



**Congressional
Research Service**

Informing the legislative debate since 1914

FDA Approval of the Pfizer-BioNTech COVID-19 Vaccine: Frequently Asked Questions

Updated September 29, 2021

Congressional Research Service

<https://crsreports.congress.gov>

R46913



FDA Approval of the Pfizer-BioNTech COVID-19 Vaccine: Frequently Asked Questions

R46913

September 29, 2021

Kevin J. Hickey
Legislative Attorney

Erin H. Ward
Legislative Attorney

Agata Bodie
Analyst in Health Policy

On August 23, 2021, the U.S. Food and Drug Administration (FDA) announced its regulatory approval of the Pfizer-BioNTech Coronavirus Disease 2019 (COVID-19) vaccine for people 16 years of age or older. The Pfizer-BioNTech vaccine is the first COVID-19 vaccine—and the first vaccine based on messenger RNA (mRNA) technology—to be licensed by FDA. Previously, the Pfizer-BioNTech vaccine was available in the United States only under an Emergency Use Authorization (EUA), a distinct regulatory pathway that allows FDA to authorize use of a drug, biologic, or medical device prior to approval during a public health emergency.

Pfizer and BioNTech are marketing their licensed vaccine under the new brand name Comirnaty (pronounced koe-MIR-na-tee). Comirnaty has the same ingredients and formulation as the Pfizer-BioNTech vaccine that is authorized under the EUA. The two products differ in branding and labeling but can be used interchangeably without any impact on safety or effectiveness.

Although Comirnaty is fully approved by FDA for administration to individuals 16 years and older, an EUA remains in effect for the Pfizer-BioNTech COVID-19 vaccine. Among other things, the reissued EUA authorizes the Pfizer-BioNTech vaccine for uses that FDA had previously authorized but fall outside the scope of FDA’s approval of Comirnaty. Such uses include the administration of the vaccine to children aged 12 to 15 and third doses of the vaccine regimen for certain immunocompromised individuals. The EUA also authorizes use of Comirnaty for those purposes to allow for interchangeable administration of the two vaccines.

To encourage rapid development and administration of medical countermeasures during a public health emergency, the Public Readiness and Emergency Preparedness Act (PREP Act) allows the Secretary of Health and Human Services to provide liability protections to manufacturers, distributors, and administrators of medical countermeasures. The Secretary invoked the PREP Act with respect to the COVID-19 pandemic in a declaration effective February 4, 2020. Under the current PREP Act declaration, manufacturers, distributors, and administrators of COVID-19 vaccines (along with other COVID-19 countermeasures) are generally immune from lawsuits based on injuries relating to the use of the vaccines. Liability immunity under the PREP Act applies to both licensed and authorized COVID-19 vaccines and thus generally applies in the same manner to both Comirnaty and the Pfizer-BioNTech vaccine. However, the PREP Act may not protect “off label” uses of the vaccine—that is, uses covered neither by the EUA nor by the biologics license.

Some employers, businesses, and schools require proof of vaccination for certain activities to protect their employees, customers, and students from COVID-19. Such “vaccine mandates” take different forms and have largely been sustained when challenged in court. As a practical matter, FDA’s approval of Comirnaty may result in greater use of vaccine mandates by these entities to the extent that some of them previously did not require vaccination because no COVID-19 vaccine had been fully licensed by FDA. FDA’s approval may also diminish uncertainty surrounding the legality of such vaccine mandates, although the legal authority for and limitations on these mandates are largely the same for both licensed and authorized vaccines.

Contents

Frequently Asked Questions	1
Has the Pfizer-BioNTech COVID-19 vaccine been fully approved by FDA?.....	1
What is Comirnaty?	2
What is the scope of FDA’s biologics license for Comirnaty?	3
Is there any difference between Comirnaty and the Pfizer-BioNTech vaccine?.....	4
If Comirnaty is now licensed, why did FDA reissue an EUA for the Pfizer-BioNTech vaccine?	4
What is the scope of the current EUA for the Pfizer-BioNTech vaccine?	6
Why did the FDA Vaccines and Related Biological Products Advisory Committee recommend booster doses only for certain categories of individuals?	8
Can COVID-19 vaccine providers use the Comirnaty-labeled vaccine interchangeably with the Pfizer-BioNTech vaccine?.....	11
Why did FDA refer to Comirnaty and the Pfizer-BioNTech vaccine as “legally distinct”?	12
What liability protections apply to COVID-19 vaccines?	13
Does FDA’s licensure of Comirnaty affect liability protections for COVID-19 vaccines under the PREP Act?	14
Do the PREP Act’s liability protections extend to off-label uses of Comirnaty?	14
Does FDA’s licensure of Comirnaty affect the authority of employers or schools to “mandate” COVID-19 vaccines?.....	16

Tables

Table 1. Comparison of Patient Populations Covered by the Pfizer-BioNTech EUA and Comirnaty BLA.....	6
---	---

Contacts

Author Information.....	18
-------------------------	----

On August 23, 2021, the U.S. Food and Drug Administration (FDA) approved the Coronavirus Disease 2019 (COVID-19) vaccine manufactured by Pfizer and BioNTech for individuals 16 years of age or older.¹ The Pfizer-BioNTech COVID-19 vaccine is the first COVID-19 vaccine—and the first vaccine based on messenger RNA (mRNA) technology—to be licensed by FDA.² Pfizer and BioNTech will market their licensed COVID-19 vaccine under the brand name Comirnaty (pronounced koe-MIR-na-tee).

Prior to approval, the Pfizer-BioNTech vaccine was available in the United States only under an Emergency Use Authorization (EUA).³ An EUA is a distinct regulatory pathway from the ordinary biologics licensure pathway that allows FDA to authorize use of a drug or biologic prior to approval in circumstances such as a public health emergency.⁴ FDA first issued an EUA for the Pfizer-BioNTech vaccine on December 11, 2020, and has reissued the EUA several times since then, such as to authorize the vaccine in additional groups—for example, children 12 to 15 years of age.⁵ A revised EUA remains in effect for the Pfizer-BioNTech vaccine.⁶

FDA's approval of Comirnaty has caused some confusion about the scope of FDA's approval, the relationship between Comirnaty and the Pfizer-BioNTech COVID-19 vaccine, and other issues.⁷ This report addresses some common questions about FDA's approval of Comirnaty.

Frequently Asked Questions

Has the Pfizer-BioNTech COVID-19 vaccine been fully approved by FDA?

Yes. On August 23, 2021, FDA licensed (i.e., approved)⁸ the first COVID-19 vaccine, Comirnaty, manufactured by Pfizer-BioNTech. The vaccine is licensed for the prevention of COVID-19, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), in individuals 16 years of age and older.⁹

¹ FDA, "FDA Approves First COVID-19 Vaccine," press release, August 23, 2021, <https://www.fda.gov/news-events/press-announcements/fda-approves-first-covid-19-vaccine>.

² FDA, "FDA Approves First COVID-19 Vaccine."

³ FDA, EUA letter to Pfizer, September 22, 2021, p. 1, <https://www.fda.gov/media/150386/download>.

⁴ 21 U.S.C. §360bbb-3.

⁵ FDA, EUA letter to Pfizer, September 22, 2021, pp. 1-2.

⁶ On the same day FDA approved the Comirnaty BLA, FDA reissued the Pfizer-BioNTech vaccine EUA to incorporate its approval of Comirnaty. FDA, EUA letter to Pfizer, August 23, 2021, pp. 1-2, <https://web.archive.org/web/20210824120845/https://www.fda.gov/media/150386/download>. On September 22, 2021, FDA reissued the EUA again to authorize third doses of the vaccine for additional categories of individuals determined to be at high risk for severe COVID, including individuals 65 years of age and older. FDA, EUA letter to Pfizer, September 22, 2021, p. 7.

⁷ See, for example, Angelo Fichera, "Researcher Distorts Facts on COVID-19 Vaccine Approval, Liability," FactCheck.org, August 30, 2021, <https://www.factcheck.org/2021/08/scicheck-researcher-distorts-facts-on-covid-19-vaccine-approval-liability/>; Reuters Fact Check, "Fact Check-Media Reports Have Not Lied about Pfizer-BioNTech's FDA Approval," August 27, 2021, <https://www.reuters.com/article/factcheck-fda-pfizer/fact-check-media-reports-have-not-lied-about-pfizer-biontechs-fda-approval-idUSL1N2PY0OL>; and Glenn Kessler, "The False Claim That the Fully-Approved Pfizer Vaccine Lacks Liability Protection," *Washington Post*, August 30, 2021, <https://www.washingtonpost.com/politics/2021/08/30/false-claim-that-fully-approved-pfizer-vaccine-lacks-liability-protection/>.

⁸ Biologics are a subset of drugs and subject to many of the same statutory requirements. However, while small molecule, chemically synthesized drugs are *approved* by FDA via a new drug application under the Federal Food, Drug, and Cosmetic Act, biologics such as vaccines are *licensed* via a biologics license application under the Public Health Service Act.

