an Emergency Use Authorization Meet Relevant Statutory Requirements

a. Vaccines that are FDA-Licensed are Safe

i. Vaccines that are FDA-Licensed Are Shown to Be Safe at the Time of Licensure

FDA has a stringent regulatory process for licensing vaccines.[6,7] 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."[8] 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 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 biologics license application (BLA) include, among other things, data derived from nonclinical and clinical studies

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Basis for Regulatory Action (SBRA) for the BioNTech application. This memorandum will be posted on fda.gov. We incorporate by reference the SBRA for the BLA.

[6] 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.

[7] FDA, V*accine Safety Questions and Answers*, last updated March 2018, https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/vaccine-safety-questions-and-answers.

[8] 42 U.S.C. § 262(a)(2)(C)(i)(I).

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.[9]

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 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.[10] Only when FDA's standards are met is a vaccine licensed.

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."[11] Therefore, the manufacturers of vaccines that have been licensed in the U.S. have necessarily demonstrated the safety of the

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[9] 21 CFR § 601.2(a).

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

[11] 21 CFR § 601.2(d) (emphasis added).

vaccines within the meaning of the applicable statutory and regulatory provisions before the vaccines were licensed and allowed to be marketed.

For more information on FDA's thorough process for evaluating the safety of vaccines, *see* Appendix I of this letter, *Aspects of Vaccine Development and Process for Licensure*.

ii. Vaccine Safety Continues to Be Monitored Post-Licensure

FDA's oversight of vaccine safety continues after licensure of the product. Once the licensed vaccine is on the market, post-marketing surveillance of vaccine safety is conducted in order to detect any rare, serious, or unexpected adverse events, as well as to monitor vaccine lots. FDA employs multiple surveillance systems and databases to continue to evaluate the safety of these vaccines. In certain cases, FDA may require the manufacturer to conduct post-marketing studies to further assess known or potential serious risks.

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

Congress established the Emergency Use Authorization (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 Food Drug & Cosmetic Act (FD&C Act) (21 U.S.C. § 360bbb-3) 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 (21 U.S.C. § 360bbb-3(b)(1)(C)), 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.[12] 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 U.S.C. § 360bbb-3(b)(1)).[13]

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[12] 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.

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

Based on this declaration and determination, under section 564(c) of the FD&C Act (21 U.S.C. § 360bbb-3(c)), 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 March 27, 2020 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.
- 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* (October 2020 Guidance), FDA has

provided recommendations that describe key information that would support issuance of an EUA for a vaccine to prevent COVID-19.[14] In the October 2020 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.[15] 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.[16]

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

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[14] *Emergency Use Authorization for Vaccines to Prevent COVID-19; Guidance for Industry*, October 2020 (October 2020 Guidance), https://www.fda.gov/media/142749/download.

[15] *Id.* at 3.

[16] *Id.* at 4.

disease will be assessed by comparing the number of cases of disease in each study group. For Phase 3 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.[17] 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.

Investigational COVID-19 vaccines continue to be studied in Phase 2 or Phase 3 trials. Following clinical trials, manufacturers analyze data prior to submitting to FDA a BLA to request approval from FDA to market the vaccine. A BLA for a new vaccine includes information and data regarding the safety, effectiveness, chemistry, manufacturing and controls, and other details regarding the product. 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.

Importantly, FDA has made clear that any vaccine that meets FDA's standards for effectiveness is also expected to meet the Agency's safety standards. FDA has stated that the duration of safety follow-up for a vaccine authorized under an EUA may be shorter than with a BLA (which the Agency expects will ultimately be submitted by manufacturers of vaccines that

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[17] *Development and Licensure of Vaccines to Prevent COVID-19; Guidance for Industry*, June 2020, https://www.fda.gov/media/139638/download.

are authorized under an EUA). Specifically, FDA's guidance to manufacturers recommends that data from Phase 3 studies to support an EUA include a median follow-up duration of at least 2 months after completion of the full vaccination regimen.[18] Furthermore, robust safety monitoring is conducted after a vaccine is made available. The monitoring systems include the Vaccine Adverse Event Reporting System (VAERS), FDA's Biologics Effectiveness and Safety (BEST) System, and the Centers for Disease Control and Prevention's (CDC) Vaccine Safety Datalink. In addition, FDA has a partnership with the Centers for Medicare & Medicaid Services (CMS) to study vaccine safety. Other tools to monitor vaccine safety are under development. Collectively, these programs will help detect any new, unusual and rare side effects after vaccination that might not have been observed during clinical trials, as well as monitor for increases in any known side effects.

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

The Petition makes a request regarding clinical trials of COVID-19 vaccines that include or propose to include children. FDA's investigational new drug process applies to the development of new drugs and biological products, including vaccines.[19]

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[18] October 2020 Guidance at 10-11.

[19] *See* 21 CFR § 312.2 (explaining that the IND regulations apply to clinical investigations of both drugs and biologics).

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[20]) 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) to FDA.[21] The IND describes the proposed clinical study in detail and, among other things, helps protect the safety and

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[20] 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.

[21] *See* 21 CFR § 312.20(a).

rights of human subjects.[22] 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 experimental 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),[23] and to adhere to the investigational new drug 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

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[22] 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.

[23] 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.

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.[24]

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 50, subpart D and only

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[24] 21 CFR § 312.22(a).

approve those clinical investigations involving children as subjects that satisfy the criteria in 21 CFR 50, subpart 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."[25]

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; 21 U.S.C. § 355(i)(3)), 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.[26]

b. The Citizen Petition

i. Petitioner's Request to Revoke all Emergency Use Authorizations for COVID-19 Vaccines and

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[25] 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.

[26] 21 CFR § 312.42(a).

Refrain from Issuing any Future EUA or Approving any Future NDA, or BLA for any COVID-19 Vaccine for all Demographic Groups because the Current Risks of Serious Adverse Events or Deaths Outweigh the Benefits, and Because Existing, Approved Drugs Provide Highly Effective Prophylaxis and Treatment against COVID-19, Mooting the EUAs

Petitioner makes several requests regarding COVID-19 vaccines in the Petition and, in support of these requests, argues that (1) the rates of serious adverse events or deaths outweigh the benefits of these vaccines and (2) approved drugs provide highly effective prophylaxis/treatment against COVID, thereby "mooting" the EUAs. We interpret this as an argument that the authorizations of COVID-19 vaccines to date did not meet the relevant legal standard. Below, we address each of Petitioner's requests and the information provided by Petitioner in support of these requests.

1. Petitioner's Request to Revoke all Emergency Use Authorizations for COVID-19 Vaccines

In this section, we address Petitioner's request that FDA "revoke all EUAs . . . for any COVID vaccine for all demographic groups because the current risks of serious adverse events or deaths outweigh the benefits, and because existing, approved drugs provide highly effective prophylaxis and treatment against COVID, mooting the EUAs." Petition at 1.

a. EUAs for COVID-19 Vaccines

As noted above in Section II above, FDA may issue an EUA during the COVID-19 public health

emergency after FDA concludes that the statutory requirements provided in section 564 of the FD&C Act are met. In an attempt to prevent the spread of disease and to control the pandemic, numerous COVID-19 vaccine candidates have been developed. COVID-19 vaccines that have been developed or are currently in development are based on various platforms and include mRNA, DNA, viral vectored, subunit, inactivated, and live-attenuated vaccines. Most COVID-19 candidate vaccines express the spike protein or parts of the spike protein, *i.e.*, the receptor binding domain, as the immunogenic determinant.

To date, FDA has issued EUAs for three COVID-19 vaccines ("the Authorized COVID-19 Vaccines"), as described in the Scope of Authorization for these COVID-19 vaccines, pursuant to section 564 of the FD&C Act. Additionally, FDA has expanded the authorized age range for one COVID-19 vaccine.

- On December 11, 2020, FDA issued an EUA for emergency use of Pfizer-BioNTech COVID-19 Vaccine for the prevention of COVID-19 in individuals 16 years of age and older.
- On May 10, 2021, FDA authorized the emergency use of Pfizer-BioNTech COVID-19 Vaccine to include individuals 12 through 15 years of age.
- On December 18, 2020, FDA issued an EUA for emergency use of Moderna COVID-19 Vaccine for the prevention of COVID-19 in individuals 18 years of age and older.
- On February 27, 2021, FDA issued an EUA for emergency use of Janssen COVID-19 Vaccine for the prevention of COVID-19 in individuals 18 years of age and older.

The Agency issued these EUAs after a thorough evaluation of scientific data regarding the safety, effectiveness, and manufacturing information (which helps ensure product quality and consistency) of these COVID-19 vaccines and after reaching a determination that these vaccines meet the statutory requirements under section 564 of the FD&C Act. This letter incorporates by reference the EUA Review Memoranda for the Authorized COVID-19 Vaccines,[27] which discuss this determination, and the data upon which it was based, in detail as well as the Summary Basis of Regulatory Action for the BioNTech COVID-19 vaccine (COVID-19 Vaccine, mRNA; Comirnaty).[28]

Petitioner argues that the authorizations for these vaccines should be revoked, and that future COVID vaccines should not be authorized or licensed, because

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[27] FDA, *Pfizer-BioNTech COVID-19 Vaccine EUA Decision Memorandum* (Dec. 11, 2020), https://www.fda.gov/media/144416/download; FDA, Pfizer-BioNTech COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization in Individuals 12-15 Years of Age (May 10, 2021), https://www.fda.gov/media/148542/download; FDA, Pfizer-BioNTech COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization of an Additional Dose in Certain Immunocompromised Individuals (August 12, 2021) https://www.fda.gov/media/151613/download; FDA, *Moderna COVID-19 Vaccine EUA Decision Memorandum* (Dec. 18, 2020), https://www.fda.gov/media/144673/download; FDA, *Moderna COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization of an Additional Dose in Certain Immunocompromised Individuals* (August 12, 2021) https://www.fda.gov/media/151611/download; FDA, *Janssen COVID-19 Vaccine EUA Decision Memorandum* (Feb. 27, 2021), https://www.fda.gov/media/146338/download.

[28] This letter incorporates by reference FDA's Summary Basis for Regulatory Action (SBRA) for the BioNTech BLA. This memorandum will be posted on www.fda.gov.

(1) "the current risks of serious adverse events or deaths outweigh the benefits," and (2) "existing, approved drugs provide highly effective prophylaxis and treatment against COVID, mooting the EUAs." We address each of Petitioner's arguments, and data submitted in the Petition in support of these arguments, below.

FDA disagrees with Petitioner's position that the Authorized COVID-19 Vaccines did not meet the statutory standard at the time of authorization, and finds no basis in the information submitted in the Petition, or in any postmarket data regarding these vaccines, to support a revocation of any of these authorizations. FDA is not aware of any information indicating that the known and potential benefits of the Authorized COVID-19 Vaccines are outweighed by their known and potential risks, nor has Petitioner provided any such information in the Petition. The known and potential benefits of the Authorized COVID-19 Vaccines continue to outweigh their known and potential risks, given the risk of COVID-19 and related, potentially severe, complications. Furthermore**,** as explained below, there is no adequate, approved, and available alternative to the Authorized COVID-19 Vaccines for preventing COVID-19. Accordingly, this request is denied.

b. Standard for Revocation of EUAs is not Met for the Authorized COVID-19 Vaccines

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.

FDA's guidance entitled *Emergency Use Authorization of Medical Products and Related Authorities* ("EUA Guidance"),[29] 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])."[30] Regarding the circumstances that would make a revision or revocation appropriate to protect the public health or safety, FDA explains in the EUA guidance 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

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[29] *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.

[30] *Id.* at 28.

> 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.

EUA guidance at 29.

Thus, in addressing Petitioner's request for FDA to revoke the Authorized COVID-19 Vaccines, we assess whether any of the statutory conditions under which FDA may revoke an EUA are met, namely: (1) whether the circumstances justifying their issuance under section 564(b)(1) of the FD&C Act no longer exist, (2) whether the criteria for their 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 Continue to Justify the Issuance of the EUAs for the Authorized COVID-19 Vaccines

As explained above in section II.b., on February 4, 2020, pursuant to section 564(b)(1)(C) of the FD&C Act (21 U.S.C. § 360bbb-3(b)(1)(C)), 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.[31] 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 564(b)(1) of the FD&C Act (21 U.S.C. § 360bbb-3(b)(1)).[32]

Based on this declaration and determination, under section 564(c) of the FD&C Act (21 U.S.C. § 360bbb-3(c)), FDA may issue an EUA during the COVID-19 pandemic after FDA concludes that the statutory requirements provided in section 564(c) are met. Section 564(b)(2) sets forth the statutory standard for termination of an EUA declaration. An EUA declaration remains in place until the earlier of: (1) a determination by the HHS Secretary that the circumstances that precipitated the declaration have ceased (after con sultation as appropriate with the Secretary of Defense) or (2) a change in the approval status of the product such that the authorized use(s) of the product are no longer unapproved. Neither of those statutory criteria is satisfied with respect to the Authorized COVID-19 Vaccines.

Thus, the circumstances described under section 564(b)(1) of the FD&C Act continue to exist. FDA therefore is not revoking the EUAs for the Authorized

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[31] 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.

[32] 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.

COVID-19 Vaccines under the authority in section 564(g)(2)(A) of the FD&C Act.

ii. The Criteria for The Issuance of the Authorized COVID-19 Vaccines Continue to Be Met

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

1. Serious or life-threatening disease or condition.

Section 564(c)(1) of the FD&C Act requires that, for an EUA to be issued for a medical product, FDA must conclude "the agent(s) referred to in [the HHS Secretary's EUA declaration] can cause a serious or life-threatening disease or condition." FDA has concluded that SARS-CoV-2, which is the subject of the EUA declaration, meets this standard.

The SARS-CoV-2 pandemic continues to present an extraordinary challenge to global health and, as of August 3, 2021, has caused more than 199 million cases of COVID-19 and claimed the lives of more than 4.2 million people worldwide.[33] In the United States, more than 34 million cases and over 611,000 deaths have been reported to the CDC.[34] On January 31,

[33] Johns Hopkins University School of Medicine, Coronavirus Resource Center, https://coronavirus.jhu.edu/map.html.

[34] CDC, *COVID Data Tracker*, https://covid.cdc.gov/covid-data-tracker/#trends_dailytrendscases.

2020, the U.S. Secretary of Health and Human Services (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.

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. Therefore, the criterion under section 564(c)(1) continues to be met with respect to the Authorized COVID-19 Vaccines.

2. Evidence of Effectiveness

Section 564(c)(2)(A) of the FD&C Act requires that, for an EUA to be issued for a medical product, FDA must conclude "based on the totality of scientific evidence available to the Secretary, including data from adequate and well-controlled trials, if available, it is reasonable to believe that the product may be effective to prevent, diagnose, or treat such serious or life-threatening disease or condition that can be caused by SARS-CoV-2."

FDA issued EUAs for the Authorized COVID-19 Vaccines after determining that, among other things, these products were demonstrated in clinical trials to prevent symptomatic and severe COVID-19 in vaccinated clinical trial subjects.[35] FDA is not aware of

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[35] FDA, *Pfizer-BioNTech COVID-19 Vaccine EUA Decision Memorandum* (Dec. 11, 2020), at 23, https://www.fda.gov/media/144416/download; FDA, *Moderna COVID-19 Vaccine EUA Decision Memorandum* (Dec. 18, 2020), at 24, https://www.fda.gov/media/

any data that changes this conclusion, nor has Petitioner provided any such data in the Petition. This section addresses Petitioner's arguments regarding the effectiveness of the Authorized COVID-19 vaccines and explains why the information submitted by Petitioner does not change FDA's analysis regarding the effectiveness of these vaccines.

After FDA approves a vaccine or authorizes a vaccine for emergency use, the vaccine continues to be studied to determine how well it works under real-world conditions. FDA, CDC, and other federal partners have been assessing, and will continue to assess, COVID-19 vaccine effectiveness under real-world conditions. Such evaluations will help us understand if vaccines are performing as expected outside the more controlled setting of a clinical trial.

Petitioner raises concerns regarding the post-market effectiveness of the Authorized COVID-19 Vaccines (Petition at 6). Petitioner points to CDC-reported "breakthrough cases" to suggest that the Authorized COVID-19 Vaccines are not effective and argues that the EUAs for the Authorized COVID-19 Vaccines should therefore be revoked because the current risks of these vaccines outweigh their benefits. This perspective fails to recognize several important points regarding the concept of breakthrough cases and regarding the CDC publication cited in the Petition.

First, we note that the Letters of Authorization for the Authorized COVID-19 Vaccines require EUA-holders to report to VAERS "cases of COVID-19 that

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144673/download; FDA, *Janssen COVID-19 Vaccine EUA Decision Memorandum* (Feb. 27, 2021), at 25, https://www.fda.gov/media/146338/download.

result in hospitalization or death, that are reported to [the EUA holder]."[36] Thus, the possibility that individuals who received one of the Authorized COVID-19 Vaccines could develop breakthrough COVID-19 cases was recognized by FDA when the Agency evaluated the EUA requests for these vaccines and determined that their known and potential benefits outweigh their known and potential and risks.

Second, the Authorized COVID-19 Vaccines are indicated to prevent symptomatic COVID-19,[37] not to prevent SARS-CoV-2 infection. Over 353 million doses of COVID-19 vaccines have been administered in the United States[38] and FDA's ongoing post authorization

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[36] *Section 8, Requirements and Instructions for Reporting Adverse Events and Vaccine Administration Errors*, Pfizer-BioNTech COVID-19 Fact Sheet for Healthcare Providers Administering Vaccine, https://www.fda.gov/media/144413/download; *Section 8, Requirements and Instructions for Reporting Adverse Events and Vaccine Administration Errors*, Moderna COVID-19 Fact Sheet for Healthcare Providers Administering Vaccine, https://www.fda.gov/media/144637/download; *Section 8, Requirements and Instructions for Reporting Adverse Events and Vaccine Administration Errors*, Janssen COVID-19 Fact Sheet for Healthcare Providers Administering Vaccine, https://www.fda.gov/media/146304/download.

[37] FDA, *Pfizer-BioNTech COVID-19 Vaccine EUA Decision Memorandum* (Dec. 11, 2020), at 23, https://www.fda.gov/media/144416/download; FDA, *Moderna COVID-19 Vaccine EUA Decision Memorandum* (Dec. 18, 2020), at 24, https://www.fda.gov/media/144673/download; FDA, J*anssen COVID-19 Vaccine EUA Decision Memorandum* (Feb. 27, 2021), at 25, https://www.fda.gov/media/146338/download.

[38] CDC, C*OVID Data Tracker Weekly Review, Interpretive Summary* for August 13, 2021, https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covidview/index.html

monitoring informs us that the known and potential benefits continue to outweigh the known and potential risks. Additionally, CDC's post-authorization data regarding the Authorized COVID-19 Vaccines continues to support FDA's conclusion that these vaccines prevent symptomatic COVID-19.[39]

Third, a vaccine does not need to be 100% effective in preventing the target disease in order to meet the licensure or EUA standard. It is expected that some vaccinated individuals will contract the target disease despite having been vaccinated against it. No FDA licensed or authorized vaccine is 100% effective, but scientific data has nevertheless demonstrated that vaccinations have been a very effective approach to protecting the public's health in the United States.[40]

Similarly, a COVID-19 vaccine need not be 100% effective in preventing symptomatic COVID19, or even close to 100% effective in doing so, in order to have a significant effect in altering the course of the COVID-19 pandemic. As FDA noted in its June 2020 Guidance for Industry, Development and Licensure of Vaccines to Prevent COVID-19, ("The Vaccine Development and Licensure Guidance") "[t]o ensure that a widely deployed COVID-19 vaccine is effective, the primary efficacy endpoint point estimate for a placebo-controlled efficacy trial should be at least 50%, and the statistical success

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[39] CDC, *COVID-19 Vaccine Effectiveness Research*, https://www.cdc.gov/vaccines/covid-19/effectiveness-research/protocols.html.

