Assessing COVID-19 Emergency Use Authorizations

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ABSTRACT

Emergency Use Authorizations (EUAs) have been integral to the federal government's response to the COVID-19 pandemic. During a public health emergency, the Federal Food, Drug, and Cosmetic Act permits the U.S. Food and Drug Administration (FDA) the authority to issue EUAs to allow the distribution of unapproved medical products, or of already-authorized products for unapproved uses, when certain criteria are met, including that there are no adequate, approved, and available alternatives. When compared to standards for FDA approval of drugs, medical devices, and vaccines, the EUA pathway has a lower statutory bar to market. This lower bar provides FDA with flexibility in responding to public health emergencies, but also permits marketing of medical products where safety and effectiveness data are less robust than with full approval. Within the first thirteen months of the pandemic, FDA issued over 400 EUAs for a wide range of medical products. Products authorized under EUAs have had varying degrees of efficacy, safety, and reliability. While some EUA medical products have been essential elements of the health and public health responses to the pandemic, others were pulled from the market because they ultimately proved to be unsafe or ineffective. This Article discusses the EUA framework and the motivations that led to its creation, examines FDA's use of the EUA process during the COVID-19 pandemic, and offers suggestions for ways that Congress and FDA can recalibrate the EUA mechanism to help it better achieve its goals.

I. INTRODUCTION

Emergency Use Authorizations (EUAs)—which permit the marketing of unapproved medical products or unapproved uses of approved medical products in the United States—have been integral to the medical and public health response to the COVID-19 pandemic.[1] Under the Federal Food, Drug, and Cosmetic Act (FDCA), the

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Secretary of the U.S. Department of Health and Human Services (HHS) has the authority to issue an emergency declaration that authorizes the U.S. Food and Drug Administration (FDA) to issue EUAs.[2] The EUA pathway has a low statutory bar to market: rather than demonstrate safety through "adequate tests by all methods reasonably applicable" and "substantial evidence" of effectiveness—as is required for FDA drug approval, for example[3]—under the EUA mechanism, a product may come to market if "it is reasonable to believe" that "the product may be effective" and that "the known and potential benefits of the product . . . outweigh [its] known and potential risks."[4]

From February 4, 2020—when then-HHS Secretary Alex Azar issued an emergency declaration for COVID-19—through March 8, 2021, FDA issued more than 400 EUAs related to COVID-19.[5] These EUAs, covering approximately the first thirteen months of the COVID-19 pandemic, authorized the distribution of a wide range of products such as ventilators, N95 respirator decontamination devices, viral detection tests, antibody tests, drugs, vaccines, and more.[6] Consistent with the low, flexible statutory threshold for issuing an EUA,[7] products authorized for use under the EUA pathway were supported by varying kinds of evidence and had varying degrees of effectiveness, safety, and reliability.

Alongside heavy use of the EUA pathway, from the onset of the COVID-19 pandemic through the end of his term, the administration of President Donald J. Trump repeatedly undermined science-based decisions and exerted political pressure on public health officials within HHS, FDA, and the U.S. Centers for Disease Control and Prevention (CDC).[8] At times, leaders within these agencies, including at FDA,

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1 21 U.S.C. § 360bbb-3.

2 *Id.*

3 21 U.S.C. § 355(d).

4 *See id.*; *see also* U.S. FOOD & DRUG ADMIN., GUIDANCE FOR EMERGENCY USE AUTHORIZATION OF MEDICAL PRODUCTS AND RELATED AUTHORITIES 8 (Jan. 2017), https://www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-medical-products-and-related-authorities [https://perma.cc/Y2A2-BTTJ] [hereinafter 2017 EUA GUIDANCE] ("The 'may be effective' standard for EUAs provides for a lower level of evidence than the 'effectiveness' standard that FDA uses for product approvals.").

5 *Coronavirus Disease 2019 (COVID-19) EUA Information, Emergency Use Authorization*, U.S. FOOD & DRUG ADMIN., https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization (last accessed Mar. 8, 2021) [hereinafter FDA COVID-19 EUA List] [https://perma.cc/UZ2B-XPKE]; *Emergency Use Authorization—Archived Information*, U.S. FOOD & DRUG ADMIN., https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization-archived-information (last accessed Mar. 8, 2021) [hereinafter FDA Revoked EUA List] [https://perma.cc/RM5Y-3LBB].

6 FDA COVID-19 EUA List, *supra* note 5.

7 21 U.S.C. § 360bbb-3.

8 *See, e.g.*, Letter from Anne Schuchat, Principal Deputy Director, Ctrs. for Disease Control & Prevention, to Rochelle P. Walensky, Director, Ctrs. for Disease Control & Prevention, and Administrator, Agency for Toxic Substances and Disease Registry, Summary of Agency Guidance Review (Mar. 10, 2021), https://www.cdc.gov/coronavirus/2019-ncov/downloads/communication/Guidance-Review.pdf (reporting

succumbed, or at least appeared to succumb, to the political pressure, for example by making public statements that drastically misrepresented scientific data supporting products issued EUAs or by issuing EUAs for products shortly after public statements from the White House urged FDA to do so.[9] The net result was diminished public trust in decisions and statements from public health agencies and officials, sentiments that carried forward into the administration of President Joseph R. Biden, Jr.[10]

Amid a raging pandemic with significant gaps in testing and treatment options, FDA was tasked with deciding between denying an EUA, and potentially delaying access to what may prove to be an effective COVID-19 countermeasure, or issuing one for a promising, but uncertain, medical product that might ultimately prove to be unsafe or ineffective. In many instances, the agency chose the latter course.[11] Yet, for any medical product—and perhaps especially during a pandemic—effectiveness and reliability issues raise significant health and public health concerns, and can contribute to unhelpful or harmful policy decisions.[12] In addition, issuance of EUAs, similar to other kinds of non-trial preapproval access, may affect clinical trial enrollment, slowing or preventing research needed to understand the safety and effectiveness of the products issued the EUAs as well as potential competitor products.[13]

Evaluating FDA's approach to COVID-19 EUAs is important as the agency continues its efforts to address the pandemic.[14] An assessment also can help identify

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the results of a 2021 review of CDC's existing COVID-19 guidance that found "a variety of issues," including "guidance that was not primarily authored by CDC staff") [https://perma.cc/Y5CA-M4WF].

9 *See infra* Section III.B.

10 *See, e.g.*, Tanya Lewis, *How the U.S. Pandemic Went Wrong—And What Went Right—During a Year of COVID*, SCI. AM. (Mar. 11, 2021), https://www.scientificamerican.com/article/how-the-u-s-pandemic-response-went-wrong-and-what-went-right-during-a-year-of-covid/ [https://perma.cc/7ZCD-TNK9]; RJ Reinhart, *More Americans Now Willing to Get COVID-19 Vaccine*, GALLUP (Nov. 17, 2020), https://news.gallup.com/poll/325208/americans-willing-covid-vaccine.aspx (reporting that only 58% of Americans reported being willing to get a COVID-19 vaccine authorized by FDA, up from 50% in September) [https://perma.cc/QE7J-9Z8W]; *7 Former FDA Commissioners: The Trump Administration is Undermining the Credibility of the FDA*, WASH. POST (Sept. 29. 2020), https://www.washingtonpost.com/opinions/2020/09/29/former-fda-commissioners-coronavirus-vaccine-trump/ [https://perma.cc/7V9L-NVL5]; *but see* Daniel Engber, *No, Public Trust in Scientific Institutions Has Not Eroded*, WIRED (Sept. 2, 2020, 8:00 AM), https://www.wired.com/story/no-public-trust-in-scientific-institutions-has-not-eroded/ [https://perma.cc/PA7X-H4MA].

11 *See infra* Section IV.

12 *Cf.* Alex John London & Jonathan Kimmelman, *Against Pandemic Research Exceptionalism*, 368 SCIENCE 476, 477 (2020) (arguing that regulatory agencies should take steps to ensure the conduct of rigorous research during pandemics).

13 *See, e.g.*, Andre C. Kalil, *Treating COVID-19—Off-Label Drug Use, Compassionate Use, and Randomized Clinical Trials During Pandemics*, 323 JAMA 1897 (2020) (describing difficulties completing well-designed clinical trials for Ebola products).

14 Indeed, this Article joins the growing body of literature that analyzes various aspects of FDA's implementation of its EUA authority during the COVID-19 pandemic. This literature includes other articles presented at the *Food and Drug Law Journal*'s 2020 annual symposium: *This Teachable Moment: How COVID-19 Provides Lessons from FDA's Past and Present That Will Benefit Its Future Preparedness*, *see, e.g.*, Yaniv Heled, Ana Santos Rustchman & Liza Vertinsky, *Regulatory Reactivity: FDA and the Response to COVID-19*, 76 FOOD & DRUG L.J. 318 (2021), as well as articles published elsewhere. *See, e.g.*, Jerry Avorn & Aaron Kesselheim, *Regulatory Decision-Making on COVID-19 Vaccines During a Public Health Emergency*, 324 JAMA 1284 (2020); Barbara J. Evans & Ellen Wright Clayton, *Deadly Delay: The FDA's*

areas for improvement in dealing with future public health emergencies. To those ends, this Article—which was prepared for the *Food and Drug Law Journal*'s 2020 annual symposium, *This Teachable Moment: How COVID-19 Provides Lessons from FDA's Past and Present That Will Benefit Its Future Preparedness*, which was held on November 12–13, 2020—examines how FDA's implementation of its EUA authorities evolved during roughly the first year that the agency issued EUAs for COVID-19 products. To help situate the Article, we note that the bulk of this Article was drafted between August–December 2020 and that the authors incorporated updates in early March 2021. Accordingly, we do not intend this Article to cover developments that post-date March 2021.

This Article proceeds in four parts. First, the Article outlines the EUA framework and the motivations that led to its creation. Second, this Article considers the overall political context in which FDA operates, as well as the risks of inappropriate political influence on FDA's decisions to issue EUAs. Third, the Article analyzes how FDA used its EUA authority during the COVID-19 pandemic through early March 2021, including several case studies of medical products for which FDA issued EUAs. Finally, building off lessons learned from the COVID-19 pandemic, the Article offers suggestions for ways Congress and FDA can recalibrate the EUA mechanism to help ensure the pathway can be used to best achieve its goals. Some of these recommendations would require statutory changes, but others could be implemented by FDA under its existing authority, such as requiring more exacting pre-market studies and post-market assessment of issued EUAs.

II. UNDERSTANDING THE EUA MECHANISM

Via the Project BioShield Act of 2004, Congress created the EUA pathway to address concerns surrounding approval of countermeasures to combat chemical, biological, radiological, and nuclear (CBRN) agents.[15] Among its provisions, the BioShield Act added Section 564 to the FDCA, which contains the statutory provisions related to EUAs.[16] During a declared emergency, EUAs may be issued for products intended to diagnose, treat, or prevent serious or life-threatening diseases when certain criteria are met, including that there are no adequate, approved, and available alternatives.[17] When the HHS Secretary determines that the emergency is over, they terminate the declaration, and all EUAs issued based on that declaration no longer remain in effect.[18] There is a long history leading up to Congress's creation of this EUA mechanism, which we briefly recount.

During the 1990s, FDA struggled to establish appropriate protocols to govern the review and approval of CBRN countermeasures. Just prior to the 1991 Gulf War, FDA

Role in America's COVID-Testing Debacle, 130 YALE L.J. F. 78 (2020); Elizabeth Y. McCuskey, *FDA in the Time of COVID-19*, 45 ABA ADMIN. & REGUL. L. NEWS (2020); Ameet Sarpatwari, Anna Kaltenboeck & Aaron S. Kesselheim, *Missed Opportunities on Emergency Remdesivir Use*, 324 JAMA 331 (2020).

[15] *See* Project BioShield Act of 2004, Pub. L. No. 108-276, 118 Stat. 835 (July 21, 2004).

[16] 21 U.S.C. § 360bbb-3.

[17] *Id.*

[18] *Id.*

amended its regulations to allow the agency the ability to issue an informed consent waiver in instances where military exigencies required mandatory administration of investigational medical products or off-label uses of approved products to counter the threat of biological and chemical warfare.[19]

Service members sued to invalidate FDA's new rule, but the United States Court of Appeals for the D.C. Circuit held that FDA's amendments to its regulations were within the agency's discretion.[20] Despite the failed legal challenge, the amendments were criticized after the war, with some researchers suggesting that the countermeasures authorized for use via the mechanism—pyridostigmine bromide and the botulinum toxoid vaccine—may have contributed to Gulf War Illness, which affected hundreds of thousands of veterans.[21] In light of the ongoing controversy, FDA revoked the informed consent waiver provision in 1999.[22]

The revocation of the rule did not eliminate the regulatory and national security concerns that initially led to its promulgation. During the late 1990s and early 2000s, FDA and the U.S. Department of Defense (DoD) discussed the creation of new mechanisms for review and approval of CBRN countermeasures for military uses.[23] These discussions included debate on how best to structure safety and effectiveness standards in instances where it may be unethical to conduct clinical trials due to the risk of serious injury or death to human participants, as may be the case when evaluating the effectiveness of CBRN countermeasures.[24]

The urgency of the matter grew exponentially following the 9/11 attacks, anthrax letter attacks in autumn 2001, and U.S. military interventions that began in the early 2000s in Afghanistan and Iraq. The EUA mechanism was one aspect of a diverse set of tools created to address challenges in the development, stockpiling, and administration of CBRN countermeasures.

A. Creation of the EUA Mechanism

Congress added the EUA provisions to the FDCA amid a legal crisis impacting DoD's anthrax vaccine immunization program (AVIP). The AVIP was launched in December 1997, and immunizations begin in March 1998.[25] Under the program, anthrax vaccine inoculation was mandatory for all 2.5 million active duty and reserve

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19 *See, e.g.*, Efthimios Parasidis, *Justice and Beneficence in Military Medicine and Research*, 73 OHIO ST. L.J. 724, 741–42 (2012).

20 Doe v. Sullivan, 938 F.2d 1370, 1381–82 (D.C. Cir. 1991).

21 *See* Efthimios Parasidis, *The Military Biomedical Complex: Are Service Members a Vulnerable Population?*, 16 HOUS. J. HEALTH L. & POL'Y 113, 137–40 (2016); RICHARD A. RETTIG, RAND, WAIVING INFORMED CONSENT: MILITARY USE OF NON-FDA APPROVED DRUGS IN COMBAT (2000).

22 Revocation of 1990 Interim Final Rule, 64 Fed. Reg. 54,180, 54,184 (Oct. 5, 1999) (to be codified at 21 C.F.R. pt. 50, 312).

23 *See, e.g.*, Parasidis, *supra* note 21, at 137–40.

24 *See id.*

25 Rempfer v. Sharfstein, 583 F.3d 860, 863–67 (D.C. Cir. 2009).

service members, as well as members of the Coast Guard and certain civilian employees, regardless of where an individual was stationed or set to deploy.[26]

At the time, the anthrax vaccine was FDA-approved to protect against cutaneous anthrax, which is anthrax that comes into contact with the skin.[27] However, DoD mandated the vaccine due to its fears regarding the potential use of airborne anthrax as a biological weapon.[28] Reports had identified several countries—including Iraq—which maintained stockpiles of weapons-grade anthrax, and U.S. authorities surmised that terrorist groups also had acquired the deadly pathogen.[29]

From the outset, the AVIP was controversial. A congressional report published in 2000 dubbed the program an "overwrought response to the threat of anthrax" and one that "compromises the practice of medicine to achieve military objectives."[30] The House Committee on Government Reform found that DoD provided service members with "[h]eavy handed, one-sided informational materials[,]" and that the military was "far more concerned with public relations than effective force protection or the practice of medicine."[31] The report noted that DoD actions fueled "suspicions the program understates adverse reaction risks in order to magnify the relative, admittedly marginal, benefits of the vaccine."[32] The committee further stated that, pursuant to FDA regulations, use of the vaccine for inhalation anthrax amounted to investigational use under the FDCA.[33] The committee recommended that DoD halt AVIP until and unless FDA approved the vaccine as prophylaxis for inhalation anthrax.[34]

Despite the scathing congressional report, DoD refused to suspend the AVIP. Moreover, within the first two years of the program, no less than twenty-four service members were discharged "under other than honorable conditions" for refusing the anthrax vaccine.[35] By 2002, disciplinary action had been taken in more than 100 Air Force cases alone, including at least one Air Force physician who refused to be

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[26] *See id.*

[27] *See id.*

[28] H.R. REP. NO. 106-556, at 5–9 (2000).

[29] *See id.*

[30] *Id.* at 2–3.

[31] *Id.* The report was based on a study conducted by the Congressional Subcommittee on National Security, Veterans Affairs, and International Relations.

[32] *Id.*

[33] *See id.*

[34] *See id.* at 4.

[35] JONATHAN D. MORENO, UNDUE RISK: SECRET STATE EXPERIMENTS ON HUMANS 269 (2000).

vaccinated.[36] Despite the disciplinary proceedings, service members continued to refuse the vaccine and challenge resulting sanctions in military courts.[37]

In 2003, six service members filed a lawsuit in a federal district court seeking to enjoin DoD from continuing the AVIP.[38] The service members argued that the program should be stopped because DoD did not adhere to legal requirements governing informed consent for off-label use of vaccines.[39] The court granted the injunction, finding that the AVIP amounted to off-label use of a vaccine and that DoD failed to comply with one of the two options regarding informed consent: 1) obtain consent from each service member; or 2) have the President of the United States issue an informed consent waiver.[40]

Eight days after the injunction, FDA classified the anthrax vaccine as safe and effective "independent of the route of exposure,"[41] a label expansion that encompassed the indication of inhalation anthrax.[42] Upon further challenge by the service members, the federal district court vacated FDA's decision on procedural grounds because the agency did not adhere to its own regulations governing such an action.[43] In short, the AVIP once again was halted by a federal court.