⁹ FDA, "FDA Approves First COVID-19 Vaccine." See also FDA, Approval Letter to BioNTech Manufacturing

To obtain licensure from FDA, BioNTech Manufacturing GmbH, in partnership with Pfizer, submitted a biologics license application (BLA) to the agency for review. The BLA for Comirnaty included clinical trial safety and effectiveness data and other information that built on data previously submitted to FDA in Pfizer-BioNTech’s November 2020 EUA request for the Pfizer-BioNTech COVID-19 vaccine.¹⁰

FDA received the BLA on May 18, 2021.¹¹ The agency granted the BLA priority review, assigning it a review goal date of January 16, 2022. FDA also had previously designated the vaccine as a fast track product.¹² Fast track designation may be granted to a vaccine that is intended to prevent a serious disease or condition and for which nonclinical or clinical data demonstrate the product’s potential to address an unmet medical need.¹³ The designation confers certain benefits, such as expedited review and eligibility for rolling review, meaning that FDA may review portions of the BLA before the completed application is submitted.¹⁴ FDA issued its decision to license Comirnaty in 97 days, or about three months after receiving the complete BLA from Pfizer-BioNTech.¹⁵

What is Comirnaty?

Comirnaty is the proprietary name (i.e., the brand name) under which the FDA-licensed vaccine that has been known as the Pfizer-BioNTech COVID-19 vaccine (or BNT162b2) will be marketed.¹⁶ The proprietary name is the exclusive name of a drug or vaccine that is owned by a company under trademark law. Pharmaceutical products are often marketed under a brand name, which the company selects and FDA approves as part of the BLA review process.¹⁷ In the BLA approval letter, FDA indicated that Pfizer and BioNTech may label and market the licensed vaccine as Comirnaty,¹⁸ which, according to the companies, “represents a combination of the terms COVID-19, mRNA, community, and immunity.”¹⁹

GmbH, Pfizer Inc., August 23, 2021, <https://www.fda.gov/media/151710/download>. The approval letter states that FDA is “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 Public Health Service 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.”

¹⁰ FDA, Approval Letter to BioNTech Manufacturing GmbH, Pfizer.

¹¹ FDA, Summary Basis for Regulatory Action—Comirnaty, p. 5, <https://www.fda.gov/media/151733/download>.

¹² FDA, Summary Basis for Regulatory Action—Comirnaty, p. 5.

¹³ 21 U.S.C. §356(b). FDA, “Guidance for Industry Expedited Programs for Serious Conditions—Drugs and Biologics,” May 2014, p. 9, <https://www.fda.gov/media/86377/download>.

¹⁴ 21 U.S.C. §356(d). FDA, “Guidance for Industry Expedited Programs for Serious Conditions—Drugs and Biologics,” p. 10.

¹⁵ FDA, “First COVID-19 Vaccine Approval Media Call,” August 23, 2021, at 19:05 minutes.

¹⁶ FDA, Summary Basis for Regulatory Action—Comirnaty, p. 3; FDA, “Comirnaty and Pfizer-BioNTech COVID-19 Vaccine,” accessed August 27, 2021, <https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/comirnaty-and-pfizer-biontech-covid-19-vaccine>; and Pfizer, “Pfizer and BioNTech Receive Authorization in the European Union for COVID-19 Vaccine,” December 21, 2020, <https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-receive-authorization-european-union>.

¹⁷ FDA, “Contents of a Complete Submission for the Evaluation of Proprietary Names,” Guidance for Industry, April 2016, pp. 5-7, <https://www.fda.gov/media/72144/download>.

¹⁸ FDA, Approval Letter to BioNTech Manufacturing GmbH, Pfizer.

¹⁹ Pfizer, “Pfizer and BioNTech Receive Authorization in the European Union for COVID-19 Vaccine,” press release, December 21, 2020, <https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-receive->

What is the scope of FDA’s biologics license for Comirnaty?

Comirnaty is licensed as a two-dose vaccine for the prevention of COVID-19 in individuals 16 years of age and older. It is *not* licensed for use in individuals under 16 years of age. It is also not licensed to be administered as a third dose to individuals who are immunocompromised, or as a booster dose to individuals determined to be at high risk for severe COVID-19. The EUA for the Pfizer-BioNTech COVID-19 vaccine, however, does cover these uses, as explained below in the section “What is the scope of the current EUA for the Pfizer-BioNTech vaccine?”

In determining whether to license a vaccine for a specific use, FDA reviews the data and information submitted by the manufacturer in the BLA and inspects the facilities in which a vaccine is made to ensure that the product meets standards for safety, purity, and potency (i.e., effectiveness).²⁰ The scope of Comirnaty’s licensure is based on the supporting data and information FDA received in Pfizer-BioNTech’s BLA. This support included data regarding the safety and effectiveness of two doses of the vaccine administered in individuals 16 years of age and older, building on the data and information previously submitted by the companies in their initial EUA request.

For example, the Pfizer-BioNTech COVID-19 vaccine EUA was granted based on safety and effectiveness data derived from an ongoing, randomized, controlled, and blinded trial of approximately 36,000 individuals 16 years of age and older who did not have evidence of SARS-CoV-2 infection within a week of receiving the second dose of the vaccine. About half of this group received the vaccine (n=18,198) and the other half placebo (n=18,325).²¹ The vaccine was found to be 95% effective at preventing symptomatic COVID-19, with eight cases of COVID-19 identified in the vaccine group and 162 in the placebo group.²²

FDA evaluated follow-up data from this trial as part of the Comirnaty BLA, with the updated analysis including approximately 19,993 individuals in the vaccine group and 20,118 in the placebo group.²³ The updated analysis found an effectiveness rate of 91%, based on the occurrence of 77 cases of COVID-19 in the vaccine group and 833 COVID-19 cases in the placebo group.²⁴ In determining whether to license the vaccine, FDA evaluated these data, along with information about the manufacturing facilities, longer term follow-up safety data from the trial, adverse events reported from use of the vaccine under EUA, and other information.

Under the terms of licensure, Comirnaty may be manufactured only in facilities identified and approved under the vaccine’s BLA.²⁵ Comirnaty’s labeling must be identical to that approved by FDA and must include warnings and precautions, contraindications, dosage and administration instructions, and storage and handling conditions, among other information.²⁶ The Comirnaty

authorization-european-union.

²⁰ 42 U.S.C. §262(a)(1)(C).

²¹ FDA, “Q&A for Comirnaty (COVID-19 Vaccine mRNA),” accessed August 30, 2021, <https://www.fda.gov/vaccines-blood-biologics/qa-comirnaty-covid-19-vaccine-mrna>. See also FDA, EUA letter to Pfizer, December 11, 2020, p. 23, <https://www.fda.gov/media/144416/download>.

²² FDA, EUA letter to Pfizer, December 11, 2020, p. 23.

²³ FDA, “Q&A for Comirnaty (COVID-19 Vaccine mRNA);” and FDA, Summary Basis for Regulatory Action—Comirnaty, p. 19.

²⁴ FDA, “Q&A for Comirnaty (COVID-19 Vaccine mRNA);” and FDA, Summary Basis for Regulatory Action—Comirnaty, p. 19.

²⁵ FDA, Approval Letter to BioNTech Manufacturing GmbH, Pfizer.

²⁶ FDA, Approval Letter to BioNTech Manufacturing GmbH, Pfizer. A vaccine manufacturer must submit proposed vaccine labeling as part of a BLA. See 21 C.F.R. §601.14. Labeling requirements for drugs and biologics are specified

approval letter also requires that any manufacturing changes that deviate from those approved under the BLA be submitted to FDA, specifies requirements for advertising and promotional labeling, and outlines postmarketing study obligations for the manufacturer.²⁷

As required for all licensed vaccines, Pfizer and BioNTech must report adverse events associated with Comirnaty to FDA.²⁸ Each serious and unexpected adverse experience must be reported as soon as possible but no later than 15 days from initial receipt of the information by the manufacturer.²⁹ Periodic safety reports are required for each adverse experience not reported in a 15-day alert report and must be submitted to FDA at quarterly intervals for the first three years following approval and at annual intervals thereafter.³⁰

Is there any difference between Comirnaty and the Pfizer-BioNTech vaccine?

The BLA-licensed vaccine Comirnaty is the same formulation as the EUA-authorized Pfizer-BioNTech COVID-19 vaccine. Specifically, both Comirnaty and the Pfizer-BioNTech vaccine contain “a nucleoside-modified messenger RNA (mRNA) encoding the viral spike glycoprotein (S) of SARS-CoV-2” formulated in the same lipids (i.e., organic compounds that are insoluble in water such as fats).³¹ Because the vaccines contain the same formulation, doses distributed under the EUA can be used interchangeably with doses licensed under the BLA without safety or effectiveness concerns.³² The distinction between Comirnaty and the Pfizer-BioNTech COVID-19 vaccine is legal rather than scientific, as further discussed in the section “Why did FDA refer to Comirnaty and the Pfizer-BioNTech vaccine as “legally distinct”?”