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

criterion should be that the lower bound of the appropriately alpha-adjusted confidence interval around the primary efficacy endpoint point estimate is >30%."[41] This statistical consideration provided in the Vaccine Development and Licensure Guidance reflects FDA's assessment that a vaccine with at least 50 percent efficacy would have a significant impact on disease, both at the individual and societal level.

Finally, we note that Petitioner refers to "CDC-reported" breakthrough cases in support of its argument that there are effectiveness concerns with the Authorized COVID-19 Vaccines but fails to acknowledge that CDC reported a set of breakthrough cases that includes a large proportion of asymptomatic individuals who tested positive for SARS-CoV-2. Petitioner thus applies a narrower definition of the term "breakthrough case" to a set of cases than CDC has in its COVID-19 Vaccine Breakthrough Case Investigation.[42] Petitioner refers to breakthrough cases in which vaccinated individuals "fall ill and potentially transmit the virus" (Petition at 6) and states that "CDC reported over 9,000 'breakthrough cases' and 132 COVID-caused deaths among vaccinated people." Petition at 6.

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[41] *Development and Licensure of Vaccines to Prevent COVID-19, Guidance for Industry*, June 2020, at 14, https://www.fda.gov/media/139638/download.

[42] CDC, *COVID-19 Vaccine Breakthrough Case Investigations and Reporting*, https://www.cdc.gov/vaccines/covid-19/health-departments/breakthrough-cases.html.

CDC's objective in the COVID-19 Vaccine Breakthrough Case Investigation is to[43] ensure the COVID-19 vaccines are working as expected and to "identify patterns or trends" in:

- Patients' characteristics, such as age or underlying medical conditions
- The specific vaccine that patients received
- Whether a specific SARS-CoV-2 variant caused the infections"[44]

The objective of this investigation is not simply to count symptomatic COVID-19 cases. Currently, COVID-19 cases are increasing again in nearly all states. The highest rate of COVID19 case spread is in areas with low vaccination rates.[45]

Petitioner's submitted data regarding CDC-reported "breakthrough cases" therefore does not present new data or information that the Agency has not previously considered regarding the effectiveness of the Authorized COVID-19 Vaccines. Available data

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[43] CDC, *COVID-19 Vaccine Breakthrough Case Investigations and Reporting*, https://www.cdc.gov/vaccines/covid-19/health-departments/breakthrough-cases.html.

[44] CDC, *COVID-19 Vaccine Breakthrough Case Investigations and Reporting*, https://www.cdc.gov/vaccines/covid-19/health-departments/breakthrough-cases.html.

[45] "As of July 22 [2021], 35% of U.S. counties are experiencing high levels of community transmission. COVID-19 cases are on the rise in nearly 90% of U.S. jurisdictions, and we are seeing outbreaks in parts of the country that have low vaccination coverage." CDC, COVID Data Tracker Weekly Review, Interpretive Summary for July 23, 2021, available at_https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covidview/index.html.

regarding effectiveness of the Authorized COVID-19 Vaccines continues to support the conclusion that these vaccines may be effective in preventing COVID-19. FDA is not aware of any data that changes this conclusion, nor has Petitioner provided any such data in the Petition. Therefore, the criterion under section 564(c)(2)(A) continues to be met with respect to the Authorized COVID-19 Vaccines.

3. Benefit-Risk Analysis

Section 564(c)(2)(B) of the FD&C Act requires that, for an EUA to be issued for a medical product, FDA must conclude "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. . . . " Petitioner argues that the current risks of serious adverse events or deaths associated with the Authorized COVID-19 Vaccines outweigh the benefits of COVID-19 vaccines. This section addresses Petitioner's arguments regarding the safety of COVID-19 vaccines and explains why the information submitted by Petitioner does not change FDA's analysis regarding the benefits and risks of the Authorized COVID-19 Vaccines.

FDA issued EUAs for the Authorized COVID-19 Vaccines after reaching a determination regarding each of these vaccines that, among other things, the known and potential benefits of the vaccine, when used to prevent COVID-19, outweigh its known and potential risks.[46] FDA is not aware of any data that

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[46] For an extensive discussion of FDA's analysis of the clinical trial data regarding the risks and benefits of each of the authorized COVID-19 Vaccines, *see* FDA, *Pfizer-BioNTech COVID-19*

changes this determination, nor has Petitioner provided any such data in the Petition. The known and potential benefits of the Authorized COVID-19 Vaccines, when used to prevent COVID-19, continue to outweigh their known and potential risks, given the risk of COVID-19 and related, potentially severe, complications.

Petitioner raises numerous concerns regarding safety of the Authorized COVID-19 Vaccines (Petition at 2-6) and asserts that the EUAs for the Authorized COVID-19 Vaccines should be revoked due in part to these safety concerns. For reasons explained below, FDA disagrees with Petitioner's assertions regarding the safety of the Authorized COVID-19 Vaccines.

As an initial matter, we note that the Petition discusses several assertions made by CDC and requests that have been directed to CDC. For requests intended for CDC, you should contact CDC directly.

a. Petitioner's Claims Regarding VAERS Data

In arguing that the Authorized COVID-19 Vaccines should be revoked due, in part, to safety concerns, Petitioners assert that "Vaccine Adverse Event Reporting System (VAERS) data reveal unprecedented

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Vaccine EUA Decision Memorandum (Dec. 11, 2020), at 49, https://www.fda.gov/media/144416/download; FDA, *Moderna COVID-19 Vaccine EUA Decision Memorandum* (Dec. 18, 2020), at 55, https://www.fda.gov/media/144673/download; FDA, *Janssen COVID-19 Vaccine EUA Decision Memorandum* (Feb. 27, 2021), at 59, https://www.fda.gov/media/146338/download. *See also*, FDA, *Pfizer-BioNTech COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization in Individuals 12-15 Years of Age* (May 10, 2021), at 38, https://www.fda.gov/media/148542/download.

levels of deaths and other adverse events since the FDA issued Emergency Use Authorizations (EUAs) for three COVID vaccines. As of May 10, 2021, VAERS reported 4,434 deaths of people who received at least one COVID vaccination." As an initial matter, we note that VAERS is a national passive surveillance vaccine safety database that receives unconfirmed reports of possible adverse events following the use of a vaccine licensed or authorized in the United States. VAERS is not designed to assess whether a reported adverse event was caused by a vaccine. This section explains vaccine safety surveillance, including VAERS, in greater detail below.

Regarding the number of VAERS reports submitted for the Authorized COVID-19 Vaccines, this figure can be attributed to multiple factors. First, we note that a large number of COVID-19 vaccine doses have been administered in the United States and that certain adverse event reporting by vaccination providers is required for the Authorized COVID-19 Vaccines. As of August 13, 2021, over 353,000,000 doses of the Authorized COVID-19 Vaccines have been administered.[47] We note that the crude number of VAERS reports of death is extremely small compared to the to the large number of people who have been vaccinated. The VAERS reporting rate for deaths (which is the number of VAERS death reports received out of the number of individuals vaccinated) for the Authorized COVID-19 Vaccines is actually very low (6,490 reports of death out of 346 million doses administered

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[47] CDC, COVID Data Tracker, COVID-19 Vaccinations in the United States, https://covid.cdc.gov/covid-data-tracker/#vaccinations_vacc-total-admin-rate-total.

(0.0019%) as of August 2, 2021).[48] Petitioner's assertion fails to account for this fact.

For licensed vaccines, healthcare providers are legally required under 42 USC 300aa-25 to report to VAERS two categories of adverse events: "[a]ny adverse event listed in the VAERS Table of Reportable Events Following Vaccination that occurs within the specified time period after vaccination [and] [a]n adverse event listed by the vaccine manufacturer as a contraindication to further doses of the vaccine"[49] Vaccine manufacturers are also required to report to VAERS all adverse events that come to their attention.[50]

Under the EUAs for the Authorized COVID-19 Vaccines, however, vaccination providers are required to report to VAERS serious adverse events following vaccination with the Authorized COVID-19 Vaccines, "irrespective of attribution to vaccination" and without a specified time period after vaccination.[51] Another

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[48] CDC, *Selected Adverse Events Reported after COVID-19 Vaccination,* https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/adverse-events.html.

[49] VAERS, Frequently Asked Questions, https://vaers.hhs.gov/faq.html (emphasis added).

[50] 21 CFR 600.80. *See also* VAERS, Frequently Asked Questions, https://vaers.hhs.gov/faq.html.

[51] *Section 8, Requirements and Instructions for Reporting Adverse Events and Vaccine Administration Errors*, Pfizer-BioNTech COVID-19 Fact Sheet for Healthcare Providers Administering Vaccine, https://www.fda.gov/media/144413/download; *Section 8, Requirements and Instructions for Reporting Adverse Events and Vaccine Administration Errors*, Moderna COVID-19 Fact Sheet for Healthcare Providers Administering Vaccine, https://www.fda.gov/media/144637/download; *Section 8, Requirements and Instructions for Reporting Adverse Events and Vaccine*

contributing factor is the v-safe system,[52] which is a new CDC smartphone-based active-surveillance system in which participants who have been vaccinated may voluntarily enroll. This system was developed for the COVID-19 vaccination program. V-safe sends text messages and web surveys to participants who can report side effects following receipt of a COVID-19 vaccine. If a participant indicates through the v-safe surveys that he or she required medical care at any time, CDC calls the participant to complete a report through VAERS. This system is unique to COVID-19 vaccines and may be contributing to the number of VAERS reports submitted for the Authorized COVID-19 Vaccines.

Finally, another potential factor is the concept of "stimulated reporting."[53] Because of extensive media

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Administration Errors, Janssen COVID-19 Fact Sheet for Healthcare Providers Administering Vaccine, https://www.fda.gov/media/146304/download.

[52] CDC, *v-safe Overview*, https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/vsafe.html.

[53] We note that an article submitted by Petitioner in support of their arguments regarding VAERS acknowledges this concept: "Like all spontaneous public health reporting systems, VAERS has limitations. VAERS is subject to reporting bias, including underreporting of adverse events – especially common, mild ones – and stimulated reporting, which is elevated reporting that might occur in response to intense media attention and increased public awareness, such as during the 2009 H1N1 pandemic influenza vaccination program" Shimabukuro et al., Safety monitoring in the Vaccine Adverse Event Reporting System (VAERS), Vaccine (Nov. 4, 2015), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4632204/. *See also* "The number of reports and reporting rate following 2009-H1N1 vaccination were higher than following 2009–2010 seasonal influenza vaccines for all age groups. These findings, however, should be interpreted in light of the publicity

coverage and awareness of the public health emergency – and of the Authorized COVID19 Vaccines and their reported side effects –vaccine recipients, health care providers, and others are more likely to report adverse events for the Authorized COVID-19 Vaccines than for other vaccines that have been widely available for longer periods of time. Additionally, one of the articles submitted by Petitioner in support of their argument actually provides support for this explanation for the number of VAERS reports submitted for the Authorized COVID-19 Vaccines. The article notes "[t]he relatively rapid increase in numbers of reports to VAERS following the introduction and initial uptake of a new vaccine, an expected occurrence, has been misinterpreted as actual increases in incidence of adverse events and vaccine related risk."[54] Petitioner's argument regarding VAERS data for the Authorized COVID-19 Vaccines is unavailing because it fails to account for the factors outlined above.

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around the 2009-H1N1 vaccine and efforts to increase reporting to VAERS. Heightened public awareness and stimulated reporting likely enhanced reporting to VAERS. Furthermore, although 2009-H1N1 was licensed similarly to seasonal influenza vaccines, it was likely perceived as a 'new' vaccine by the public and susceptible to the known tendency (*i.e.*, the Weber effect) for adverse events to be reported more frequently following newly licensed products." Vellozzi, et al*., Adverse events following influenza A (H1N1) 2009 monovalent vaccines reported to the Vaccine Adverse Event Reporting System*, United States, October 1, 2009–January 31, 2010, Vaccine (Oct. 21, 2010), https://www.sciencedirect.com/science/article/pii/S0264410X10013319.

[54] Shimabukuro et al., *Safety monitoring in the Vaccine Adverse Event Reporting System (VAERS)*, Vaccine (Nov. 4, 2015), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4632204/ (emphasis added).

In addressing Petitioner's assertion regarding VAERS claims, this section addresses the extensive vaccine safety surveillance efforts, in addition to VAERS, that are in place for the Authorized COVID-19 Vaccines.[55] FDA is monitoring the safety of the Authorized COVID-19 Vaccines through both passive and active safety surveillance systems. FDA is doing so in collaboration with the Centers for Disease Control and Prevention (CDC), the Centers for Medicare and Medicaid Services (CMS), the Department of Veterans Affairs (VA), and other academic and large non-government healthcare data systems.

In addition, FDA participates actively in ongoing international pharmacovigilance efforts, including those organized by the International Coalition of Medicines Regulatory Authorities (ICMRA) and the World Health Organization (WHO). These efforts are in addition to the pharmacovigilance efforts being undertaken by the individual manufacturers for authorized vaccines. A coordinated and overlapping approach using state-of the art technologies has been implemented. As part of our efforts to be transparent about our COVID-19 vaccine safety monitoring activities, FDA is posting summaries of the key safety monitoring findings on the FDA website.[56]

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[55] FDA, *COVID-19 Vaccine Safety Surveillance*, https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/covid-19-vaccine-safety-surveillance.

[56] FDA, *COVID-19 Vaccine Safety Surveillance*, https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/covid-19-vaccine-safety-surveillance

i. Vaccine Safety Surveillance

Passive Surveillance

VAERS is a national passive surveillance vaccine safety database that receives unconfirmed reports of possible adverse events following the use of a vaccine licensed or authorized in the United States. Passive surveillance is defined as unsolicited reports of adverse events that are sent to a central database or health authority. In the United States, these are received and entered into VAERS, which is co-managed by FDA and CDC. In the current pandemic, these reports are being used to monitor the occurrence of both known and unknown adverse events, as providers of COVID-19 vaccines are required to report serious adverse events to VAERS.

As part of FDA and CDC's multi-system approach to post-licensure and post-authorization vaccine safety monitoring, VAERS is designed to rapidly detect unusual or unexpected patterns of adverse events, also known as "safety signals." VAERS reports generally cannot be used to determine if a vaccine caused or contributed to an adverse event or illness. If the VAERS data suggest a possible link between an adverse event and vaccination, the relationship may be further studied in a controlled fashion.[57]

Anyone can make a report to VAERS, including vaccine manufacturers, private practitioners, state and local public health clinics, vaccine recipients, and their parents or caregivers. Surveillance programs like VAERS perform a critical function by generating signals

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[57] FDA, VAERS Overview, https://www.fda.gov/vaccines-blood-biologics/vaccine-adverse-events/vaers-overview.

of potential problems that may warrant further investigation.

VAERS is not designed to assess causality. It is often difficult to determine with certainty if a vaccine caused an adverse event reported to VAERS. Many events that occur after vaccination can happen by chance alone. Some adverse events are so rare that their association with a vaccine is difficult to evaluate. In addition, we often receive reports where there is no clear clinical diagnosis. FDA draws upon multiple sources of data and medical and scientific expertise to assess the potential strength of association between a vaccine, including COVID-19 vaccines, and a possible adverse event.

If VAERS monitoring suggests that a vaccine might be causing a health problem, additional scientifically rigorous studies or investigations can be performed by FDA and CDC. Monitoring and analysis of VAERS reports typically includes daily in-depth medical review of all serious reports, statistical data mining techniques, and epidemiological analysis. We look for patterns and similarities in the onset timing and clinical description. We review published literature to understand possible biologic hypotheses that could plausibly link the reported adverse event to the vaccine. We review the pre-licensure or pre-authorization data and any other post-marketing studies that have been conducted. We also consider "background rate," meaning the rate at which a type of adverse event occurs in the unvaccinated general population. When necessary, we discuss the potential adverse event with our federal and international safety surveillance partners. We also carefully evaluate unusual or unexpected reports, as well as reports of "positive re-challenges" (adverse

events that occur in the same patient after each dose received). When there is sufficient evidence for a potential safety concern, we may proceed to conduct large studies, and we may coordinate with our federal, academic, and private partners to further assess the potential risk after vaccination. In addition, when potential safety issues arise, they are often presented to various U.S. government advisory committees, including the Vaccines and Related Biological Products Advisory Committee, the Advisory Committee on Immunization Practices (ACIP), and the Advisory Committee on Childhood Vaccines, and are often discussed with experts from other countries and from the World Health Organization. Federal agencies that assist in population-based vaccines safety studies include the CDC, Centers for Medicaid and Medicare (CMS), the Department of Defense (DoD), and the Indian Health Services (IHS). In addition, we generally communicate and work with international regulatory authorities and international partners to conduct studies in vaccine safety.

Active Surveillance

Active surveillance involves proactively obtaining and rapidly analyzing information related to millions of individuals and recorded in large healthcare data systems to verify safety signals identified through passive surveillance or to detect additional safety signals that may not have been reported as adverse events to passive surveillance systems. FDA is conducting active surveillance using the Sentinel BEST (Biologics Effectiveness and Safety) System and the CMS system, and is also collaborating with other federal and non-federal partners.

BEST

To elaborate further, the BEST system,[58] which is part of the Sentinel initiative,[59] comprises large-scale claims data, electronic health records (EHR), and linked claims-EHR databases with a data lag of approximately three months. The system makes use of multiple data sources and enables rapid queries to detect or evaluate adverse events as well as studies to answer specific safety questions for vaccines. The linked claims-EHR database makes it possible to study the safety of vaccines in sub-populations with pre-existing conditions or in pregnant women. The major partners for BEST currently are Acumen, IBM Federal HealthCare, IQVIA, and Columbia University and many affiliated partners such as MedStar Health, BlueCross BlueShield of America, the Observational Health Data Sciences and Informatics (OHDSI), OneFlorida, University of California and several others.[60]

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[58] CBER Biologics Effectiveness and Safety (BEST) System, https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/cber-biologics-effectiveness-and-safety-best-system.

[59] FDA's Sentinel Initiative, https://www.fda.gov/safety/fdas-sentinel-initiative.

[60] To confirm the utility of the BEST system for situations such as COVID-19 vaccine surveillance, a test case was conducted. This study aimed to replicate a previous study by the CDC's Vaccine Safety Datalink (VSD) (Klein et al. Pediatrics 2010) that examined the databases and analytic capabilities of the new system. The objective of this study was to test the new system's ability to reproduce the increased risk of febrile seizures in children receiving the first dose of measles-mumps-rubella-varicella (MMRV) vaccine, compared to that of MMR and varicella vaccines separately but on the same day. The results of

Using BEST, CBER plans to monitor about 15 adverse events[61] that have been seen with the deployment of previous vaccines but have yet to be associated with a safety concern for an authorized COVID-19 vaccine at this time. CBER further plans to use the BEST system to conduct more in-depth analyses should a safety concern be identified from sources such as VAERS.

CMS

FDA has worked over the past several years with CMS to develop capabilities for routine and time-sensitive assessments of the safety of vaccines for people 65 years of age and older using the Medicare Claims database.[62] Because it was already in place, this system was immediately put into use for COVID-19 vaccine surveillance to monitor for adverse events.[63]

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the study met the objectives and demonstrated the ability of the BEST Initiative data network to run a complex study protocol at multiple sites using a distributed data network and the Observational Medical Outcomes Partnership Common Data Model (organizing disparate data sources into the same database design using a common format).

[61] *Background Rates of Adverse Events of Special Interest for COVID-19 Vaccine Safety Monitoring, Draft Protocol* (December 31, 2020), https://www.bestinitiative.org/wp-content/uploads/2021/01/C19-Vaccine-Safety-AESI-Background-Rate-Protocol-2020.pdf.