Thereafter, Congress stepped in with legislation that aided DoD—the Project BioShield Act of 2004.[44] Among its provisions, the law expedited procurement and grant funding for medical countermeasures to combat CBRN agents, guaranteed government purchasing of CBRN countermeasures, and amended the FDCA to grant FDA the ability to issue EUAs.[45] Although a mechanism like the EUA pathway had been discussed within DoD and FDA for years, the court-mandated pause of the AVIP created an urgency that motivated the new legislation. The first EUA issued by FDA authorized the anthrax vaccine for inhalation anthrax, a move that mooted the court order and allowed the AVIP to resume.[46] Although it was military exigencies that

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[36] *See* Bates v. Rumsfeld, 271 F. Supp. 2d 54, 57–58 (D.D.C. 2004); United States v. Washington, 57 M.J. 394, 400 (C.A.A.F. 2002); *See also* Randall D. Katz, *Friendly Fire: The Mandatory Military Anthrax Vaccination Program*, 50 DUKE L. J. 1835, 1837 (2001).

[37] Doe v. Rumsfeld, 341 F. Supp. 2d 1, 3 (D.D.C. 2004).

[38] *Id.*

[39] *Id.*

[40] *Id.* at 6.

[41] *Id.*

[42] *Id.*

[43] *Id.* at 13–16. Notably, the court also rejected the DoD's arguments that a soldier's refusal to submit to the order to be inoculated with the anthrax vaccine would "undermine a key component of military readiness and defense" and that "requiring the DoD to obtain informed consent will interfere with the smooth functioning of the military." Doe v. Rumsfeld, 297 F. Supp. 2d 119, 123, 134–35 (D.D.C. 2003).

[44] Project BioShield Act, 118 Stat. 835 (2004).

[45] *Id.*

[46] *See* Stuart L. Nightingale, Joanna M. Prasher & Stewart Simonson, *Emergency Use Authorization (EUA) to Enable Use of Needed Products in Civilian and Military Emergencies, United States*, 13 EMERGING INFECTIOUS DISEASES 1046, 1046 (July 2007). The DoD administered more than 100,000

precipitated passage of the EUA provision, the law was written broadly to encompass the authorization of medical products for civilian use in emergency contexts.[47] In the years that followed, FDA has utilized the EUA mechanism for countermeasures in various military and public health emergencies, including, for example, for products to prevent or treat Ebola, MERS, Zika virus, and nerve agents.[48]

B. The EUA Regulatory Framework

Section 564 of the FDCA allows FDA to issue EUAs for unapproved products or for unapproved uses of products, but only in certain circumstances.[49] FDA may issue EUAs when the HHS Secretary determines that the "circumstances exist justifying" such authorizations.[50] The HHS Secretary may find that these circumstances exist on the basis of various determinations by either the Secretaries of Homeland Security, Defense or HHS, such as a determination by the HHS Secretary that there is a "public health emergency, or a significant potential for a public health emergency."[51]

When the HHS Secretary has declared that circumstances justify issuing EUAs, FDA is permitted to issue an EUA only when various other criteria have been met as well.[52] These include that FDA determines that "there is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating [the relevant] disease or condition."[53] FDA also must determine, "based on the totality of scientific evidence available," that "it is reasonable to believe" that "the known and potential benefits of the product . . . outweigh [its] known and potential risks" for the emergency use and that "it is reasonable to believe" "the product may be effective"

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anthrax vaccinations during the pendency of the EUA. *See id.* at 1050. Moreover, while the EUA for the anthrax vaccine was active, FDA categorized the anthrax vaccine as safe and effective regardless of the route of exposure. Rempfer v. Sharfstein, 583 F.3d 860, 864 (D.D.C. 2009). Service members again challenged FDA's decision, but the U.S. Court of Appeals for the D.C. Circuit dismissed the action because it found that FDA did not act arbitrarily or capriciously in authorizing the new indication during the agency's second review. *Id.* at 868.

47 Project BioShield Act, 118 Stat. 835 (2004).

48 *See* FDA COVID-19 EUA List, *supra* note 5. The list of instances identified in the text is not exhaustive. *See id.*

49 21 U.S.C. § 360bbb-3(a)(2). Under the terms of the statute, certain devices are cleared for use through demonstrating substantial equivalence to existing, legally marketed devices, rather than "approved" based on independent evidence of safety and effectiveness, but for the sake of simplicity we use the term "approved" to encompass both here.

50 21 U.S.C. § 360bbb-3(b).

51 *Id.*

52 To be more precise, the FDCA authorizes the HHS Secretary to issue an EUA when the statutory criteria are met. The Secretary, however, has delegated that authority to FDA and, as discussed in more detail in this Article, has rarely used its legal authority to overturn an FDA decision about a product authorization. *Delegations of Authority*, U.S. FOOD & DRUG ADMIN., https://www.fda.gov/about-fda/staff-manual-guides/delegations-authority-volume-ii-1400 (last updated Sept. 20, 2021) [https://perma.cc/P8UG-2VED].

53 21 U.S.C. § 360bbb-3(c)(3).

for the relevant condition.[54] This bar is decidedly lower than the evidence of effectiveness required for FDA approval.[55] Importantly, FDA's EUA authority is permissive, not mandatory—that is, FDA may issue an EUA when these criteria are met, but the agency is not required to do so.[56]

FDA also may impose conditions on products authorized for use via the EUA pathway, such as mandatory post-market surveillance and analysis, as well as restrictions on who can administer or receive the product.[57] Such conditions are analogous to requirements that the agency may impose in other contexts, such as through requiring Risk Evaluation and Mitigation Strategies (REMS) for certain products approved under new drug applications or biologics license applications.[58] Additionally, the FDCA requires that FDA "periodically" review the EUAs that it has issued and allows the agency to revoke or revise EUAs at any time if appropriate to protect public health or safety.[59] Thus, although the standard that must be met to issue an EUA is low, once an EUA is issued, FDA has broad power to shape how medical products distributed under EUAs are used, and the agency can change conditions or revoke permission to distribute more easily than it can for approved products.

To be clear, EUAs are not the only way that patients may access unapproved products or unapproved uses of approved products during public health emergencies.[60] Patients also may receive wholly unapproved products absent an EUA and outside a clinical trial through either the expanded access or the Right to Try pathways, assuming relevant criteria are met and the manufacturer is willing to provide the product.[61] For example, before FDA issued EUAs for remdesivir and convalescent

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[54] 21 U.S.C. § 360bbb-3(c).

[55] *See, e.g.*, 2017 EUA GUIDANCE, *supra* note 4; *see also* Patricia J. Zettler, Micah L. Berman & Efthimios Parasidis, *Drug and Vaccine Development and Access*, *in* ASSESSING LEGAL RESPONSES TO COVID-19, 163, 163–69 (Scott Burris et al., eds., 2020) (describing the standards). Because of this lower standard, the EUA mechanism can be understood as a special form of non-trial preapproval access available during public health emergencies.

[56] 21 U.S.C. § 360bbb-3(c) ("The Secretary may issue an authorization under this section . . . if . . . the Secretary concludes . . . ").

[57] 21 U.S.C. § 360bbb-3(c).

[58] 21 U.S.C. § 355-1.

[59] 21 U.S.C. § 360bbb-3(g).

[60] *See, e.g.*, *Understanding the Regulatory Terminology of Potential Preventions and Treatments for COVID-19*, U.S. FOOD & DRUG ADMIN., https://www.fda.gov/consumers/consumer-updates/understanding-regulatory-terminology-potential-preventions-and-treatments-covid-19 (last updated Nov. 22, 2020) (describing approval, EUAs, expanded access, and off-label use) [https://perma.cc/S2ND-CEEH].

[61] *See* 21 U.S.C. §§ 360bbb, 360bbb-0a; 21 C.F.R. pt. 312, subpt I; 21 C.F.R. § 812.36; U.S. FOOD & DRUG ADMIN., *supra* note 60. For an overview of the differences between the expanded access and federal 'right to try' pathways, see Holly Fernandez Lynch, Ameet Sarpatwari & Patricia J. Zettler, *Promoting Patient Interests in Implementing the Federal Right to Try Act*, 320 JAMA 869 (2018). Under the expanded access pathway, FDA may authorize a sponsor to provide its investigational drug or device, outside a clinical trial, to a patient with a serious or life-threatening disease or condition who lacks comparable alternatives if FDA determines that the potential benefits justify the potential risks and providing the product will not interfere with clinical trials, among other things. *See, e.g.*, *id.* The Right to Try pathway, similarly, permits

plasma for COVID-19, both products were available to certain patients under expanded access programs.[62] Some experts have advocated for greater use of the expanded access pathway (instead of EUAs) for potential COVID-19 products because of the requirements in FDA expanded access regulations meant to prevent such access from interfering with continued conduct of clinical trials.[63] Others have argued that EUAs are more appropriate for the widespread distribution needed for many COVID-19 products, and that FDA's authority to impose restrictions on EUA products can achieve similar protections for patients as expanded access requirements do, and can similarly help to ensure continued research.[64] Sponsors also may prefer the EUA pathway because, unlike products provided under expanded access or the right to try pathway, products provided under EUAs do not come with limits on how much sponsors may charge.[65]

As with wholly unapproved products, COVID-19 patients may access unauthorized uses of already approved products absent EUAs in certain circumstances. This is because health care professionals typically can prescribe and dispense already-authorized products for off-label emergency uses without an EUA.[66] For example, one study published relatively early in the pandemic—in May 2020—identified dozens of treatments that had been used off-label in COVID-19 patients.[67] Nevertheless, there are various reasons why sponsors may seek EUAs, and FDA may find it beneficial to issue EUAs instead of providing access without an EUA.[68] In the absence of an EUA,

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a sponsor to provide an investigational drug, outside a clinical trial, to a patient with a life-threatening condition, but FDA authorization is not required, among other differences. *See, e.g.*, *id.*

[62] *See, e.g.*, Matthew Herper, *Gilead Pauses Access to Experimental COVID-19 Drug Due to Overwhelming Demand*, STAT (Mar. 22, 2020); Press Release, U.S. Food & Drug Admin., FDA Issues Emergency Use Authorization for Convalescent Plasma as Potential Promising COVID-19 Treatment, Another Achievement in Administration's Fight Against Pandemic (Aug. 23, 2020), https://www.fda.gov/news-events/press-announcements/fda-issues-emergency-use-authorization-convalescent-plasma-potential-promising-covid-19-treatment [https://perma.cc/S6US-SK5A].

[63] *See, e.g.*, Jon Cohen, '*There's Only One Chance to Do This Right'—FDA Panel Wrestles With COVID-19 Vaccine Issues*, SCIENCE (Oct. 23, 2020); Lisa Kearns & Alison Bateman-House, *Drug Companies Shouldn't Play Favorites in Granting Access to Experimental COVID-19 Treatments,* MIT TECH. REV. (Oct. 24, 2020); Matthew W. McCarthy, David Oshinsk & Arthur Caplan, Vaccine Working Group on Ethics and Policy, *Make Pre-approval COVID-19 Vaccines Available Through Expanded Access, Not An EUA*, STAT (Nov. 9, 2020), https://www.statnews.com/2020/11/09/expanded-access-not-eua-for-distributing-preapproval-covid-19-vaccines/ [https://perma.cc/FGA4-TN9W].

[64] *See, e.g.*, Steve Usdin, *Expanded Access to COVID-19 Vaccines*, BIOCENTURY (Oct. 30, 2020), https://www.biocentury.com/article/631556/expanding-access-to-covid-19-vaccines [https://perma.cc/X8VT-3MMU].

[65] *Compare* 21 U.S.C. § 360bbb-0a & 21 C.F.R. § 312.8 (2021) *with* 21 U.S.C. § 360bbb-3.

[66] *See, e.g.*, David C. Fajgenbaum, Johnson S. Khor, Alexander Gorzewski, Mark-Avery Tamakloe, Victoria Powers, Joseph J. Kakkis, Mileva Repasky, Anne Taylor, Alexander Beschloss, Laura Hernandez-Miyares, Beatrice Go, Vivek Nimgaonkar, Madison S. McCarthy, Casey J. Kim, Ruth-Anne Langan Pai, Sarah Frankl, Philip Angelides, Joanna Jiang, Rozena Rasheed, Erin Napier, Duncan Mackay & Sheila K. Pierson, *Treatments Administered to the First 9152 Reported Cases of COVID-19: A Systemic Review*, 9 INFECTIOUS DISEASE & THERAPY 435, 435–36 (2020).

[67] *Id.* As the article notes, this was not merely an American phenomenon. *See id.*

[68] *See, e.g.*, Zettler, Berman & Parasidis, *supra* note 55, at 164.

for example, the federal government could not stockpile and distribute products for the off-label use through the Strategic National Stockpile, and liability protections for manufacturers and health care professionals may not be available.[69]

C. PREP Act Legal Immunities

An evaluation of the EUA mechanism must account for the legal shields embedded in the Public Readiness and Emergency Preparedness Act of 2005 (PREP Act).[70] Notwithstanding extensive lobbying from biopharmaceutical companies, the Project BioShield Act of 2004 did not afford legal immunities to manufacturers of CBRN countermeasures.[71] Seventeen months after enactment of the BioShield Act, as relentless lobbying continued, Congress enacted the PREP Act.[72] The liability shield in the PREP Act encompasses "all claims for loss caused by, arising out of, relating to, or resulting from the administration to or the use by an individual of a covered countermeasure."[73] The protections extend to any individual or entity "involved in the development, manufacture, testing, distribution, administration, and use of . . . countermeasures" described in a PREP Act declaration issued by the HHS Secretary.[74]

The legal shields are extremely broad, and a lawsuit is permitted only if a person who died or is seriously injured can demonstrate that the company engaged in "willful misconduct"[75]—a very high legal bar that can be satisfied only if a plaintiff can prove the manufacturer intentionally caused harm by disregarding a known or obvious risk.[76] Even this small window of claims is closed if the manufacturer abided by regulatory requirements prior to marketing the countermeasure.[77] Damages for pain and suffering

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[69] *See, e.g.*, *id.* In practice, however, liability may not be a significant concern for some of the other available access pathways. In particular, there are no publicly documented instances of successful products liability claims arising from the expanded access program, and the federal "Right to Try" pathway provides express liability protections. *See, e.g.*, Lynch, Sarpatwari & Zettler, *supra* note 61, at 870; Amy E. McKee, André O. Markon, Kirk M. Chan-Tack & Peter Lurie, *How Often Are Drugs Made Available Under the Food and Drug Administration's Expanded Access Process Approved?*, 57 J. CLINICAL PHARMACOLOGY S136, S136–40 (2017).

[70] Public Readiness and Emergency Preparedness Act, Pub. L. No. 109-148, 119. Stat. 2818 (2005).

[71] *See, e.g.*, *Immunity Sought as Avian Flu Shadow Approaches*, THE HILL (Oct. 12, 2005, 12:00 AM), https://thehill.com/business-a-lobbying/2718-immunity-sought-as-avian-flu-shadow-approaches [https://perma.cc/4759-BQT8].

[72] *See id.*

[73] 42 U.S.C. § 247d-6d(a)(1).

[74] U.S. FOOD & DRUG ADMIN., EMERGENCY USE AUTHORIZATION OF MEDICAL PRODUCTS AND RELATED AUTHORITIES: DRAFT GUIDANCE FOR INDUSTRY AND PUBLIC HEALTH STAKEHOLDERS 39–40 (2016).

[75] 42 U.S.C. § 247d-6d(c)(3).

[76] *See, e.g.*, Efthimios Parasidis, *Big Pharma's Safety Pledge Isn't Enough to Build Public Confidence in COVID-19 Vaccine—Here's What Will*, THE CONVERSATION (Sept. 14, 2020, 7:55 AM), https://theconversation.com/big-pharmas-safety-pledge-isnt-enough-to-build-public-confidence-in-covid-19-vaccine-heres-what-will-145822 [https://perma.cc/LZ88-3LT7].

[77] 42 U.S.C. § 247d-6d(c)(5)(A).

are precluded, and a person cannot obtain legal redress in court unless and until HHS or the U.S. Department of Justice (DoJ) also has sued and imposed penalties on the manufacturer.[78] These stringent requirements make a lawsuit all but impossible.

A lawsuit likewise is precluded if a person injured by a countermeasure has accepted compensation from the Countermeasures Injury Compensation Program (CICP).[79] The CICP is administered by HHS's Health Resources and Services Administration (HRSA).[80] Funding for CICP is provided by the U.S. Treasury in accordance with the HHS Secretary's determination on the scope of legal immunity for a particular declared emergency.[81] Claims must be filed within a one-year statute of limitations that begins from the date a person is administered the countermeasure.[82] The legal shields in the PREP Act have been invoked for several medical products, including the anthrax vaccine, smallpox vaccine, botulism countermeasures, pandemic influenza vaccines, countermeasures for acute radiation syndrome, and COVID-19 countermeasures.[83]

The CICP has been criticized as a narrow program that affords fewer remedies than, for example, the Vaccine Injury Compensation Program (VICP).[84] The CICP also has been criticized for lacking transparency and being a difficult vehicle for obtaining redress.[85] According to one recent report, the CICP has afforded compensation in only 10% of claims.[86] In one example, a person who had a baseball-size growth on his arm

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78 *See* KEVIN J. HICKEY, CONG. RSCH. SERV., LSB10443, THE PREP ACT AND COVID-19: LIMITING LIABILITY FOR MEDICAL COUNTERMEASURES 3–4 (2021) [hereinafter CRS, COVID-19 PREP ACT REPORT].