If Comirnaty is now licensed, why did FDA reissue an EUA for the Pfizer-BioNTech vaccine?

There are several reasons FDA reissued the Pfizer-BioNTech vaccine EUA when it licensed the Comirnaty vaccine under the BLA. In the August 23, 2021 letter, FDA stated that it reissued the EUA “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.”³³ Reissuing the EUA has several legal and practical effects.

First, the EUA allows the Pfizer-BioNTech vaccine and Comirnaty to be used for patient populations and clinical situations that are not included in the Comirnaty BLA.³⁴ FDA approved Comirnaty to be marketed only for a two-dose regimen for individuals 16 years of age and older.³⁵ The EUA authorizes both the Pfizer-BioNTech vaccine and Comirnaty to be used for a two-dose regimen for individuals 12 to 15 years of age, for certain immunocompromised

in 21 C.F.R. §§201.56, 201.57, for example.

²⁷ FDA, Approval Letter to BioNTech Manufacturing GmbH, Pfizer.

²⁸ FDA, Approval Letter to BioNTech Manufacturing GmbH, Pfizer.

²⁹ 21 C.F.R. §600.80(c).

³⁰ 21 C.F.R. §600.80(c).

³¹ FDA, Summary Basis for Regulatory Action—Comirnaty, p. 3; and FDA, EUA letter to Pfizer, December 11, 2020, p. 11.

³² FDA, EUA letter to Pfizer, September 22, 2021, p. 3.

³³ FDA, EUA letter to Pfizer, August 23, 2021, p. 2. See also FDA, EUA letter to Pfizer, September 22, 2021, p. 2, n. 9.

³⁴ FDA, EUA letter to Pfizer, September 22, 2021, p. 2.

³⁵ FDA, Approval Letter to BioNTech Manufacturing GmbH, Pfizer.

individuals to receive a third dose of the vaccine, and for single booster doses at least six months after the primary vaccination series for certain individuals determined to be at high risk for severe COVID.³⁶ Without the EUA, individuals 12 to 15 years of age would not be authorized or approved to receive a Pfizer-manufactured COVID-19 vaccine, nor could any individuals receive a third dose or booster. (For a summary of the populations covered by the EUA and the approved BLA, see **Table 1**.)

Second, reissuing the EUA allows vaccine administrators to use the remaining doses of the Pfizer-BioNTech vaccine that have not yet been administered. FDA notes in the EUA that there “remains a significant amount of Pfizer-BioNTech COVID-19 vaccine that was manufactured and labeled in accordance with” the EUA.³⁷ The Pfizer-BioNTech vaccine has the same formulation as Comirnaty but is legally distinct and can be manufactured, marketed, distributed, and administered only pursuant to the EUA.³⁸ (For more information on what it means for the two vaccines to be legally distinct, see “Why did FDA refer to Comirnaty and the Pfizer-BioNTech vaccine as “legally distinct”?”) If FDA had revoked the EUA when it approved the Comirnaty BLA, the remaining Pfizer-BioNTech vaccine doses would have been unauthorized and unable to be used.

Third, the EUA facilitates the logistics of distributing and administering Pfizer-manufactured COVID-19 vaccines. The EUA authorizes use of Comirnaty for the patient populations and clinical situations for which the Pfizer-BioNTech vaccine is authorized but that are not covered by the BLA: a two-dose regimen for individuals 12 to 15 years of age, a third dose for certain immunocompromised individuals 12 years and older, and a booster dose for certain individuals 18 years and older determined to be at high risk of severe COVID.³⁹ By authorizing Comirnaty for these uses, and clarifying that Comirnaty is interchangeable with the Pfizer-BioNTech vaccine, the EUA allows vaccine administrators to use whichever vaccine is available—whether it is labeled Comirnaty or Pfizer-BioNTech—which may avoid potential shortages or other logistical complications.⁴⁰

³⁶ FDA, EUA letter to Pfizer, September 22, 2021, p. 7.

³⁷ FDA, EUA letter to Pfizer, September 22, 2021, p. 13.

³⁸ FDA, EUA letter to Pfizer, September 22, 2021, p. 3, n. 10; 42 U.S.C. §360bbb-3.

³⁹ FDA, EUA letter to Pfizer, September 22, 2021, p. 7.

⁴⁰ FDA, EUA letter to Pfizer, September 22, 2021, pp. 2 and 7.

Table 1. Comparison of Patient Populations Covered by the Pfizer-BioNTech EUA and Comirnaty BLA

Patient Population	Pfizer-BioNTech EUA		Comirnaty BLA
	Pfizer-BioNTech	Comirnaty	
Individuals 0 to 11	x	x	x
Individuals 12 to 15	√	√	x
Individuals 16 and older	√	x	√
Third dose for certain immunocompromised individuals	√	√	x
Single booster dose at least six months after completing the primary vaccination series for certain individuals determined to be at high risk for severe COVID-19	√	√	x

Source: CRS.

Notes: EUA = Emergency Use Authorization; BLA = biologics license application. On August 12, 2021, FDA authorized third doses for individuals 12 years of age and older who have undergone solid organ transplants or been diagnosed with similarly immunocompromising conditions. On September 22, 2021, FDA reissued the EUA to authorize a single booster dose at least six months after completing the primary vaccination series for (1) individuals 65 years of age or older, (2) individuals 18 to 64 years of age who are at high risk of severe COVID-19, and (3) individuals 18 to 64 years of age whose institutions or occupations involve frequent exposure to SARS-CoV-2 such that they are at high risk of serious complications of COVID-19.

What is the scope of the current EUA for the Pfizer-BioNTech vaccine?

The Pfizer-BioNTech vaccine EUA, as reissued on September 22, 2021, authorizes a two-dose regimen of the Pfizer-BioNTech vaccine for individuals 12 years or age and older, a third dose of the Pfizer-BioNTech vaccine for individuals 12 years of age and older who have undergone solid organ transplants or been diagnosed with similarly immunocompromising conditions, and single booster doses at least six months after completing the primary vaccination series for certain categories of individuals determined to be at high risk for severe COVID. Specifically, the EUA authorizes booster doses for (1) individuals 65 years of age or older, (2) individuals 18 to 64 years of age who are at high risk of severe COVID-19, and (3) individuals 18 to 64 years of age whose institutions or occupations involve frequent exposure to SARS-CoV-2 such that they are at high risk of serious complications of COVID including severe COVID-19.⁴¹ The EUA also authorizes a two-dose regimen of Comirnaty for individuals 12 to 15 years of age, a third dose of Comirnaty for individuals 12 years or age and older who have undergone solid organ transplants or have been diagnosed with similarly immunocompromising conditions, and a single booster dose six months after the primary vaccination series for the same categories authorized for the Pfizer-

⁴¹ FDA, EUA letter to Pfizer, September 22, 2021, p. 7. The September 22, 2021, EUA revises the existing EUA, which FDA originally issued for the Pfizer-BioNTech vaccine on December 11, 2020, for a two-dose regimen in individuals 16 years of age or older. FDA, EUA letter to Pfizer, December 11, 2020. Since the initial EUA, FDA has amended the EUA several times and issued three additional decision memoranda. The first, issued May 10, 2021, authorized the Pfizer-BioNTech vaccine to be used in individuals 12 to 15 years of age. FDA, EUA letter to Pfizer, May 10, 2021, <https://www.fda.gov/media/148542/download>. The second, issued August 12, 2021, authorized a third dose of the Pfizer-BioNTech vaccine to be administered to individuals who have undergone solid organ transplants or have been diagnosed with similarly immunocompromising conditions. FDA, EUA letter to Pfizer, August 12, 2021, <https://www.fda.gov/media/151613/download>.

BioNTech vaccine.⁴² These uses are not included in the approved Comirnaty BLA (see “What is the scope of FDA’s biologics license for Comirnaty?”).

The scope of the Pfizer-BioNTech vaccine EUA is based on the supporting data and information submitted to FDA by the companies in their EUA requests. As FDA has received additional data to support that the vaccine may be effective in preventing COVID-19 in certain pediatric populations (i.e., 12 to 15 year olds) and under expanded dosing regimens (i.e., a third dose for certain immunocompromised individuals and single booster doses for individuals determined to be at high risk for severe COVID-19), the agency has amended and reissued the original Pfizer-BioNTech vaccine EUA to include these indications.