[62] CMS, *Standard Analytical Files (Medicare Claims) – LDS*, https://www.cms.gov/Research-Statistics-Data-and-Systems/Files-for-Order/LimitedDataSets/StandardAnalyticalFiles.

[63] As one example of the capabilities of this system, FDA, CMS, and CDC evaluated the risk of Guillain-Barré syndrome (GBS) following influenza vaccination after CDC's Vaccine Safety Datalink, identified safety signals suggesting an increased risk

During the current pandemic, FDA, CMS, and CDC have already used the Medicare data to publish a study showing that frailty, comorbidities, and race/ethnicity were strong risk factors of COVID-19 hospitalization and death among the U.S. elderly.[64]

VSD

In addition, the Vaccine Safety Datalink (VSD) is a collaborative project between CDC's Immunization Safety Office and nine health care organizations. As noted on the CDC's webpage, the VSD started in 1990 and continues today in order to monitor safety of vaccines and conduct studies about rare and serious adverse events following immunization.

The VSD uses electronic health data from each participating site. This includes information on vaccines: the kind of vaccine given to each patient, date of vaccination, and other vaccinations given on the same day. The VSD also uses information on medical illnesses that have been diagnosed at doctors' offices, urgent care visits, emergency department visits, and

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of GBS following high-dose influenza vaccinations and Shingrix vaccinations during the 2018-2019 influenza season. CBER, CDC, and CMS formed working groups in February 2019 to refine these safety signals in the CMS data.

[64] Hector S Izurieta, David J Graham, Yixin Jiao, Mao Hu, Yun Lu, Yue Wu, Yoganand Chillarige, Michael Wernecke, Mikhail Menis, Douglas Pratt, Jeffrey Kelman, Richard Forshee, *Natural History of Coronavirus Disease 2019: Risk Factors for Hospitalizations and Deaths Among >26 Million US Medicare Beneficiaries*, The Journal of Infectious Diseases, Volume 223, Issue 6, 15 March 2021, Pages 945-956, https://doi.org/10.1093/infdis/jiaa767 https://academic.oup.com/jid/article/223/6/945/6039057.

hospital stays. The VSD conducts vaccine safety studies based on questions or concerns raised from the medical literature and reports to the Vaccine Adverse Event Reporting System (VAERS). When there are new vaccines that have been recommended for use in the United States or if there are changes in how a vaccine is recommended, the VSD will monitor the safety of these vaccines.

The VSD has a long history of monitoring and evaluating the safety of vaccines. Since 1990, investigators from the VSD have published many studies to address vaccine safety concerns.[65]

In summary, in collaboration and coordination with several different partners, FDA has assembled passive surveillance systems-including VAERS-and active surveillance systems that can detect and refine safety findings with the Authorized COVID-19 Vaccines in a relatively rapid manner. These systems can also potentially be leveraged to assess safety in specific subpopulations and to assess vaccine effectiveness.

ii. Articles Submitted in Petition Regarding Vaccine Surveillance

We note at the outset that Petitioner raises concerns regarding the methodology by which CDC calculated rates of anaphylactic adverse events post-vaccination. Such concerns are best directed to CDC and are outside the scope of FDA's Petition response.

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[65] *See, e.g.,* CDC, *White Paper on the Safety of the Childhood Immunization Schedule*, Vaccine Safety Datalink, available at https://www.cdc.gov/vaccinesafety/pdf/WhitePaperSafety_WEB.pdf.

Regarding Petitioner's contention that a low percentage of adverse events have been reported to VAERS and that therefore "the safety of COVID vaccines is considerably worse than it currently appears" (Petition at 4), as explained in detail above in this section, VAERS is only one part of a multi-tiered vaccine safety surveillance system, so the information derived from VAERS reports does not represent the full extent of vaccine safety information being monitored by FDA and its federal partners.

Specifically, Petitioner cites to three studies in support of the argument that "[g]iven that only 1 to 13% of adverse reactions have been reported to the FDA and CDC via the VAERS passive reporting system, according to Lazarus et al., the high number of adverse events and deaths following COVID vaccines is alarming." Petition at 5. The articles cited by Petitioner in support of this contention do not support Petitioner's position that, due to underreporting of adverse events, the rate of reported adverse events associated with COVID-19 vaccination is low in comparison to the actual rate of adverse events. As discussed above in this section, there are several factors unique to the surveillance of the Authorized COVID-19 Vaccines that have contributed to the number of VAERS reports submitted for these vaccines. Petitioner's argument that adverse events associated with the Authorized COVID-19 Vaccines are underreported because of the figures presented in the articles cited fail to account for any of those factors that are unique to the Authorized COVID-19 Vaccines.

Petitioner cites to a publication from the Agency for Healthcare Research and Quality (Lazarus et al.) in support of the argument that deaths and adverse

events associated with the Authorized COVID-19 Vaccines are underreported because "only 1 to 13% of adverse reactions have been reported to the FDA and CDC via the VAERS passive reporting system" (Petition at 5), and therefore the actual rate of COVID-19 Vaccine adverse events is significantly higher than reported.[66] As an initial matter, we note that the language cited from the Lazarus article is referring to adverse event reporting for drugs and vaccines, not just vaccine adverse events reported to VAERS.[67] Furthermore, as explained in detail above, several factors have contributed to the number of VAERS reports submitted for the Authorized COVID-19 Vaccines. The issues raised in this article regarding underreporting of drug adverse event reporting are not directly relevant to the claims Petitioner makes regarding adverse event reporting for the Authorized COVID-19 Vaccines. The article was published in 2010 and does not consider the numerous factors outlined above regarding reporting of adverse events following COVID-19 vaccination.

Petitioner cites to a journal article in the publication *Vaccine*[68] regarding VAERS safety monitoring in support of their argument that adverse

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[66] Lazarus et al., *Electronic Support for Public Health-Vaccine Adverse Event Reporting System*, Agency for Healthcare Research and Quality, HHS (Sept. 30, 2010), https://digital.ahrq.gov/ahrq-funded-projects/electronic-support-public-health-vaccine-adverse-event-reporting-system.

[67] *Id.* at 6.

[68] Shimabukuro et al., *Safety monitoring in the Vaccine Adverse Event Reporting System (VAERS)*, Vaccine (Nov. 4, 2015), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4632204/.

event reports for the Authorized COVID-19 Vaccines are underreported. This article generally discusses the limitations of VAERS and passive surveillance, which are well-understood by the FDA and which are discussed in this letter. Additionally, this article notes "[p]erhaps the two most common misconceptions about VAERS are that temporally associated reports represent true adverse reactions caused by vaccination, and that VAERS reports equate to rates of adverse events or indicate risk of adverse events associated with vaccination."[69] This statement from the article demonstrates the flaws underlying Petitioner's claims that the Authorized COVID-19 Vaccines are unsafe due to the number of serious adverse events reported to VAERS following administration of these vaccines. Additionally, the article notes "[t]he relatively rapid increase in numbers of reports to VAERS following the introduction and initial uptake of a new vaccine, an expected occurrence, has been misinterpreted as actual increases in incidence of adverse events and vaccine related risk."[70] Thus, the article cited by Petitioner directly contradicts Petitioner's claims regarding the safety of the Authorized COVID-19 Vaccines based on the number of VAERS adverse event reports associated with these vaccines.

Finally, Petitioner also cites to a journal article in the American Journal of Public Health.[71] This article

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[69] *Id.* at 9.

[70] *Id.*

[71] S. Rosenthal and R. Chen, T*he reporting sensitivities of two passive surveillance systems for vaccine adverse events*, American Journal of Public Health (Dec. 1995), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1615747/.

does not raise issues that have not already been addressed in this letter's discussion of safety surveillance. For instance, the article notes that passive surveillance has several limitations, specifically, passive surveillance may involve underreporting of adverse events, and passive surveillance data is not adequate to determine causation. Additionally, this article notes that passive surveillance can provide valuable information, "[n]evertheless, if reporting is reasonably consistent, it may be possible to detect changes in trends of known common adverse events."[72]

Therefore, the articles submitted by Petitioner do not present data or information regarding the Authorized COVID-19 Vaccines that change the Agency's analysis regarding the benefits and risks of the Authorized COVID-19 Vaccines.

Petitioner further asserts that extensive safety information regarding vaccines is inaccessible to the public ("the VAERS database is the only safety database to which the public has access. The government withholds extensive safety information from the public despite having at least ten additional data sources and expert consultants to analyze these data. . . . " Petition at 2.). This contention represents a misunderstanding by Petitioner of the sources of data analyzed by FDA and its federal partners, and of the types of information available to the public.

As noted above, Petitioner's questions regarding databases operated by other federal partners, such as DOD, CMS, CDC, VA, should be directed to those federal entities. Regarding FDA's BEST system, Petitioner

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[72] *Id.*

erroneously claims that the public does not have access to the information on this system. As noted above, the BEST system,[73] which is part of the Sentinel initiative,[74] comprises large-scale claims data, electronic health records (EHR), and linked claims-EHR databases with a data lag of approximately three months. The system makes use of multiple data sources and enables rapid queries to detect or evaluate adverse events as well as studies to answer specific safety questions for vaccines. The system is not intended to be a source of raw EHR data. Instead, as explained on FDA's webpage describing the BEST system, the purpose of the BEST system is to: (1) build data, analytics, infrastructure for an active, large-scale, efficient surveillance system for biologic products; and (2) develop innovative methods to utilize electronic health records (EHR) effectively and establish automated adverse events reporting, utilizing natural language processing and artificial intelligence.[75] BEST does not have access to the raw, identifiable data. BEST data partners analyze the raw data per publicly posted protocols and send the results in aggregated form to BEST for review. The information is summarized in either final reports, manuscripts or public presentations. BEST publicly posts study protocols of surveillance activities on the

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[73] CBER *Biologics Effectiveness and Safety (BEST) System*, https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/cber-biologics-effectiveness-and-safety-best-system.

[74] FDA's Sentinel Initiative, https://www.fda.gov/safety/fdas-sentinel-initiative.

[75] CBER Biologics Effectiveness and Safety (BEST) System, https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/cber-biologics-effectiveness-and-safety-best-system.

BEST site with open public comments regarding the protocols, final reports and manuscripts as well as communication on CBER safety site and public meetings, *e.g.*, VRBPAC, where appropriate. These protocols delineate the scientific approach to analyzing the raw data, where in the raw form is of limited utility to the public, to generate information on vaccine safety. The final reports and manuscripts summarize the information and conclusions inferred from well-conducted surveillance studies.

iii. FDA Has Responded to Safety Signals Related to the Authorized COVID-19 Vaccines by Extensively Reviewing Data, Updating the Authorized Labeling, and Communicating to the Public

Petitioner further asserts that "FDA and CDC have not responded to these data by issuing any warnings or restricting the use of these vaccines." Petition at 2. This assertion is inaccurate. As explained in detail above, FDA and its federal partners, including CDC, have closely monitored post-market safety data regarding the Authorized COVID-19 Vaccines. FDA has worked to identify and investigate serious adverse events occurring in people after receiving the Authorized COVID-19 Vaccines, and to communicate these risks to the public and revise the authorized labeling to reflect these risks in a timely fashion.[76] The

[76] Janssen COVID-19 Vaccine Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers), Sections 5.2 and 5.3 Warnings and Precautions Regarding Thrombosis with Thrombocytopenia and GBS, https://www.fda.gov/media/146304/download; Pfizer-BioNTech COVID-19 Vaccine Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination

surveillance systems that are in place to monitor the safety of COVID-19 vaccines authorized for emergency use are working, as demonstrated by FDA's and CDC's work to identify and investigate these serious adverse events in a timely manner.

Adverse events reported to VAERS following administration of one of the authorized COVID-19 vaccines are reviewed to assess possible safety concerns. Such review of VAERS data regarding the authorized COVID-19 vaccines has been conducted since these vaccines were authorized. Such review has prompted the Agency to take action with respect to the currently authorized COVID-19 vaccines:

- On April 13, 2021, FDA and CDC recommended a pause in the use of the Janssen COVID-19 vaccine following six VAERS reports in the U.S. of thrombosis with thrombocytopenia.[77] The FDA and CDC thoroughly reviewed VAERS and other post-authorization information and data related

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Providers), Section 5.2, Warning and Precautions Regarding Myocarditis and Pericarditis, https://www.fda.gov/media/144413/download; Moderna COVID-19 Vaccine Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers), Section 5.2, Warning and Precautions Regarding Myocarditis and Pericarditis, https://www.fda.gov/media/144637/download.

[77] We note that Petitioner mentions that Denmark, among other nations, has "banned" the Janssen COVID-19 vaccine. To the extent Petitioner relies on this ban as support for Petitioner's request that FDA revoke the EUA for this vaccine, we note that Denmark and other nations' actions with respect to the use of this vaccine are outside purview of FDA's work, so we cannot comment on decisions they make under their public health regulatory framework.

to the Janssen COVID-19 vaccine during the recommended pause. This review included two meetings of ACIP. Following a thorough safety review, FDA determined that the available data show that the Janssen COVID-19 vaccine's known and potential benefits outweigh its known and potential risks in individuals 18 years of age and older. As a result of this review, the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) was updated to include a Warning pertaining to the risk of thrombosis with thrombocytopenia. The Fact Sheet for Recipients and Caregivers was also updated to include information about these serious adverse events. The FDA and CDC conducted extensive outreach to providers and clinicians to ensure they were made aware of the potential for these adverse events and could properly recognize and manage thrombosis with thrombocytopenia in individuals who receive the Janssen COVID-19 Vaccine.

- On June 25, 2021, following review of VAERS reports, FDA required revisions to the authorized labeling for the Pfizer-BioNTech COVID-19 vaccine and the Moderna COVID-19 vaccine to add a warning regarding the suggested increased risks of myocarditis and pericarditis. This update to the authorized labeling for these vaccines followed an extensive review of information and the discussion by CDC's ACIP meeting on June 23, 2021. As of July 26, 2021, the FDA and the Centers for Disease Control and Prevention (CDC) have received 1,194 reports of myocarditis or pericarditis occurring among people ages 30 and

younger who received either Moderna or Pfizer-BioNTech COVID-19 vaccines, particularly following the second dose.[78] Through follow-up, including medical record reviews, the FDA and CDC had confirmed 699 cases of myocarditis or pericarditis.[79]

- On July 13, 2021, FDA required revisions to the vaccine recipient and vaccination provider fact sheets for the Janssen COVID-19 Vaccine to include information pertaining to a suggested increased risk of Guillain-Barré Syndrome (GBS) during the 42 days following vaccination. Based on an analysis of Vaccine Adverse Event Reporting (VAERS) data, at that time, there had been 100 reports of presumptive GBS following vaccination with the Janssen vaccine after approximately 12.5 million doses administered. Of these reports, 95 of them were serious and required hospitalization. There was one reported death. As noted in the Janssen Fact Sheet for Healthcare Providers Administering Vaccine, because these reactions are reported voluntarily, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure. Each year in the United States, an estimated 3,000 to 6,000 people develop GBS. Most people fully recover from the disorder. FDA publicly presented this issue, and information

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[78] CDC, *COVID-19 Reported Adverse Events*, https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/adverse-events.html.

[79] *Id.*

regarding these 100 reports of presumptive GBS, to the ACIP on July 22, 2021.[80]

During each of these post-authorization reviews and labeling changes, the FDA has evaluated the available post-authorization information for the authorized COVID-19 Vaccines and continues to find the known and potential benefits clearly outweigh the known and potential risks.

iv. Petitioner's Claims Regarding Anaphylaxis

Petitioner cites to a study of acute allergic reactions to mRNA COVID-19 vaccines in support of their argument that adverse event rates for COVID-19 vaccines have been miscalculated by CDC.[81] As stated above, questions relating to CDC are best directed to that Agency. We note, however, that this journal article states, immediately after the sentence quoted by Petitioner, "[h]owever, the overall risk of anaphylaxis to an mRNA COVID-19 vaccine remains extremely low and largely comparable to other common health care exposures. Although cases were clinically compatible with anaphylaxis, the mechanism of these reactions is unknown." The paper further states, in describing the limitations of the study, that "[a]

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[80] FDA, CDC ACIP Meeting Presentation, Guillain-Barré Syndrome (GBS) after Janssen COVID-19 Vaccine: Vaccine Adverse Event Reporting System (VAERS), July 22, 2021, https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-07/02-COVID-Alimchandani-508.pdf.

[81] Blumenthal KG, Robinson LB, Camargo CA, et al., *Acute Allergic Reactions to mRNA COVID-19 Vaccines*, JAMA. 2021;325(15):1562–1565. doi:10.1001/jama.2021.3976, https://jamanetwork.com/journals/jama/fullarticle/2777417.

northeastern US cohort may not be generalizable." Thus, Petitioner is inappropriately generalizing the results of this study in an attempt to compare the results to the CDC's reported data and conclude that the safety of COVID vaccines is "considerably worse than it currently appears." Petition at 4.

Additionally, we note that the authorized labeling for all the Authorized COVID-19 vaccines already contain warnings regarding the risk of anaphylaxis as a potential adverse event. Thus, the risk of anaphylaxis is a potential safety issue FDA is already aware of, and Petitioner's argument, and the article submitted in support of this argument, does not change FDA's conclusions regarding the safety of the Authorized COVID-19 vaccines.

v. Animal Toxicology and Pharmacokinetic Studies of COVID-19 Vaccines

Petitioner raises concerns regarding FDA's vaccine safety assessment. Specifically, Petitioner states that other "problems with vaccine safety assessment may exist because of inadequate animal toxicology and pharmacokinetic studies of COVID vaccines." Petition at 5; emphasis added. As an initial matter, we note that Petitioner's concerns regarding the vaccine safety assessment for COVID-19 vaccines involves speculation regarding whether problems actually exist ("problems with vaccine safety assessment may exist . . . "), and Petitioner fails to point to any specific problems that result or may result from the allegedly inadequate studies.

Regarding Petitioner's claims, in general, when evaluating the safety data regarding a vaccine, FDA

considers data from animal studies (if such pre-clinical studies were performed) as one part of the full body of evidence regarding the vaccine. In addition to data from animal studies, if available, FDA evaluates data from in vitro studies and conducts a safety assessment of data from clinical studies.

Thus, although Petitioner raises several concerns and cites to several articles regarding risks of COVID-19 vaccination, FDA is not aware of any information indicating that the known and potential benefits of the Authorized COVID-19 Vaccines are outweighed by their known and potential risks, nor has Petitioner provided any such information in the Petition. Therefore, the criterion under section 564(c)(2)(B) continues to be met with respect to the Authorized COVID-19 Vaccines.

4. No Alternatives

As noted above, Petitioner requests that "FDA should revoke all EUAs and refrain from approving any future EUA . . . for any COVID vaccine for all demographic groups because the current risks of serious adverse events or deaths outweigh the benefits, and because existing, approved drugs provide highly effective prophylaxis and treatment against COVID, mooting the EUAs." Petition at 1. Section 564(c)(3) of the FD&C Act provides one of the required statutory factors that must be met in order for a product to be granted an EUA. This statutory provision requires that "there is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating [the serious or life-threatening disease or

condition]."[82] To the extent Petitioner's contention can be interpreted as an argument that there are adequate, approved, available drugs indicated for the prevention of COVID-19 (and that therefore the requirement in section 564(c)(3) of the FD&C Act that there is no "adequate, approved, and available alternative to the Authorized COVID-19 Vaccines for preventing COVID-19 is not met), this argument is erroneous.