79 *See id.* at 3. Additionally, creating international liability protection and injury compensation programs for COVID-19 products—specifically for COVID-19 vaccine candidates—has been discussed. *See* Sam Halabi, Andrew Heinrich & Saad B. Omer, *No-Fault Compensation for Vaccine Injury—The Other Side of Equitable Access to Covid-19 Vaccines*, 383 N. ENG. J. MED. e125(1), e125(1) (2020).

80 *See* CRS, COVID-19 PREP ACT REPORT, *supra* note 78, at 4.

81 *See id.*

82 *See Countermeasures Injury Compensation Program (CICP): Frequently Asked Questions*, HEALTH RES. & SERVS. ADMIN., https://www.hrsa.gov/cicp/faq (last visited Aug. 30, 2021) [https://perma.cc/LBE3-7D9X].

83 *See Countermeasures Injury Compensation Program*, HEALTH RES. & SERVS. ADMIN., https://www.hrsa.gov/sites/default/files/hrsa/cicp/cicpfactsheet.pdf (last visited Aug. 30, 2021) [https://perma.cc/U2L8-L73V].

84 *See* Katharine Van Tassel, Carmel Shachar & Sharona Hoffman, *Covid-19 Vaccine Injuries—Preventing Inequities in Compensation*, 384 N. ENG. J. MED. e34(1), e34(2) (2021); Sharon Lerner, *Drug Companies Continue to Shed Liability for Rushed Coronavirus Treatments*, INTERCEPT (Aug. 28, 2020, 11:08 AM), https://theintercept.com/2020/08/28/coronavirus-vaccine-prep-act/ [https://perma.cc/BT2R-CK4K]; Tom Hals, *COVID-19 Era Highlights U.S. 'Black Hole' Compensation Fund for Pandemic Vaccine Injuries*, REUTERS (Aug. 21, 2020, 7:08 AM), https://www.reuters.com/article/us-health-coronavirus-vaccines-liability/covid-19-era-highlights-u-s-black-hole-compensation-fund-for-pandemic-vaccine-injuries-idUSKBN25H1E8 [https://perma.cc/N5E4-PKDH]. To be sure, the VICP likewise has been criticized as a lackluster system for affording individuals compensation for vaccine-induced injuries. *See* Efthimios Parasidis, *Recalibrating Vaccination Laws*, 97 B.U. L. REV. 2153, 2154 (2017).

85 *See* Hals, *supra* note 84.

86 *See id.*

after a H1N1 vaccine was denied compensation when he filed the claim shortly after the one-year statute of limitations had elapsed—because he had difficulty figuring out how to the file the claim.[87] Although state statutes of limitations for tort claims typically impose limits on how long after an injury a claim can be filed, and thus whether compensation is available,[88] such harsh outcomes may be more concerning when imposed on people administered unproven products under EUAs, particularly if partly caused by the byzantine nature of the compensation program itself.

For COVID-19, the HHS Secretary invoked the PREP Act's protections on February 4, 2020, the same day the Secretary first issued a declaration authorizing FDA to utilize the EUA mechanism for certain COVID-19 products.[89] The COVID-19 legal shield encompasses "any antiviral, any other drug, any biologic, any diagnostic, any other device, or any vaccine, used to treat, diagnose, cure, prevent, or mitigate COVID-19, or the transmission of SARS-CoV-2 or a virus mutating therefrom, or any device used in the administration of any such product, and all components and constituent materials of any such product."[90]

As of March 8, 2021, the HHS Secretary had amended the COVID-19 PREP Act declaration six times.[91] The amendments expanded the scope of individuals and entities afforded immunity, as well as the realm of products eligible for the legal immunities.[92] As a practical matter, the HHS Secretary's declarations cast a wide net of legal shields for products, people, and entities for all COVID-19 countermeasures authorized via an EUA—broad immunities that several articles criticized in the context of COVID-19.[93]

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[87] *See id.*

[88] *See, e.g.*, Jing Liu & David A. Hyman, *The Impact of Medical Malpractice Reforms*, 16 ANN. REV. L. & SOC. SCI. 405, 406–08 (2020).

[89] Declaration Under the Public Readiness and Emergency Preparedness Act for Medical Countermeasures Against COVID-19, 85 Fed. Reg. 15,198, 15,198 (March 17, 2020).

[90] *Id.* at 15,202.

[91] Amendment to Declaration Under the Public Readiness and Emergency Preparedness Act for Medical Countermeasures Against COVID-19, 85 Fed. Reg. 21,012, 21,012–14 (Apr. 15, 2020); Second Amendment to Declaration Under the Public Readiness and Emergency Preparedness Act for Medical Countermeasures Against COVID-19, 85 Fed. Reg. 35,100, 35,100–02 (June 8, 2020); Third Amendment to Declaration Under the Public Readiness and Emergency Preparedness Act for Medical Countermeasures Against COVID-19, 85 Fed. Reg. 52,136, 52,136–41 (Aug. 24, 2020); Fourth Amendment to Declaration Under the Public Readiness and Emergency Preparedness Act for Medical Countermeasures Against COVID-19 and Republication of the Declaration, 85 Fed. Reg. 79,190, 79,190–98 (Dec. 9, 2020); Fifth Amendment to Declaration Under the Public Readiness and Emergency Preparedness Act for Medical Countermeasures Against COVID-19, 86 Fed. Reg. 7,872, 7,872–76 (Feb. 2, 2021); Sixth Amendment to Declaration Under the Public Readiness and Emergency Preparedness Act for Medical Countermeasures Against COVID-19, 86 Fed. Reg. 9,516, 9,516–20 (Feb. 16, 2021).

[92] *See* CRS, COVID-19 PREP ACT REPORT, *supra* note 78, at 5–6.

[93] *See, e.g.*, Hals, *supra* note 84; Lerner, *supra* note 84; Parasidis, *supra* note 76.

III. THE ROLE OF POLITICAL INFLUENCE

As the history of the EUA pathway illustrates, the EUA mechanism has been political, to some extent, from the very beginning. Moreover, the EUA pathway may be more prone to political influence than standard FDA approval processes. This is because the statutory standard for issuing an EUA leaves more room for FDA discretion and because public health emergencies often, and understandably, generate immense political pressure to make medical countermeasures available as quickly as possible.[94] For these reasons, we examine the value of FDA independence from inappropriate political pressure and the ways in which political interference with FDA's work arose during the start of the COVID-19 pandemic through early March 2021.

A. Political Influence, FDA Decision-Making, and Reputation

Given the immense economic and societal importance of its work—FDA describes the products within its jurisdiction as accounting for "about 25 cents of every dollar spent by American consumers each year"[95]—it is hard to imagine FDA ever fully separating itself from political influence.[96] As a government agency that is part of the executive branch and dependent on Congress for funding, FDA must—and arguably should—be responsive to the policy priorities of democratically elected officials.[97] Similarly, the uncertainty intrinsic to the scientific process and scientific evidence

[94] For example, in 2014, when two U.S. citizens survived Ebola after being treated with an experimental treatment, it "generat[ed] intense global pressure to use this product and other unproven treatments." Jesse L. Goodman & Luciana Borio, *Finding Effective Treatments for COVID-19: Scientific Integrity and Public Confidence in a Time of Crisis*, 323 JAMA 1899, 1899 (2020). The resulting pressure to abandon clinical trials for potential therapies made it so that "it is still not known whether other experimental Ebola treatments are of value or may be injurious." *Id.* As discussed *infra*, in the face of President Trump's repeated claims that a COVID-19 vaccine would soon be available, "many . . . started to wonder whether the US Food and Drug Administration (FDA) [could] withstand this type of political pressure." Gail R. Wilensky & Brian J. Miller, *The Public Can Trust the FDA's Vaccine Review Process*, 1(10) JAMA HEALTH F. 1, 1 (2020).

[95] *Executive Summary: Strategic Plan for Regulatory Science*, U.S. FOOD & DRUG ADMIN. (Mar. 29, 2018), https://www.fda.gov/science-research/advancing-regulatory-science/executive-summary-strategic-plan-regulatory-science [https://perma.cc/X62T-X2AZ].

[96] *See, e.g.*, James S. Marks, *Epidemiology, Public Health, and Public Policy*, 6 PREVENTING CHRONIC DISEASE 1, 1 (2009) (describing Bill Foege, former CDC director, as having the "conviction that public health was inherently political, inescapably political"); Holly Fernandez Lynch, Steven Joffee & Matthew S. McCoy, *The Limits of Acceptable Political Influence over the FDA*, 27 NATURE MED. 188, 188–89 (2021) ("The FDA cannot make decisions on the basis of science alone, and political considerations sometimes do have a role to play.").

[97] *See, e.g.*, Eli Y. Adashi, Rohit S. Rajan & I. Glenn Cohen, *When Science and Politics Collide: Enhancing the FDA*, 364 SCIENCE 628, 630 (2019); *see also* Jerry L. Mashaw, *Prodelegation: Why Administrators Should Make Political Decisions*, 1 J. L. ECONS. & ORG. 81, 95–99 (1985) (suggesting that broad delegation to administrative agencies is "a device for facilitating responsiveness to voter preferences expressed in presidential election," and that such delegation, "far from taking decisions out of politics, seeks to give political choice a form in which potential collective agreement can be discovered and its benefits realized").

means that FDA decision-making inherently involves the agency using its discretion and making judgment calls.[98]

Structurally, there are many means through which FDA is subject to the influence of elected or politically appointed actors—some of which may be viewed as appropriate or acceptable.[99] For example, as with any statute, Congress can amend the FDCA, thereby changing FDA's mandate and authority.[100] As another example, since 1988, federal law has required that the FDA Commissioner be appointed by the President and confirmed by the Senate.[101] As is true of other executive agencies, FDA is subject to the structures and policies of the Office of Management and Budget (OMB), which is part of the White House.[102] And, as an agency within HHS, FDA is subject to the policies of the HHS Secretary, often including HHS review of its regulations and guidance documents.[103]

At the same time, throughout its history, FDA has sought to build and sustain its reputation as an agency that makes independent, science-based decisions in the public's interest, and is therefore deserving of the public's trust.[104] The importance of FDA's reputation was the thesis of political scientist Daniel Carpenter's groundbreaking book, *Reputation and Power*.[105] In Carpenter's view, the central pillars of FDA's reputation—including "a demonstrated capacity for citizen protection, a vigilance against threats to drug safety and medicinal effect, [and] an enduring commitment to scientific principles of assessment"—are critical sources of its immense power.[106] Though FDA has extensive statutory authority, its reputation—and the respect accorded to FDA when it issues its decisions (e.g., to authorize or to block the sale of a new drug)—provides it with influence that "vastly outstrips the

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[98] For example, FDA regulations regarding new drug applications make clear that the agency has tremendous discretion to decide what kinds of evidence are needed to satisfy the approval standard, explaining that "[w]hile the statutory standards apply to all drugs, the many kinds of drugs that are subject to the statutory standards and the wide range of uses for those drugs demand flexibility in applying the standards. Thus FDA is required to exercise its scientific judgment to determine the kind and quantity of data and information an applicant is required to provide for a particular drug to meet the statutory standards." 21 C.F.R. § 314.105(c) (2021).

[99] *See, e.g.*, Dan Troy, Dan Mendelson & David Beier, *FDA Reform: It's Time to Act, but Not as an Independent Agency*, HEALTH AFFS. (Mar. 19, 2019), https://www.healthaffairs.org/do/10.1377/hblog20190312.542301/full/ [https://perma.cc/5FUQ-GE3R].

[100] *See id.*

[101] Health Omnibus Programs Extension Act, Pub. L. No. 100-607, § 503, 102 Stat. 3048, 3121 (1988) (codified as amended at 21 U.S.C. § 393); *see also* Adashi, Rajan & Cohen, *supra* note 97, at 629.

[102] *See id.* at 629–30.

[103] *See id.* at 629.

[104] *Cf.* Kirti Datla & Richard L. Revesz, *Deconstructing Independent Agencies (and Executive Agencies)*, 98 CORNELL L. REV. 769, 817 (2013) (describing FDA as an "executive agency that has enjoyed a great deal of practical independence from presidential influence").

[105] DANIEL CARPENTER, REPUTATION AND POWER: ORGANIZATIONAL IMAGE AND PHARMACEUTICAL REGULATION AT THE FDA (2010).

[106] *Id.* at 730.

[formal statutory] authority and resources given to the agency."[107] Accordingly, the imperative to preserve the agency's reputation, and hence its power, has "governed and animated FDA's behavior . . . for much of the last half-century."[108] Consistent with Carpenter's thesis, FDA's staff handbook states that "[s]hielding the agency's science and its scientific staff from political influence" is one of the agency's "key principles."[109]

The logical corollary to Carpenter's thesis is that actions that undermine FDA's reputation for scientific integrity are incredibly costly to the agency. FDA's high profile misfires—such as its slow response to evidence that the anti-arthritis drug Vioxx was increasing heart attack risk—have been considered crises that risked breaking the "covenant of trust" between FDA and the public.[110] Likewise, instances of overt political interference,[111] such as when HHS Secretary Kathleen Sebelius overruled FDA in 2011 and blocked over-the-counter approval for all ages for the "morning-after pill" levonorgestrel, have been truly rare.[112] Indeed, then-Secretary Sebelius's decision was reportedly "the first time in American history [that] a cabinet

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[107] *Id.* at 750.

[108] *Id.* at 66.

[109] U.S. FOOD & DRUG ADMIN., SMG 9001.1, SCIENTIFIC INTEGRITY 2 (2012), https://www.fda.gov/media/82932/download. [https://perma.cc/F9SV-VY68].

[110] Richard Horton, *Vioxx, the Implosion of Merck, and Aftershocks at the FDA*, 364 LANCET 1995, 1995–96 (2004).

[111] There are also instances in which FDA, arguably, has more opaquely incorporated inappropriate social political considerations into its decisions. *See, e.g.*, Patricia J. Zettler, Margaret Foster Riley & Aaron S. Kesselheim, *Implementing a Public Health Perspective in FDA Drug Regulation*, 73 FOOD & DRUG L. J. 221, 253–55 (2018). For example, scholars—and more recently, litigants—have argued that FDA's REMS requirement (and before that, the RiskMAP) for mifepristone is driven by political concerns about abortion rather than the risks of the drug. *See, e.g.*, *id.* at 254; *see also* Plaintiffs' Memorandum of Law in Support of Motion for Preliminary Injunction at 16–19, Am. College of Obstetricians & Gynecologists v. Food & Drug Admin., No. 8:20-cv-01320-TDC (D. Md. Jul. 13, 2020); Beatrice L. Brown, Susan F. Wood & Ameet Sarpatwari, *Ensuring Safe Access to Mifepristone During the Pandemic and Beyond*, ANNALS OF INTERNAL MED. (Oct. 21, 2020), https://www.acpjournals.org/doi/10.7326/M20-6671 [https://perma.cc/ZG7W-8338]; Greer Donley, *Early Abortion Exceptionalism*, 107 CORNELL L. REV. (forthcoming 2021), https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3795414; Lars Noah, *A Miscarriage in the Drug Approval Process?: Mifepristone Embroils the FDA in Abortion Politics*, 36 WAKE FOREST L. REV. 571, 571–74 (2001). As another example, FDA's policy restricting blood donation by men who have sex with men has been criticized as both out of step with current science and stigmatizing. *See, e.g.*, Doron Dorfman, *Can the COVID-19 Interstate Travel Restrictions Help Lift the FDA's Blood Ban?*, 7 J. L. & BIOSCIENCE 1, 1–11 (2020); *see also* I. Glenn Cohen, Jeremy Feigenbaum & Eli Y. Adashi, *Reconsideration of the Lifetime Ban on Blood Donation by Men Who Have Sex With Men*, 312 JAMA 337, 337–38 (2014) (criticizing FDA's previous lifetime ban).

[112] *See, e.g.*, Lisa Heinzerling, *The FDA's Plan B Fiasco: Lessons for Administrative Law*, 102 GEO. L.J. 927, 947 (2014); Tummino v. Hamburg, 936 F. Supp. 2d 162, 167–70 (E.D.N.Y. 2013). For another example of interference—by members of Congress rather than the Secretary—see Gardiner Harris & David M. Halbfinger, *F.D.A. Reveals it Fell to a Push by Lawmakers*, N.Y. TIMES, Sept. 25, 2009, at A1 (describing how, in response to "extreme" pressure from political actors, FDA management overruled scientific reviewers who had expressed concerns about the safety of a patch for knee injuries); *see also* Ivy Sports Med., LLC v. Burwell, 767 F.3d 81, 85 (D.C. Cir. 2014); U.S. FOOD & DRUG ADMIN., REVIEW OF THE REGEN MENAFLEX: DEPARTURES FROM PROCESSES, PROCEDURES, AND PRACTICES LEAVE THE BASIS FOR A REVIEW DECISION IN QUESTION 1–2 (2009), https://www.fda.gov/media/77734/download [https://perma.cc/8GJM-4MUY].

secretary—and by extension, a president—has overruled a drug-approval decision by the Food and Drug Administration."[113] No one questioned the legal authority of then-Secretary Sebelius to overrule FDA, but it was a shocking departure from the norm of FDA independence.