FDA initially granted the Pfizer-BioNTech vaccine EUA on December 11, 2020, based on safety and effectiveness data in individuals 16 years of age and older.⁴³ FDA subsequently reissued the EUA on May 10, 2021, to authorize the use of the vaccine in individuals 12 to 15 years of age based on clinical trial safety and effectiveness data in more than 2,000 individuals in this age group.⁴⁴ FDA again amended the Pfizer-BioNTech vaccine EUA on August 12, 2021, as requested by Pfizer, to allow for the use of a third dose of the vaccine in certain immunocompromised individuals based on safety and effectiveness data in the published literature.⁴⁵

On August 23, 2021, FDA reissued the EUA after it approved the Comirnaty BLA “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.”⁴⁶ FDA reissued the EUA again on September 22, 2021, to authorize single booster doses at least six months after the primary vaccination series for certain categories of individuals determined to be at high risk for severe COVID-19.⁴⁷

Under the terms of the EUA, the Pfizer-BioNTech vaccine may be manufactured only in a facility identified and agreed upon in Pfizer’s EUA request.⁴⁸ The Pfizer-BioNTech vaccine vial label and carton labels must be clearly marked for “Emergency Use Authorization.”⁴⁹ Pfizer must distribute the Pfizer-BioNTech vaccine to emergency response stakeholders directly or through authorized distributors as directed by the U.S. government, such as the Centers for Disease Control and Prevention (CDC).⁵⁰ The Pfizer-BioNTech vaccine must be administered by vaccine providers, as

⁴² FDA, EUA letter to Pfizer, September 22, 2021, p. 7.

⁴³ FDA, EUA letter to Pfizer, December 11, 2020.

⁴⁴ FDA, EUA letter to Pfizer, May 10, 2021.

⁴⁵ FDA, EUA letter to Pfizer, August 12, 2021.

⁴⁶ FDA, EUA letter to Pfizer, August 23, 2021, p. 2.

⁴⁷ FDA, EUA letter to Pfizer, September 22, 2021, p. 7.

⁴⁸ FDA, EUA letter to Pfizer, September 22, 2021, p. 8.

⁴⁹ FDA, EUA letter to Pfizer, September 22, 2021, p. 8.

⁵⁰ FDA, EUA letter to Pfizer, September 22, 2021, pp. 6-7. Pfizer and the U.S. government determine which entities are “authorized distributor(s).” FDA, EUA letter to Pfizer, September 22, 2021, p. 6, n.14. The letter defines *emergency response stakeholder* as public health agencies and their delegates. FDA, EUA letter to Pfizer, September 22, 2021, p. 6, n. 15.

defined by the EUA.⁵¹ Fact sheets must be made available to vaccination providers and recipients.⁵²

The EUA imposes reporting requirements on Pfizer in connection with adverse events.⁵³ It also imposes conditions on emergency response stakeholders and vaccination providers to distribute and administer the Pfizer-BioNTech vaccine in accordance with the EUA's terms and to provide relevant information to stakeholders and recipients.⁵⁴ The EUA further provides conditions related to advertising, promoting, and exporting the Pfizer-BioNTech vaccine.⁵⁵ Finally, the EUA requires that Comirnaty vaccines be manufactured, distributed, and administered in accordance with the EUA terms when administered for uses authorized by the EUA (i.e., for individuals 12 to 15 years of age, third doses for certain immunocompromised individuals, and single booster doses for certain individuals determined to be at high risk for severe COVID-19), except that Comirnaty vaccines manufactured and labeled in accordance with the BLA are deemed to meet the EUA's manufacturing, labeling, and distribution requirements.⁵⁶

Unlike the BLA, which will remain in effect indefinitely unless it is withdrawn for safety or efficacy reasons, the EUA remains in effect only until the Secretary revokes the declaration that an emergency exists due to the COVID-19 pandemic that justifies the emergency use of unapproved drugs and biological products.⁵⁷

Why did the FDA Vaccines and Related Biological Products Advisory Committee recommend booster doses only for certain categories of individuals?

The Vaccines and Related Biological Products Advisory Committee (VRBPAC) made its recommendation as to booster doses of the Pfizer-BioNTech vaccine based on the data available from clinical trials and real-world case studies, as well as on statutory standards for approving or authorizing biologics such as vaccines.

On September 17, 2021, FDA convened a meeting of the VRBPAC to discuss the supplemental BLA submitted by Pfizer-BioNTech for approval of a single booster dose of Comirnaty for individuals 16 years of age and older.⁵⁸ Pfizer and BioNTech initiated submission of their

⁵¹ FDA, EUA letter to Pfizer, September 22, 2021, p. 7. As defined in the EUA, for vaccines administered in the United States, a vaccination provider is "a facility, organization, or healthcare provider licensed or otherwise authorized by the emergency response stakeholder ... to administer or provide vaccination services" and "who is enrolled in the CDC COVID-19 Vaccination Program." FDA, EUA letter to Pfizer, September 22, 2021, p. 7, n. 16.

⁵² Specifically, vaccination providers must be provided with a fact sheet titled "Fact Sheet for Healthcare Providers Administering Vaccine (Vaccine Providers): Emergency Use Authorization (EUA) of Pfizer-BioNTech COVID-19 Vaccine to Prevent Coronavirus Disease 2019 (COVID-19)." Vaccine recipients must be provided with a fact sheet titled "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)." FDA, EUA letter to Pfizer, September 22, 2021, p. 8.

⁵³ FDA, EUA letter to Pfizer, September 22, 2021, p. 10.

⁵⁴ FDA, EUA letter to Pfizer, September 22, 2021, pp. 11-12.

⁵⁵ FDA, EUA letter to Pfizer, September 22, 2021, pp. 13.

⁵⁶ FDA, EUA letter to Pfizer, September 22, 2021, p. 13-14.

⁵⁷ FDA, EUA letter to Pfizer, September 22, 2021, p. 14; 42 U.S.C. §300bbb-3.

⁵⁸ FDA, "Vaccines and Related Biological Products Advisory Committee September 17, 2021 Meeting Announcement," accessed on September 27, 2021, <https://www.fda.gov/advisory-committees/advisory-committee-calendar/vaccines-and-related-biological-products-advisory-committee-september-17-2021-meeting-announcement#event-materials>.

supplemental BLA to FDA on August 25, 2021.⁵⁹ After consideration of the available data, as well as the statutory standards for approving or authorizing biologics such as vaccines, VRBPAC voted *not* to recommend approval of a single booster for individuals 16 years of age and older. VRBPAC instead voted to recommend an EUA for single booster doses for individuals 65 years of age and older and for individuals 18 to 64 years of age at high risk for severe COVID-19 or with frequent exposure to SARS-CoV-2 in their institution or occupation that put them at high risk of serious complications from COVID-19, including severe COVID-19.⁶⁰ FDA reissued the Pfizer-BioNTech vaccine EUA on September 22, 2021, with new authorizations consistent with VRBPAC’s recommendations.⁶¹

During the September 17, 2021 hearing, FDA and Pfizer-BioNTech presented the data available on changes in immunity over time after full vaccination and side effects associated with administering booster doses.⁶² The Committee also heard presentations on data from the United Kingdom regarding real-world effectiveness of COVID-19 vaccines and on data from Israel regarding the protection provided by booster doses against infection and severe cases of COVID-19.⁶³ The hearing also included a presentation on the epidemiology of the pandemic and comments from members of the public.⁶⁴

The standards for approving a biologic under a BLA are different from those for authorizing a medical countermeasure, such as a vaccine, for emergency use under an EUA. To approve a BLA (or supplemental BLA) under the Public Health Service (PHS) Act, FDA must determine that the sponsor has demonstrated the product (e.g., a vaccine) is safe and effective.⁶⁵ EUAs are subject to a different standard for authorization. To issue an EUA, FDA must determine, among other things, that the known and potential benefits of using the countermeasure to diagnose, treat, or prevent the relevant disease or condition outweigh the known and potential risks of such use.⁶⁶ Thus, to issue an EUA for a booster dose of the Pfizer-BioNTech vaccine, FDA would have to determine that the known and potential benefits of administering a single booster dose to

⁵⁹ Pfizer and BioNTech, “Pfizer and BioNTech Initiate Rolling Submission of Supplemental Biologics License Application to U.S. FDA for Booster Dose of Comirnaty in Individuals 16 and Older,” press release, August 25, 2021, <https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-initiate-rolling-submission>.

⁶⁰ FDA, “Vaccines and Related Biological Products Advisory Committee,” September 17, 2021, at 7:51-7:52 minutes, <https://www.youtube.com/watch?v=WFph7-6t34M>.

⁶¹ FDA, EUA letter to Pfizer, September 22, 2021, p. 3.

⁶² FDA, “Comirnaty (COVID-19 Vaccine, mRNA) Supplemental Biologics License Application for a Booster Dose in Individuals 16 Years of Age and Older,” presentation, September 17, 2021, p. 6, <https://www.fda.gov/media/152242/download> (hereinafter *VRBPAC Meeting Agenda*); FDA, “Application for Licensure of a Booster Dose of COMIRNATY, COVID-19 Vaccine, mRNA,” presentation, September 17, 2021, <https://www.fda.gov/media/152238/download>; FDA, “FDA Review of Effectiveness and Safety of COMIRNATY (COVID-19 Vaccine, mRNA) Booster Dose Biologics License Application Supplement,” presentation, September 17, 2021, <https://www.fda.gov/media/152239/download>; Pfizer and BioNTech, “BNT162b2 [COMIRNATY (COVID-19 Vaccine, mRNA)] Booster (Third) Dose,” presentation, September 17, 2021, <https://www.fda.gov/media/152240/download>.