As explained in the Decision Review Memoranda for the Authorized COVID-19 Vaccines, at the time each COVID-19 vaccine EUA was issued, there were no FDA-approved drugs or biological products indicated to prevent COVID-19 in any population because no vaccine or other medical product was the subject of an approved marketing application for prevention of COVID-19.[83] This is still true today, with the exception of the BLA for BioNTech's COVID-19 vaccine (COVID-19 Vaccine, mRNA; Comirnaty), which is now approved for the prevention of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. The EUA for Pfizer-BioNTech COVID-

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[82] The term "approved," for purposes of section 564(c) of the FD&C Act, means a product is approved, licensed, or cleared by FDA under section 505, 510(k), or 515 of the FD&C Act or section 351 of the PHS Act, as applicable, and this term is indication-specific. *See*, section 564(a)(2) of the FD&C Act. *See also,* EUA guidance at 3.

[83] FDA, P*fizer-BioNTech COVID-19 Vaccine EUA Decision Memorandum* (Dec. 11, 2020), at 8-9, https://www.fda.gov/media/144416/download; FDA, M*oderna COVID-19 Vaccine EUA Decision Memorandum* (Dec. 18, 2020), at 9, https://www.fda.gov/media/144673/download; FDA, *Janssen COVID-19 Vaccine EUA Decision Memorandum* (Feb. 27, 2021), at 9, https://www.fda.gov/media/146338/download.

19 Vaccine remains in effect. This EUA will continue to cover individuals 12 through 15 years of age, to cover the administration of a third dose to certain immunocompromised individuals 12 years of age and older, and to cover individuals 16 years of age and older until sufficient approved vaccine can be manufactured and distributed. Similarly, the EUA for the Moderna COVID-19 Vaccine and the Janssen COVID-19 Vaccine remain in effect for individuals 18 years of age and older. Although FDA has approved one new drug application (NDA) for remdesivir for use in adult and pediatric patients 12 years of age and older and weighing at least 40 kilograms for the treatment of COVID-19 requiring hospitalization, this drug is not for prevention of COVID-19. Several other therapies are currently available under EUA, but not FDA approved, for treatment of COVID-19, and one is available under EUA, but not FDA approved, for post-exposure prophylaxis in a limited population. These products that are available under EUA are not considered "approved" products for purposes of section 564(c)(3) because they are not the subject of an approved marketing application (*i.e.*, they are not approved under an NDA or BLA).

Thus, Petitioner's assertion that the EUAs for the Authorized COVID-19 Vaccines are "mooted" by the existence of drugs approved to prevent COVID-19 is incorrect.

5. 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 other 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.[84]

As of the date of this writing, FDA has not identified any such circumstances that would make revocation of any of the Authorized COVID-19 Vaccines appropriate to protect the public health or safety. As stated previously in this response, FDA determined

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84 EUA Guidance at 29.

the EUA standard is met for the three authorized COVID-19 vaccines because data submitted by the sponsors demonstrated in a clear and compelling manner that the known and potential benefits of these products, when used to prevent COVID-19, outweigh the known and potential risks of these products, and that there is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating COVID-19.

As described in detail in section III.b.i.1.b above, FDA has identified circumstances that have made revision of the EUAs for the Authorized COVID-19 Vaccines appropriate, and, accordingly, has required changes to the authorized labeling for the Authorized COVID-19 Vaccines.[85]

Additionally, as explained above, FDA finds no basis in the information submitted in the Petition, or in any postmarket data regarding the Authorized COVID-19 Vaccines, to support a revocation of any of these EUAs, nor has Petitioner provided any such information in the Petition. FDA is not aware of any information indicating that the known and potential benefits of the Authorized COVID-19 Vaccines are

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[85] FDA, Pfizer-BioNTech COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization in Individuals 12-15 Years of Age (May 10, 2021), Section 4.6, EUA Prescribing Information and Fact Sheets, https://www.fda.gov/media/148542/download; FDA, Pfizer-BioNTech COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization of an Additional Dose in Certain Immunocompromised Individuals (August 12, 2021), https://www.fda.gov/media/151613/download; FDA, Moderna COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization of an Additional Dose in Certain Immunocompromised Individuals (August 12, 2021), https://www.fda.gov/media/151611/download.

outweighed by their known and potential risks, nor has Petitioner provided any such information in the Petition. Furthermore, there are no other circumstances that make a revision or revocation appropriate to protect the public health or safety, nor has Petitioner provided any information about such circumstances.

FDA therefore sees no justifiable basis upon which to take any action based on Petitioner's request with respect to the any of the Authorized COVID-19 Vaccines. Accordingly, as noted above, we deny Petitioner's request for FDA to "revoke all EUAs . . . for any COVID vaccine for all demographic groups because existing, approved drugs provide highly effective prophylaxis and treatment against COVID, mooting the EUAs."

2. Petitioner's Request to Refrain from Granting any Future EUA for a COVID-19 Vaccine for any Population Because Approved Drugs Exist for COVID-19 Prevention

Petitioner also requests in the Petition that FDA "refrain from approving any future EUA . . . for any COVID vaccine for all demographic groups because the current risks of serious adverse events or deaths outweigh the benefits, and because existing, approved drugs provide highly effective prophylaxis and treatment against COVID, mooting the EUAs."[86] Petition at 1.

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[86] FDA authorization of an EUA request is not FDA approval. FDA does not "approve" an EUA request. Rather, FDA authorizes the emergency use of a product following review of data and information submitted in an EUA request.

Petitioner has provided no evidence that would provide a basis for FDA to conclude that no future COVID-19 vaccine candidate could meet the EUA standard. Indeed, FDA is not aware of any information indicating that the known and potential benefits of the Authorized COVID-19 Vaccines are outweighed by their known and potential risks, nor has Petitioner provided any such information in the Petition.

Additionally, as explained above in section III.b.i.1.b. of this letter, to the extent Petitioner's contention can be interpreted as an argument that there are FDA-approved drugs indicated for the prevention of COVID-19 (and that therefore the requirement in section 564(c)(3) of the FD&C Act that there is no "adequate, approved, and available alternative" could not be met), this argument fails. Should FDA receive future requests for EUAs for COVID-19 vaccine candidates, FDA would consider such requests on a case-by-case basis.[87] Accordingly, Petitioner's request is denied.

3. Petitioner's Request to Refrain from Approving any Future NDA for any COVID-19 Vaccine for any Population

Petitioner's request regarding "any future . . . NDA . . . for any COVID Vaccine for all demographic groups" is moot because vaccines are biological products subject to licensure under the PHS Act and

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[87] FDA has issued guidance describing factors the Agency intends to use in determining how to prioritize EUA requests for COVID-19 vaccine candidates. See October 2020 Guidance at 5 (citing EUA Guidance at 18-20).

are not subject to approval under section 505 of the FD&C Act.

4. Petitioner's Request to Refrain from Licensing any Future BLA for any COVID-19 Vaccine for any Population

Petitioner requests that FDA "refrain from approving any future . . . BLA for any COVID vaccine for all demographic groups because the current risks of serious adverse events or deaths outweigh the benefits, and because existing, approved drugs provide highly effective prophylaxis and treatment against COVID, mooting the EUAs." Petition at 1. To the extent this request can be interpreted as asserting that the risks of serious adverse events or deaths associated with any COVID-19 vaccine would necessarily outweigh the benefits of any COVID-19 vaccine and therefore FDA should refrain from approving any BLA for any COVID-19 vaccine, this section explains why this argument is unavailing and why we are denying Petitioner's request.

To the extent this request can be interpreted as also asserting, in addition to the assertion above, that, because approved drugs provide effective prophylaxis and treatment of COVID-19, the approval of a BLA for a COVID-19 vaccine would be "moot," this section explains why such a position is flawed and why FDA is not granting this request.

a. Petitioner's Request that FDA Refrain from Approving any BLA for any COVID-19 Vaccine because the Current Risks Outweigh the Benefits

Petitioner requests that FDA "refrain from approving any future BLA . . . for any COVID vaccine for all demographic groups" because the risks of serious adverse events or deaths associated with any COVID-19 vaccine outweigh the benefits of any COVID-19 vaccine. Petitioner has provided no evidence that would provide a basis for FDA to conclude that no COVID-19 vaccine could meet the BLA approval standard, however. Indeed, FDA has now approved a BLA for BioNTech's COVID-19 vaccine (COVID-19 Vaccine, mRNA; Comirnaty) because, among other things, the data and information in the application demonstrated the safety and effectiveness of the vaccine.[88] Thus, Petitioner's request that FDA refrain from approving any BLAs for COVID-19 vaccines is denied.

In Appendix I to this letter, we have provided additional background information about FDA's regulatory framework for the review of vaccine BLAs.

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[88] See FDA's Summary Basis for Regulatory Action (SBRA) for the BioNTech BLA. This memorandum will be posted on www.fda.gov.

b. Petitioner's Request that FDA Refrain from Approving any BLA for any COVID-19 Vaccine because the Current Risks Outweigh the Benefits and because Currently-Approved Drugs are Effective in Preventing COVID-19

To the extent Petitioner is arguing that FDA should also refrain from approving a BLA for any COVID-19 vaccine because of the existence of FDA-approved drugs that are effective in preventing COVID-19, this argument is unavailing. As described above in section III.b.i.1, there are no FDA-approved drugs that are effective in preventing COVID-19 (other than BioNTech'sCOVID-19 vaccine [COVID-19 Vaccine, mRNA; Comirnaty], which is now approved for the prevention of COVID-19 caused by SARS-CoV-2 in individuals 16 years of age and older.).

For the reasons outlined in this section, FDA denies Petitioner's requests to refrain from licensing any BLAs for a COVID-19 vaccine.

ii. Petitioner's Requests Regarding COVID-19 Vaccines in Children

1. Request to Immediately Refrain from Allowing COVID-19 Vaccine Trials to Include Pediatric Subjects

In the Petition, Petitioner requests that FDA "immediately refrain from allowing minors to participate in COVID vaccine trials. . . . " Petition at 1. To the extent that the Petition can be interpreted to request that FDA suspend any COVID-19 vaccine clinical trial that includes pediatric subjects, this section

explains why FDA is not at this time ordering that these clinical trials be suspended.

As explained above in section III.a., with certain exceptions, clinical investigations in which a drug is administered to human subjects must be conducted under an IND submitted to FDA by the sponsor. FDA's review of an IND includes a review of the study protocol which describes, among other things, the design of the clinical study, including the identified endpoints and methods for assessing the safety and effectiveness of the investigational product. The Petition requests that FDA adopt a universal approach toward all clinical trials of COVID-19 vaccines. Under FDA's regulations, however, the Agency examines each Investigational New Drug (IND) Application individually and considers the IND in the context of the standards in the regulation.

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; 21 U.S.C. 355(i)(3)). FDA's implementing regulations in 21 CFR 312.42 identify the circumstances that may justify a clinical hold. In this section of this letter, we explain why, at this time, FDA has not granted Petitioner's request to place all proposed or ongoing studies of COVID-19 vaccines enrolling pediatric subjects on clinical hold under 21 CFR 312.42(b).

The grounds for placing a proposed or ongoing study, including an ongoing Phase 3 study, on clinical hold are provided in 21 CFR 312.42(b). Specifically, 21 CFR 312.42(b)(1)(i) through (b)(1)(v) provides grounds for imposition of a clinical hold of a Phase 1 study. Additionally, as stated in 21 CFR 312.42(b)(2), FDA

may place a proposed or ongoing Phase 2 or 3 investigation on clinical hold if it finds that: (i) any of the conditions in 21 CFR 312.42(b)(1)(i) through (b)(1)(v) apply; or (ii) the plan or protocol for the investigation is clearly deficient in design to meet its stated objectives. As indicated in more detail below, at this time, FDA has not granted Petitioner's request to place all proposed or ongoing studies of COVID-19 vaccines enrolling pediatric subjects on clinical hold under 21 CFR 312.42(b).

- 21 CFR 312.42(b)(1)(i): Human subjects are or would be exposed to an unreasonable and significant risk of illness or injury.

  > FDA continues to evaluate all available information and, based on this evaluation thus far, does not believe that human subjects in any COVID-19 vaccine study that includes pediatric subjects are or would be exposed to an unreasonable and significant risk of illness or injury. The Agency reviews the protocols for COVID-19 vaccine clinical trials proposing to enroll pediatric subjects when they are submitted to the IND, in addition to any subsequent protocol amendments. For those clinical trials that have proceeded to studying COVID-19 vaccines in pediatric populations, FDA has determined that, based on all information currently available to FDA, the studies do not expose subjects to unreasonable risks.

- 21 CFR 312.42(b)(1)(ii): The clinical investigators named in the IND are not qualified by

reason of their scientific training and experience to conduct the investigation described in the IND.

> The Petitioner has not provided evidence and FDA is currently aware of no other information indicating that clinical investigators named in the IND for any COVID-19 vaccine clinical trial including pediatric subjects are not qualified by reason of their scientific training and experience to conduct the investigation described in the INDs.

- 21 CFR 312.42(b)(1)(iii): The investigator brochure is misleading, erroneous, or materially incomplete.

  > The Petitioner has not provided evidence and FDA is currently aware of no other information indicating that the investigator brochures for any ongoing COVID-19 vaccine investigation which includes or proposes to include pediatric subjects are misleading, erroneous, or materially incomplete.

- 21 CFR 312.42(b)(1)(iv): The IND does not contain sufficient information required under 312.23 to assess the risks to subjects of the proposed studies.

  > The Petitioner has not provided evidence and FDA is currently aware of no other information indicating that the IND for any ongoing COVID-19 vaccine in which pediatric subjects are enrolled contains insufficient information required under 21 CFR 312.23 to assess the risks to pediatric subjects participating in the studies.

- 21 CFR 312.42(b)(1)(v) [provides, in part, that]: The IND is for the study of an investigational drug intended to treat a life-threatening disease or condition that affects both genders, and men or women with reproductive potential who have the disease or condition being studied are excluded from eligibility because of a risk or potential risk from use of the investigational drug of reproductive toxicity (*i.e.*, affecting reproductive organs) or developmental toxicity (*i.e.*, affecting potential offspring). . . .

  > The Petitioner has not provided evidence and FDA is currently aware of no other information indicating that any COVID-19 vaccine studies enrolling pediatric subjects are excluding from eligibility men or women – including male and female adolescents and teenagers-with reproductive potential.

- 21 CFR 312.42(b)(2)(ii): The plan or protocol for the Phase 2 or Phase 3 investigation is clearly deficient in design to meet its stated objectives.

  > The Agency reviewed the protocols for the COVID-19 vaccine investigations involving pediatric subjects at the time they were submitted to the INDs, as well as any subsequent amendments as they were submitted, and has determined that the study designs meets their stated objectives.
  >
  > At this time, the Agency is aware of no information to indicate that the protocols for any ongoing clinical investigations of

> COVID-19 vaccines involving pediatric subjects are clearly deficient in design to meet their stated objectives.

FDA has reviewed the issues raised in the Petition relating to the request to "immediately refrain from allowing minors to participate in COVID vaccine trials." Petition at 1. For the reasons outlined above, and in light of information currently available to FDA, FDA has determined that grounds do not exist to grant Petitioner's request to place all COVID-19 vaccine clinical investigations involving pediatric subjects on clinical hold pursuant to 21 CFR 312.42.

2. Request that FDA Refrain from Issuing EUA Amendments for Authorized COVID-19 Vaccines to Include Indications for Pediatric Populations

The Petition requests, among other things, that "[g]iven the extremely low risk of COVID illness in children, FDA should . . . immediately refrain from amending EUAs to include children. . . . " Petition at 1. To the extent that the Petition requests that FDA refrain from issuing EUA amendments for any of the Authorized COVID-19 Vaccines to include an indication for use in pediatric populations, this section explains why FDA is not granting this request.

In determining whether to issue an EUA for a product, including an amendment to an EUA in order to include additional populations within the indication, the FDA evaluates the available evidence and assesses, among other things, any known or potential risks and any known or potential benefits. Once a manufacturer submits an EUA request for a COVID-19 vaccine, the FDA then evaluates the request and determines

whether the relevant statutory criteria are met, taking into account the totality of the scientific evidence about the vaccine that is available to the agency.

As noted in Section II.b. above, in the October 2020 Guidance, FDA provided recommendations that describe key information that would support issuance of an EUA for a vaccine to prevent COVID-19.[89] In this guidance, FDA explained that, in the case of such 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 pre-clinical and human clinical study data on the product, and the totality of the available scientific evidence relevant to the product.[90] 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.[91]

a. Information Submitted by Petitioner Regarding the Safety of COVID-19 Vaccines in Pediatric Populations

Petitioner argues that, for children, the risks of COVID-19 vaccines outweigh the benefits because the risk of severe COVID in children is "extremely low."

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[89] October 2020 Guidance at 6-7.

[90] *Id.* at 3.

[91] *Id.* at 4.

Petition at 1. Petitioner cites to several sources of information in support of this argument (Petition at 12-13), which FDA has reviewed and considered.

Petitioner cites to CDC data[92] regarding death rates of children in the United States due to COVID-19 and compares the number of children who have died involving COVID-19 to the number of Americans of all ages who have died of COVID-19. Petitioner's approach of simply comparing raw numbers of deaths involving COVID-19 in the U.S. pediatric population against the raw numbers of deaths involving COVID-19 in the overall U.S. population (all sexes and all ages), does not provide a sufficient scientific basis upon which to conclude, as Petitioner contends, that the "relative risk for children due to COVID is very low." Petition at 12. Additionally, as discussed in further detail below, based on available data and information, we have concluded that COVID-19 is a serious or life-threatening disease or condition in the 12-17 age group.

As a preliminary matter, we note that petitioner's claim that "the death rate following either vaccination in this age group, assuming these children were trial enrollees, is approximately 2 in 2,000 or 0.1%." (Petition at 13) is erroneous. Our review of the submitted clinical trial data associated with the Pfizer-BioNTech COVID-19 Vaccine has not identified any deaths among adolescent or young adult vaccinees.[93]

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[92] CDC, National Center for Health Statistics, Weekly Updates by Select Demographic and Geographic Characteristics,_https://www.cdc.gov/nchs/nvss/vsrr/covid_weekly/index.htm#SexAndAge.

[93] FDA, *Pfizer-BioNTech COVID-19 Vaccine EUA Decision Memorandum* (Dec. 11, 2020), https://www.fda.gov/media/144416/

Additionally, as described in a NEJM article regarding the Moderna COVID-19 vaccine, no deaths were reported among vaccine recipients enrolled in the clinical trial of Moderna COVID-19 Vaccine.[94] Investigational New Drug (IND) application sponsors are required to notify FDA in a written safety report of any adverse experience associated with the use of the drug that is both serious and unexpected.[95] Any death that occurs in a vaccine clinical trial therefore must be reported to FDA and is then thoroughly evaluated by FDA to determine the cause and whether or not the death is plausibly related to the vaccine.

Additionally, we note that Petitioner raised concerns regarding VAERS reports in arguing that COVID-19 vaccines should not be authorized for pediatric populations because, Petitioner argues, "[a]vailable evidence strongly suggests that the vaccine is much more dangerous to children than the disease." Petition at 12. VAERS data reviewed to date has not identified risks related to vaccination that would cause the Agency to change its view that the benefits of vaccination with the Pfizer-BioNTech COVID-19 vaccine outweigh the risks of vaccination in individuals 12-17 years of age.

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download (stating that there were two deaths in vaccine recipients, both >55 years of age). FDA, *Pfizer-BioNTech COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization in Individuals 12-15 Years of Ag*e (May 10, 2021), https://www.fda.gov/media/148542/download (stating that there were no deaths among vaccine recipients 12-15 years of age during the follow-up period).

[94] K. Ali, et al., *Evaluation of mRNA-1273 SARS-CoV-2 Vaccine in Adolescents*, NEJM (Aug. 11, 2021), DOI: 10.1056/NEJMoa2109522, https://www.nejm.org/doi/10.1056/NEJMoa2109522.