Ensuring FDA's independence from inappropriate political influence, and its scientific grounding, is not only important for the preservation of the agency's power—it is also critical to public health. A substantial and growing body of evidence suggests that trust in government agencies is a "predictor of a wide variety of health behaviors and outcomes."[114] For example, "individuals with higher levels of social trust in the FDA" demonstrate a "greater intention to get immunized [for influenza] and perceive[] vaccines to be less risky compared to those less trusting of the authority."[115] Specific to the public health emergency context, researchers found that during the 2009–2010 H1N1 influenza pandemic, "a higher level of trust in the FDA was a powerful predictor of willingness" to try antiviral drug peramivir if prescribed by a physician.[116]

Maintaining public trust, therefore, is essential for ensuring that COVID-19 devices, drugs, or vaccines authorized by FDA are actually used by the appropriate patient populations.[117] For example, at the October 22, 2020 meeting of FDA's Vaccine and Related Biological Products Advisory Committee (VRBPAC), in which the agency sought general advice about the development of COVID-19 vaccines, a representative from the Reagan Udall Foundation raised concerns, and presented research, regarding the relationship between public perceptions and mistrust in COVID-19 vaccine

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[113] Daniel Carpenter, *Free the FDA*, N.Y. TIMES, Dec. 14, 2011, at A35. Then-Secretary Sebelius' rejection of FDA's decision to approve over-the-counter (OTC) access for all ages, including minors younger than 17, was not the first controversy regarding approval of the product (and FDA's attempt to approve the drug OTC for all ages came only after years of litigation). Several years earlier, in 2005, then-FDA Commissioner Lester Crawford overruled the agency's scientific reviewers, and rejected the advice of its advisory committee, by blocking the approval of levonorgestrel for OTC use. This was also seen a disturbing departure from FDA norms. Dr. Susan Wood, Director of the Office of Women's Health at FDA, resigned in protest, noting that "recommendations of an advisory committee that are strongly supported by the FDA's review staff have rarely, if ever, been overturned at the highest level of the agency." Susan F. Wood, *Women's Health and the FDA*, 353 N. ENG. J. MED. 1650–51 (2005).

[114] Sarah D. Kowitt, Allison M. Schmidt, Anika Hannan & Adam O. Goldstein, *Awareness and Trust of the FDA and CDC: Results from a National Sample of US Adults and Adolescents*, 12 PLOS ONE 1, 9 (2017).

[115] Nien-Tsu Nancy Chen, *Predicting Vaccination Intention and Benefit and Risk Perceptions: The Incorporation of Affect, Trust, and Television Influence in a Dual-Mode Model*, 35 RISK ANALYSIS 1268, 1277 (2015).

[116] FDA had issued an EUA for peramivir, an unapproved drug then in clinical trials, for IV use by patients hospitalized with severe cases of H1N1 influenza. Sandra Crouse Quinn, Karen Hilyard, Nestor Castaneda-Angarita & Vicki S. Freimuth, *Public Acceptance of Peramivir During the 2009 H1N1 Influenza Pandemic: Implications for Other Drugs or Vaccines Under Emergency Use Authorizations*, 9 DISASTER MED. & PUB. HEALTH PREPAREDNESS 166, 172 (2015).

[117] Maintaining trust in FDA is valuable to the pharmaceutical industry as well. Carpenter quotes Pfizer's chief medical officer as stating that the company "can't afford" a loss of public trust in FDA, because "[w]hen our medicines come out, we want people to understand they have gone through a rigorous review process." CARPENTER, *supra* note 105, at 740.

candidates and willingness to be vaccinated.[118] Such concerns may be particularly salient for racial and ethnic minority groups, which—due to a history of racism, exploitation, and marginalization by government and public health authorities—tend to express lower levels of trust in FDA and other governmental public health institutions.[119]

B. Political Influence During the COVID-19 Pandemic

Notwithstanding the importance of public trust in FDA, inappropriate political interference with FDA decision-making reached a high-water mark, at least for the modern era, during the Trump Administration.[120] Specific examples of efforts to influence EUA decisions are discussed in Part IV of this Article. But these examples must be viewed in the context of a broader assault on—and politicization of—scientific decision-making throughout the entire executive branch, both before and after the arrival of SARS-CoV-2.[121] For FDA in particular, the response to COVID-19 through early March 2021 was characterized by unprecedented involvement of HHS and White House officials in FDA decision-making. Consider for example, the following news clips from only the fall of 2020:

- "Health and Human Services Secretary Alex Azar led an escalating pressure campaign against his own Food and Drug

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[118] *See* Susan C. Winckler, *COVID-19 Vaccine Confidence Project*, REAGAN-UDALL FOUND., https://www.fda.gov/media/143531/download (last visited Sept. 2, 2021) [https://perma.cc/RB7E-QGGN]; *see also* Sarah Karlin-Smith (@SarahKarlin), TWITTER (Oct. 22, 2020, 1:39 PM), https://twitter.com/SarahKarlin/status/1319332534250070017 [https://perma.cc/H8XP-ZNPQ].

[119] *See, e.g.*, Vicki S. Freimuth, Amelia M. Jamison, Ji An, Gregory R. Hancock & Sandra Crouse Quinn, *Determinants of Trust in the Flu Vaccine for African Americans and Whites*, 193 SOC. SCI. & MED. 70, 79 (2017); Amelia M. Jamison, Sandra Crouse Quinn & Vicki S. Freimuth, *"You Don't Trust a Government Vaccine": Narratives of Institutional Trust and Influenza Vaccination among African American and White Adults*, 221 SOC. SCI. & MED. 87, 94 (2019). *But see* Juana Summers, *Little Difference in Vaccine Hesitancy Among White and Black Americans, Poll Finds*, NPR (Mar. 12, 2021, 5:00 AM), https://www.npr.org/sections/coronavirus-live-updates/2021/03/12/976172586/little-difference-in-vaccine-hesitancy-among-white-and-black-americans-poll-find [https://perma.cc/MQ43-J7V7].

[120] Lev Facher, *Trump Has Launched an All-Out Attack on the FDA. Will Its Scientific Integrity Survive?*, STAT (Aug. 27, 2020) (quoting former FDA Commissioner Margaret Hamburg stating that political influence "has been an issue in past administrations Republican and Democratic . . . . But never at this level, and never accompanied with the kind of public derision and undermining of both the employees who work at the agency and, frankly, the very mission of the agency"), https://www.statnews.com/2020/08/27/trump-has-launched-an-all-out-attack-on-the-fda-will-its-scientific-integrity-survive/ [https://perma.cc/DP24-9U98].

[121] The examples are too numerous to review, but for summaries, see, e.g., James Bandler, Patricia Callahan, Sebastian Rotella & Kirsten Berg, *Inside the Fall of the CDC*, PROPUBLICA (Oct. 15, 2020), https://www.propublica.org/article/inside-the-fall-of-the-cdc [https://perma.cc/V6WN-HY56]; *A Four-Year Timeline of Trump's Impact on Science*, NATURE (Oct. 5, 2020), https://www.nature.com/articles/d41586-020-02814-3 [https://perma.cc/K57K-JPNC]; Ed Pilkington, *Pandemic Brings Trump's War on Science to the Boil—But Who Will Win?*, THE GUARDIAN (May 3, 2020, 5:00 AM), https://www.theguardian.com/us-news/2020/may/03/science-donald-trump-coronavirus [https://perma.cc/AZ4J-9V7E]; Brad Plumer & Coral Davenport, *Science Under Attack: How Trump is Sidelining Researchers and Their Work*, N.Y. TIMES (Dec. 28, 2019), https://www.nytimes.com/2019/12/28/climate/trump-administration-war-on-science.html [https://perma.cc/DZ2R-XB2U]; *see also* Adashi, Rajan & Cohen, *supra* note 97, at 629 (describing the progressive curtailing of FDA independence since the 1960s).

> Administration this spring and summer, urging the agency to abandon its responsibility for ensuring the safety and accuracy of a range of coronavirus tests as the pandemic raged."[122]
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> - "In a stunning declaration of authority, Alex M. Azar II, the secretary of health and human services, this week barred the nation's health agencies, including the Food and Drug Administration, from signing any new rules regarding the nation's foods, medicines, medical devices and other products, including vaccines."[123]
> - "On Saturday, [President] Trump, with no evidence, accused the FDA of taking part in a 'deep state' political conspiracy to harm his reelection campaign. And two key White House aides, including Trump's chief of staff, have taken the rare step of criticizing the agency publicly, with one reportedly advocating for the approval of an unproven plant extract as a COVID-19 cure."[124]

Seven former FDA commissioners, appointed by both Democratic and Republican presidents, considered these actions (and many others) to be so alarming that they issued forceful public rebukes in written op-eds and television newscasts, even making a joint public statement to warn that "[t]he Trump administration is undermining the credibility of the FDA."[125] Interference with FDA's scientific judgments, particularly in the vaccine review process, they warned, ultimately "prolongs the pandemic and erodes our public health institutions."[126]

Following the former FDA commissioners' statement, FDA took numerous steps to reassure the public of the integrity of its decision-making, particularly with respect to drugs and vaccines. These included announcing its intent to be as transparent as the

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[122] Adam Cancryn & Sarah Owermohle, *HHS Chief Overrode FDA Officials to Ease Testing Rules*, POLITICO (Sept. 15, 2020, 3:21 PM), https://www.politico.com/news/2020/09/15/hhs-alex-azar-overrode-fda-testing-rules-415400 [https://perma.cc/MB5Q-6XN6].

[123] Sheila Kaplan, *In 'Power Grab,' Health Secretary Azar Asserts Authority Over F.D.A.*, N.Y. TIMES (Sept. 19, 2020), https://www.nytimes.com/2020/09/19/health/azar-hhs-fda.html [https://perma.cc/L3LX-KF44]. The memorandum issued by HHS Secretary Azar related to new "rules," and thus did not change the processes for medical product approvals or authorizations (which are governed in part by existing regulations but are not themselves "rules"). Nonetheless, the memorandum was, in the words of Peter Lurie of the Center for Science in the Public Interest (and a former FDA official), "a slap in the face to the people at the FDA." Jason Mast & Arsalan Arif, *Azar Falls in Line Under Trump Again. Experts Say He's Reinforcing a Dark Signal Sent to the FDA*, ENDPOINTS NEWS (Sept. 24, 2020, 11:04 AM), https://endpts.com/azar-falls-in-line-under-trump-again-experts-say-hes-reinforcing-a-dark-signal-sent-to-the-fda/ [https://perma.cc/2VQ5-5KTR]. The White House during the Trump Administration also separately sought to influence the vaccine authorization process. *See, e.g.*, Sharon LaFraniere & Noah Weiland, *White House Blocks F.D.A. Rules that Would Push Vaccine Release Past Election*, N.Y. TIMES, Oct. 6, 2020, at A11.

[124] Facher, *supra* note 120. The Trump Administration also "installed a right-wing journalist best known for her gun-rights advocacy as the FDA's top spokeswoman—empowering her to aggressively reshape the FDA's typically nonpolitical, straight-laced public messaging." *Id.*

[125] *7 Former FDA Commissioners*, *supra* note 10.

[126] *Id.*

law permits about the bases for the agency's decisions on EUAs for drugs and vaccines,[127] as well as holding the October 2020 meeting of the VRBPAC to discuss COVID-19 vaccine development generally.[128] The agency also held VRBPAC meetings to discuss the EUAs that Pfizer, Moderna, and Johnson & Johnson submitted for their vaccine candidates.[129] Notwithstanding FDA's actions to alleviate the public's concerns, HHS and the White House continued to take steps to influence—or try to influence—FDA decision-making. For example, in the lead up to the December 10, 2020 and December 17, 2020 VRBPAC meetings concerning EUAs for Pfizer and Moderna's vaccine candidates, the White House called a "vaccine summit" to meet with manufacturers.[130] Pfizer and Moderna declined to participate.[131]

Ultimately, respect for FDA's independence is a longstanding, bipartisan norm, but it is not a legal requirement—unlike, for example, with the Federal Reserve, which is formally constituted as an independent agency and structurally buffered from short-term political pressures.[132] Political interference with FDA's scientific work may not register high on the long list of norm-shattering actions by the Trump Administration, which included undermining scientific and agency decision-making of all sorts. But the short- and long-term consequences of undermining FDA's decision-making autonomy should not be underestimated. Michael Ryan, a physician and executive director of the World Health Organization's Health Emergency Program, recently referred to the maxim that "it a takes years to build trust, and seconds to lose it."[133] Though he was not speaking directly to FDA, he reflected the sentiments that agency

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[127] Press Release, U.S. Food & Drug Admin., COVID-19 Update: FDA's Ongoing Commitment to Transparency for COVID-19 EUAs (Nov. 17, 2020), https://www.fda.gov/news-events/press-announcements/covid-19-update-fdas-ongoing-commitment-transparency-covid-19-euas [https://perma.cc/U7V4-2Z62].

[128] *Advisory Committee Calendar*, U.S. FOOD & DRUG ADMIN., https://www.fda.gov/advisory-committees/advisory-committee-calendar, https://www.fda.gov/advisory-committees/advisory-committee-calendar (last updated Sept. 9, 2021) [https://perma.cc/33E7-TNWR]. Such advisory committee meetings permit the agency to obtain advice from outside experts and also promote transparency, because the Federal Advisory Committee Act generally requires that they be open to the public.

[129] *Id.*

[130] *See, e.g.*, Lev Facher, *Leading COVID-19 Vaccine Makers Pfizer and Moderna Decline Invitations to White House 'Vaccine Summit,'* STAT (Dec. 7, 2020), https://www.statnews.com/2020/12/07/pfizer-moderna-decline-white-house-vaccine-summit/ [https://perma.cc/9LWQ-MD32].

[131] *See id.*

[132] *What Does it Mean that the Federal Reserve is "Independent Within the Government"?*, THE FED. RSRV., https://www.federalreserve.gov/faqs/about_12799.htm (last updated Mar. 1, 2017) [https://perma.cc/F8NG-9LHF].

[133] World Health Organization, *Media Briefing on COVID-19*, YOUTUBE 50:45 (Sept. 7, 2020), available at https://youtu.be/JTAKQyClEto [https://perma.cc/R79T-JZF4].

leaders,[134] former FDA staff,[135] former commissioners,[136] and others also have been expressing:

> Good governments build trust with communities by only providing them with verified, evidence-based information. Because if things go wrong, communities will understand. But if communities perceive that they're getting information that is being politically manipulated, or that is being managed in a way that is distorting evidence, then unfortunately that comes back to roost . . . . That has been the case around the world and for many different disasters over time.[137]

Because this Article was drafted and edited during the COVID-19 pandemic, which continues at the time of publication of this Article, we cannot fully analyze the long-term impact on public trust in FDA, CDC, and other public health agencies. Nonetheless, it appears that in the first year of the pandemic, a growing lack of trust in FDA hindered its effectiveness. For example, upon issuance of the first COVID-19 vaccine EUA, vaccine hesitancy was at an "all-time high."[138] This was particularly true amongst the poor and people of color, groups that have suffered disproportionally from the pandemic and have long been marginalized and exploited by the health care system.[139] In turn, state and local governments exerted significant efforts to encourage vaccination and reassure the public that COVID-19 vaccines are safe and effective.

Regulatory policy is inherently political, in the sense that "regulatory regimes are deeply and fundamentally enmeshed with political processes, concerns, and pathways."[140] Although some may regard undue political interference as particularly egregious during the Trump Administration, it is easy to imagine a future administration, faced with its own public health emergency, similarly pressuring FDA to produce regulatory "wins" quickly.

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[134] Patrizia Cavazzoni, Peter Marks, Susan Mayne, Judy McMeekin, Jeff Shuren, Steven Solomon, Janet Woodcock & Mitch Zeller, *Senior FDA Career Executives: We're Following the Science to Protect Public Health in Pandemic*, USA TODAY (Sept. 10, 2020), https://www.usatoday.com/story/opinion/2020/09/10/sound-science-to-meet-covid-challenges-fda-career-officials-column/5756948002/ (joint public statement by eight senior career civil servants at FDA) [https://perma.cc/PE4Y-EQ4S].

[135] Jessie Hellman, *Ex-FDA Employees Express Worries to Congress Over Politicization of Vaccines*, THE HILL (Sept. 30, 2020), https://thehill.com/policy/healthcare/518979-ex-fda-employees-express-worries-to-congress-over-politicization-of [https://perma.cc/PLZ7-2636].

[136] *7 Former FDA Commissioners*, *supra* note 10.

[137] World Health Organization, *supra* note 133, at 50:59–51:33.

[138] Stacy Wood & Kevin Schulman, *Beyond Politics—Promoting Covid-19 Vaccination in the United States*, 384 NEW ENG. J. MED. e23 (2021).

[139] *See, e.g.*, Ruqaiijah Yearby & Seema Mohapatra, *Law, Structural Racism, and the COVID-19 Pandemic*, 7 J. L. & BIOSCIENCES l (2020).

[140] *See, e.g.*, Daniel S. Goldberg, *Against the Very Idea of the Politicization of Public Health Policy*, 102 AM. J. PUB. HEALTH 44, 46 (2012); *see also* Lawrence O. Gostin, *Language, Science, and Politics: The Politicization of Public Health*, 319 JAMA 541, 542 (2018) ("The politicization of science, of course, has occurred in prior administrations [before the Trump Administration].").

IV. COVID-19 EUAS

Assessing all of the 400+ COVID-19 EUAs issued as of March 8, 2021 is beyond the scope of this Article. Rather, we focus on a subset of EUAs that highlight clinical, ethical, public health, and regulatory issues that can help identify aspects of the EUA mechanism that may need recalibrating. We begin by discussing drug and biologic products: chloroquine phosphate, hydroxychloroquine sulfate, remdesivir, COVID-19 convalescent plasma, and monoclonal antibodies. We then outline the categories of medical devices that had received EUAs as of March 8, 2021 and discuss some of the challenges faced by the health and public health communities following issuance of some of those device EUAs. Next, we examine the enormous efforts to develop COVID-19 vaccines, review the robust debates regarding COVID-19 vaccine research and development, and explore issues raised by the vaccine EUAs.