⁶³ VRBPAC Meeting Agenda, p. 5; Jonathan Sterne, University of Bristol, “Real-World Effectiveness of COVID-19 Vaccines,” presentation, September 17, 2021, <https://www.fda.gov/media/152241/download>; Israel MOH, Weizmann Institute of Science, Gertner Institute, Hebrew University, and Technion, “Booster Protection Against Confirmed Infections and Severe Disease – Data from Israel,” presentation, September 17, 2021, <https://www.fda.gov/media/152205/download>.

⁶⁴ VRBPAC Meeting Agenda, p. 5; Sara Oliver, CDC, “Updates to COVID-19 Epidemiology and COVID-19 Vaccines,” presentation, September 17, 2021, <https://www.fda.gov/media/152243/download>.

⁶⁵ 42 U.S.C. §262(a); 21 U.S.C. §355.

⁶⁶ 21 U.S.C. §360bbb-3(c)(2)(B).

individuals 18 years of age and older outweigh the known and potential risks of administering the booster dose.

During the Committee discussion, VRBPAC members raised concerns about the available data's adequacy, particularly with respect to the risks and benefits for younger individuals not at high risk for severe COVID-19. Committee members expressed concerns that the value for younger individuals with lower risks of COVID-19 complications was not as clear, and that such individuals might be at higher risk for adverse events from additional doses.⁶⁷ In particular, multiple Committee members raised concerns about whether the risk of myocarditis (inflammation of the heart muscle)—particularly for men under the age of 40—might be increased with a third dose.⁶⁸ Others observed that myocarditis is a short-term condition, versus the potential longer-term consequences of COVID-19, and that the infrequency of myocarditis as a side effect may mean that sufficient data are obtainable only through widespread use of boosters rather than clinical trials.⁶⁹ The Committee noted that the pathogenesis of myocarditis is poorly understood, and more data are needed before moving forward with a booster dose in the general population.⁷⁰ In addition, Committee members observed that Pfizer's clinical trial was small, so it provided limited data on risks associated with boosters, particularly in younger age groups.⁷¹

Given that unauthorized booster doses have been administered to healthy individuals, some Committee members were surprised about the lack of strong safety evidence presented, and indicated that FDA's failure to request such data was a missed opportunity.⁷² A related challenge noted by members was that additional data and studies were forthcoming, but not yet available to inform the Committee's deliberations.⁷³ Finally, some members questioned whether there were adequate data about whether and how much the immune response decreased over time after the primary vaccination series, primarily due to reliance on measuring antibody levels rather than assessing cell-mediated immunity.⁷⁴

Due to the limitations of the Pfizer clinical trial data presented, the Committee also considered Israeli data.⁷⁵ Committee members observed that because Israel had administered booster doses beginning with older populations, limited data were available about the risks and benefits for younger populations.⁷⁶ Committee members also questioned whether the Israeli data were representative of the expected risks and benefits for the U.S. population, which has a lower vaccination rate. In particular, in the United States, transmission is driven primarily by unvaccinated individuals, and thus providing a third dose to the already vaccinated may provide only a marginal benefit for reducing overall disease burden.⁷⁷ Members observed that those who

⁶⁷ FDA, "Vaccines and Related Biological Products Advisory Committee," September 17, 2021, at 6:18-6:19.

⁶⁸ FDA, "Vaccines and Related Biological Products Advisory Committee," September 17, 2021, at 6:24-6:30, 6:39-40.

⁶⁹ FDA, "Vaccines and Related Biological Products Advisory Committee," September 17, 2021, at 6:45-6:46, 6:53-6:54.

⁷⁰ FDA, "Vaccines and Related Biological Products Advisory Committee," September 17, 2021, at 6:25.

⁷¹ FDA, "Vaccines and Related Biological Products Advisory Committee," September 17, 2021, at 6:14-6:15, 6:45, 6:56.

⁷² FDA, "Vaccines and Related Biological Products Advisory Committee," September 17, 2021, at 6:14-6:15.

⁷³ FDA, "Vaccines and Related Biological Products Advisory Committee," September 17, 2021, at 6:38.

⁷⁴ FDA, "Vaccines and Related Biological Products Advisory Committee," September 17, 2021, at 6:17-6:18, 6:35.

⁷⁵ FDA, "Vaccines and Related Biological Products Advisory Committee," September 17, 2021, at 6:14-6:15, 7:05.

⁷⁶ FDA, "Vaccines and Related Biological Products Advisory Committee," September 17, 2021, at 6:30-6:32, 7:05.

⁷⁷ FDA, "Vaccines and Related Biological Products Advisory Committee," September 17, 2021, at 6:17-6:18, 6:30-6:32, 6:35, 6:37.

stand to benefit most from additional doses that reduce the disease's severity are those at highest risk of severe complications from COVID-19.⁷⁸ This approach may be reevaluated as more data become available.⁷⁹

Following the presentations and public comments provided at the hearing, VRBPAC voted on whether the safety and effectiveness data from the Pfizer-BioNTech clinical trial (C4591001) supported the *approval* of a Comirnaty booster dose administered at least six months after completing the primary vaccination series for use in individuals 16 years of age and older.⁸⁰ Two Committee members voted to approve the supplemental BLA and sixteen voted not to approve it.⁸¹ Following a discussion of the first voting question, FDA recognized that Committee members had several concerns related to the benefit-risk balance of a booster in the population of individuals 16 years and older, as well as concerns about the data and level of evidence available to support the safety and effectiveness of a booster dose.⁸² Given this, FDA formulated a new question involving an EUA. The second voting question asked whether, based on the totality of scientific evidence available, including from clinical trial C4591001, the known and potential benefits outweighed the known and potential risks of providing a Pfizer-BioNTech vaccine booster at least six months after the primary vaccination series to individuals 65 years of age and older and individuals at high risk of severe COVID-19.⁸³ The Committee unanimously voted yes, recommending issuance of an EUA of a booster dose for those populations.⁸⁴

VRBPAC's recommendation to authorize booster doses only for certain populations was based on the data available and presented on September 17, 2021. The Committee could vote in a future meeting to modify its recommendations regarding such doses based on additional data on declining immunity, the effectiveness of booster doses after various intervals following the primary vaccination series, or the side effects of booster doses. Similarly, VRBPAC could vote to recommend approving booster doses for the population covered by the September 22, 2021 EUA or some other population, pursuant to a resubmitted supplemental BLA. While FDA takes VRBPAC's recommendation into consideration, it is not binding on the agency. As such, FDA may choose to expand the EUA or approve the vaccine for additional uses even if VRBPAC does not recommend such uses.

Can COVID-19 vaccine providers use the Comirnaty-labeled vaccine interchangeably with the Pfizer-BioNTech vaccine?

Yes. The revised EUA states that Comirnaty can be used interchangeably with the Pfizer-BioNTech vaccine because it is the same formulation.⁸⁵ This means vaccine administrators may use Comirnaty for the first dose and Pfizer-BioNTech vaccine for the second dose, or vice versa, "without presenting any safety or effectiveness concerns."⁸⁶ Similarly, either the Comirnaty or

⁷⁸ FDA, "Vaccines and Related Biological Products Advisory Committee," September 17, 2021, at 6:30-6:32.

⁷⁹ *Ibid.*

⁸⁰ FDA, "Vaccines and Related Biological Products Advisory Committee," September 17, 2021, at 6:57.

⁸¹ FDA, "Vaccines and Related Biological Products Advisory Committee," September 17, 2021, at 7:00-7:02.

⁸² FDA, "Vaccines and Related Biological Products Advisory Committee," September 17, 2021, at 7:42-7:43.

⁸³ FDA, "Vaccines and Related Biological Products Advisory Committee," September 17, 2021, at 7:50.

⁸⁴ FDA, "Vaccines and Related Biological Products Advisory Committee," September 17, 2021, at 7:51-7:52.

⁸⁵ FDA, EUA letter to Pfizer, September 22, 2021, p. 3.

⁸⁶ FDA, EUA letter to Pfizer, September 22, 2021, p. 3, n. 10. In the context of biological products, the standard for interchangeability is that (1) the biological product is biosimilar to the reference (i.e., brand-name) product; (2) the biological product can be expected to produce the same clinical result in any given patient as the reference product; and

Pfizer-BioNTech vaccine may be used for any third doses regardless of which vaccine was used for the original two-dose regimen.

Why did FDA refer to Comirnaty and the Pfizer-BioNTech vaccine as “legally distinct”?