[95] 21 CFR § 312.32(c)(1)(i).

VAERS data is evaluated thoroughly, and as described in greater detail above, FDA acts on safety signals. VAERS reports, however, are not used in isolation to draw an association between a vaccine and a possible adverse event.

Finally, we note that petitioner cites to an opinion piece published in the British Medical Journal, which presents the authors' opinion that the benefits of COVD-19 vaccination are outweighed by its risks in pediatric populations.[96] FDA has reviewed this article and determined it does not present evidence that the EUA standard could not be met for pediatric populations. Indeed, as explained in the FDA Decision Memorandum for the Pfizer-BioNTech COVID-19 Vaccine EUA, based on FDA's review of all available data regarding the benefits and risks of the use of the Pfizer-BioNTech COVID-19 vaccine in individuals 12 through 17 years of age, we have determined that this EUA meets the statutory criteria for individuals in this age range.[97]

Petitioner has failed to present data demonstrating that, for children, the risks of COVID-19 vaccines outweigh their benefits because the risk of severe COVID

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[96] W. Pegden, V. Prasad, S. Baral, *Covid vaccines for children should not get emergency use authorization*, BMJ (May 7, 2021), https://blogs.bmj.com/bmj/2021/05/07/covid-vaccines-for-children-should-not-get-emergency-use-authorization/.

[97] FDA, *Pfizer-BioNTech COVID-19 Vaccine EUA Decision Memorandum* (Dec. 11, 2020), https://www.fda.gov/media/144416/download; FDA, *Pfizer-BioNTech COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization in Individuals 12-15 Years of Age* (May 10, 2021), https://www.fda.gov/media/148542/download.

in children is "extremely low." Petition at 1. As explained in this section, the information submitted by Petitioner does not support this contention. As explained in further detail below, data reviewed by the Agency demonstrates that the Pfizer-BioNTech COVID-19 Vaccine, which is authorized for use in individuals 12 years of age and older, continues to demonstrate that the known and potential benefits of this vaccine outweigh its known and potential risks in this population. Any other EUA requests for COVID-19 vaccine candidates for use in pediatric populations will be reviewed on a case-by-case basis under the applicable statutory standards. Therefore, we deny Petitioner's request to refrain from amending any EUA for a COVID-19 vaccine to include a pediatric indication.

3. Request that FDA Immediately Revoke all EUAs for COVID19 Vaccines with Pediatric Indications

Petitioner requests that FDA "immediately revoke all EUAs that permit vaccination of children under 16 for the Pfizer vaccine and under 18 for other COVID vaccines." Petition at 1. Currently, only the Pfizer-BioNTech COVID-19 vaccine is indicated for the prevention of COVID-19 in pediatric populations. This vaccine is indicated for individuals 12 years of age and older. As explained in section III.B.i.1.b above, in addressing this request, it is necessary to consider the EUA revocation standard provided in section 564(g)(2) of the FD&C Act. In this section, we assess whether any of these statutory conditions under which FDA may revoke an EUA are met with respect to the pediatric indication for the Pfizer-BioNTech COVID-19 Vaccine EUA and explain why the EUA revocation standard is not met for this vaccine.

a. Standard for Revocation of EUAs is not Met for the Authorized COVID-19 Vaccines with Pediatric Indications

As explained above in section III.b.i.1.b of this letter, 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.

As explained above in section II.b., the EUA Guidance 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])."[98]

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[98] EUA Guidance at 28.

i. Circumstances Continue to Justify the Issuance of the EUAs for the Authorized COVID-19 Vaccine with Pediatric Indications

As explained in detail above in section III.b.i.1.b., section 564(b)(2) of the FD&C Act sets forth the statutory standard for termination of an EUA declaration. This provision provides that an EUA declaration remains in place until the earlier of: (1) a determination by the HHS Secretary, in consultation with the Secretary of Defense, that the circumstances that precipitated the declaration have ceased or (2) a change in the approval status of the product such that the authorized use(s) of the product are no longer unapproved. Neither of those statutory criteria is satisfied with respect to the Authorized COVID-19 Vaccine with a pediatric indication. Thus, the circumstances described under section 564(b)(1) of the FD&C Act continue to exist. FDA therefore is not revoking the EUA for the Authorized COVID-19 vaccine with a pediatric indication under the authority in section 564(g)(2)(A) of the FD&C Act.

1. The Criteria for The Issuance of the Authorized COVID-19 Vaccine with Pediatric Indications Continues to Be Met

This section describes in detail why the criteria under section 564(c) of the FD&C Act continue to be met with respect to the pediatric indication for the Pfizer-BioNTech COVID-19 Vaccine EUA and why, therefore, FDA may not revoke this EUA under the authority in section 564(g)(2)(B) of the FD&C Act.

a. Serious or life-threatening disease or condition.

As explained above in section III.b.i.1 of this letter, section 564(c)(1) of the FD&C Act requires that, for an EUA to be issued for a medical product, "the agent(s) referred to in [the HHS Secretary's EUA declaration] can cause a serious or life-threatening disease or condition." FDA has concluded that SARS-CoV-2, which is the subject of the EUA declaration, meets this standard. 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 August 3, 2021, has caused more than 199 million cases of COVID-19 and claimed the lives of more than 4.2 million people worldwide.[99] In the United States, more than 34 million cases and over 611,000 deaths have been reported to the CDC.[100] On January 31, 2020, the U.S. Secretary of Health and Human Services (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 FDA

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[99] Johns Hopkins University School of Medicine, Coronavirus Resource Center, https://coronavirus.jhu.edu/map.html.

[100] CDC, COVID Data Tracker, https://covid.cdc.gov/covid-data-tracker/#trends_dailytrendscases.

Decision Memoranda for the Authorized COVID-19 Vaccines.[101]

Since March 1, 2020, approximately 1.7 million COVID-19 cases in individuals 12 to 17 years of age have been reported to the Centers for Disease Control and Prevention (CDC). Among these cases approximately 11,700 resulted in hospitalization, with more than 691 ICU admissions and more than 100 deaths. It is difficult to estimate the incidence of COVID-19 among children and adolescents because they are frequently asymptomatic and infrequently tested. Chil dren and adolescents appear less susceptible to SARS-CoV-2 infection and have a milder COVID-19 disease course as compared with adults. However, as with adults, children and adolescents 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 illness from COVID-19, most have had underlying medical 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

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101 FDA, *Pfizer-BioNTech COVID-19 Vaccine EUA Decision Memorandum* (Dec. 11, 2020), https://www.fda.gov/media/144416/download; FDA, *Pfizer-BioNTech COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization in Individuals 12-15 Years of Age* (May 10, 2021), https://www.fda.gov/media/148542/download; FDA, *Moderna COVID-19 Vaccine EUA Decision Memorandum* (Dec. 18, 2020), https://www.fda.gov/media/144673/download; FDA, *Janssen COVID-19 Vaccine EUA Decision Memorandum* (Feb. 27, 2021), https://www.fda.gov/media/146338/download.

June 28, 2021, the CDC received reports of 4196 cases and 37 deaths that met the definition for MIS-C.

Both FDA and CDC have convened advisory committee meetings to discuss the use of COVID-19 vaccines in pediatric populations. Overall, these advisory committees agreed that there is a serious risk of severe COVID-19 in the pediatric population. In particular, the June 23, 2021 ACIP meeting discussed the benefits and risks of the use of COVID-19 mRNA vaccines in adolescents and young adults.[102] This discussion raised the point that adolescents and young adults have the highest COVID-19 incidence rates, and that these populations are an increasing proportion of COVID-19 cases reported. COVID-19-associated deaths continue to occur in these populations; since April 2021, 316 deaths have been reported among persons aged 12-29 years. Additionally, post-COVID conditions—such as Multisystem Inflammatory Syndrome in Children (MIS-C) and Multisystem Inflammatory Syndrome in Adults (MIS-A)—can occur in these populations following COVID-19.

Therefore, the criterion under section 564(c)(1) continues to be met with respect to the Authorized COVID-19 Vaccines with Pediatric Indications.

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[102] CDC, Megan Wallace and Sara Oliver, CDC ACIP Meeting Presentation, *COVID-19 mRNA Vaccines in Adolescents and Young Adults: Benefit-Risk Discussion*, (June 23, 2021), https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-06/05-COVID-Wallace-508.pdf; CDC, ACIP Meeting Slides, (June 23, 2021), https://www.cdc.gov/vaccines/acip/meetings/slides-2021-06.html.

b. Evidence of Effectiveness

As explained above in section III.b.i.1.b of this letter, Section 564(c)(2)(A) of the FD&C Act requires that, for an EUA to be issued for a medical product, FDA must conclude "based on the totality of scientific evidence available to the Secretary, including data from adequate and well-controlled trials, if available, it is reasonable to believe that the product may be effective to prevent, diagnose, or treat such serious or life-threatening disease or condition that can be caused by SARS-CoV-2." 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 Pfizer-BioNTech COVID-19 vaccine may be effective to prevent, diagnose, or treat such serious or life-threatening disease or condition in the 12 through 17 years of age population.[103] The basis for this determination is explained in detail in FDA's decision memoranda regarding the Pfizer BioNTech COVID-19 Vaccine EUA.[104] Section III.b.ii of this letter explains why Petitioner's arguments regarding the effectiveness of the Authorized COVID-

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[103] FDA, *Pfizer-BioNTech COVID-19 Vaccine EUA Decision Memorandum* (Dec. 11, 2020), https://www.fda.gov/media/144416/download; FDA, *Pfizer-BioNTech COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization in Individuals 12-15 Years of Age* (May 10, 2021), https://www.fda.gov/media/148542/download.

[104] FDA, *Pfizer-BioNTech COVID-19 Vaccine EUA Decision Memorandum* (Dec. 11, 2020), https://www.fda.gov/media/144416/download; FDA, *Pfizer-BioNTech COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization in Individuals 12-15 Years of Age* (May 10, 2021), https://www.fda.gov/media/148542/download.

19 Vaccines, and the information submitted by Petitioner in support of this argument, does not change FDA's analysis regarding the effectiveness of the Pfizer-BioNTech COVID-19 vaccine in individuals 12 through 17 years of age.

Therefore, the criterion under section 564(c)(2)(A) continues to be met with respect to the Authorized COVID-19 Vaccines.

c. Benefit-Risk Analysis

Section 564(c)(2)(B) of the FD&C Act requires that, for an EUA to be issued for a medical product, FDA must conclude "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. . . . " Petitioner argues that the current risks of serious adverse events or deaths associated with the authorized COVID-19 vaccines outweigh the benefits of COVID-19 vaccines in the pediatric population. Section III.b.i.1.b.ii above addresses these arguments insofar as they apply to the Authorized COVID-19 Vaccines generally and explains why they are unavailing. Section III.b.ii above addresses Petitioner's arguments regarding the safety of COVID-19 vaccines in the pediatric population, and explains why the information submitted by Petitioner does not change FDA's analysis regarding the benefits and risks of the authorized COVID-19 vaccines in the pediatric population.

d. No Alternatives

Section 564(c)(3) of the FD&C Act provides one of the required statutory factors that must be met in

order for a product to be granted an EUA. This statutory provision requires that "there is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating [the serious or life-threatening disease or condition]." To the extent Petitioner's contention can be interpreted as an argument that there are FDA-approved drugs indicated for the prevention of COVID-19 in pediatric populations (and that therefore the requirement in section 564(c)(3) of the FD&C Act is not met with respect to the Authorized COVID-19 Vaccine with a pediatric indication), this argument is erroneous.

As described above in section III.b.i.1.b, there are no FDA-approved drugs or biological products indicated to prevent COVID-19 in any population, other than the newly-approved BioNTech COVID-19 vaccine (COVID-19 Vaccine, mRNA; Comirnaty). That vaccine is approved for the prevention of COVID-19 caused by SARS-CoV-2 in individuals 16 years of age and older.[105] The EUA for Pfizer-BioNTech COVID-19 Vaccine remains in effect to cover those 12 through 15 years of age, the administration of a third dose to certain immunocompromised individuals 12 years of age and older, and until sufficient approved vaccine can be manufactured and distributed for use in those 16 years of age and older. Similarly, the EUA for the Moderna COVID-19 Vaccine and the Janssen COVID-19 Vaccine

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[105] FDA, *Pfizer-BioNTech COVID-19 Vaccine EUA Decision Memorandum* (Dec. 11, 2020), at 8-9, https://www.fda.gov/media/144416/download; FDA, Moderna *COVID-19 Vaccine EUA Decision Memorandum* (Dec. 18, 2020), at 9, https://www.fda.gov/media/144673/download; FDA, *Janssen COVID-19 Vaccine EUA Decision Memorandum* (Feb. 27, 2021), at 9, https://www.fda.gov/media/146338/download.

remain in effect for individuals 18 years of age and older. Therefore, there is no adequate, approved, and available alternative to the Authorized COVID-19 Vaccines for preventing COVID-19.

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

As noted above in section III.b.i.1.b of this letter, 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 other 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.[106]

As of the date of this writing, FDA has not identified any such circumstances that would make revocation of the pediatric indication for the Pfizer-BioNTech COVID-19 Vaccine EUA appropriate to protect the public health or safety. As stated previously in this response, FDA determined the EUA standard is met for the Pfizer-BioNTech COVID-19 Vaccine in individuals 12 through 17 years of age because data submitted by the sponsors demonstrated in a clear and compelling manner that the known and potential benefits of this vaccine, when used to prevent COVID-19, outweigh the known and potential risks of this vaccine in individuals 12 through 17 years of age, and that there is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating COVID-19 in this population.

As described in detail in section III.b.i.1 above, FDA has identified circumstances that have made revision of the EUAs for the Authorized COVID-19 Vaccines appropriate, and, accordingly, has required changes to the authorized labeling for the Authorized COVID-19 Vaccines.[107]

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[106] EUA Guidance at 29.

[107] FDA, *Pfizer-BioNTech COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization in Individuals 12-15 Years of Age* (May 10, 2021), https://www.fda.gov/media/148542/download; FDA, *Pfizer-BioNTech COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization of an Additional Dose in Certain Immunocompromised Individuals* (August 12, 2021), https://www.fda.gov/media/151613/download; FDA, *Moderna COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization of an Additional Dose in Certain*

Additionally, as explained above, FDA finds no basis in the information submitted in the Petition, or in any postmarket data regarding the Pfizer-BioNTech COVID-19 Vaccine, to support a revocation of the pediatric indication for the Pfizer-BioNTech COVID-19 Vaccine EUA, nor has Petitioner provided any such information in the Petition. FDA is not aware of any information indicating that the known and potential benefits of Pfizer-BioNTech COVID-19 Vaccine in the 12-17 years of age population are outweighed by their known and potential risks, nor has Petitioner provided any such information in the Petition. Furthermore, there are no other circumstances that make a revision or revocation of the pediatric indication for the Pfizer-BioNTech COVID-19 Vaccine EUA appropriate to protect the public health or safety, nor has Petitioner provided any information about such circumstances. FDA therefore sees no justifiable basis upon which to take any action based on Petitioner's request with respect to the pediatric indication for the Pfizer-BioNTech COVID-19 Vaccine EUA. Accordingly, as noted above, we deny Petitioner's request that FDA "immediately revoke all EUAs that permit vaccination of children under 16 for the Pfizer vaccine and under 18 for other COVID vaccines." Petition at 1.

Immunocompromised Individuals (August 12, 2021), https://www.fda.gov/media/151611/download; FDA, *Janssen COVID-19 Vaccine EUA Decision Memorandum* (Feb. 27, 2021), https://www.fda.gov/media/146338/download.

iii. Petitioner's Request that FDA Immediately Revoke Tacit Approval that Pregnant Women may Receive any EUA or Licensed COVID-19 Vaccines and Immediately Issue Public Guidance

Petitioner requests that FDA "immediately revoke tacit approval that pregnant women may receive any EUA or licensed COVID vaccines and immediately issue public guidance to that effect." Petition at 1. Because "tacit approval," or revocation thereof, is not a concept that exists in applicable statutes or regulations governing FDA-regulated products, FDA interprets this as a request that the labeling for the Authorized COVID-19 Vaccines, and any COVID-19 vaccine that may be licensed in the future, contain a contraindication for use during pregnancy.

In addressing Petitioner's request for a contraindication, we first discuss the risks posed to pregnant women by COVID-19. We then provide an explanation of the regulatory framework for prescription drug labeling for approved and licensed products, including the standard for inclusion of contraindications in such labeling to inform health care providers of information such as known hazards in the use of a particular drug as well as the requirements for pregnancy and lactation information in such labeling. We then discuss labeling for products made available under an EUA and explain why a contraindication for use in pregnant women was not included in the labeling for the Authorized COVID-19 Vaccines. This section concludes with an explanation for why Petitioner's requests for a contraindication for use during pregnancy in the labeling for the Authorized COVID-19 Vaccines –

and BioNTech's COVID-19 vaccine (COVID-19 Vaccine, mRNA; Comirnaty)-is denied.

1. COVID-19 in Pregnancy

As a preliminary matter, we note that COVID-19 poses significant risks to pregnant women. CDC explains that "observational data regarding COVID-19 during pregnancy demonstrate that pregnant people with COVID-19 have an increased risk of severe illness, including illness resulting in intensive care admission, mechanical ventilation, extracorporeal membrane oxygenation, or death, though the absolute risk for these outcomes is low. Additionally, they are at increased risk of preterm birth and might be at an increased risk of adverse pregnancy complications and outcomes, such as preeclampsia, coagulopathy, and stillbirth."[108]

2. Certain Content and Format Requirements for Prescription Drug Labeling for Products Approved Under NDAs or BLAs

As FDA explains in the draft guidance for industry, Pregnancy, Lactation, and Reproductive Potential: Labeling for Human Prescription Drug and Biological Products – Content and Format, ("Pregnancy and Lactation Guidance") "[p]rescription

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[108] CDC, *Interim Clinical Considerations for Use of COVID-19 Vaccines Currently Authorized in the United States, Vaccination of Pregnant or Lactating People*, https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fvaccines%2Fcovid-19%2Finfo-by-product%2Fclinical-considerations.html#pregnant.

drug labeling is a communication tool. Its principal objective is to make available to health care providers the detailed prescribing information necessary for the safe and effective use of a drug, in a manner that is clear and useful to providers when prescribing for and counseling patients."[109] In order to achieve this objective, prescription labeling must be based on scientific data, and it must not be inaccurate, false, or misleading.[110]

FDA regulations govern the content and format of prescription drug labeling for approved drugs and biological products (*see*, *e.g.*, §§ 201.56 and 201.57 (21 CFR 201.57); *see also* 21 CFR 201.100(c)). The regulations are intended to organize labeling information to more effectively communicate to health care professionals the "information necessary for the safe and effective use of prescription drugs."[111] FDA regulations

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[109] *Pregnancy, Lactation, and Reproductive Potential: Labeling for Human Prescription Drug and Biological Products-Content and Format Guidance for Industry*, Draft Guidance, July 2020, at 2, https://www.fda.gov/media/90160/download.

[110] 21 CFR § 201.56(a)(2) "The labeling must be informative and accurate and neither promotional in tone nor false or misleading in any particular. In accordance with §§ 314.70 and 601.12 of this chapter, the labeling must be updated when new information becomes available that causes the labeling to become inaccurate, false, or misleading."