A. Drug and Therapeutic Biologic Products

On March 27, 2020, the HHS Secretary determined that circumstances existed justifying EUAs for drug and biologic products and issued a declaration authorizing FDA to issue such EUAs.[141] At the outset of the COVID-19 pandemic, there were no known drugs or biologic products that could treat or prevent COVID-19.[142] FDA used EUAs to fill this gap—to enable patients to access promising but unproven drugs and biologic products. Taken together, the EUAs that FDA issued through March 8, 2021 for these products highlight the low statutory standard for authorization, the broad discretion afforded to FDA to issue and revoke EUAs, and the ways in which that discretion creates opportunities for undue political influence.

1. Chloroquine Phosphate and Hydroxychloroquine Sulfate

On March 28, 2020, FDA issued EUAs for two pharmaceuticals—chloroquine phosphate (CQ) and hydroxychloroquine sulfate (HCQ)—the first EUAs for potential COVID-19 treatments.[143] At the time the EUAs were issued, CQ and HCQ were FDA-approved for various non-COVID indications, including preventing and treating

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[141] Emergency Use Authorization Declaration, 85 Fed. Reg. 18,250, 18,250 (Apr. 1, 2020).

[142] A year into the pandemic, despite a major public-private partnership called Accelerating COVID-19 Interventions and Vaccines (ACTIV), among other initiatives, more effective therapeutics were still needed, especially for the most serious cases of COVID-19. *See* Karen Weintraub, *Treatment for COVID-19 is Better than a Year Ago, But It Still Has a Long Way to Go*, USA TODAY (Mar. 14, 2021), https://www.usatoday.com/in-depth/news/health/2021/03/14/covid-treatments-have-improved-but-more-rigorous-study-trials-needed/4433230001/ [https://perma.cc/D3DH-S7R2] (discussing some of the difficulties of developing and studying therapeutics in the midst of an ongoing pandemic).

[143] The EUA was technically granted at the request of the Biomedical Advanced Research and Development Authority (BARDA), but in his whistleblower complaint, former BARDA director Rick Bright details that he pursued an EUA in order to head off a plan by HHS leadership to establish a "a Nationwide Expanded Access Investigational New Drug ('IND') protocol for [CQ and HCQ], which would provide significantly greater access to the drug than would an EUA." Dr. Bright had deep concerns about the EUA as well, and he clarified in the application letter that BARDA was making the EUA request only because it had been directed to do so. Addendum to the Complaint of Prohibited Personnel Practice and other Prohibited activity by the Department of Health and Human Services Submitted by Dr. Rick Bright to the U.S. Off. Special Couns. (2020), https://www.kmblegal.com/sites/default/files/NEW%20R.%20Bright%20OSC%20Complaint_Redacted.pdf [https://perma.cc/N5EH-E8HY].

malaria and treating lupus and rheumatoid arthritis.[144] Because CQ and HCQ are approved drugs, health care professionals generally could have prescribed and dispensed them off-label to treat COVID-19 without FDA issuing the March 2020 EUA.[145] Yet, as noted above, there are reasons why the EUAs were nonetheless sought.[146]

The EUAs for CQ and HCQ for COVID-19 were based on limited data of effectiveness from one randomized pilot study of thirty subjects that found little to no effect of the drugs in COVID-19, and an open-label, non-randomized study in thirty-six subjects.[147] FDA issued the EUAs notwithstanding several known risks of the drugs, including risks of serious heart arrhythmias.[148] Moreover, FDA issued the EUAs only nine days after President Trump publicly touted the drugs as safe and effective COVID-19 countermeasures.[149] According to a whistleblower complaint filed by the former director of BARDA, the Trump Administration exerted relentless and improper political pressure on FDA to issue the EUAs.[150]

Following issuance of the EUAs, additional studies found that the suggested dosage regimens were unlikely to produce an antiviral effect sufficient to treat COVID-19.[151] Although initial research found decreased viral shedding when CQ and HCQ were administered, subsequent studies did not replicate these findings.[152] Moreover, data from a large randomized controlled trial found no evidence of benefit of HCQ treatment in hospitalized patients with COVID-19 in terms of mortality or other clinical outcomes such as length of hospital stay or need for mechanical ventilation.[153]

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144 *See, e.g.*, Lara Bull-Otterson, Elizabeth B. Gray, Daniel S. Budnitz, Heather M. Strosnider, Lyna Z. Schieber, Joseph Courtney, Macarena C. García, John T. Brooks, William R. Mac Kenzie & Adi V. Gundlapalli, *Hydroxychloroquine and Chloroquine Prescribing Patterns by Provider Specialty Following Initial Reports of Potential Benefit for COVID-19 Treatment—United States, January–June 2020*, 69 MORBIDITY & MORTALITY WKLY. REP. 1210, 1211 (2020).

145 *See, e.g.*, *id.* at 1210.

146 *See supra* note 69 and accompanying text.

147 *See, e.g.*, Bull-Otterson et al., *supra* note 144, at 1210; Zahra Hirji, Dan Vergano & Jason Leopold, *Internal FDA Documents Show How Little Evidence the Agency had before Allowing Malaria Drugs to be Used to Treat COVID-19*, BUZZFEED (June 1, 2020), https://www.buzzfeednews.com/article/zahrahirji/fda-eua-hydroxychloroquine-chloroquine.

148 *See, e.g.*, Zettler et al., *supra* note 55, at 165.

149 *See, e.g.*, *id.*

150 Laurel Wamsley, *Rick Bright, Former Top Vaccine Scientist, Files Whistleblower Complaint*, NPR (May 5, 2020), https://www.npr.org/sections/coronavirus-live-updates/2020/05/05/850960344/rick-bright-former-top-vaccine-scientist-files-whistleblower-complaint [https://perma.cc/GYE2-RJ5L].

151 *See Frequently Asked Questions on the Revocation of the Emergency Use Authorization for Hydroxychloroquine Sulfate and Chloroquine Phosphate*, U.S. FOOD & DRUG ADMIN., https://www.fda.gov/media/138946/download (last updated June 19, 2020) [https://perma.cc/94GL-FYSC].

152 *Id.*

153 *Id.*

According to FDA, administration of CQ and HCQ also was linked to "ongoing reports" of "serious cardiac adverse events and other serious side effects."[154]

In light of the safety and effectiveness concerns, on June 15, 2020, FDA revoked the EUAs for CQ and HCQ.[155] Notwithstanding revocation of the EUAs, patients in the midst of treatment with CQ and HCQ were permitted the ability to continue with treatment, and FDA allowed to proceed clinical trials studying whether CQ and HCQ can treat or prevent COVID-19.[156] Moreover, as of December 2020, some physicians continued to push CQ and HCQ as promising COVID-19 treatments or preventions, notwithstanding the lack of supporting evidence regarding effectiveness and documented evidence of harm.[157] In March 2021, World Health Organization (WHO) guidelines developed to guide treatment of COVID-19 explained that there is "high certainty evidence" that "hydroxychloroquine had a small or no effect on mortality and admission to hospital" and that "this drug is no longer a research priority and . . . resources should rather be oriented to evaluate other more promising drugs to prevent COVID-19."[158]

2. Remdesivir

On May 1, 2020, FDA issued an EUA for remdesivir, an anti-viral drug that inhibits viral RNA synthesis.[159] At the time, remdesivir was not approved for any indication, though for years the drug has been studied in clinical trials to gauge treatment potential for Ebola, SARS, and MERS.[160] On April 29, 2020, the National Institute of Allergy

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[154] *Id.*

[155] *Id.*

[156] *Id.*

[157] *See Early Outpatient Treatment: An Essential Part of a COVID-19 Solution, Part II*, *Before the S. Comm. on Homeland Sec. & Gov't Affs.* 116th Cong. (Dec. 8, 2020), at 29:00, https://www.hsgac.senate.gov/early-outpatient-treatment-an-essential-part-of-a-covid-19-solution-part-ii [https://perma.cc/G3D2-CEN4]; *see also* Brown School of Public Health, *Why Scientific Evidence Matters in a Pandemic*, GLOB. EPIDEMICS, https://globalepidemics.org/2020/12/07/why-scientific-evidence-matters-in-a-pandemic [https://perma.cc/3J7Y-8KZ9]. Moreover, one study found that administration of CQ and HCQ to COVID-19 patients was associated with unusually high rates of psychiatric disorders and suicidal tendencies. *See* Carlo Martuscelli, *Drugs Hypes as Coronavirus Treatment Linked to Psychiatric Disorders, Says EU Agency*, POLITICO (Nov. 27, 2020), https://www.politico.eu/article/drugs-hyped-as-coronavirus-treatment-linked-to-psychiatric-disorders-says-ema/ [https://perma.cc/6QKL-ANGB].

[158] François Lamontagne, Thomas Agoritsas, Reed Siemieniuk, Bram Rochwerg, Jessica Bartoszko, Lisa Askie, Helen Macdonald, Wagdy Amin, Frederique Jacquerioz Bausch, Erlina Burhan, Maurizio Cecconi, Duncan Chanda, Vu Quoc Dat, Bin Du, Heike Geduld, Patrick Gee, Harley Nerina, Madiha Hashimi, Beverley J Hunt, Sushil Kabra, Seema Kanda, Leticia Kawano-Dourado, Yae-Jean Kim, Niranjan Kissoon, Arthur Kwizera, Yee-Sin Leo, Imelda Mahaka, Hela Manai, Greta Mino, Emmanuel Nsutebu, Natalia Pshenichnaya, Nida Qadir, Shalini Sri Ranganathan, Saniya Sabzwari, Rohit Sarin, Michael Sharland, Yinzhong Shen, Joao Paulo Souza, Miriam Stegemann, Sebastian Ugarte, Sridhar Venkatapuram, Dubula Vuyiseka, Jacobus Preller, Romina Brignardello-Petersen, Elena Kum, Anila Qasim, Dena Zeraatkar, Andrew Owen, Gordon Guyatt, Lyubov Lytvyn, Janet Diaz, Per Olav Vandvik & Michael Jacobs, *A Living WHO Guideline on Drugs to Prevent COVID-19*, 372 BRIT. MED. J. n526 (2021).

[159] *See* Letter from U.S. Food & Drug Admin. to Gilead Sciences (Aug. 28, 2020). Remdesivir's trade name is Veklury. *Id.*

[160] *See id.*; *see also* Search Results for "remdesivir" from clinicaltrials.gov, https://clinicaltrials.gov/ct2/results?cond=&term=remdesivir [https://perma.cc/H5ZY-7G6T]; Authorizations and Revocation of

and Infectious Diseases (NIAID), which is part of the National Institutes of Health (NIH), released a preliminary data analysis from a NIAID-led study involving over 1,000 hospitalized patients with COVID-19.[161] The preliminary analysis provided some evidence that patients hospitalized with COVID-19 recovered faster when provided remdesivir when compared to patients who received a placebo.[162] In the study, the average recovery time for hospitalized patients that survived a COVID-19 infection was eleven days on remdesivir and fifteen days on a placebo.[163] The analysis also found that, for hospitalized patients, the difference in mortality rate between remdesivir and the placebo was not statistically significant.[164] Previous studies, conducted in the United States and China, returned mixed results on remdesivir's effectiveness for hospitalized patients.[165]

Based on the preliminary data, NIAID decided to halt its study, determining that it was unethical not to offer remdesivir to patients in the placebo arm.[166] The decision was controversial. Within days, several scientists lambasted NIAID's reliance on what they viewed as an unhelpful study endpoint—days to recovery for hospitalized patients who survived a COVID-19 infection—rather than a more meaningful endpoint such as the ability of remdesivir to lower mortality from COVID-19.[167] Moreover, of the 1,063 participants in the study, less than half (480) had recovered at the time of the preliminary analysis.[168] Nevertheless, following issuance of the EUA, demand for remdesivir exploded, with shortages reported throughout the United States and the rest of the world.[169]

The EUA for remdesivir that was issued in May 2020 limited drug access to patients with severe COVID-19, which was defined as patients with low blood oxygen levels

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Emergency Use of Drugs During the COVID-19 Pandemic, 85 Fed. Reg. 56,231, 56,250 (Sept. 11, 2020). Prior to issuance of the EUA, some patients in the United States gained access to the drug via FDA's expanded access program. Gilead began to wind down its expanded access program for remdesivir once FDA issued the EUA.

161 *See* Press Release, NIH Clinical Trial Shows Remdesivir Accelerates Recovery from Advanced COVID-19, Nat'l Inst. of Allergy & Infectious Diseases (Apr. 29, 2020).

162 *See id.*

163 *See, e.g.*, Matthew Herper & Adam Feuerstein, *Critical Study of Gilead's Covid-19 Drug Shows Patients are Responding to Treatment, NIH Says*, STAT (Apr. 29, 2020), https://www.statnews.com/2020/04/29/gilead-says-critical-study-of-covid-19-drug-shows-patients-are-responding-to-treatment/ [https://perma.cc/9AV6-V22K].

164 *Id.* Although the rate was not statistically significant, the study found the mortality rate to be 8% for the remdesivir group as compared to 11.6% for the placebo group. *Id.*

165 *Id.*

166 *See, e.g.*, Matthew Herper, *Inside the NIH's Controversial Decision to Stop its Big Remdesivir Study*, STAT (May 11, 2020), https://www.statnews.com/2020/05/11/inside-the-nihs-controversial-decision-to-stop-its-big-remdesivir-study/ [https://perma.cc/X23P-JJQQ].

167 *See id.*

168 *See id.*

169 *See, e.g.*, Janice Hopkins Tanne, *U.S. Should End Gilead's Monopoly on Producing Remdesivir, Report Says*, 370 BRIT. MED. J. m3537 (Sept. 10, 2020).

or patients who needed oxygen therapy or mechanical ventilation.[170] Following additional studies, on August 28, 2020, FDA expanded the EUA to encompass all hospitalized adult and pediatric patients with suspected or confirmed COVID-19, regardless of the severity of the disease.[171]

Following the EUA expansion for remdesivir, some physicians indicated that they were not changing their prescribing practices because they believed that the data did not show that remdesivir provided a clinical benefit across all hospitalized COVID-19 patients.[172] In October 2020, interim results of the WHO's Solidarity Therapeutics Trial, the largest randomized controlled trial of potential COVID-19 treatments, suggested that remdesivir "appeared to have little or no effect . . . [on] overall mortality, initiation of ventilation and duration of hospital stay."[173]

Shortly thereafter, on October 22, 2020, FDA approved a new drug application (NDA) for remdesivir for hospitalized COVID-19 patients, making remdesivir the first product fully approved for a COVID-19 treatment indication.[174] In a *New England Journal of Medicine* article, FDA officials described the approval as "an important step toward addressing the needs of patients with Covid-19" while also acknowledging the Solidarity trial and "the need for continued therapeutic development" due to "the absence of a demonstrated survival benefit."[175] Several commentators criticized the approval because of questions about remdesivir's effectiveness and because FDA failed to consult an advisory committee before making its approval decision.[176] Following FDA approval, a WHO advisory committee recommended against use of remdesivir to treat COVID-19, finding that the treatment "has no meaningful effect on mortality or on other important outcomes for patients."[177]

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[170] *See* Press Release, U.S. Food & Drug Admin., FDA Broadens Emergency Use Authorization for Veklury (remdesivir) to Include All Hospitalized Patients for Treatment of COVID-19 (Aug. 28, 2020), https://www.fda.gov/news-events/press-announcements/covid-19-update-fda-broadens-emergency-use-authorization-veklury-remdesivir-include-all-hospitalized [https://perma.cc/4SVP-XWLF].

[171] *Id.*

[172] *See, e.g.*, Deena Beasley, *U.S. Hospitals Turn Down Remdesivir, Limit Use to Sickest COVID-19 Patients*, REUTERS (Sept. 11, 2020), https://www.reuters.com/article/health-coronavirus-remdesivir/exclusive-u-s-hospitals-turn-down-remdesivir-supplies-limit-use-to-sickest-covid-19-patients-idUSL1N2G728H [https://perma.cc/7A4V-J7FP].

[173] WHO Solidarity Trial Consortium, *Repurposed Antiviral Drugs for COVID-19—Interim WHO Solidarity Trial Results*, 384 NEW ENG. J. MED. 497, 497 (2021).

[174] U.S. FOOD & DRUG ADMIN., VEKLURY LABELING DOCUMENT (2020), https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/214787Orig1s000lbl.pdf [https://perma.cc/5GPQ-NVB5].

[175] Daniel Rubin, Kirk Chan-Tack, John Farley & Adam Sherwat, *FDA Approval of Remdesivir—A Step in the Right Direction*, 383 NEW ENG. J. MED. 2598 (2020).

[176] *See, e.g.*, Jon Cohen & Kai Kupferschmidt, *'A Very, Very Bad Look' for Remdesivir*, 370 SCIENCE 642, 642 (2020).

[177] Mike Murphy, *WHO Advisers Recommend Against Gilead's Remdesivir for Treating Covid-19*, MKT. WATCH (Nov. 19, 2020, 9:17 PM), https://www.marketwatch.com/story/who-advisers-recommend-against-gileads-remdesivir-for-treating-covid-19-11605834767 [https://perma.cc/7AMU-S8RV].

Even before FDA approved remdesivir, concerns were raised about the cost of the drug, which was $2,340 to $3,120 per patient.[178] Reports indicated that the cost to manufacture the drug was $0.93 per dose.[179] By the time FDA expanded the remdesivir EUA in August 2020, the supply issues from earlier in the summer had been rectified and there was a surplus of the drug in the United States.[180] Nevertheless, some hospitals began stockpiling the drug in anticipation of increasing cases in fall 2020.[181] Meanwhile, eleven states asked the manufacturer, Gilead, to lower its price for the drug, stating that the price was "disconnected from market forces" and brought the company "unreasonable profits."[182] Allegations of profiteering were paired with claims that high prices for remdesivir would set a pandemic precedent for additional therapies that may be authorized for use.[183] Gilead denied that the cost was unreasonable and, as of March 2021, did not lower the price.[184]

3. Convalescent Plasma

On August 23, 2020, FDA issued an EUA for COVID-19 convalescent plasma, which is human plasma collected from individuals who have survived a COVID-19 infection and have SARS-CoV-2 antibodies.[185] Treatment with convalescent plasma has been studied in several viruses, including Ebola, MERS, SARS, and H1N1 influenza.[186] From an early stage of the COVID-19 epidemic, scientists considered whether convalescent plasma might be a helpful treatment for individuals hospitalized due to COVID-19.[187]

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[178] *See, e.g.*, Tanne, *supra* note 169.