In the EUA, FDA states that the Comirnaty and Pfizer-BioNTech vaccines “are legally distinct with certain differences that do not impact safety or effectiveness.”⁸⁷ While the Comirnaty and Pfizer-BioNTech vaccines have the same formulation, they are legally allowed to be marketed and used pursuant to different legal authorities.⁸⁸ Specifically, Comirnaty is licensed pursuant to a BLA issued under the PHS Act (42 U.S.C. §262).⁸⁹ The Pfizer-BioNTech vaccine is authorized for emergency use pursuant to the Federal Food, Drug, and Cosmetic (FD&C) Act (21 U.S.C. §360bbb-3).⁹⁰

Each product must be manufactured, labeled, marketed, distributed, and administered in accordance with the requirements of the legal regime under which it was approved or authorized. These requirements may differ in a number of ways. For example, under the EUA, the Pfizer-BioNTech vaccine must be accompanied by fact sheets for the vaccine administrator and recipient informing them, among other things, of the product’s emergency authorization, known and anticipated risks and benefits, and the right to decline the vaccine.⁹¹ Comirnaty need not be accompanied by this information if it is being administered pursuant to the BLA rather than the EUA; instead, the PHS Act and other FDA regulatory labeling requirements apply.⁹²

As another example, the Pfizer-BioNTech vaccine may be manufactured only at facilities identified and agreed upon in Pfizer’s EUA request, must be distributed directly by Pfizer or through authorized distributors to emergency response stakeholders (as defined in the EUA) as directed by the U.S. government, and must be administered by vaccination providers (as defined in the EUA) only to individuals 12 years of age and older in accordance with the uses authorized by the EUA.⁹³ These limitations do not apply to Comirnaty vaccines manufactured and distributed pursuant to the BLA; instead, the PHS Act and FD&C Act requirements apply. Comirnaty may be manufactured only at facilities identified and approved in the BLA.⁹⁴

(3) if administered more than once to an individual (as the Pfizer-BioNTech and Comirnaty vaccines are due to the two-dose regimen), the risk of safety and diminished efficacy from switching between the biosimilar and reference product is not greater than when using the reference product alone. 42 U.S.C. §262(k)(4). FDA appears to have used the same standard to determine that the Comirnaty and Pfizer-BioNTech vaccines are interchangeable.

⁸⁷ FDA, EUA letter to Pfizer, September 22, 2021, p. 3, n. 10.

⁸⁸ FDA, EUA letter to Pfizer, September 22, 2021, p. 3.

⁸⁹ FDA, Approval Letter to BioNTech Manufacturing GmbH, Pfizer, August 23, 2021; 42 U.S.C. §262.

⁹⁰ FDA, EUA letter to Pfizer, September 22, 2021.

⁹¹ FDA, EUA letter to Pfizer, September 22, 2021, p. 8; FDA, “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-2019),” September 22, 2021, <https://www.fda.gov/media/144413/download>; FDA, “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),” September 22, 2021, <https://www.fda.gov/media/144414/download>.

⁹² FDA, EUA letter to Pfizer, September 22, 2021, p. 14.

⁹³ FDA, EUA letter to Pfizer, September 22, 2021, pp. 6-7.

⁹⁴ FDA, Approval Letter to BioNTech Manufacturing GmbH, Pfizer, August 23, 2021.

What liability protections apply to COVID-19 vaccines?

Under the Public Readiness and Emergency Preparedness Act (PREP Act), the Secretary of Health and Human Services (HHS) has the authority to limit legal liability for losses relating to the administration of medical countermeasures—such as diagnostics, treatments, and vaccines—during a public health emergency.⁹⁵ In a declaration effective February 4, 2020, the Secretary invoked the PREP Act and declared COVID-19 to be a public health emergency warranting liability protections for manufacturers, distributors, and administrators of covered countermeasures (along with other covered persons).⁹⁶ If covered by the terms of such a declaration, the PREP Act generally immunizes a covered person from legal liability for all claims for loss relating to the administration or use of a covered countermeasure.⁹⁷

Under the current PREP Act declaration for COVID-19, covered countermeasures include “any drug, any biologic ... or any vaccine manufactured, used, designed, [or] developed ... [t]o diagnose, mitigate, prevent, treat, or cure COVID-19.”⁹⁸ Covered persons include manufacturers, distributors, and qualified persons authorized to administer covered countermeasures by federal, state, tribal, and local public health agencies.⁹⁹

Thus, vaccine manufacturers, distributors, and authorized health care providers administering the Pfizer-BioNTech COVID-19 vaccine or Comirnaty are generally immune from legal claims for injury or other losses resulting from the administration of the vaccine.¹⁰⁰ For example, an individual who suffers an adverse allergic reaction to a COVID-19 vaccine—such as the rare reported cases of anaphylaxis¹⁰¹—generally cannot sue the vaccine manufacturer for damages resulting from the injury. Instead, while the declared public health emergency remains in effect, monetary compensation for any deaths or serious injuries caused by COVID-19 vaccines may be available from the federal government through the Countermeasures Injury Compensation Program.¹⁰²

⁹⁵ 42 U.S.C. §§247d-6d, 247d-6e. For more detail on the scope of liability protections for COVID-19 countermeasures under the PREP Act, see generally CRS Legal Sidebar LSB10443, *The PREP Act and COVID-19: Limiting Liability for Medical Countermeasures*, by Kevin J. Hickey.

⁹⁶ HHS, “Declaration Under the Public Readiness and Emergency Preparedness Act for Medical Countermeasures Against COVID-19,” 85 *Federal Register* 15198, March 10, 2020. The PREP Act declaration has been subsequently amended nine times to expand the scope of its liability protection in various ways. See HHS, “Public Readiness and Emergency Preparedness Act,” accessed September 8, 2021, <https://www.phe.gov/Preparedness/legal/prepact/Pages/default.aspx> (linking to the PREP Act declaration amendments).

⁹⁷ 42 U.S.C. §247d-6d(a)(1).

⁹⁸ 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 *Federal Register* 79190, 79196, December 3, 2020. (Subsequent amendments have not altered this section of the declaration.)

⁹⁹ HHS, “Ninth Amendment to Declaration Under the Public Readiness and Emergency Preparedness Act for Medical Countermeasures Against COVID-19,” 86 *Federal Register* 51160, 51163, September 14, 2021.

¹⁰⁰ 42 U.S.C. §247d-6d(a)(1); see generally CRS Report R46399, *Legal Issues in COVID-19 Vaccine Development and Deployment*, by Kevin J. Hickey, Wen W. Shen, and Erin H. Ward, at pp. 32-36. The “sole exception to the immunity” is a claim for willful misconduct. See 42 U.S.C. §247d-6d(d)(1). “Willful misconduct” as defined in the PREP Act requires that the covered person acted (i) intentionally to achieve a wrongful purpose; (ii) knowingly without legal or factual justification; and (iii) 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. 42 U.S.C. §247d-6d(c)(1)(A).

¹⁰¹ CDC and FDA, “Allergic Reactions Including Anaphylaxis After Receipt of the First Dose of Pfizer-BioNTech COVID-19 Vaccine—United States, December 14-23,” *Morbidity and Mortality Weekly Report*, vol. 70, no. 2 (January 15, 2021), pp. 46-51, <https://www.cdc.gov/mmwr/volumes/70/wr/mm7002e1.htm>.

¹⁰² Health Resources and Services Administration, “Countermeasures Injury Compensation Program,” accessed September 8, 2021, <https://www.hrsa.gov/cicp>; see generally CRS Legal Sidebar LSB10584, *Compensation Programs*

Does FDA’s licensure of Comirnaty affect liability protections for COVID-19 vaccines under the PREP Act?

Generally speaking, it does not. Under the PREP Act, “covered countermeasures” include both (1) “qualified pandemic or epidemic products” and (2) biological products authorized for emergency use under an EUA.¹⁰³

Comirnaty is a biological product licensed by FDA to prevent COVID-19 (see “What is the scope of FDA’s biologics license for Comirnaty?”). It meets the definition of *qualified pandemic or epidemic product* and is thus a covered countermeasure under the PREP Act while the PREP Act declaration remains in effect. For its part, the Pfizer-BioNTech vaccine is authorized under an EUA to prevent COVID-19 (see “What is the scope of the current EUA for the Pfizer-BioNTech vaccine?”). It, too, meets the definition of *covered countermeasure* under the PREP Act.

Because Comirnaty and the Pfizer-BioNTech COVID-19 vaccine are both covered countermeasures, the liability protections under the PREP Act apply to both products. That is, assuming that all the other elements for immunity under the PREP Act are met,¹⁰⁴ whether the vaccine’s use is licensed by FDA or authorized under an EUA does not affect the PREP Act’s liability protections.

Do the PREP Act’s liability protections extend to off-label uses of Comirnaty?