[111] Preamble to final rule, "Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products" (71 FR 3922 at 3928, January 24, 2006) (Physician Labeling Rule). For the content and format requirements for the labeling of older prescription drug products that are not subject to the labeling requirements in § 201.57, see § 201.80 (21 CFR 201.80). The specific labeling requirements for older drug

require that the labeling of most prescription drug products include Highlights of Prescribing Information, which are intended to summarize the information that is most important for prescribing the drug safely and effectively and to facilitate access to the more detailed information within product labeling (see § 201.57(a)). FDA regulations further require that the labeling for most prescription drugs include, among other information, the following sections: Contraindications; Warnings and Precautions; Adverse Reactions; and Use in Specific Populations, which includes a subsection on Pregnancy (see § 201.57(c)(1), (5), (6), (7), and (9)(i)).

a. Contraindications

The Contraindications section must describe any situations in which the drug should not be used because the risk of use "clearly outweighs any possible therapeutic benefit" (§ 201.57(c)(5)). This section should include observed and anticipated risks, but not theoretical risks.[112] This could include, for example, a situation where animal data raise substantial concern about the potential for occurrence of the adverse reaction in humans (*e.g.*, animal data demonstrate that the drug has teratogenic effects) and those risks

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products differ in certain respects, and generally are not referenced in this response.

[112] See § 201.57(c)(5); *see also* FDA guidance for industry, Warnings and Precautions, Contraindications, and Boxed Warning Sections of Labeling for Human Prescription Drug and Biological Products-Content and Format; Guidance for Industry, October 2011 (Warnings Guidance), at 8, https://www.fda.gov/media/71866/download.

do not outweigh any potential benefit of the drug to any patient.[113]

b. Pregnancy

The Pregnancy subsection is located under the Use in Specific Populations section (*see* § 201.57 (c)(9)(i)). On December 4, 2014, FDA issued a final rule amending the regulations on the requirements for pregnancy and lactation information in prescription drug and biological product labeling (Pregnancy and Lactation Labeling Rule (PLLR)).[114] The PLLR revisions to the regulations were intended "to create a consistent format for providing information about the effects of a drug on pregnancy and lactation that would be useful for decision making by health care providers and their patients."[115] The labeling content and format requirements in § 201.57(c)(9)(i), as revised by the PLLR, took effect on June 30, 2015, with a phased implementation schedule for drugs (including biological products) that are the subject of NDAs, BLAs, and efficacy supplements that had been approved on or after June 30, 2001.[116] The PLLR also requires for all

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[113] See Warnings Guidance at 8.

[114] Final rule, "Content and Format of Labeling for Human Prescription Drug and Biological Products; Requirements for Pregnancy and Lactation Labeling" (PLLR) (79 FR 72064, December 4, 2014), https://www.federalregister.gov/documents/2014/12/04/2014-28241/content-and-format-of-labeling-for-human-prescription-drug-and-biological-products-requirements-for.

[115] *Id.* at 72066.

[116] *See* §§ 201.56(b) and 201.57(c)(9)(i).

human prescription drug and biological products, including those for which an application was approved before June 30, 2001, that the Pregnancy subsection of labeling be revised to remove the pregnancy letter categories A, B, C, D, and X.[117]

Information in the Pregnancy subsection of labeling may present, in greater detail, a topic that is briefly summarized in another section of labeling (*e.g.*, Warnings and Precautions).[118] FDA has explained that when a topic is discussed in more than one section of labeling, the section containing the most important information relevant to prescribing should typically include a succinct description and should cross-reference sections that contain additional detail.[119]

Under current labeling requirements, information in the Pregnancy subsection of labeling is presented under the following subheadings: Pregnancy Exposure Registry; Risk Summary; Clinical Considerations; and Data.[120] The labeling for the Authorized COVID-19 Vaccines includes the Pregnancy Exposure Registry and the Risk Summary subheadings. We briefly describe these subheadings below.

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[117] §§ 201.57(c)(9) and 201.80; *see also* 79 FR 72064 at 72095 (December 4, 2014).

[118] PLLR, 79 FR 72064 at 72085 (December 4, 2014).

[119] See FDA guidance for industry, Labeling for Human Prescription Drug and Biological Products-Implementing the PLR Content and Format Requirements; Guidance for Industry, February 2013, https://www.fda.gov/media/71836/download.

[120] § 201.57(c)(9)(i).

i. Pregnancy Exposure Registry

If there is a scientifically acceptable pregnancy exposure registry for the drug, the labeling must state that fact and provide contact information needed for enrolling in or obtaining information about the registry.

ii. Risk Summary

The Risk Summary subheading is required under the Pregnancy subsection because certain statements must be included even when no product-specific data are available, given that all pregnancies have a background risk of birth defect, loss, or other adverse outcomes.[121] The Risk Summary must contain risk statement(s) that describe for the drug the risk of adverse developmental outcomes based on all relevant human data, animal data, and/or the drug's pharmacology.[122] When multiple data sources are available, the risk statements are required to be presented in the following order: human, animal, and pharmacologic.[123]

When human data are available that establish the presence or absence of any adverse developmental outcome(s) associated with maternal use of the drug, a risk statement based on human data must summarize the specific developmental outcome(s) and include its incidence and the effects of dose, duration of exposure, and gestational timing of exposure.[124] If human data indicate that there is an increased risk for a specific

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[121] § 201.57(c)(9)(i)(B).

[122] *Id.*

[123] *Id.*

[124] § 201.57(c)(9)(i)(B)(1).

adverse developmental outcome in infants born to women exposed to the drug during pregnancy, the risk summary must contain a quantitative comparison of that risk to the risk for the same outcome in infants born to women who were not exposed to the drug, but who have the disease or condition for which the drug is indicated to be used.[125] When risk information is not available for women with the disease or condition(s) for which the drug is indicated, the risk summary must contain a comparison of the specific outcome in women exposed to the drug during pregnancy against the rate at which the outcome occurs in the general population.[126]

When animal data are available, the risk statement based on such data must describe the potential risk for adverse developmental outcomes in humans and summarize the available data.[127] This statement must include: the number and type(s) of species affected; timing of exposure; animal doses expressed in terms of human dose or exposure equivalents; and outcomes for pregnant animals and offspring.[128]

With respect to pharmacology, when the drug has a well-understood pharmacologic mechanism of action that may result in adverse developmental outcomes,

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[125] *Id.*

[126] *Id.*

[127] § 201.57(c)(9)(i)(B)(2).

[128] *Id.*

the Risk Summary must explain the mechanism of action and the potential associated risks.[129]

3. Inclusion of Contraindications and Pregnancy Information in the Labeling for the Authorized COVID-19 Vaccines

For the emergency use of an unapproved product, section 564(e)(1)(A)(i) of the FD&C Act requires that FDA must—to the extent practicable given the applicable circumstances of the emergency, and as FDA finds necessary and appropriate to protect the public health—establish appropriate conditions designed to ensure that health care professionals administering the authorized product are informed:

That FDA has authorized the emergency use of the product (including the product name and an explanation of its intended use);

Of the significant known and potential benefits and risks of the emergency use of the product, and the extent to which such benefits and risks are unknown; and

Of available alternatives and their benefits and risks.

Therefore, as explained in the EUA Guidance, FDA recommends that "a request for an EUA include a 'Fact Sheet' for health care professionals or authorized dispensers that includes essential information about the product. In addition to the required information, Fact Sheets should include . . . any contraindications

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[129] § 201.57(c)(9)(i)(B)(3).

or warnings."[130] The EUA guidance also recommends that, for unapproved drugs that do not have "FDA-approved labeling for any indication . . . in addition to the brief summary information found in a Fact Sheet, the sponsor also develop more detailed information similar to what health care professionals are accustomed to finding in FDA-approved package inserts."[131]

The sponsors for all the Authorized COVID-19 Vaccines submitted such prescribing information in the EUA requests, and FDA reviewed and authorized this labeling. The Fact Sheets for Healthcare Providers Administering Vaccine for all of the Authorized COVID-19 Vaccines contain Contraindications and Warnings and Precautions sections because FDA determined that sufficient data existed for inclusion of such information in the authorized labeling for these vaccines.[132]

FDA did not, however, require inclusion of a contraindication for pregnancy in the authorized

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[130] EUA Guidance at 22.

[131] EUA Guidance at 23.

[132] Janssen COVID-19 Vaccine Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers), Sections 5.2 and 5.3 Warnings and Precautions Regarding Thrombosis with Thrombocytopenia and GBS, https://www.fda.gov/media/146304/download; Pfizer-BioNTech COVID-19 Vaccine Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers), Section 5.2, Warning and Precautions Regarding Myocarditis and Pericarditis, https://www.fda.gov/media/144413/download Moderna COVID-19 Vaccine Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers), Section 5.2, Warning and Precautions Regarding Myocarditis and Pericarditis, https://www.fda.gov/media/144637/download.

labeling. The authorized COVID-19 vaccines are authorized for use in an age range that includes women of childbearing age and are not contraindicated for use in pregnant women because FDA is not aware of any evidence that suggests the risk of use of the Authorized COVID-19 Vaccines in pregnant women would clearly outweigh any possible therapeutic benefit.[133] Nor has the Petitioner presented any such evidence in the Petition. Accordingly, this request is denied.

4. Inclusion of Contraindications and Pregnancy Information in the Labeling for Licensed COVID-19 Vaccines

With respect to Petitioner's request that FDA "immediately revoke tacit approval that pregnant women may receive any EUA or licensed COVID vaccines and immediately issue public guidance to that effect" (Petition at 1; emphasis added), as explained above in this section, FDA regulations require the Contraindications section of the labeling for an approved drug or biological product to describe any situations in which the drug or biological product should not be used because the risk of use "clearly outweighs any possible therapeutic benefit" (§ 201.57(c)(5)).

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[133] FDA's decision memoranda for the Authorized COVID-19 Vaccines discuss FDA's analysis of all available data regarding the use of the Authorized COVID-19 Vaccines in pregnancy. *See*, FDA, *Pfizer-BioNTech COVID-19 Vaccine EUA Decision Memorandum* (Dec. 11, 2020), https://www.fda.gov/media/144416/download; FDA, *Moderna COVID-19 Vaccine EUA Decision Memorandum* (Dec. 18, 2020), https://www.fda.gov/media/144673/download; FDA, *Janssen COVID-19 Vaccine EUA Decision Memorandum* (Feb. 27, 2021), https://www.fda.gov/media/146338/download.

This section should include observed and anticipated risks, but not theoretical risks.[134] The approved COVID-19 vaccine (COVID-19 Vaccine, mRNA; Comirnaty) is indicated for use in an age range that includes women of childbearing age and is not contraindicated for use in pregnant women because FDA is not aware of any evidence that suggests the risk of use of BioNTech's COVID-19 vaccine in pregnant women would clearly outweigh any possible therapeutic benefit,[135] nor has the Petitioner presented any such evidence in the Petition.

In its review of a BLA for any future COVID-19 vaccine candidate, FDA will apply the regulatory standards outlined above in determining, on a case-by-case basis, whether to include a contraindication in pregnancy, or any other contraindications, in the approved labeling for such a vaccine. Accordingly, Petitioner's request is denied.

iv. Petitioner's Request that FDA Immediately Amend its Guidance regarding Certain Approved Drugs [chloroquine drugs, ivermectin, "and any other drugs demonstrated to be safe and effective against COVID"]

Petitioner requests that the Agency "immediately amend its existing guidance for the use of the chloroquine drugs, ivermectin, and any other drugs demonstrated to be safe and effective against COVID, to

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[134] See § 201.57(c)(5); *see also* Warnings Guidance at 8.

[135] See FDA's Summary Basis for Regulatory Action (SBRA) for the BioNTech BLA. This memorandum will be posted on www.fda.gov.

comport with current scientific evidence of safety and efficacy at currently used doses and immediately issue notifications to all stakeholders of this change." Petition at 2. FDA has not issued "guidance for the use of chloroquine drugs, ivermectin, and other drugs demonstrated to be safe and effective against COVID."[136] FDA has, however, analyzed adverse event information and made publicly available safety issues regarding the use of hydroxychloroquine and chloroquine to treat patients with COVID-19.[137] FDA has

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[136] Under FDA's good guidance practices regulations, a "guidance document" is defined as "documents prepared for FDA staff, applicants/sponsors, and the public that describe the agency's interpretation of or policy on a regulatory issue." 21 CFR 10.115(a)(b)(1). The regulation provides further that "[g]uidance documents include, but are not limited to, documents that relate to: The design, production, labeling, promotion, manufacturing, and testing of regulated products; the processing, content, and evaluation or approval of submissions; and inspection and enforcement policies." Importantly, the provision at 21 CFR 10.115(b)(3), excludes from the definition of "guidance document" general information documents provided to consumers or health professionals, such as those communications that have been provided to the public regarding the use of hydroxychloroquine, chloroquine, and ivermectin to treat patients with COVID-19. 21 CFR 10.115(b)(3) states: "[g]uidance documents do not include: Documents relating to internal FDA procedures, agency reports, general information documents provided to consumers or health professionals, speeches, journal articles and editorials, media interviews, press materials, warning letters, memoranda of understanding, or other communications directed to individual persons or firms." (Emphasis added.)

[137] FDA Drug Safety Communication, FDA cautions against use of hydroxychloroquine or chloroquine for COVID-19 outside of the hospital setting or a clinical trial due to risk of heart rhythm problems, April 24, 2020, updated June 15, 2020 and July 1, 2020, https://www.fda.gov/drugs/drug-safety-and-availability/fda-cautions-against-use-hydroxychloroquine-or-chloroquine-

also informed the public that it has received multiple reports of patients who have required medical support and been hospitalized after self-medicating with ivermectin intended for horses, that taking large doses of ivermectin can cause serious harm, that ivermectin is not authorized or approved by FDA to treat COVID-19, and that using any treatment for COVID-19 that is not approved or authorized by the FDA, unless part of a clinical trial, can cause serious harm.[138] You have not provided any evidence to suggest that the safety information in these communications is inaccurate. Thus, to the extent you are requesting that FDA withdraw or revise these previous safety communications, that request is denied.

v. Petitioner's Request that FDA Issue Guidance to the Secretary of Defense and the President

Petitioner requests that FDA "issue guidance to the Secretary of the Defense and the President not to grant an unprecedented Presidential waiver of prior

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covid-19-outside-hospital-setting-or; FDA, CDER Office of Surveillance and Epidemiology Pharmacovigilance Memorandum, May 19, 2020, https://www.accessdata.fda.gov/drugsatfda_docs/nda/2020/OSE%20Review_Hydroxychloroquine-Cholorquine%20-%2019May2020_Redacted.pdf.

[138] FDA Consumer Update, Why You Should Not Use Ivermectin to Treat or Prevent COVID-19, March 5, 2021, https://www.fda.gov/consumers/consumer-updates/why-you-should-not-use-ivermectin-treat-or-prevent-covid-19; FDA Letter to Stakeholders, Do Not Use Ivermectin Intended for Animals as Treatment for COVID-19 in Humans, April 10, 2020, https://www.fda.gov/animal-veterinary/product-safety-information/fda-letter-stakeholders-do-not-use-ivermectin-intended-animals-treatment-covid-19-humans.

consent regarding COVID vaccines for Servicemembers under 10 U.S.C. § 1107(f) or 10 U.S.C. § 1107a." Petition at 2.

FDA denies this request because FDA, an agency within the U.S. Department of Health and Human Services, does not issue guidance of the type requested to the President of the United States or to other Departments in the executive branch of the U.S. federal government.

vi. Petitioner's Request that FDA Issue Guidance to Stakeholders Regarding the Option to Refuse or Accept Administration of Investigational COVID-19 Vaccines

Petitioner requests that FDA "issue guidance to all stakeholders in digital and written formats to affirm that all citizens have the option to accept or refuse administration of investigational COVID vaccines without adverse work, educational or other non-health related consequences, under 21 U.S.C. § 360 bbb-3(e)(1)(a)(ii)(III) 1 and the informed consent requirements of the Nuremberg Code."[139] We interpret this request to relate to the Authorized COVID-19 Vaccines and third parties' decisions with respect to unvaccinated individuals' participation in certain activities. Such decisions by third parties with respect to employment, education, and other nonFDA-regulated activities would not be within FDA's purview. Accordingly, FDA denies Petitioner's request.

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[139] Concerns about potential State vaccine requirements are better directed to the States. FDA does not mandate use of vaccines.

vii. Petitioner's Request that FDA Issue Guidance Regarding Marketing and Promotion of COVID-19 Vaccines

FDA notes that your Petition discusses statements made by CDC. For requests intended for CDC, you should contact CDC directly.

As explained above in section III.b.i.1.b of this response, the EUA revocation standard in section 564(g)(2) of the FD&C Act is not met for any of the Authorized COVID-19 Vaccines. With respect to Petitioner's request to issue guidance pending revocation of the EUAs for the Authorized COVID-19 Vaccines, we note that the EUA Guidance contains a section regarding advertising for EUA products. As explained in the EUA guidance, FDA may, under section 564(e)(1)(B) of the FD&C Act, on a case-by-case basis and to the extent feasible given the circumstances of a particular public health emergency, establish certain additional conditions that FDA finds to be necessary or appropriate to protect the public health.[140] The EUA guidance explains that, under section 564(e)(4) of the FD&C Act, FDA may place conditions on "advertisements and other promotional descriptive printed matter (*e.g.*, press releases issued by the EUA sponsor) relating to the use of an EUA product, such as requirements applicable to prescription drugs under section 502(n). . . . "[141] FDA's authority under section 564(e)(4) ordinarily does not extend to statements by third parties who have no direct connection with the EUA sponsor.

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[140] EUA Guidance at 26.

[141] *Id.* at 27.

For the Authorized COVID-19 Vaccines, FDA has determined that such conditions are necessary to protect the public health. Accordingly, the Letter of Authorization for each of the Authorized COVID-19 Vaccines contains conditions related to printed matter, advertising, and promotion.[142] Given the current public health emergency, FDA does not see a need to expend the resources necessary to develop and issue additional guidance on this topic. Thus, because FDA has already issued guidance addressing advertising and promotion of EUA products, and because FDA has established conditions related to printed matter, advertising, and promotion for all of the Authorized COVID-19 Vaccines, FDA denies Petitioner's request to issue additional guidance on this issue.

c. Conclusion

FDA has considered Petitioner's requests as they relate to the Authorized COVID-19 Vaccines and the approved COVID-19 Vaccine. For the reasons given in this letter, FDA denies the requests in Petitioner's citizen petition. Therefore, we deny the Petition in its entirety.

Sincerely,

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

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[142] FDA, *Pfizer-BioNTech COVID-19 Vaccine Letter of Authorization* (Aug. 12, 2021), https://www.fda.gov/media/150386/download; FDA, *Moderna COVID-19 Vaccine Letter of Authorization* (Aug. 12, 2021), https://www.fda.gov/media/144636/download; FDA, *Janssen COVID-19 Vaccine Letter of Authorization* (June 10, 2021), https://www.fda.gov/media/146303/download.

Appendix I: Aspects of Vaccine Development and Process for Licensure

A. Vaccines are Biologics and Drugs

Vaccines are both biological products under the Public Health Service Act (PHS Act) (42 U.S.C. § 262) and drugs under the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. § 321). The PHS Act defines a "biological product" as including a "vaccine . . . or analogous product . . . applicable to the prevention, treatment, or cure of a disease or condition of human beings." 42 U.S.C. § 262(i)(1). The FD&C Act defines drug to include "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man." 21 U.S.C. § 321(g)(1)(B).

Under the PHS Act, a biological product may not be introduced or delivered for introduction into interstate commerce unless a biologics license is in effect for the product. 42 U.S.C. § 262(a)(1)(A).

B. Clinical Investigations of Vaccines

Before a vaccine is licensed (approved) by FDA and can be used by the public, FDA requires that it undergo a rigorous and extensive development program that includes laboratory research, animal studies, and human clinical studies to determine the vaccine's safety and effectiveness.