[179] *See id.* Patients typically receive five doses during the course of treatment with the drug. *See id.*

[180] *See* Beasley, *supra* note 172.

[181] *See id.*

[182] Ed Silverman, *State Treasurers Urge Gilead to Lower the Price of Remdesivir and Not Pursue "Unreasonable Profits"*, STAT (Sept. 17, 2020), https://www.statnews.com/pharmalot/2020/09/17/gilead-remdeisivir-covid19-fda-coronavirus-pandemic/ [https://perma.cc/482M-E529].

[183] *Id.*

[184] *Id.*

[185] Press Release, U.S. Food & Drug Admin., FDA Issues Emergency Use Authorization for Convalescent Plasma as Potential Promising COVID–19 Treatment, Another Achievement in Administration's Fight Against Pandemic (Aug. 23, 2020), https://www.fda.gov/news-events/press-announcements/fda-issues-emergency-use-authorization-convalescent-plasma-potential-promising-covid-19-treatment [https://perma.cc/LGL4-HHLZ].

[186] *See, e.g.*, Long Chen, Jing Xiong, Lei Bao & Yuan Shi, *Convalescent Plasma as a Potential Therapy for COVID-19*, 20 LANCET 398, 398–99 (Apr. 2020).

[187] *See* Michael Greshko, *Blood Plasma Touted as COVID-19 Breakthrough: But Does it Work?*, NAT'L GEOGRAPHIC (Aug. 24, 2020), https://www.nationalgeographic.com/science/article/convalescent-blood-plasma-touted-coronavirus-breakthrough-does-it-work-cvd [https://perma.cc/B2G9-5XXS]; *see also* Chenguang Shen, Zhaoqin Wang, Fang Zhao, Yang Yang, Jinxiu Li, Jing Yuan, Fuxiang Wang, Delin Li, Minghui Yang, Li Xing, Jinli Wei, Haixia Xiao, Yan Yang, Jiuxin Qu, Ling Qing, Li Chen, Zhixiang Xu, Ling Peng, Yanjie Li, Haixia Zheng, Feng Chen, Kun Huang, Yujing Jiang, Dongjing Liu, Zheng Zhang,

As of late August 2020—despite over seventy clinical trials that evaluated the effectiveness of convalescent plasma as a treatment for COVID-19—not one study had confirmed the effectiveness of the treatment.[188] The primary study upon which FDA based the EUA was an observational study led by the Mayo Clinic. The study, which was not peer-reviewed, enrolled over 35,000 participants who were hospitalized with COVID-19.[189] The study built off an expanded access program, which provided COVID-19 patients non-trial preapproval access to convalescent plasma.[190] More than 2,700 hospitals across the country signed up to participate in the expanded access program, and by August 17, 2020 more than 97,000 patients were treated with convalescent plasma for COVID-19.[191] Some physicians expressed concern with the widespread, non-trial preapproval use of convalescent plasma in light of the lack of data on effectiveness.[192]

A preliminary analysis of the Mayo Clinic study, publicized in mid-August 2020, found that patients who were administered convalescent plasma within three days of a COVID-19 diagnosis had a seven-day death rate of 8.7%, whereas patients who were administered the treatment more than four days after being hospitalized had a death rate of 11.9%.[193] The analysis found this distinction to be statistically significant.[194] However, the study had a major flaw—it did not have a control arm.[195] Without a control arm, it is difficult to accurately assess whether the treatment itself was responsible for the decreased death rate.[196] Another design flaw in the study involved a discrepancy in the level of antibodies in the plasma that was provided to patients in the two different groups.[197] The study did not randomize the administration of the plasma, and thus conclusions could not be drawn related to the ideal antibody levels

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Yingxia Liu & Lei Liu, *Treatment of 5 Critically Ill Patients with COVID-19 with Convalescent Plasma*, 323 JAMA 1582 (2020) (citing a study conducted in China from January to March 2020).

[188] *See* Greshko, *supra* note 187.

[189] *See* Damian Garde & Matthew Herper, *Large Study Suggests Convalescent Plasma Can Help Treat Covid-19, But Experts Have Doubts*, STAT (Aug. 13, 2020), https://www.statnews.com/2020/08/13/large-study-suggests-convalescent-plasma-can-help-treat-covid-19-with-caveats/ [https://perma.cc/BL65-8PV3].

[190] *See id.*

[191] *See* Adam Rogers, *97,000 People Got Convalescent Plasma: Who Knows If it Works?*, WIRED (Aug. 21, 2020), https://www.wired.com/story/97000-people-got-convalescent-plasma-who-knows-if-it-works/ [https://perma.cc/2SUQ-73SC].

[192] *See id.*

[193] *See* Garde & Herper, *supra* note 189.

[194] *See id.*

[195] *See id.*

[196] *See id.*

[197] *See* Heidi Ledford, *Evidence for Convalescent Plasma Coronavirus Treatment Lags Behind Excitement*, SCI. AM. (Aug. 24, 2020), https://www.scientificamerican.com/article/evidence-for-convalescent-plasma-coronavirus-treatment-lags-behind-excitement/?print=true [https://perma.cc/HHE4-QLY5].

in the plasma and the ideal date at which the treatment should begin.[198] As Peter Bach, director of Memorial Sloan Kettering's Center for Health Policy and Outcomes, remarked days before the EUA was issued: "If we had just done the randomized control trials, we would know the answers we are still guessing at."[199]

Because of the serious questions regarding the effectiveness of convalescent plasma for COVID-19, in mid-August 2020, leaders at the NIH and NIAID—including NIH Director Francis Collins and NIAID Director Anthony Fauci—advised that FDA proceed cautiously before issuing an EUA.[200] One important concern was that an EUA would make it even more difficult to conduct necessary clinical trials.[201] President Trump lambasted what he viewed as an unnecessary delay, dubbing it a "deep state" conspiracy to undermine his reelection campaign.[202] Days later—without any new evidence on the effectiveness of the treatment and without a clear plan to help ensure that continued clinical trial enrollment was feasible—FDA issued the EUA.[203] In a press release accompanying the issuance of the EUA, HHS Secretary Azar heralded the EUA as "a milestone achievement in President Trump's efforts to save lives."[204]

That same day, FDA Commissioner Stephen Hahn grossly over-stated the potential benefits of the treatment, claiming that convalescent plasma would save 35 of 100 lives that would have been lost to COVID-19—when in reality the evidence supporting convalescent plasma's potential benefits was far more modest.[205] Immediately, leaders

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[198] *See id.*

[199] Garde & Herper, *supra* note 189.

[200] Noah Weiland, Sharon LaFraniere & Sheri Fink, *FDA's Emergency Approval of Blood Plasma is Now on Hold*, N.Y. TIMES (Aug. 19, 2020), https://www.nytimes.com/2020/08/19/us/politics/blood-plasma-covid-19.html [https://perma.cc/9P89-6ZS6].

[201] *See id.*

[202] *See* Noah Higgins-Dunn & Christina Farr, *Trump Says FDA Hold on Blood Treatment Therapy Use for Coronavirus Patients 'Could Be a Political Decision'*, CNBC (Aug. 19, 2020), https://www.cnbc.com/2020/08/19/trump-says-fda-hold-on-blood-treatment-therapy-use-for-coronavirus-patients-could-be-a-political-decision.html [https://perma.cc/RU4P-X2K5]; Jonathan Lemire & Mike Stobbe, *Trump Announces Plasma Treatment Authorized for COVID-19*, AP NEWS (Aug. 23, 2020), https://apnews.com/article/virus-outbreak-health-ap-top-news-politics-3296040fb1225ee7fa465d7baa5057da [https://perma.cc/8D6M-6TNA]. It was reported that President Trump personally pressured NIH Director Frances Collins to facilitate the EUA authorization. Sharon LaFraniere, Noah Weiland & Michael D. Shear, *Trump Pressed for Plasma Therapy. Officials Worry, Is an Unvetted Vaccine Next?*, N.Y. TIMES (Sept. 12, 2020), https://www.nytimes.com/2020/09/12/us/politics/trump-coronavirus-treatment-vaccine.html [https://perma.cc/9EQQ-D2XM].

[203] Lemire & Stobbe, *supra* note 202.

[204] Press Release, U.S. Food & Drug Admin., FDA Issues Emergency Use Authorization for Convalescent Plasma as Potential Promising COVID-19 Treatment, Another Achievement in Administration's Fight Against Pandemic (Aug. 23, 2020), https://www.fda.gov/news-events/press-announcements/fda-issues-emergency-use-authorization-convalescent-plasma-potential-promising-covid-19-treatment [https://perma.cc/Q7LV-275D].

[205] *See* Richard Harris, *FDA's Hahn Apologizes for Overselling Plasma's Benefits as a COVID-19 Treatment*, NPR (Aug. 25, 2020), https://www.npr.org/sections/health-shots/2020/08/25/905792261/fdas-hahn-apologizes-for-overselling-plasmas-benefits-as-a-covid-19-treatment [https://perma.cc/68XP-M2WY].

in the scientific community criticized the statements.[206] For example, Eric Topol of the Scripps Translational Research Institute was quoted as saying, "I can't remember a mistake by FDA or the commissioner as serious as this one."[207] Commissioner Hahn walked back his claims the following day.[208] Notably, the announcement of the convalescent plasma EUA came on the eve of the Republican National Convention, where the Trump Administration was expected to be praised for its response to the pandemic and President Trump was expected to be formally nominated as the Republican candidate for the 2020 election.[209]

Within days of FDA's issuance of the COVID-19 convalescent plasma EUA, the NIH's COVID-19 Treatment Guidelines Panel issued a statement wherein it underscored that "[t]here are currently no data from well-controlled, adequately powered randomized clinical trials that demonstrate the efficacy and safety of convalescent plasma for the treatment of COVID-19."[210] The NIH further stated that "[t]here are insufficient data to recommend either for or against the use of convalescent plasma for the treatment of COVID-19."[211] Accordingly, the NIH panel stated that "[c]onvalescent plasma should not be considered standard of care for the treatment of patients with COVID-19."[212]

Following the NIH panel's recommendations, dozens of leading hospitals from across the country indicated that they would work together to construct a randomized controlled trial to evaluate the effectiveness of convalescent plasma as a treatment for hospitalized COVID-19 patients.[213] Within weeks, the NIH announced it was providing nearly $50 million to support two randomized controlled trials.[214] Due to access to the treatment via the newly issued EUA, however, enrolling participants in the trials was challenging.[215] And, three months after issuance of the EUA, a study

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[206] *Id.*

[207] *Id.*

[208] *See id.* Hahn stated: "What I should have said better is that the data show a relative risk reduction not an absolute risk reduction." However, even this explanation did not line up with the data. *Id.*

[209] *See, e.g.*, Efthimios Parasidis, *The Trump Administration's FDA is Both Victim and Villain*, BARRON'S (Aug. 26, 2020), https://www.barrons.com/articles/the-trump-administrations-fda-is-both-victim-and-villain-51598478351 [https://perma.cc/55X2-JSGR].

[210] NAT'L INSTS. HEALTH, THE COVID-19 TREATMENT GUIDELINES PANEL'S STATEMENT ON THE EMERGENCY USE AUTHORIZATION OF CONVALESCENT PLASMA FOR THE TREATMENT OF COVID-19 (2020).

[211] *Id.*

[212] *Id.*

[213] The trial was led by Vanderbilt University Medical Center and included forty-five hospitals. *See* JoNel Aleccia, *Dozens of U.S. Hospitals Poised to Defy FDA's Directive on COVID Plasma*, KAISER HEALTH NEWS (Sept. 3, 2020), https://khn.org/news/dozens-of-u-s-hospitals-poised-to-defy-fdas-directive-on-covid-plasma/ [https://perma.cc/Y3NL-PCEG].

[214] Press Release, Nat'l Insts. Health, NIH Expands Clinical Trials to Test Convalescent Plasma Against COVID-19 (Sept. 22, 2020), https://www.nih.gov/news-events/news-releases/nih-expands-clinical-trials-test-convalescent-plasma-against-covid-19 [https://perma.cc/3ZFU-DN27].

[215] *See* Aleccia, *supra* note 213.

published in the *New England Journal of Medicine* found no significant difference in disease burden or overall mortality between patients treated with COVID-19 convalescent plasma and those that received a placebo.[216]

On March 2, 2021—more than six months after FDA issued the EUA for COVID-19 convalescent plasma—the NIH halted clinical trials because it concluded that the treatment "provides no significant benefit" to patients with mild-to-moderate COVID-19.[217] Specifically, data from the clinical trial, which enrolled patients from forty-seven emergency departments from across the United States, found that COVID-19 convalescent plasma did not reduce disease burden, did not reduce the need for further emergency care, did not reduce hospitalization, and did not reduce death due to COVID-19.[218] Despite the NIH's findings, several other clinical trials remained active as of March 2021, seeking to find a subset of patients for which COVID-19 convalescent plasma might be effective.[219]

4. Monoclonal Antibody Products

In November 2020, FDA issued EUAs for Eli Lilly and Regeneron's monoclonal antibody products for mild to moderate COVID-19, some of which involved combination treatments.[220] Monoclonal antibodies are synthetic versions of antibodies that the human immune system produces to ward off pathogens.[221] The monoclonal

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[216] *See* V.A. Simonovich, L.D. Burgos Pratx, P. Scibona, M.V. Beruto, M.G. Vallone, C. Vázquez, N. Savoy, D.H. Giunta, L.G. Pérez, M..L. Sánchez, A.V. Gamarnik, D.S. Ojeda, D.M. Santoro, P.J. Camino, S. Antelo, K. Rainero, G.P. Vidiella, E.A. Miyazaki, W. Cornistein, O.A. Trabadelo, F.M. Ross, M. Spotti, G. Funtowicz, W.E. Scordo, M.H. Losso, I. Ferniot, P.E. Pardo, E. Rodriguez, P. Rucci, J. Pasquali, N.A. Fuentes, M. Esperatti, G.A. Speroni, E.C. Nannini, A. Matteaccio, H.G. Michelangelo, D. Follmann, H.C. Lanec & W.H. Belloso, *A Randomized Trial of Convalescent Plasma in Covid-19 Severe Pneumonia*, 384 NEW ENG. J. MED. 619, 619 (2020).

[217] Press Release, Nat'l Insts. Health, NIH Halts Trial of COVID-19 Convalescent Plasma in Emergency Department Patients with Mild Symptoms (Mar. 2, 2021), https://www.nih.gov/news-events/news-releases/nih-halts-trial-covid-19-convalescent-plasma-emergency-department-patients-mild-symptoms [https://perma.cc/UJX3-D8L8].

[218] *Id.*

[219] *See* Richard Harris, *Convalescent Plasma Strikes Out as COVID-19 Treatment*, NPR (Mar. 10, 2021), https://www.npr.org/sections/health-shots/2021/03/10/975365309/convalescent-plasma-strikes-out-as-covid-19-treatment [https://perma.cc/45KP-FYN2]; *Emergency Use Authorization*, U.S. FOOD & DRUG ADMIN., https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#coviddrugs (last updated Nov. 15, 2021) (listing EUA for convalescent plasma) [https://perma.cc/8A66-6TVU].

[220] *See* U.S. FOOD & DRUG ADMIN., LETTER OF EMERGENCY USE AUTHORIZATION FOR BAMLANIVIMAB, (2021); U.S. FOOD & DRUG ADMIN., LETTER OF EMERGENCY USE AUTHORIZATION FOR CASIRIVIMAB AND IMDEVIMAB (2020). In November 2020, FDA also issued an EUA for the use of baricitinib, a Janus kinase inhibitor, in combination with remdesivir for certain COVID-19 patients. U.S. FOOD & DRUG ADMIN., LETTER OF EMERGENCY USE AUTHORIZATION FOR BARICITINIB (2021). When President Trump was hospitalized with COVID-19 in October 2020, he received Regeneron's products through expanded access. *See, e.g.*, Katie Thomas & Noah Weiland, *Eli Lilly's Antibody Treatment Gets Emergency FDA Approval*, N.Y. TIMES (Nov. 9, 2020), https://www.nytimes.com/2020/11/09/health/covid-antibody-treatment-eli-lilly.html [https://perma.cc/22KG-XBDN].