It is not clear whether off-label uses of otherwise covered countermeasures, such as Comirnaty, would receive the same liability protections under the PREP Act as authorized and approved uses. Off-label use generally refers to the practice of prescribing or administering a drug or biologic (such as a vaccine) for a use other than the one or more specific uses FDA approved.¹⁰⁵ Such off-label uses are generally considered to be within the scope of the practice of medicine, with the physician exercising professional judgment about treatment, and therefore not in violation of the FD&C Act’s marketing restrictions.¹⁰⁶

Following the licensure of Comirnaty, there were reports of parents expressing interest in vaccinating their younger children who are not covered by the scope of the licensed vaccine or the EUA-authorized vaccine (i.e., children under 12 years of age) through off-label use of Comirnaty.¹⁰⁷ The CDC has noted that such uses of Comirnaty are not authorized and indicated that off-label uses therefore “may not be covered” under the PREP Act.¹⁰⁸

for *Potential COVID-19 Vaccine Injuries*, by Kevin J. Hickey and Erin H. Ward.

¹⁰³ 42 U.S.C. §247d-6d(i)(1)(A), (C). A “qualified pandemic product” is defined to include a “biological product that is ... manufactured, used, designed, [or] developed ... to diagnose, mitigate, prevent, treat, or cure a pandemic or epidemic” and that is approved or licensed by FDA. 42 U.S.C. §247d-6d(i)(7)(A)-(B).

¹⁰⁴ See CRS Legal Sidebar LSB10443, *The PREP Act and COVID-19: Limiting Liability for Medical Countermeasures*, by Kevin J. Hickey, for a discussion of those other elements (such as the claim being against a “covered person” and a causal relationship between the loss and the use of the covered countermeasure).

¹⁰⁵ FDA, “Understanding Unapproved Use of Approved Drugs ‘Off Label,’” accessed September 1, 2021, <https://www.fda.gov/patients/learn-about-expanded-access-and-other-treatment-options/understanding-unapproved-use-approved-drugs-label>.

¹⁰⁶ See, for example, *Buckman Co. v. Plaintiffs’ Legal Comm.*, 531 U.S. 341, 350 (2001).

¹⁰⁷ See, for example, Theresa Gaffney, “‘Tired of Worrying’: As Some Parents Press for Vaccines Off-Label, Pediatricians Call for Patience,” *STAT News*, August 27, 2021, <https://www.statnews.com/2021/08/27/covid19-vaccine-off-label-kids/>.

¹⁰⁸ CDC, “COVID-19 Vaccine FAQs for Healthcare Professionals” (see section “Off-Label Use”), accessed August 30,

The CDC’s statement reflects legal uncertainty as to whether PREP Act immunity extends to claims for injuries resulting from off-label uses of a covered countermeasure. For immunity under the PREP Act to apply, the activity at issue must relate to the administration or use of a covered countermeasure for which the Secretary of HHS has issued a PREP Act declaration.¹⁰⁹ If providers knowingly administer vaccines to populations currently outside of the EUA or the approved biologics license for Comirnaty, they would arguably fall outside of the current PREP Act declaration and therefore not be immunized from liability. In particular, the declaration contains language excluding uses that exceed the scope of authorization by the relevant public health authority. For example, the declaration states that “liability protections are afforded to Covered Persons only for” covered countermeasures that (1) “are related to activities authorized in accordance with the public health and medical response of the Authority Having Jurisdiction” or (2) are administered “pursuant to the FDA licensure, approval, clearance, or authorization.”¹¹⁰ The “Authority Having Jurisdiction” refers to the state, federal, tribal, or local “public agency ... that has legal responsibility and authority for responding to an incident.”¹¹¹ Thus, if providers intentionally engage in activities that the relevant public health authorities—here, the CDC and FDA—did *not* authorize, they may not be immune from claims of legal liability under the PREP Act declaration for those actions.

Off-label use generally refers to a situation where the provider exercises professional judgment to prescribe or administer a drug or biologic for an unapproved use. A potentially distinct scenario may occur when an otherwise-authorized health care provider unknowingly administers the vaccine to a recipient outside of the currently authorized population. For example, anecdotal media reports indicate instances of parents misrepresenting the ages of their children to obtain COVID-19 vaccines.¹¹² In that situation, the health care provider administering the vaccine may have no reason to know that the vaccine administration was unauthorized under the EUA and current CDC guidance.

Language in the PREP Act declaration arguably allows health care providers to retain legal immunity in this situation. The current PREP Act declaration purports to provide immunity even if the vaccine recipient is outside the covered population if the “qualified person reasonably could have believed the recipient was in this population.”¹¹³ The PREP Act declaration would therefore arguably reach authorized health care providers who unwittingly administer COVID-19 vaccines to populations beyond those currently authorized. As the former general counsel of HHS explained in an advisory opinion (later explicitly incorporated into the operative PREP Act declaration¹¹⁴), PREP Act immunity should apply to persons who “reasonably could have

2021, <https://www.cdc.gov/vaccines/covid-19/hcp/faq.html#off-label-use>.

¹⁰⁹ 42 U.S.C. §247d-6d(a)(1), (b)(1).

¹¹⁰ 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,” at 79196-97. There are other covered activities and distribution channels in the PREP Act declaration—such as activities relating to federal contracts—but these do not appear relevant to the off-label use scenario.

¹¹¹ 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,” at 79197.

¹¹² See, for example, Brett Kast, “Some Michigan Parents Reportedly Lying About Their Child’s Age to Get Them COVID Vaccine,” WXYZ, August 18, 2021, <https://www.wxyz.com/news/coronavirus/covid-19-vaccine/some-michigan-parents-reportedly-lying-about-their-childs-age-to-get-them-covid-vaccine>.

¹¹³ 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,” at 79197.

¹¹⁴ 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” at 79195, n. 19.

believed” they were covered persons administering a covered countermeasure, even if that belief later proved mistaken.¹¹⁵ Given the limited case law on the PREP Act, however, it is difficult to determine whether a court would agree with these constructions of the PREP Act declaration and statute.¹¹⁶

Separately from the PREP Act issue, the CDC has stated that knowing off-label uses “would be in violation of the CDC COVID-19 Vaccination Program provider agreement and therefore may not be reimbursable, and may impact the ability of a provider to remain in the CDC Program, in addition to other potential sanctions.”¹¹⁷ Thus, whether or not PREP Act immunity applies, providers engaging in intentional off-label use may be in violation of their contractual obligations.

VRBPAC, the FDA’s vaccine advisory committee, may ultimately recommend authorizing additional uses for the Pfizer-BioNTech and other COVID-19 vaccines—such as administration of the vaccine to children aged 5 to 11 or booster shots for the general adult population that is not determined to be at high risk for severe COVID-19. FDA would then likely reissue the currently operative EUA to authorize these additional uses. At that point, such uses would no longer be off-label but within the scope of an EUA and covered by the PREP Act.

Does FDA’s licensure of Comirnaty affect the authority of employers or schools to “mandate” COVID-19 vaccines?

As explained in more detail in other CRS products, federal law does not generally preclude private employers from requiring that their employees be vaccinated but may require these entities to provide appropriate exemptions based on medical disabilities or religious beliefs.¹¹⁸ As to government employers and public schools, modern courts have relied on *Jacobson v. Massachusetts*—a 1905 Supreme Court ruling holding that the Constitution does not preclude state governments from mandating vaccination¹¹⁹—to uphold such vaccine mandates (with

¹¹⁵ HHS, “Advisory Opinion on the Public Readiness and Emergency Preparedness Act and the March 10, 2020 Declaration under the Act,” May 19, 2020, p. 2, <https://www.hhs.gov/sites/default/files/prep-act-advisory-opinion-hhs-ogc.pdf>. HHS’s interpretation draws on the statutory provision that provides immunity under “circumstances in which ... the covered person reasonably could have believed that the countermeasure was administered or used in accordance with” population or geographical limitations in the PREP Act Declaration. 42 U.S.C. §247d-6d(a)(4)(B).

¹¹⁶ For example, assuming the PREP Act declaration is read to cover this situation, the liability protections must still accord with the statute. To be a covered countermeasure under the PREP Act, the vaccine must be approved, licensed, or authorized for emergency use by FDA. 42 U.S.C. §247d-6d(i)(1)(C), (7)(B). Comirnaty and the Pfizer-BioNTech vaccine are licensed and authorized for emergency use by FDA, respectively, and are thus covered countermeasures. Read literally, the PREP Act’s definition of *covered countermeasure* requires only that “the biological product ... is authorized” (or licensed) and does not speak to the authorization of particular uses. 42 U.S.C. §247d-6d(i)(1)(C), (7)(B)(i). That said, a court might understand the word *authorized* (or *licensed*) to imply that the actual use at issue must be within the scope of the EUA (or approved biologics license) in order to be a “covered countermeasure.”

¹¹⁷ CDC, “COVID-19 Vaccine FAQs for Healthcare Professionals” (see section “Off-Label Use”).

¹¹⁸ See CRS Legal Sidebar LSB10573, *COVID-19 Vaccination Requirements: Potential Constraints on Employer Mandates Under Federal Law*, by April J. Anderson and Victoria L. Killion; see also Equal Employment Opportunity Commission, “What You Should Know About COVID-19 and the ADA, the Rehabilitation Act, and Other EEO Laws,” accessed September 9, 2021, <https://www.eeoc.gov/wysk/what-you-should-know-about-covid-19-and-ada-rehabilitation-act-and-other-eeo-laws> (“The federal [employment laws] do not prevent an employer from requiring all employees physically entering the workplace to be vaccinated for COVID-19, subject to the reasonable accommodation provisions of Title VII [relating to religious objections] and the ADA [relating to disabilities].”).