The PHS Act and the FD&C Act provide FDA with the authority to promulgate regulations that provide a pathway for the study of unapproved new drugs and biologics. 42 U.S.C. § 262(a)(2)(A) and 21 U.S.C. § 355(i). The regulations on clinical investigations require the submission of an Investigational New

Drug application (IND), which describes the protocol, and, among other things, assures the safety and rights of human subjects. These regulations are set out at 21 CFR Part 312. *See* 21 CFR § 312.2 (explaining that the IND regulations apply to clinical investigations of both drugs and biologics).

The 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, Phase 1 studies typically enroll fewer than 100 participants and are designed to look for very common side effects and preliminary evidence of an immune response to the candidate vaccine. 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 are usually of sufficient size to detect less common adverse events.

If product development is successful and the clinical data are supportive of the proposed indication, the completion of all three phases of clinical development can be followed by submission of a Biologics License Application (BLA) pursuant to the PHS Act (42 U.S.C. § 262(a)), as specified in 21 CFR § 601.2.

C. Biologics License Applications

A BLA must include data demonstrating that the product is safe, pure, and potent and that the facility in which the product is manufactured "meets standards designed to assure that the biological product continues to be safe, pure, and potent." 42 U.S.C. § 262(a)(2)(C)(i). FDA does not consider an application to be filed until FDA determines that all pertinent information and data have been received. 21 CFR § 601.2. FDA's filing of an application indicates that the application is complete and ready for review but is not an approval of the application.

Under § 601.2(a), FDA may approve a manufacturer's application for a biologics license only after the manufacturer submits an application accompanied by, among other things, "data derived from nonclinical laboratory and clinical studies which demonstrate that the manufactured product meets prescribed requirements of safety, purity, and potency." The BLA must provide the multidisciplinary FDA reviewer team (medical officers, microbiologists, chemists, biostatisticians, etc.) with the Chemistry, Manufacturing, and Controls (CMC)[143] and clinical information necessary to make a benefit-risk assessment, and to determine whether "the establishment(s) and the product meet the applicable requirements established in [FDA's regulations]." 21 CFR § 601.4(a).

FDA generally conducts a pre-license inspection of the proposed manufacturing facility, during which production of the vaccine is examined in detail. 42 U.S.C. § 262(c). In addition, FDA carefully reviews

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[143] Also referred to as Pharmaceutical Quality/CMC.

information on the manufacturing process of new vaccines, including the results of testing performed on individual vaccine lots.

FDA scientists and physicians evaluate all the information contained in a BLA, including the safety and effectiveness data and the manufacturing information, to determine whether the application meets the statutory and regulatory requirements. FDA may also convene a meeting of its advisory committee to seek input from outside, independent, technical experts from various scientific and public health disciplines that provide input on scientific data and its public health significance.

As part of FDA's evaluation of a vaccine as a whole, FDA takes all of a vaccine's ingredients into account (including preservatives and adjuvants). FDA licenses a vaccine only after the Agency has determined that the vaccine is safe and effective for its intended use, in that its benefits outweigh its potential risks.

EXHIBIT 5
FDA APPROVAL OF BIONTECH
BIOLOGICS LICENSE APPLICATION

BLA APPROVAL

August 23, 2021

BioNTech Manufacturing GmbH
Attention: Amit Patel
Pfizer Inc.
235 East 42nd Street
New York, NY 10017

Dear Mr. Patel:

Please refer to your Biologics License Application (BLA) submitted and received on May 18, 2021, under section 351(a) of the Public Health Service Act (PHS Act) for COVID-19 Vaccine, mRNA.

Licensing

We are issuing Department of Health and Human Services U.S. License No. 2229 to BioNTech Manufacturing GmbH, Mainz, Germany, under the provisions of section 351(a) of the PHS Act controlling the manufacture and sale of biological products. The license authorizes you to introduce or deliver for introduction into interstate commerce, those products for which your company has demonstrated compliance with establishment and product standards.

Under this license, you are authorized to manufacture the product, COVID-19 Vaccine, mRNA, which is indicated for active immunization to prevent

coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

The review of this product was associated with the following National Clinical Trial (NCT) numbers: NCT04368728 and NCT04380701.

Manufacturing Locations

Under this license, you are approved to manufacture COVID-19 Vaccine, mRNA drug substance at (b)(4)XXXXXXXXXXXXThe final formulated product will be manufactured, filled, labeled and packaged at Pfizer (b)(4)XXXXXXXXXXXThe diluent, 0.9% Sodium Chloride Injection, USP, will be manufactured at (b)(4)XXXXXXXXXXXXXXXXXXXXYou may label your product with the proprietary name, COMIRNATY, and market it in 2.0 mL glass vials, in packages of 25 and 195 vials.

We did not refer your application to the Vaccines and Related Biological Products Advisory Committee because our review of information submitted in your BLA, including the clinical study design and trial results, did not raise concerns or controversial issues that would have benefited from an advisory committee discussion.

Dating Period

The dating period for COVID-19 Vaccine, mRNA shall be 9 months from the date of manufacture when stored between-90°C to-60°C (-130°F to-76°F). The date of manufacture shall be no later than the date of final sterile filtration of the formulated drug product (at (b)(4)XXXXXXXXXXX, the date of manufacture is

defined as the date of sterile filtration for the final drug product; at (b)(4) Pfizer (b)(4)XXXXXXXXXXX, it is defined as the date of the XXXXXXXXXXXXXX Following the final sterile filtration, (b)(4)XXXXX XXXXXXX, no reprocessing/reworking is allowed without prior approval from the Agency. The dating period for your drug substance shall be (b)(4)XXX when stored at (b)(4)XXXX We have approved the stability protocols in your license application for the purpose of extending the expiration dating period of your drug substance and drug product under 21 CFR 601.12.

FDA Lot Release

Please submit final container samples of the product in final containers together with protocols showing results of all applicable tests. You may not distribute any lots of product until you receive a notification of release from the Director, Center for Biologics Evaluation and Research (CBER).

Biological Product Deviations

You must submit reports of biological product deviations under 21 CFR 600.14. You should identify and investigate all manufacturing deviations promptly, including those associated with processing, testing, packaging, labeling, storage, holding and distribution. If the deviation involves a distributed product, may affect the safety, purity, or potency of the product, and meets the other criteria in the regulation, you must submit a report on Form FDA 3486 to the Director, Office of Compliance and Biologics Quality, electronically through the eBPDR web application or at the address below. Links for the instructions on completing the electronic form (eBPDR) may be found on CBER's

web site at https://www.fda.gov/vaccines-blood-biologics/report-problem-center-biologics-evaluation-research/biological-product-deviations:

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
10903 New Hampshire Ave.
WO71-G112
Silver Spring, MD 20993-0002

Manufacturing Changes

You must submit information to your BLA for our review and written approval under 21 CFR 601.12 for any changes in, including but not limited to, the manufacturing, testing, packaging or labeling of COVID-19 Vaccine, mRNA, or in the manufacturing facilities.

Labeling

We hereby approve the draft content of labeling including Package Insert, submitted under amendment 74, dated August 21, 2021, and the draft carton and container labels submitted under amendment 63, dated August 19, 2021.

Content of Labeling

As soon as possible, but no later than 14 days from the date of this letter, please submit the final content of labeling (21 CFR 601.14) in Structured Product Labeling (SPL) format via the FDA automated drug registration and listing system, (eLIST) as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the Package Insert submitted on August 21, 2021. Information on submitting

SPL files using eLIST may be found in the guidance for industry *SPL* Standard for Content of Labeling Technical Qs and As at http://www.fda.gov/downloads /Drugs/GuidanceCompliance RegulatoryInformation/ Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

Carton and Container Labels

Please electronically submit final printed carton and container labels identical to the carton and container labels submitted on August 19, 2021, according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications* at https: //www.fda.gov/regulatory-information/search-fda-guidance-documents/providing-regulatory-submissions-electronic-format-certain-human-pharmaceutical-product-applications.

All final labeling should be submitted as Product Correspondence to this BLA STN BL 125742 at the time of use and include implementation information on Form FDA 356h.

Advertising and Promotional Labeling

You may submit two draft copies of the proposed introductory advertising and promotional labeling with Form FDA 2253 to the Advertising and Promotional Labeling Branch at the following address:

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center

10903 New Hampshire Ave.
WO71-G112
Silver Spring, MD 20993-0002

You must submit copies of your final advertising and promotional labeling at the time of initial dissemination or publication, accompanied by Form FDA 2253 (21 CFR 601.12(f)(4)).

All promotional claims must be consistent with and not contrary to approved labeling. You should not make a comparative promotional claim or claim of superiority over other products unless you have substantial evidence or substantial clinical experience to support such claims (21 CFR 202.1(e)(6)).

Adverse Event Reporting

You must submit adverse experience reports in accordance with the adverse experience reporting requirements for licensed biological products (21 CFR 600.80), and you must submit distribution reports at monthly intervals as described in 21 CFR 600.81. For information on adverse experience reporting, please refer to the guidance for industry *Providing Submissions in Electronic Format —Postmarketing Safety Reports for Vaccines* at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/providing-submissions-electronic-format-postmarketing-safety-reports-vaccines. For information on distribution reporting, please refer to the guidance for industry *Electronic Submission of Lot Distribution Reports* at http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Post-MarketActivities/LotReleases/ucm061966.htm.

Pediatric Requirements

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are deferring submission of your pediatric studies for ages younger than 16 years for this application because this product is ready for approval for use in individuals 16 years of age and older, and the pediatric studies for younger ages have not been completed.

Your deferred pediatric studies required under section 505B(a) of the Federal Food, Drug, and Cosmetic Act (FDCA) are required postmarketing studies. The status of these postmarketing studies must be reported according to 21 CFR 601.28 and section 505B(a)(4)(C) of the FDCA. In addition, section 506B of the FDCA and 21 CFR 601.70 require you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

Label your annual report as an "*Annual Status Report of Postmarketing Study Requirement/Commitments*" and submit it to the FDA each year within 60 calendar days of the anniversary date of this letter until all Requirements and Commitments subject to the reporting requirements under section 506B of the FDCA are released or fulfilled. These required studies are listed below:

1. Deferred pediatric Study C4591001 to evaluate the safety and effectiveness of COMIRNATY in children 12 years through 15 years of age.

Final Protocol Submission: October 7, 2020
Study Completion: May 31, 2023
Final Report Submission: October 31, 2023

2. Deferred pediatric Study C4591007 to evaluate the safety and effectiveness of COMIRNATY in infants and children 6 months to <12 years of age.

Final Protocol Submission: February 8, 2021
Study Completion: November 30, 2023
Final Report Submission: May 31, 2024

3. Deferred pediatric Study C4591023 to evaluate the safety and effectiveness of COMIRNATY in infants <6 months of age.

Final Protocol Submission: January 31, 2022
Study Completion: July 31, 2024
Final Report Submission: October 31, 2024

Submit the protocols to your IND 19736, with a cross-reference letter to this BLA STN BL 125742 explaining that these protocols were submitted to the IND. Please refer to the PMR sequential number for each study/clinical trial and the submission number as shown in this letter.

Submit final study reports to this BLA STN BL 125742. In order for your PREA PMRs to be considered fulfilled, you must submit and receive approval of an efficacy or a labeling supplement. For administrative purposes, all submissions related to these required pediatric postmarketing studies must be clearly designated as:

- Required Pediatric Assessment(s)

We note that you have fulfilled the pediatric study requirement for ages 16 through 17 years for this application.

Postmarketing Requirements Under Section 505(o)

Section 505(o) of the Federal Food, Drug, and Cosmetic Act (FDCA) authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute (section 505(o)(3)(A), 21 U.S.C. 355(o)(3)(A)).

We have determined that an analysis of spontaneous postmarketing adverse events reported under section 505(k)(1) of the FDCA will not be sufficient to assess known serious risks of myocarditis and pericarditis and identify an unexpected serious risk of subclinical myocarditis.

Furthermore, the pharmacovigilance system that FDA is required to maintain under section 505(k)(3) of the FDCA is not sufficient to assess these serious risks.

Therefore, based on appropriate scientific data, we have determined that you are required to conduct the following studies:

4. Study C4591009, entitled "A Non-Interventional Post-Approval Safety Study of the Pfizer-BioNTech COVID-19 mRNA Vaccine in the United States," to evaluate the occurrence of myocarditis and pericarditis following administration of COMIRNATY.

We acknowledge the timetable you submitted on August 21, 2021, which states that you will conduct this study according to the following schedule:

Final Protocol Submission: August 31, 2021
Monitoring Report Submission: October 31, 2022
Interim Report Submission: October 31, 2023
Study Completion: June 30, 2025
Final Report Submission: October 31, 2025

5. Study C4591021, entitled "Post Conditional Approval Active Surveillance Study Among Individuals in Europe Receiving the Pfizer-BioNTech Coronavirus Disease 2019 (COVID-19) Vaccine," to evaluate the occurrence of myocarditis and pericarditis following administration of COMIRNATY.

We acknowledge the timetable you submitted on August 21, 2021, which states that you will conduct this study according to the following schedule:

Final Protocol Submission: August 11, 2021
Progress Report Submission: September 30, 2021
Interim Report 1 Submission: March 31, 2022
Interim Report 2 Submission: September 30, 2022
Interim Report 3 Submission: March 31, 2023
Interim Report 4 Submission: September 30, 2023
Interim Report 5 Submission: March 31, 2024
Study Completion: March 31, 2024
Final Report Submission: September 30, 2024

6. Study C4591021 substudy to describe the natural history of myocarditis and pericarditis following administration of COMIRNATY.

We acknowledge the timetable you submitted on August 21, 2021, which states that you will conduct this study according to the following schedule:

Final Protocol Submission: January 31, 2022
Study Completion: March 31, 2024
Final Report Submission: September 30, 2024

7. Study C4591036, a prospective cohort study with at least 5 years of follow-up for potential long-term sequelae of myocarditis after vaccination (in collaboration with Pediatric Heart Network).

We acknowledge the timetable you submitted on August 21, 2021, which states that you will conduct this study according to the following schedule:

Final Protocol Submission: November 30, 2021
Study Completion: December 31, 2026
Final Report Submission: May 31, 2027

8. Study C4591007 substudy to prospectively assess the incidence of subclinical myocarditis following administration of the second dose of COMIRNATY in a subset of participants 5 through 15 years of age.

We acknowledge the timetable you submitted on August 21, 2021, which states that you will conduct this assessment according to the following schedule:

Final Protocol Submission: September 30, 2021
Study Completion: November 30, 2023
Final Report Submission: May 31, 2024

9. Study C4591031 substudy to prospectively assess the incidence of subclinical myocarditis following administration of a third dose of COMIRNATY in a subset of participants 16 to 30 years of age.

We acknowledge the timetable you submitted on August 21, 2021, which states that you will conduct this study according to the following schedule:

Final Protocol Submission: November 30, 2021

Study Completion: June 30, 2022
Final Report Submission: December 31, 2022

Please submit the protocols to your IND 19736, with a cross-reference letter to this BLA STN BL 125742 explaining that these protocols were submitted to the IND. Please refer to the PMR sequential number for each study/clinical trial and the submission number as shown in this letter.

Please submit final study reports to the BLA. If the information in the final study report supports a change in the label, the final study report must be submitted as a supplement to this BLA STN BL 125742. For administrative purposes, all submissions related to these postmarketing studies required under section 505(o) must be submitted to this BLA and be clearly designated as:

- Required Postmarketing Correspondence under Section 505(o)
- Required Postmarketing Final Report under Section 505(o)
- Supplement contains Required Postmarketing Final Report under Section 505(o)

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. In addition, section 506B of the FDCA and 21 CFR 601.70 require you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

You must describe the status in an annual report on postmarketing studies for this product. Label your annual report as an *Annual Status Report of Postmarketing Requirements/Commitments* and submit it to the FDA each year within 60 calendar days of the anniversary date of this letter until all Requirements and Commitments subject to the reporting requirements of section 506B of the FDCA are fulfilled or released. The status report for each study should include:

- the sequential number for each study as shown in this letter;
- information to identify and describe the postmarketing requirement;
- the original milestone schedule for the requirement;
- the revised milestone schedule for the requirement, if appropriate;
- the current status of the requirement (i.e., pending, ongoing, delayed, terminated, or submitted); and,
- an explanation of the status for the study or clinical trial. The explanation should include how the study is progressing in reference to the original projected schedule, including, the patient accrual rate (*i.e.*, number enrolled to date and the total planned enrollment).

As described in 21 CFR 601.70(e), we may publicly disclose information regarding these postmarketing studies on our website at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PostmarketingPhaseIVCommitments/default.htm.

We will consider the submission of your annual report under section 506B of the FDCA and 21 CFR

601.70 to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in section 505(o) and 21 CFR 601.70. We remind you that to comply with section 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to periodically report on the status of studies or clinical trials required under section 505(o) may be a violation of FDCA section 505(o)(3)(E)(ii) and could result in regulatory action.

Postmarketing Commitments Subject to Reporting Requirements Under Section 506B

We acknowledge your written commitments as described in your letter of August 21, 2021 as outlined below:

10. Study C4591022, entitled "Pfizer-BioNTech COVID-19 Vaccine Exposure during Pregnancy: A Non-Interventional Post-Approval Safety Study of Pregnancy and Infant Outcomes in the Organization of Teratology Information Specialists (OTIS)/ MotherToBaby Pregnancy Registry."

Final Protocol Submission: July 1, 2021
Study Completion: June 30, 2025
Final Report Submission: December 31, 2025

11. Study C4591007 substudy to evaluate the immunogenicity and safety of lower dose levels of COMIRNATY in individuals 12 through <30 years of age.

Final Protocol Submission: September 30, 2021
Study Completion: November 30, 2023
Final Report Submission: May 31, 2024

12. Study C4591012, entitled "Post-emergency Use Authorization Active Safety Surveillance Study Among Individuals in the Veteran's Affairs Health System Receiving Pfizer-BioNTech Coronavirus Disease 2019 (COVID-19) Vaccine."

Final Protocol Submission: January 29, 2021
Study Completion: June 30, 2023
Final Report Submission: December 31, 2023

13. Study C4591014, entitled "Pfizer-BioNTech COVID-19 BNT162b2 Vaccine Effectiveness Study-Kaiser Permanente Southern California."

Final Protocol Submission: March 22, 2021
Study Completion: December 31, 2022
Final Report Submission: June 30, 2023

Please submit clinical protocols to your IND 19736, and a cross-reference letter to this BLA STN BL 125742 explaining that these protocols were submitted to the IND. Please refer to the PMC sequential number for each study/clinical trial and the submission number as shown in this letter.

If the information in the final study report supports a change in the label, the final study report must be submitted as a supplement. Please use the following designators to prominently label all submissions, including supplements, relating to these postmarketing study commitments as appropriate:

- Postmarketing Commitment – Correspondence Study Update
- Postmarketing Commitment – Final Study Report
- Supplement contains Postmarketing Commitment – Final Study Report

For each postmarketing study subject to the reporting requirements of 21 CFR 601.70, you must describe the status in an annual report on postmarketing studies for this product. Label your annual report as an *Annual Status Report of Postmarketing Requirements/Commitments* and submit it to the FDA each year within 60 calendar days of the anniversary date of this letter until all Requirements and Commitments subject to the reporting requirements of section 506B of the FDCA are fulfilled or released. The status report for each study should include:

- the sequential number for each study as shown in this letter;
- information to identify and describe the postmarketing commitment;
- the original schedule for the commitment;
- the status of the commitment (i.e., pending, ongoing, delayed, terminated, or submitted); and,
- an explanation of the status including, for clinical studies, the patient accrual rate (*i.e.*, number enrolled to date and the total planned enrollment).

As described in 21 CFR 601.70(e), we may publicly disclose information regarding these postmarketing studies on our website at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PostmarketingPhaseIVCommitments/default.htm.