[221] *See* Matthew S. Schwartz, *FDA Grants Emergency Authorization for 2nd COVID-19 Antibody Treatment*, NPR (Nov. 22, 2020), https://www.npr.org/2020/11/22/937746317/fda-grants-emergency-authorization-for-a-second-covid-19-antibody-treatment [https://perma.cc/ZF44-YHQP].

antibody EUAs were based on studies showing reductions in COVID-19-related hospitalizations and emergency room visits, though after issuance of the EUAs, additional studies on safety and efficacy were conducted to confirm the findings from the early trials.[222] Both therapies were authorized for use to treat mild to moderate COVID-19 cases in individuals aged twelve and over who are at high risk of developing more severe symptoms.[223] Neither was authorized for use in hospitalized patients or patients who require supplemental oxygen.[224]

Following issuance of the EUAs, experts raised concerns about the "sparse" data to support use of the treatments.[225] The EUAs were based on very limited clinical trial data, and no evidence of mortality benefit.[226] Moreover, the EUAs authorized use of the products in cases that went beyond where the data showed effectiveness.[227] For example, both treatments were authorized for use in children, even though no children were enrolled in the clinical trials and there were no data on safety and effectiveness in children.[228] And, the EUAs allowed administration of the antibodies up to ten days after the onset of symptoms, a window longer than that which the data showed the therapies might be beneficial.[229] This is significant because, among other reasons, the treatments were "costly, time-consuming, and in short supply."[230]

In February 2021, FDA issued another EUA, this one for a combination monoclonal antibody cocktail comprised of bamlanivimab and etesevimab.[231] The EUA was based on a study that revealed clinical benefits for high risk patients who receive the cocktail prior to hospitalization for COVID-19 and/or prior to administration of supplemental oxygen.[232] After issuance of the EUA, data from a Phase III clinical trial likewise found that, for high-risk patients recently diagnosed with COVID-19 who had yet to receive supplemental oxygen and yet to be hospitalized, the combination treatment

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[222] *See* Matthew Perrone, *US Allows 1st Emergency Use of a Covid-19 Antibody Drug*, AP NEWS (Nov. 10, 2020), https://apnews.com/article/us-1st-emergency-use-virus-antibody-drug-9022befe889c4c54a95301v5535ffea4c [https://perma.cc/D8MF-CRVU].

[223] *See* LETTER OF EMERGENCY USE AUTHORIZATION FOR BAMLANIVIMAB, *supra* note 220.

[224] *See id.*

[225] *See* Colette DeJong, Bernard Lo & Alice Hm Chen, *Emergency Use Authorization for Covid-19 Monoclonal Antibodies: Challenges and Lessons Learned*, HEALTH AFFS. (Dec. 17, 2020), https://www.healthaffairs.org/do/10.1377/hblog20201216.328379/full/ [https://perma.cc/ZG59-N9Z4].

[226] *See id.*

[227] *See id.*

[228] *See id.*

[229] *See id.*

[230] *See id.*

[231] U.S. FOOD & DRUG ADMIN., LETTER OF EMERGENCY USE AUTHORIZATION FOR BAMLANIVIMAB AND ETESEVIMAB (2021).

[232] *See id.*

reduced the risk of hospitalization and death by 87%.[233] The study involved 769 patients who were categorized as high risk due to comorbidities such as obesity, diabetes, chronic kidney disease.[234]

B. Medical Devices

Similar to COVID-19 drugs and therapeutic biological products, for medical devices, FDA faced pressure to authorize EUAs expeditiously. As with drugs and therapeutic biological products, FDA's decisions to issue certain device EUAs based on sparse evidence were met with criticism. Ultimately, FDA needs to balance allowing access to necessary medical devices with sufficient processes to ensure that those products are reliable and, in the case of personal protective equipment (PPE), provide adequate protection. The examples outlined herein illustrate the difficulty of successfully navigating between those competing concerns in the pressurized context of a pandemic.

1. Diagnostic Tests

The first EUA issued during the COVID-19 pandemic was for an in vitro diagnostic test.[235] On February 4, 2020, FDA issued an EUA for a test developed by the CDC as a real-time PCR test, which is a molecular test that detects genetic material of the COVID-19 virus in a person's saliva or mucus.[236] Prior to issuance of the EUA, testing in the United States for COVID-19 was limited to the CDC's laboratories.[237] Through February 4, 2020, the CDC had conducted about 500 COVID-19 tests, twelve of which were positive.[238] Once the authorization was issued, however, testing could be conducted at any CDC-qualified lab across the country.[239] Given manufacturing limitations and a lack of reagents and other essential test kit materials, however, few

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[233] *Lilly's Bamlanivimab and Etesevimab Together Reduced Hospitalizations and Death in Phase 3 Trial for Early COVID-19*, PR NEWSWIRE (Mar. 10, 2021), https://www.prnewswire.com/news-releases/lillys-bamlanivimab-and-etesevimab-together-reduced-hospitalizations-and-death-in-phase-3-trial-for-early-covid-19-301243984.html [https://perma.cc/ET26-RM4F].

[234] *See id.*; *Frequently Asked Questions on the EUA for Bamlanivimab and Etesevimab*, U.S. FOOD & DRUG ADMIN. (Feb. 22, 2021), https://www.fda.gov/media/145808/download [https://perma.cc/EK88-JSZK].

[235] FDA COVID-19 EUA List, *supra* note 5.

[236] Authorization of Emergency Use of Certain Medical Devices During COVID-19, 85 Fed. Reg. 34,638, 34,639 (June 5, 2020).

[237] Press Release, U.S. Food & Drug Admin., FDA Takes Significant Step in Coronavirus Response Efforts, Issues Emergency Use Authorization for the First 2019 Novel Coronavirus Diagnostic (Feb. 4, 2020), https://www.fda.gov/news-events/press-announcements/fda-takes-significant-step-coronavirus-response-efforts-issues-emergency-use-authorization-first [https://perma.cc/H7C5-QSAW].

[238] *See* Robert P. Baird, *What Went Wrong with Coronavirus Testing in the U.S.*, NEW YORKER (Mar. 16, 2020), https://www.newyorker.com/news/news-desk/what-went-wrong-with-coronavirus-testing-in-the-us [https://perma.cc/SW7F-S5KS].

[239] *See id.*

tests were ready for use.[240] CDC therefore imposed limiting criteria on test eligibility.[241]

The CDC test was developed in "record time," according to then-CDC Director Robert Redfield—within ten days from the day the agency obtained access to the COVID-19 genetic sequence.[242] Rather than adopt a test blueprint endorsed by the WHO, the CDC created its own test.[243] Yet, the tests that FDA authorized with its first EUA—and that the CDC then shared across the country to detect COVID-19—largely did not work.[244]

Of the fifty state and local public health agencies that received tests in early February 2020, no more than eight were able to verify that the tests worked as intended.[245] Despite this immediate sign of problems, the CDC waited eight days to publicly announce the shortcomings.[246] It then took weeks for the CDC to correct the test kit errors.[247] Moreover, the EUA that FDA issued specified that positive tests for COVID-19 must be confirmed through retesting in a CDC lab.[248] This double-testing hindered testing efforts and reporting of COVID-19 cases, because only confirmed cases were reported.[249] All of these factors complicated the early public health response to the pandemic.

FDA also issued many additional EUAs for devices to detect COVID-19, or COVID-19 antibodies, in the early months of the pandemic. Between issuance of the initial EUA for the CDC test on February 4, 2020 and the wave of COVID-19 stay-at-

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[240] *See id.*; Lydia DePillis & Caroline Chen, *The FDA is Forcing the CDC to Waste Time Double Testing Some Coronavirus Cases*, PROPUBLICA (Mar. 12, 2020), https://www.propublica.org/article/the-fda-is-forcing-the-cdc-to-waste-time-double-testing-some-coronavirus-cases [https://perma.cc/JP75-MX3V].

[241] *See* Caroline Chen, Marshall Allen, Lexi Chruchill & Isaac Arnsdorf, *Key Missteps at the CDC Have Set Back Its Ability to Detect the Potential Spread of Coronavirus*, PROPUBLICA (Feb. 28, 2020), https://www.propublica.org/article/cdc-coronavirus-covid-19-test [https://perma.cc/DF87-KTJ]. As a point of comparison, by the end of January 2020, China had five commercial tests on the market and was conducting nearly 1.6 million tests per week. Jon Cohen, *The United States Badly Bungled Coronavirus Testing—But Things May Soon Improve*, SCIENCE (Feb. 28, 2020), https://www.science.org/news/2020/02/united-states-badly-bungled-coronavirus-testing-things-may-soon-improve [https://perma.cc/PT2K-G3HF].

[242] *See* Michelle Cortez & John Tozzi, *What Happened to the CDC?: The Storied Disease Agency is Taking a Back Seat in the U.S. Response to the Coronavirus*, FORTUNE (Apr. 12, 2020), https://fortune.com/2020/04/12/cdc-coronavirus-testing-us-covid-19-response-trump-american-government/ [https://perma.cc/N8WV-A5LF]. The CDC finalized its test on January 21, 2020, the same day that German researchers published a paper describing a COVID-19 diagnostic test design. *See* Baird, *supra* note 238. The WHO utilized the protocols outlined in the German paper in its testing guidelines. *See id.*

[243] *See* DePillis & Chen, *supra* note 240.

[244] *See id.*

[245] *See* Baird, *supra* note 238.

[246] *See id.*

[247] *See id.*

[248] *See* DePillis & Chen, *supra* note 240.

[249] *See id.*

home orders issued during March 17–23, 2020, FDA authorized over a dozen additional EUAs for COVID-19 in vitro diagnostic tests.[250] Ten more tests were authorized for use over the next two weeks, and by May 1, 2020, more than fifty additional tests were added to the list.[251] By the end of September 2020, FDA had issued more than 250 EUAs for tests, including PCR diagnostic tests, the generally-less-sensitive antigen diagnostic tests that detect viral proteins rather than the virus's genetic material, and serologic tests that detect antibodies rather than active infection.[252]

In part, the influx of tests was due to FDA's use of an "Umbrella EUA," in which, rather than authorizing tests on a case-by-case basis, FDA granted blanket EUA authorization for all independently validated SARS-CoV-2 serologic, or "antibody," tests. FDA issued the "Umbrella EUA" on April 28, 2020,[253] a point in the pandemic when some argued there was a dire need for antibody tests. FDA then revoked the Umbrella EUA on July 21, 2020 in order "to protect the public health."[254] This broad statement reflected the individual and public health dangers that resulted from inaccurate antibody tests flooding the market. Thereafter, FDA indicated that each antibody test must apply individually for an EUA.[255] Coupled with the revocation of the Umbrella EUA, FDA also revoked the EUA for two individual antibody tests due to post-market analysis that revealed poor accuracy and specificity.[256]

Partly for these reasons, through early March 2021, it was challenging for public health administrators, employers, universities, K-12 schools, and others involved in return-to-school and return-to-work programs to be able to judge the reliability and accuracy of tests—perhaps particularly so for antigen diagnostic tests and serologic antibody tests—which were deemed as essential for such programs.[257]

Additionally, in some cases, verification studies of marketed tests were being conducted after the EUAs were issued and while the tests were being used to screen

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[250] FDA COVID-19 EUA List, *supra* note 5.

[251] *See id.*

[252] *See id.*

[253] U.S. FOOD & DRUG ADMIN., LETTER OF UMBRELLA EMERGENCY USE AUTHORIZATION FOR BAMLANIVIMAB, FOR INDEPENDENTLY VALIDATED SEROLOGY TESTS FOR SARS-COV-2 (2020); FDA Revoked EUA List, *supra* note 5.

[254] U.S. FOOD & DRUG ADMIN., FDA LETTER TO MANUFACTURERS AND OTHER STAKEHOLDERS (2020); FDA Revoked EUA List, *supra* note 5.

[255] U.S. FOOD & DRUG ADMIN., FDA LETTER TO MANUFACTURERS AND OTHER STAKEHOLDERS (2020); FDA Revoked EUA List, *supra* note 5.

[256] Letter from Denise Hinton, Chief Scientist, U.S. Food & Drug Admin., to Chembio Diagnostic Systems, Revocation of EUA200179 (June 16, 2020), https://www.fda.gov/media/139109/download#:~:text=Accordingly%2C%20FDA%20revokes%20EUA200179%20for,no%20longer%20authorized%20by%20FDA; Letter from Denise Hinton, Chief Scientist, Food & Drug Admin., Revocation of EUA200349 (Aug. 6, 2020), https://www.fda.gov/media/140908/download#:~:text=Accordingly%2C%20FDA%20revokes%20EUA200349%20for,no%20longer%20authorized%20by%20FDA; FDA Revoked EUA List, *supra* note 5.

[257] Particularly early in the pandemic, media reports often conflated emergency use authorization with FDA approval, and people likewise may have misunderstood the meaning of an EUA.

people for COVID-19. For example, although many PCR tests have generally performed well, for one widely used rapid PCR test for which FDA issued an EUA—Abbott's ID Now rapid test, which disclosed results in as little as five minutes—post-market studies indicated false negative rates as high as 20%.[258] In other words, in as many as one in five instances in which a person who was in fact COVID-positive took the test, it incorrectly provided a COVID-negative result.[259] FDA issued a warning about the false negatives but did not revoke the EUA, even with other tests on the market that were 99% accurate.[260] Rather, FDA issued a statement that the test was still useful even if it had a false negative rate of 20%.[261] This decision contradicted an FDA policy that diagnostic tests should be at least 95% accurate in identifying COVID-positive individuals.[262]

By mid-June 2020, HHS alone had spent over $200 million to purchase hundreds of thousands of the Abbott tests.[263] This test was widely used by the Trump Administration and governmental agencies to screen personnel and guests, and some experts surmise the reliability issues contributed to the fall 2020 COVID outbreak within the White House that infected President Trump, Melania Trump, and dozens of others.[264] Analogous concerns have been raised about rapid antigen tests, which are generally less sensitive than PCR tests because a person typically must have a higher

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[258] *See* Matthew Herper, *FDA Says Abbott's 5-Minute Covid-19 Test May Miss Infected Patients*, STAT NEWS (May 15, 2020), https://www.statnews.com/2020/05/15/fda-says-abbotts-5-minute-covid-19-test-may-miss-infectedpatients/#:~:text=The%20Food%20and%20Drug,the%20novel%20coronavirus%20are%20not.

[259] *See id.*

[260] *See* Rachana Pradhan, *As Problems Grow with Abbott's Fast Covid Test, FDA Standards are Under Fire*, KAISER HEALTH NEWS (June 22, 2020). For additional discussion of concerns associated with test reliability, particularly for direct-to-consumer tests, see Louiza Kalokairinou, Patricia J Zettler, Ashwini Nagappan, Moira A Kyweluk & Anna Wexler, *The Promise of Direct-to-Consumer COVID-19 Testing: Ethical and Regulatory Issues*, 7 J.L. BIOSCIS. (published online; forthcoming in print), https://academic.oup.com/jlb/advance-article/doi/10.1093/jlb/lsaa069/5910046 [https://perma.cc/S9XX-UJQF]. Indeed, in March 2021, FDA issued the first EUA for a full direct-to-consumer—non-prescription, and at-home—COVID test. Press Release, U.S. Food & Drug Admin., Coronavirus (COVID-19) Update: FDA Issues Authorization for First Molecular, Non-Prescription, At-Home Test (Mar. 5, 2021), https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-issues-authorization-first-molecular-non-prescription-home-test [https://perma.cc/6UBH-HWQC].

[261] *See* Pradhan, *supra* note 260. To be clear, it may be that a less reliable, but widely available, test that provides results within minutes could have had public health benefits at the time if users understood the limits of the test and did not rely on it for diagnostic purposes. But it was not clear that the Abbott test provided such benefits.

[262] *See id.*

[263] *See id.*

[264] *See id.*; Katherine J. Wu, *The White House Bet on Abbott's Rapid Tests: It Didn't Work Out*, N.Y. TIMES (Oct. 6, 2020), https://www.nytimes.com/2020/10/06/health/covid-white-house-testing.html [https://perma.cc/6EQQ-EVAA]; Alana Wise, *White House Adviser Stephen Miller Tests Positive for the Coronavirus*, NPR (Oct. 7, 2020), https://www.npr.org/2020/10/06/920960047/wh-adviser-stephen-miller-tests-positive-for-the-coronavirus [https://perma.cc/9PLT-43XW].

viral load for the antigen test to detect COVID-19.[265] By September 2020, the federal government had spent over $760 million to purchase more than 150 million rapid antigen tests for distribution in nursing homes, health care settings, schools, and elsewhere.[266] While such tests can be important tools for detecting and stemming outbreaks when users understand their limitations and appropriate uses, following distribution of the tests, locations across the country struggled to deal with the reliability issues, prompting criticism about FDA's approach to pre-market review and post-market surveillance.[267]

Alongside concerns about whether FDA's approach has been adequate to help ensure test reliability and promote understanding of tests' limits, FDA also has been criticized for unnecessarily slowing the distribution of tests early in the pandemic by requiring EUAs for diagnostic tests developed and offered by laboratories regulated pursuant to the Clinical Laboratory Improvement Amendments (CLIA) Act.[268] FDA's authority to regulate these tests—known as laboratory developed tests (LDTs)—has long been disputed.[269] Consistent with this long-standing controversy, early in the pandemic, scholars criticized FDA for requiring EUAs for COVID-19 tests that qualified as LDTs on the ground that the agency lacked the statutory authority to do so.[270]

Then, in August 2020, HHS published a paragraph-long statement on its website rescinding FDA's guidance documents on LDTs and explaining that HHS had determined that, going forward, FDA would not require premarket review of any LDTs, including those intended for COVID-19.[271] This HHS statement was issued

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[265] *See* Lisa Song, *Rapid Testing is Less Accurate than the Government Wants to Admit*, PROPUBLICA (Nov. 16, 2020), https://www.propublica.org/article/rapid-testing-is-less-accurate-than-the-government-wants-to-admit [https://perma.cc/YKW2-BLH5].

[266] *See id.*

[267] *See id.*

[268] *See, e.g.*, Evans & Clayton, *supra* note 14.

[269] *See, e.g.*, *id.*; *see also* Barbara J. Evans, Wylie Burke & Gail P. Jarvik, *The FDA and Genomic Tests—Getting Regulation Right,* 372 NEW ENG. J. MED. 2258, 2258 (2015); James P. Evans & Michael S. Watson, *Genetic Testing and FDA Regulation: Overregulation Threatens the Emergence of Genomic Medicine*, 313 JAMA 669, 669 (2015); PAUL D. CLEMENT & LAURENCE H. TRIBE, LABORATORY TESTING SERVICES, AS THE PRACTICE OF MEDICINE, CANNOT BE REGULATED AS MEDICAL DEVICES 11 (2015), http://www.acla.com/wp-content/uploads/2015/01/Tribe-Clement-White-Paper-1-6-15.pdf [https://perma.cc/56NJ-HA6C]; Catherine M. Sharkey, *Direct-to-Consumer Genetic Testing: The FDA's Dual Role As Safety and Health Information Regulator*, 68 DEPAUL L. REV. 343, 362 (2019); *cf.* Patricia J. Zettler, *Pharmaceutical Federalism*, 92 IND. L.J. 845, 890 (2017) (expressing skepticism about the argument that FDA cannot regulate LDTs because they are medical practice, rather than medical products).