¹¹⁹ *Jacobson v. Massachusetts*, 197 U.S. 11, 26–31 (1905); *Zucht v. King*, 260 U.S. 174, 176 (1922) (“[*Jacobson*] settled that it is within the police power of a State to provide for compulsory vaccination.”).

appropriate exemptions).¹²⁰ Based on this precedent, legal challenges to public schools' and employers' COVID-19 vaccine mandates have largely been rejected by courts in early stages of litigation.¹²¹

Prior to FDA approval of the Pfizer-BioNTech COVID-19 vaccine, some commentators argued that the mandates for EUA-authorized vaccines may not be legal under the EUA statute.¹²² In particular, Section 564(e)(1)(A)(ii)(III) of the FD&C Act requires the Secretary of HHS to ensure that individuals receiving EUA products “are informed ... of the option to accept or refuse administration of the product, of the consequences, if any, of refusing administration of the product, and of the alternatives to the product that are available and of their benefits and risks.”¹²³ In these commentators' view, this language might suggest that mandating EUA products is “categorically prohibited” because the recipient must have the “option to accept or refuse administration of the product.”¹²⁴ Others read this provision not to prohibit schools' or employers' vaccine requirements but merely to require that vaccine recipients receive appropriate information—such as the FDA fact sheets for COVID-19 vaccines.¹²⁵

In a recent opinion, the Office of Legal Counsel (OLC)—the division of the Department of Justice that provides legal advice to the President—considered and rejected the argument that Section 564(e)(1)(A)(ii)(III) prohibits vaccine mandates.¹²⁶ In OLC's view, this section “concerns only the provision of information to potential vaccine recipients and does not prohibit public or private entities from imposing vaccination requirements.”¹²⁷ Consistent with this view, at least two district courts have rejected this statutory argument.¹²⁸

¹²⁰ See CRS Report R46745, *State and Federal Authority to Mandate COVID-19 Vaccination*, by Wen W. Shen, pp. 3-4 (collecting cases). Presuming that it acts pursuant to valid statutory and constitutional authority, *Jacobson* implies that the federal government has power to require vaccination in some circumstances—for example, for federal employees. See Executive Order on Requiring Coronavirus Disease 2019 Vaccination for Federal Employees, September 9, 2021, <https://www.whitehouse.gov/briefing-room/presidential-actions/2021/09/09/executive-order-on-requiring-coronavirus-disease-2019-vaccination-for-federal-employees/>; see generally CRS Legal Sidebar LSB10633, *Federal Employees and COVID-19 Vaccination Attestations: Immediate Takeaways*, by April J. Anderson, Wen W. Shen, and Jon O. Shimabukuro.

¹²¹ See, for example, *Klaassen v. Trustees of Indiana Univ.*, No. 1:21-CV-238 DRL, 2021 WL 3073926 (N.D. Ind. July 18, 2021) (denying preliminary injunction against Indiana University's COVID-19 vaccine mandate for students), *motion for injunction pending appeal denied*, 7 F.4th 592, 593 (7th Cir. 2021) (“Given [*Jacobson*], there can't be a constitutional problem with [requiring] vaccination against SARS-CoV-2.”); *Bridges v. Houston Methodist Hosp.*, No. CV H-21-1774, 2021 WL 2399994, at *1 (S.D. Tex. June 12, 2021) (dismissing wrongful termination claim based on private-employer COVID-19 vaccine mandate); *Harris v. Univ. of Massachusetts*, No. 21-CV-11244-DJC, 2021 WL 3848012, at *1 (D. Mass. Aug. 27, 2021) (denying preliminary injunction against University of Massachusetts' COVID-19 vaccine mandate for students); *Norris v. Stanley*, No. 1:21-CV-756, 2021 WL 3891615, at *1 (W.D. Mich. Aug. 31, 2021) (denying temporary restraining order against COVID-19 vaccine mandate for Michigan State University employees); *Valdez v. Grisham*, No. 21-cv-783, 2021 WL 4145746, at *13 (D.N.M. September 13, 2021) (denying temporary restraining order and preliminary injunction against COVID-19 vaccine mandate for school workers, certain health care workers, the governor's office, and state fair attendees).

¹²² Efthimos Parasidis and Aaron S. Kesselheim, “Assessing the Legality of Mandates for Vaccines Authorized Via an Emergency Use Authorization,” <https://www.healthaffairs.org/doi/10.1377/hblog20210212.410237/full/>.

¹²³ 21 U.S.C. §360bbb-3(e)(1)(A)(ii)(III).

¹²⁴ Parasidis and Kesselheim, footnote 122.

¹²⁵ Anderson, Shen, and Shimabukuro, footnote 120, at 6 (explaining this argument).

¹²⁶ OLC, “Whether Section 564 of the Food, Drug, and Cosmetic Act Prohibits Entities from Requiring the Use of a Vaccine Subject to an Emergency Use Authorization,” July 6, 2021, <https://www.justice.gov/olc/file/1415446/download> (hereinafter *OLC Section 564 Opinion*).

¹²⁷ *OLC Section 564 Opinion*, p. 7.

¹²⁸ *Bridges v. Houston Methodist Hosp.*, No. CV H-21-1774, 2021 WL 2399994, at p. *2 (S.D. Tex. June 12, 2021);

It is therefore not clear that the EUA status of a vaccine has any bearing on the authority of schools and employers to mandate that vaccine. Now that FDA has approved Comirnaty, legal arguments against vaccine mandates that relied on COVID-19 vaccines' EUA status are now largely moot.¹²⁹ To that extent, FDA's approval of Comirnaty may reduce any legal uncertainty surrounding vaccine mandates.

For the most part, however, the legal authority for COVID-19 vaccine mandates—and the statutory or constitutional constraints on them—are the same before and after Comirnaty's licensure.¹³⁰ As a practical matter, to the extent that some employers and schools previously refrained from vaccination mandates because no COVID-19 vaccine had been fully approved by FDA, the approval of Comirnaty may result in greater use of vaccine mandates.¹³¹

Author Information

Kevin J. Hickey
Legislative Attorney

Agata Bodie
Analyst in Health Policy

Erin H. Ward
Legislative Attorney

Valdez v. Grisham, No. 21-cv-783, 2021 WL 4145746, at *5 (D.N.M. September 13, 2021).

¹²⁹ At the time of this writing, Comirnaty is the only FDA-approved COVID-19 vaccine. The Moderna and Johnson & Johnson COVID-19 vaccines are available only under an EUA. However, the argument against vaccine mandates based on the EUA statute would appear to be precluded as long as the vaccine mandate at issue accepts an available FDA-approved option (here, Comirnaty). See *Norris v. Stanley*, No. 1:21-CV-756, 2021 WL 3891615, at p. *2 (W.D. Mich. Aug. 31, 2021) (“[S]hould Plaintiff be offered the FDA-approved Pfizer Comirnaty vaccine, her argument under the EUA statute would be moot....”). The legal issue may remain open with respect to vaccine mandates imposed on individuals 12 to 15 years old, however, as no vaccine is approved for use in this age group. See “If Comirnaty is now licensed, why did FDA reissue an EUA for the Pfizer-BioNTech vaccine?”

¹³⁰ There are some exceptions, such as where particular statutory authorities (or, in the employment context, contractual requirements such as collective bargaining agreements) distinguish between authorized and approved vaccines. For example, the Department of Defense interprets Title 10, Section 1107a, of the *U.S. Code* to preclude a mandate for EUA vaccines unless the President issues a waiver. See *OLC Section 564 Opinion*, pp. 16-17.

¹³¹ See, for example, Deepa Shivaram, “Why Pfizer’s FDA Approval Matters and What It Means for Vaccine Mandates,” NPR, August 24, 2021, <https://www.npr.org/sections/coronavirus-live-updates/2021/08/24/1030267314/pfizer-vaccine-covid-fda-approval-kids-faq-mandate> (“It’s likely we’ll see more vaccine requirements put in place now that there is one vaccine with full FDA approval.”).

Disclaimer

This document was prepared by the Congressional Research Service (CRS). CRS serves as nonpartisan shared staff to congressional committees and Members of Congress. It operates solely at the behest of and under the direction of Congress. Information in a CRS Report should not be relied upon for purposes other than public understanding of information that has been provided by CRS to Members of Congress in connection with CRS's institutional role. CRS Reports, as a work of the United States Government, are not subject to copyright protection in the United States. Any CRS Report may be reproduced and distributed in its entirety without permission from CRS. However, as a CRS Report may include copyrighted images or material from a third party, you may need to obtain the permission of the copyright holder if you wish to copy or otherwise use copyrighted material.