Post Approval Feedback Meeting

New biological products qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and

marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, please contact the Regulatory Project Manager for this application.

Sincerely,

Mary A. Malarkey
Director
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research

Marion F. Gruber, PhD
Director
Office of Vaccines Research and Review
Center for Biologics Evaluation
and Research

EXHIBIT 6
FDA Q&A COMMENTS ON COMINARTY

Q&A FOR COMIRNATY (COVID-19 VACCINE MRNA)

How did the FDA arrive at the decision to approve Comirnaty (COVID-19 Vaccine mRNA)? What is different now when compared to the December 2020 authorization of Pfizer-BioNTech COVID-19 Vaccine?

FDA conducted a thorough evaluation of the data and information submitted in the Biologics License Application (BLA) for Comirnaty before making a determination that the vaccine is safe and effective in preventing COVID-19 in individuals 16 years of age and older.

The EUA for the Pfizer-BioNTech COVID-19 Vaccine for individuals 16 years of age and older was based on safety and effectiveness data from a randomized, controlled, blinded ongoing clinical trial in approximately 18,000 individuals who received the vaccine and approximately 18,000 who received a placebo. The vaccine was 95% effective in preventing COVID-19 disease among these clinical trial participants with eight COVID-19 cases in the vaccine group and 162 in the placebo group. The duration of safety follow-up for the vaccinated and placebo participants was a median of two months after receiving the second dose.

Follow-up data from this ongoing clinical trial was analyzed by FDA to determine the safety and effectiveness of Comirnaty. The updated analysis to determine effectiveness for individuals 16 years of age and older included approximately 20,000 Comirnaty and 20,000 placebo recipients who did not have evidence

of SARS-CoV-2 infection through seven days after the second dose. Overall, the vaccine was 91% effective, with 77 cases of COVID-19 occurring in the vaccine group and 833 COVID-19 cases in the placebo group.

The safety was evaluated in approximately 22,000 Comirnaty and 22,000 placebo recipients 16 years of age and older. More than half of the vaccine and placebo recipients were followed for safety for at least four months after the second dose. After issuance of the EUA, participants were unblinded in a phased manner over a period of months to offer placebo participants Comirnaty. Overall, in blinded and unblinded follow-up, approximately 12,000 Comirnaty recipients have been followed for at least 6 months.

What are the most commonly reported side effects by those received Comirnaty (COVID-19 Vaccine mRNA)?

The most commly reported side effects by those clinical trials participants who received Comirnaty were pain, redness and swelling at the injection site, fatigue, headache, muscle pain, chills, joint pain, and fever.

How safe and effective is Comirnaty (COVID-19 Vaccine mRNA)?

Overall, the vaccine was 91% effective in preventing COVID-19 disease, with 77 cases of COVID-19 occurring in the vaccine group and 833 COVID-19 cases in the placebo group.

The most commonly reported side effects by those clinical trial participants who received Comirnaty were pain, redness and swelling at the injection site, fatigue, headache, muscle pain, chills, joint pain and fever.

The FDA conducted a rigorous evaluation of post-authorization safety surveillance data pertaining to myocarditis and pericarditis following administration of Pfizer-BioNTech COVID-19 Vaccine and determined that the data demonstrate increased risks, particularly within the seven days following the second dose. The observed risk is higher among males under 40 years of age compared to females and older males. The observed risk is highest in males 12 through 17 years of age. Available data from short-term follow-up suggest that most individuals have had resolution of symptoms. However, some individuals required intensive care support. Information is not yet available about potential long-term health outcomes. The Comirnaty Prescribing Information includes a warning about these risks.

Will the emergency use authorization (EUA) for Pfizer-BioNTech COVID-19 Vaccine remain in effect after the approval?

The EUA will continue to cover adolescents 12 through 15 years of age and the administration of a third dose to certain immunocompromised individuals 12 years of age and older. Additionally, for logistical reasons, the EUA will continue to cover the use of the Pfizer-BioNTech COVID-19 Vaccine in individuals 16 years of age and older; this use is also now approved.

How is Comirnaty (COVID-19 VACCINE, mRNA) related to the PFIZER-BIONTECH COVID-19 VACCINE?

The FDA-approved Pfizer-BioNTech product Comirnaty (/vaccines-blood-biologics/comirnaty) (COVID-19 Vaccine, mRNA) and the FDA-authorized Pfizer-BioNTech COVID-19 Vaccine under EUA have the same formulation and can be used interchangeably

to provide the COVID-19 vaccination series without presenting any safety or effectiveness concerns. Therefore, providers can use doses distributed under EUA to administer the vaccination series as if the doses were the licensed vaccine. For purposes of administration, doses distributed under the EUA are interchangeable with the licensed doses. The Vaccine Information Fact Sheet for Recipients and Caregivers (/media/144414/download) provides additional information about both the approved and authorized vaccine.

After FDA granted the emergency use authorization of the Pfizer BioNTech COVID-19 Vaccine were clinical trial participants unblinded so that the placebo recipients could be offered the vaccine?

Yes. After issuance of the EUA, clinical trial participants were unblinded in a phased manner over a period of months to offer the authorized Pfizer-BioNTech COVID-19 Vaccine to placebo participants. These participants were followed for safety outcomes. Overall, in blinded and unblinded follow-up, approximately 12,000 Pfizer-BioNTech COVID-19 Vaccine recipients have been followed for at least 6 months.

EXHIBIT 7
PREP ACT Q&A, U.S. DEPARTMENT OF HEALTH AND HUMAN RESOURCES

The following is intended to address an overview of the PREP Act and frequently asked questions from the manufacturing industry, the healthcare community, and state and local government officials. It is not an exhaustive review of the PREP Act's provisions in all contexts or a protocol for the HHS's implementation of the PREP Act. In addition, other legal protections may be available at the federal, state, and local government level.

The Public Readiness and Emergency Preparedness Act (PREP Act):

> adds new legal authorities to the Public Health Service (PHS) Act
>
> provides liability immunity related to the manufacture, testing, development, distribution, administration and use of medical countermeasures against chemical, biological, radiological and nuclear agents of terrorism, epidemics, and pandemics
>
> adds authority to establish a program to compensate eligible individuals who suffer injuries from administration or use of products covered by the PREP Act's immunity provisions

The PREP Act authorizes the Secretary of the Department of Health and Human Services (Secretary) (HHS) to issue a PREP Act Declaration ("Declaration") that provides immunity from liability for any loss caused, arising out of, relating to, or resulting from administration or use of countermeasures to diseases,

threats and conditions determined in the Declaration to constitute a present or credible risk of a future public health emergency.

Liability Immunity and Compensation

In general, the liability immunity applies to entities and individuals involved in the development, manufacture, testing, distribution, administration, and use of medical countermeasures described in a Declaration. The only statutory exception to this immunity is for actions or failures to act that constitute willful misconduct.

The PREP Act also authorizes a United States Treasury fund that compensates eligible individuals for serious physical injuries or deaths directly caused by administration or use of a countermeasure covered by the Declaration.

PREP Declaration

1. What Information is Included in a PREP Act Declaration?
2. Where is the Declaration Published?
3. What Factors Are Considered by the Secretary?
4. How is a PREP Act Declaration Different from a Declaration of Public Health Emergency under section 319 of the Public Health Service Act?

Immunity

1. What is Immunity from Liability?
2. Who May be Afforded Immunity from Liability under a PREP Act Declaration?

3. Are There Any Limitations on Immunity from Liability?
4. What Countermeasures May be Covered by Immunity from Liability?
5. When Does Immunity Under the PREP Act Become Available?

Claims and Compensation

1. Is There Any Compensation for Injury?
2. How Does an Individual File a Claim for Benefits?
3. What Options does an Injured Individual have if Congress has not funded the Compensation Fund? Can I receive funding priority in another way?

Litigation

1. Has there been any litigation related to the PREP Act?

PREP Declaration

1. What Information is Included in a PREP Act Declaration?

   A Declaration includes:

   A determination that a disease or health condition or threat to health constitutes a public health emergency, or that there is a credible risk that it will in the future constitute an emergency;

   The category of diseases, health conditions, or health threats for which administration and use of the countermeasure is recommended. During

the time period covered by the Declaration, it is presumed that the recommended countermeasure;

The effective time period (the Secretary may specify an extended time period for manufacturers to dispose of the countermeasure and for others to cease administration and use of the countermeasure); The population of individuals receiving the countermeasure and the geographic area of administration and use of the countermeasure for which immunity from liability is in effect for program planners and qualified persons (manufacturers and distributors are provided liability immunity regardless of who receives the countermeasure or where it is administered or used);

Limitations (if any) on the geographic area or areas for which immunity is in effect with respect to administration or use of the countermeasure;

Limitations (if any) on the means of distribution;

Any additional persons identified as qualified to prescribe, dispense, or administer the countermeasure; and

Any other limitations or conditions.

2. Where is the Declaration Published?

   The Declaration and any amendments are published in the Federal Register. It is important to note, however, that unless the Declaration specifies otherwise, it is effective upon the Secretary's signature, not upon publication in the Federal Register.

3. What Factors Are Considered by the Secretary?

In deciding whether to issue a PREP Act Declaration, HHS must consider the desirability of encouraging the design, development, clinical testing or investigation, manufacture, labeling, distribution, formulation, packaging, marketing, promotion, sale, purchase, donation, dispensing, prescribing, administering, licensing, and use of the countermeasure recommended in the Declaration. HHS may also consider other relevant factors.

4. How is a PREP Act Declaration Different from a Declaration of Public Health Emergency under section 319 of the Public Health Service Act?

Under section 319 of the Public Health Service Act, HHS may issue a declaration of a public health emergency based upon a determination that a:

disease or disorder presents a public health emergency; or

public health emergency, including significant outbreaks of infectious disease or bioterrorist attacks, otherwise exists.

Following a section 319 declaration, the HHS can take a number of emergency actions, including:

Waiving certain Medicare, Medicaid, State Children's Health Insurance Program, and Health Insurance Portability and Accountability Act requirements;

Allowing States and localities to temporarily reassign personnel supported with federal funds during the period of the emergency.

A determination of a public health emergency is different from a PREP Act declaration. The declarations are made on different public health determinations, and have different legal effects. A PREP Act Declaration may be made in advance of a public health emergency and may provide liability immunity for activities both before and after a declared public health emergency. A separate declaration under section 319 or other statutes is not needed for immunity under the PREP Act to take effect unless the PREP Act Declaration states that a public health or other emergency Declaration is needed to trigger immunity.

Immunity

1. What is immunity from Liability?

Immunity means that courts must dismiss claims brought against any entity or individuals covered by the PREP Act. Claims that courts must dismiss include claims for any loss that is related to any stage of design, development, testing, manufacture, labeling, distribution, formulation, labeling, packaging, marketing, promotion, sale, purchase, donation, dispensing, prescribing, administration, licensing or use of a courtemeasure recommended in a Declaration. This includes, but is not limited to, claims for:

Death;

Physical, mental, or emotional injury, illness, disability, or condition or fear of any such injury, illness, disability, or condition;

Any need for medical monitoring; or

Property damage or loss, including business interruption loss.

The only exception is for claims of willful misconduct. (See Question: Are There Any Limitations n Immunity From Liability?)

2. Who May be Afforded Immunity from Liability under a PREP Act Declaration?

A Declaration may provide liability immunity for covered persons. Covered persons may include, at the Secretary's discretion:

Manufactures of countermeasures;

Distributors of countermeasures;

Program planners, ie., individuals and entities involved in planning, administering, or supervising programs for distribution of a countermeasure (e.g., State or local governments, Indian tribes, or private sector employers or community groups that establish requirements or provide guidance, technical or scientific advice or assistance, or provide a facility);

Qualified persons, i.e., persons who prescribe, administer, or dispense countermeasures such as healthcare and other providers or other categories of persons named in a Declaration, e.g., volunteers;

Officials, agents, and employees of any of these entities or persons; and

The United States.

3. Are There Any Limitations on Immunity from Liability?

Immunity from liability under the PREP Act is not available for death or serious physical injury caused by willful misconduct. A "serious physical injury" is one that is life-threatening, or results in or requires medical or surgical intervention to preclude permanent impairment of a body function or results in permanent damage to a body structure. Willful misconduct is misconduct that is greater than any form of recklessness or negligence. It is defined in the PREP Act as an act or failure to act that is taken:

> intentionally to achieve a wrongful purpose;
>
> knowingly without legal or factual justification; and
>
> in disregard of a known or obvious risk that is so great as to make it highly probable that the harm will outweigh the benefit. All three of these conditions must be proven with clear and convincing evidence. Willful misconduct cannot be found against:

A manufacturer or distributor for actions regulated by HHS under the Public Health Service Act or the Federal Food, Drug and Cosmetic Act, if HHS chooses not to take an enforcement action against the manufacturer or distributor, or if HHS terminates or settles an enforcement action without imposing a criminal, civil, or administrative penalty; or

A program planner or qualified person who acts in accordance with applicable directions, guidelines, or recommendations issued by the HHS regarding administration and use of a countermeasure as long as HHS or the State or local

health authority is notified about the serious injury or death within seven days of its discovery.

In addition, immunity is not available for claims based on activities that fall outside the scope of the applicable Declaration. As described below (5. "When Does Immunity Under the PREP Act Become Available?"), the Declaration can specify the conditions under which a Declaration will provide immunity, such as the effective dates and geographic area for which immunity will be available. Immunity is not available for claims that fall outside these conditions.

Immunity is not available for claims of loss unrelated to the design, development, testing, manufacture, distribution, formulation, labeling, packaging, marketing, promotion, sale, purchase, donation, dispensing, prescribing, administration, licensing or use of a countermeasure recommended in a Declaration.

Immunity from liability also is not available for foreign claims where the U.S. has no jurisdiction. Immunity may be available for administration or use of a countermeasure outside the United States if the claim is based on events that take place in U.S. territory or there is another link to the U.S. that makes it reasonable to apply U.S. law to the claim.

In addition, immunity is not available for claims based on activities that fall outside the scope of the applicable Declaration. As described below (5. "When Does Immunity Under the PREP Act Become Available?"), the Declaration can specify the conditions under which a Declaration will

provide immunity, such as the effective dates and geographic area for which immunity will be available. Immunity is not available for claims that fall outside these conditions.

4. What Countermeasures May be Covered by Immunity from Liability?

A "covered countermeasure" may be:

A qualified pandemic or epidemic product;

A security countermeasure;

An unapproved drug, biological product, or device used under an Emergency Use Authorization (EUA) issued by FDA;

An approved drug, biological product, or device used pursuant to Federal law in conditions that are in consistent with its approval; or

An unapproved drug, biological product, or device, or an approved drug, biological product, or device intended for an unapproved use, that is intended for emergency use and shipped and held by a government agency or someone working on that agency's behalf for use only when that use is authorized.

In general, these are products that are approved, cleared, or licensed by FDA; authorized for investigational use, i.e. an Investigational New Drug ("IND") or Investigational Device Exemption ("IDE"), by FDA, authorized under an EUA by FDA, or otherwise permitted to be held or used for emergency use in accordance with Federal law.

However, each has a specific legal definition. See the PREP Act Glossary for more information.

5. When Does Immunity Under the PREP Act Become Available?

Immunity under the PREP Act becomes available when HHS issues a Declaration, beginning on the effective date or other triggering event stated in the Declaration. For example, the Declaration may specify that activities such as manufacture and testing are covered on the effective date of the Declaration, but emergency uses such as mass dispensing are covered following a declared public health or other emergency.

Claims and Compensation

1. Is There Any Compensation for Injury?

The PREP Act authorized a "Covered Countermeasures Process Fund" to compensate eligible individuals who suffer injuries as the direct result of a countermeasure administered or used under the Declaration. Funds must be appropriated by Congress into this account to pay claims. If funds are appropriated, compensation for serious physical injuries may then be available to eligible requesters under the HRSA's Countermeasures Injury Compensation Program (CICP). Requests for Benefits must be made to HRSA's CICP.

Serious physical injury means an injury that warranted hospitalization (whether or not the person was actually hospitalized) or that led to a significant loss of function or disability. The CICP pays reasonable and necessary medical benefits,

and/or lost wages for eligible injured countermeasure recipients. Death benefits may also be available to certain survivors of eligible individuals who died as a direct result of the administration or use of a covered countermeasure.

The CICP is payer of last resort, so benefits are reduced by the amounts payable by all other public and private third-party payers (such as health insurance and workers' compensation). The regulations implementing the CICP are at 42 CFR part 110.

2. How Does an Individual File a Claim for Benefits?

An individual who may have suffered a serious physical injury from the administration or use of a countermeasure under a Declaration may seek compensation by filing a Request for Benefits with the CICP. A Request for Benefits form must be filed within one year of receiving the countermeasure.

A legal or personal representative may file on the individual's behalf, but is generally not required unless the injured person is a minor or an adult who lacks legal capacity to receive payments. If the injured person has died (regardless of cause of death), the executor or administrator of the estate may file for benefits on behalf of the estate. If the injured person died as a direct result of receiving the countermeasure, certain survivors may file a request for death benefits.

As well as filing a Request for Benefits Form, the requester must submit all required medical

records and other supporting documentation. Further information on filing a Request for Benefits is available on the CICP's website

3. What Options does an Injured Individual have if Congress has not funded the Compensation Fund?

   If no funds have been appropriated to the compensation program, or the Secretary does not make a final determination on the individual's request within 240 days, or the individual decides not to accept the compensation, the injured individual or his representative may pursue a tort claim in the United States District Court for the District of Columbia, but only if the claim involves willful misconduct and meets the other requirements for suit under the PREP Act. If the individual accepts compensation from the CICP, or if there is no willful misconduct, the individual does not have a tort claim that can be filed in a United States Federal or a State court.

   Any award is reduced by public or private insurance or worker's compensation available to the injured individual. Awards for non-economic damages, such as pain, suffering, physical impairment, mental anguish, and loss of consortium are also limited.

Litigation

1. Has there been any litigation related to the PREP Act?

   On November 21, 2012, the Appellate Division of the New York Supreme Court in Parker v. St. Lawrence County Public Health Department, 102 A.D.3d 140 (2012) upheld PREP Act protections

for a county that conducted a school based vaccination clinic in response to the H1N1 outbreak.

During the clinic, a nurse employed by St. Lawrence County inadvertently vaccinated a kindergartener in the absence of parental informed consent. The child's mother filed suit, arguing that the county had committed negligence and battery. The county moved to dismiss the complaint on the basis that the claim was preempted under the PREP Act. The lower court denied the defendant's motion to dismiss, asserting that the PREP Act was not intended by Congress to protect against claims arising from failure to obtain informed consent. The county appealed and the United States submitted an amicus brief supporting the county.

The appellate court dismissed the plaintiff's claims, finding that the federal PREP Act preempted the claims under state law and that the breadth of liability immunity provided under the PREP Act precluded the plaintiff's claims of negligence and battery. The court noted the alternative remedy provided by the countermeasure injury compensation program and the possibility of a federal cause of action for willful misconduct claims.

The period for appeal of the case has expired.

In another case, *Kehler v. Hood*, 2012 WL 1945952 (E.D. Mo.), plaintiffs alleged that the physician and her employing hospital were negligent in failing to obtain the adult patient's informed consent and a consult from a specialist prior to the administration of the vaccination, which resulted in a severe case of transverse myelitis to the patient,

and loss of consortium to the spouse. Defendants then brought third party product liability/failure to warn claims against the manufacturer.

The parties did not dispute that the manufacturer, was protected by the PREP Act, nor did they allege that it engaged in willful misconduct. As a result, the federal Eastern District Court of Missouri dismissed the claim against the manufacturer. Finding that it had no jurisdiction over plaintiffs' remaining claims, the federal court remanded the case to state court for further consideration of the plaintiffs' claims.