[270] Evans & Clayton, *supra* note 14.

[271] *Rescission of Guidances and Other Informal Issuances Concerning Premarket Review of Laboratory Developed Tests*, U.S. DEP'T HEALTH & HUM. SERVS., https://www.hhs.gov/coronavirus/testing/recission-guidances-informal-issuances-premarket-review-lab-tests/index.html (last visited Oct. 2, 2021) [https://perma.cc/BJ53-JRS6]; *see also* Memorandum from Robert Charrow, HHS General Counsel to Stephen Hahn, FDA Commission (June 22, 2020) (concluding that FDA's authority to regulate LDTs "is not uniform and not as plenary as for a traditional device").

despite strong objections from FDA[272] and sparked yet more concerns about political efforts to undermine FDA's public health mission.[273] As of March 2021, the statement remained on the HHS website, and confusion about the regulatory landscape, as well as ongoing concerns about the reliability of available COVID-19 diagnostic and serological tests, persisted.[274] According to whistleblowers, HHS Secretary Azar overruled the FDA Commissioner's decision to set parameters for ensuring the safety and effectiveness of tests for political, rather than scientific, reasons.[275]

2. Personal Protective Equipment

In addition to the hundreds of EUAs issued for COVID-19 diagnostic and serologic tests, as of March 8, 2021, FDA issued twenty-eight EUAs for personal protective equipment (PPE) and related devices.[276] These EUAs include respirators for use in health care settings, decontamination systems for N95 respirator masks, face shields, hospital gowns, shoe covers, operating room shoes, surgical caps and helmets, surgical masks, and other products.[277] These EUAs posed somewhat different questions than the EUAs for drugs, biologics, and tests—although PPE products were known to be effective for a particular use, at least if manufactured well (e.g., N95s of appropriate quality are known to protect the wearer from airborne particles),[278] the products authorized under traditional mechanisms were in short in supply.

Nevertheless, FDA's decision to issue some of these EUAs, and the agency's post-EUA surveillance, raised significant concerns. For example, FDA's decisions to issue EUAs for certain N95 masks, many of which were used in health care settings, were criticized because the EUAs were supported by third-party certification, often conducted outside the United States.[279] Once the masks were on the market and being used in the United States, tests performed by FDA and CDC revealed the masks did not adequately filter a sufficient percentage of particles.[280] Although FDA ultimately

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[272] *See* Adam Cancryn & Sarah Owermohle, *HHS Chief Overrode FDA Officials to Ease Testing Rules*, POLITICO (Sept. 15, 2020), https://www.politico.com/news/2020/09/15/hhs-alex-azar-overrode-fda-testing-rules-415400 [https://perma.cc/L6W6-J5TS].

[273] *See* Dan Diamond & David Lim, *Memo Details HHS Push to Upend FDA's Testing Oversight*, POLITICO (Oct. 2, 2020), https://www.politico.com/news/2020/10/02/hhs-memo-fda-testing-oversight-425139 [https://perma.cc/X6G9-9EG4].

[274] *See id.*

[275] *See* Cancryn & Owermohle, *supra* note 272. Additionally, the publicly available internal document justifying the new position on LDT regulation offers legal analyses, but not explanations of how the position would serve public health or otherwise would be scientifically justified. *See* Diamond & Lim, *supra* note 273.

[276] FDA COVID-19 EUA List, *supra* note 5; FDA Revoked EUA List, *supra* note 5.

[277] *See id.*

[278] *See* Jack Nicas & Sheila Kaplan, *FDA Bans Faulty Masks, 3 Weeks After Failed Tests*, BALT. SUN (May 7, 2020), https://www.baltimoresun.com/coronavirus/ct-nw-nyt-faulty-masks-fda-ban-kn95-n95-20200508-4peghbpcunfnjkisgw7li2d5xy-story.html [https://perma.cc/H4T8-NXTQ].

[279] *See id.*

[280] *See id.*

revoked the EUAs, in some instances, the agency allowed the masks to remain on the market for weeks after test results revealed these flaws.[281] This created risks for individuals who used the masks, particularly health care workers, at a time when vaccination was not yet available.[282]

Controversy also surrounded an N95 decontamination system created by Battelle, a private nonprofit company based in Columbus, Ohio that has a long history of working closely with the government and military, dating back to the Manhattan Project.[283] Battelle's research found that its decontamination system could allow N95 masks to be reused twenty times.[284] However, the study was based on masks worn by mannequins.[285] A field trial in a Massachusetts hospital with actual health care workers revealed that the masks could be used only four times before losing their fit or ability to filter particles.[286] In March 2020, as FDA was considering an EUA for the Battelle decontamination system, President Trump and Ohio Governor Mike DeWine chastised FDA for what they deemed to be a slow review.[287] Both politicians argued that FDA should halt its follow-up safety review in light of mask shortages across the country.[288] Within hours, FDA indicated that it would forgo additional review and issue the EUA.[289] Thereafter, Battelle increased the cost per machine from $1 million to $6.8 million and entered into a $413 million contract with the U.S. government.[290]

Meanwhile, health care workers remained uncertain about the ability of the reused masks to safely offer protection against COVID-19.[291] These concerns continued long after FDA issued an EUA for Battelle's decontamination system. For example, in

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[281] *See id.*

[282] *See* Shira Feder, *The US Has Imported Millions of Low-Quality Masks That Don't Block Virus Particles Enough, Putting Lives at Risk*, BUS. INSIDER (May 4, 2020), https://www.businessinsider.com/many-n95-masks-fail-block-out-95-of-air-particles-2020-5 [https://perma.cc/LNR2-46C8].

[283] *See* Jonathan Allen, Phil McCausland & Cyrus Farivar, *Trump Administration Paying Huge Premium for Mask-Cleaning Machines, Which Don't Do the Job*, NBC NEWS (May 20, 2020), https://www.nbcnews.com/politics/white-house/trump-administration-paying-huge-premium-mask-cleaning-machines-which-don-n1210896 [https://perma.cc/9YAX-J6EC].

[284] *See id.*

[285] *See id.*

[286] *See id.*

[287] *See id.*

[288] *See id.*

[289] *See id.*

[290] *See id.* According to a report, the cost increase was "due to the inclusion of operating costs for six months, shipping, and logistics tails to be covered up front." *Id.* "Logistics tails" is a phrase frequently used by the military to describe the chain of goods and people supporting a mission. *Id.*

[291] *See id.*

August 2020, FDA officials met with Battelle to express concern over the system.[292] FDA noted several instances where health care workers who re-used masks decontaminated via Battelle's system suffered adverse reactions from the chemical decontaminants, and where decontaminated masks could not be reused due to damage that prevented adequate filtering.[293] Battelle failed to remedy the issues, and on October 7, 2020, FDA issued a warning letter to the company.[294] This was the first warning letter issued for a medical product under an EUA.[295] The warning letter directed Battelle to take corrective measures and report back to FDA, but there was no announced recall of the devices.[296]

3. Ventilators and Other Medical Devices

As of March 8, 2021, FDA had issued twenty-seven EUAs for ventilators and other moderate-to-high risk medical devices, such as blood purification devices, infusion pumps, diaphragm pacing systems, remote patient monitoring devices, and respiratory muscle stimulators.[297] Unlike the other EUAs issued for devices, as of March 8, 2021, few, if any, concerns were raised about these EUAs.

C. Vaccines

The decision about whether to utilize the EUA pathway to authorize emergency use of COVID-19 vaccines is one of the most consequential decisions FDA has made during the pandemic. Because of the hope (and, for some, an expectation) that a vaccine would provide the "silver bullet" to end the pandemic, this is perhaps the area where FDA has been subjected to the most intense and persistent political pressure and public scrutiny.

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[292] *See* Michael Mezher, *FDA Warns Battelle over EUA Conditions for N95 Decontamination System*, REGUL. FOCUS (Oct. 7, 2020), https://www.raps.org/news-and-articles/news-articles/2020/10/fda-warns-battelle-over-eua-conditions-for-n95-dec [https://perma.cc/ST8G-PB3E].

[293] *See id.*

[294] *FDA Issues Warning Letter to Battelle Memorial Institute, A Manufacturer of an Authorized Decontamination System Used on Respirators*, U.S. FOOD & DRUG ADMIN. (Oct. 7, 2020), https://www.fda.gov/news-events/press-announcements/fda-issues-warning-letter-battelle-memorial-institute-manufacturer-authorized-decontamination-system [https://perma.cc/P9VM-6YC4].

[295] Mezher, *supra* note 292. That a warning letter was issued to an entity marketing a product pursuant to an EUA, however, is not necessarily in and of itself surprising. FDA commonly issues warning letters to achieve voluntary compliance with federal law, and it is not unexpected that, with hundreds of products being marketed under EUAs by October 2020, FDA would find violations for one that warranted a warning letter. *Cf.* U.S. FOOD & DRUG ADMIN., REGULATORY PROCEDURES MANUAL 4-1: ADVISORY ACTIONS: WARNING LETTERS (2021) (describing Warning Letters).

[296] *See* Mezher, *supra* note 292.

[297] FDA COVID-19 EUA List, *supra* note 5; FDA Revoked EUA List, *supra* note 5. One of the EUAs, issued on May 13, 2020, was an Umbrella EUA for infusion pump and infusion pump accessories. *See id.* FDA revoked the Umbrella EUA on September 21, 2020 and indicated that thereafter the agency would review such devices on an individual basis. *See id.* The Umbrella EUA was revoked because it was not utilized by industry. *See* Greg Slabodkin, *FDA Revokes Umbrella EUA for Infusion Pumps Due to Lack of Industry Use*, MEDTECHDIVE (Sept. 24, 2020), https://www.medtechdive.com/news/fda-aims-to-thwart-infusion-pump-shortage-with-new-industrywide-emergency-u/578033/ [https://perma.cc/PD2B-JS82].

Taken together, the use of EUAs for COVID-19 vaccines largely has been a story of success. The availability of vaccines under EUAs has provided the public with an avenue to escape the wrath of the pandemic. The safety and effectiveness of the vaccines available under EUAs can be attributed, at least in part, to FDA's insistence on requiring a higher standard of evidence than the statute sets as a baseline for an EUA, even with the intense political pressure that the agency faced and the immense workload for agency staff during the pandemic. Indeed, as several former FDA officials explained in February 2021, "[d]espite numerous failures during the pandemic, the U.S. succeeded in developing safe and effective vaccines."[298]

At the same time, it is important to acknowledge that it was not inevitable the vaccines would prove to be as safe and effective as revealed in studies conducted pre- (and then post-) EUA issuance. Recognizing that reality and with an eye toward improving such processes for future pandemics, we consider the criticisms raised about the design of the clinical trials supporting the vaccine EUAs, the concerns about the EUAs posing challenges for generating robust safety and effectiveness information, and the overall political context in which the vaccines were developed and authorized, through March 2021.

In March 2020, the U.S. government began allocating hundreds of millions of dollars to private vaccine manufacturers to support COVID-19 vaccine research and development.[299] By the end of May 2020, the allocation had surpassed $2 billion.[300] The extensive funding was a component of Operation Warp Speed—a partnership between HHS, DoD, and the private sector—that was officially launched on May 15, 2020.[301] As of October 2020, worldwide there were 194 COVID-19 vaccine candidates in development.[302] Of these, 42 were in clinical trials and 152 were in preclinical evaluation.[303]

Operation Warp Speed was heralded as a scientific program of size and scope unparalleled since the Manhattan Project.[304] Part of the goal was to deliver tens of millions of vaccine doses by the end of 2020 and to have approximately 300 million

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[298] Joshua M. Sharfstein, Jesse L. Goodman & Luciana Borio, *The US Regulatory System and COVID-19 Vaccines: The Importance of a Strong and Capable FDA*, 325 JAMA 1153, 1154 (2021).

[299] *See* U.S. DEP'T HEALTH & HUM. SERVS., FACT SHEET: EXPLAINING OPERATION WARP SPEED (Sept. 24, 2020), https://www.nihb.org/covid-19/wp-content/uploads/2020/08/Fact-sheet-operation-warp-speed.pdf [https://perma.cc/GDQ8-VGZJ].

[300] *See id.*

[301] *See* Moncef Slaoui & Matthew Hepburn, *Developing Safe and Effective Covid Vaccines—Operation Warp Speed's Strategy and Approach*, 383 NEW ENG. J. MED. 1701 (2020). The DoD has played a significant role in Operation Warp Speed. *See* Nicholas Florko, *New Document Reveals Scope and Structure of Operation Warp Speed and Underscores Vast Military Involvement*, STAT NEWS (Sept. 28, 2020), https://www.statnews.com/2020/09/28/operation-warp-speed-vast-military-involvement/ [https://perma.cc/2SJQ-45UW].

[302] *See The COVID-19 Vaccine Race—Weekly Update*, GAVI (Nov. 10, 2021), https://www.gavi.org/vaccineswork/covid-19-vaccine-race [https://perma.cc/7K9V-32RP].

[303] *See id.*

[304] *See Operation Warp Speed Accelerated COVID-19 Vaccine Development Status and Efforts to Address Manufacturing Challenges*, U.S. GOV'T ACCOUNTABILITY OFF. (Feb. 2021), https://www.gao.gov/assets/gao-21-319.pdf [https://perma.cc/958P-TJBL].

doses available by mid-2021.[305] By early September 2020, the U.S. government had spent over $10 billion to achieve these goals.[306] This included a commitment to buy 800 million doses of vaccines that were in development—with no guarantee that the vaccines would gain FDA approval or authorization for use—and an option to buy an additional 1.6 billion doses.[307] To expedite vaccine development and review, FDA authorized several vaccine manufacturers to combine Phase II and Phase III studies.[308]

From the outset of the pandemic through early March 2021, intense debate centered on vaccine development and the scientific evidence that would be sufficient to qualify a vaccine candidate for emergency authorization. In June 2020, as the vaccine race was accelerating, FDA issued guidance for industry on the development and licensure of COVID-19 vaccines.[309] As is typically the case for FDA guidance documents, the guidance did not create legally binding obligations for vaccine manufacturers.[310] Nevertheless, the White House rebuked the guidance document as scientifically unnecessary and politically motivated.[311]

Throughout the summer of 2020, the Trump Administration reportedly pressured FDA to expedite review of vaccine candidates, regardless of the scientific expectations outlined in FDA's June 2020 guidance.[312] Consistent with these reports, in one of the presidential debates during fall 2020, President Trump downplayed the importance of robust FDA review, noting that he trusted vaccine manufacturers to only bring to market safe and effective vaccines.[313]

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[305] *See id.*

[306] *See id.*

[307] *See id.*

[308] *See, e.g.*, Amy McKeever, *Dozens of COVID-19 Vaccines are in Development: Here are the Ones to Follow*, NAT'L GEOGRAPHIC (Oct. 2, 2020), https://www.nationalgeographic.com/science/article/coronavirus-vaccine-tracker-how-they-work-latest-developments-cvd [https://perma.cc/FLX6-MJZP].

[309] *See* U.S. FOOD & DRUG ADMIN., DEVELOPMENT AND LICENSURE OF VACCINES TO PREVENT COVID-19: GUIDANCE FOR INDUSTRY (June 2020).

[310] *See, e.g.*, *id.*

[311] *See* Lauren Morello & Adam Cancryn, *Trump Says He Might Reject Stricter FDA Vaccine Guidelines*, POLITICO (Sept. 23, 2020), https://www.politico.com/news/2020/09/23/trump-vaccine-fda-guidelines-420803 [https://perma.cc/K2B5-LMNA].

[312] *See, e.g.*, Kevin Liptak & Kaitlin Collins, *Trump Puts Pressure on FDA for Coronavirus Silver Bullet Ahead of Election Day*, CNN (Sept. 3, 2020), https://www.cnn.com/2020/09/03/politics/white-house-fda-coronavirus-vaccine/index.html ("In meetings focused on vaccine development throughout the spring and summer, Trump has consistently pressed officials to speed up their timeline for developing a vaccine, administration officials said, saying the President appeared intent on being able to deliver at least the solid promise of an effective vaccine by the time he faces reelection.") [https://perma.cc/LM4X-5DNF]; Will Feuer, *Trump Says 'No President's Ever Pushed' the FDA Like Him, Vaccine Coming 'Very Shortly'*, CNBC (Oct. 17, 2020), https://www.cnbc.com/2020/10/07/trump-says-no-presidents-ever-pushed-the-fda-like-him-vaccine-coming-very-shortly.html [https://perma.cc/3UV4-39TX].

[313] Matthew Herper, *Eager for a Covid Vaccine, Trump Now Trusts Drug Companies He Previously Vilified*, STAT NEWS (Sept. 30, 2020), https://www.statnews.com/2020/09/30/covid-vaccine-trump-trusts-drug-companies-vilified/ [https://perma.cc/BMW2-9U3W]. Rhetoric questioning the value of FDA oversight has also arisen in non-COVID-19 contexts in recent years. For example, those supporting the Federal Right to Try Act, which created a pathway for non-trial preapproval access without FDA authorization and has been widely criticized as undermining FDA's public health mission without offering

In addition, the executive branch—via HHS—triggered PREP Act immunity for vaccine manufacturers and several other stakeholders in the chain of vaccine development and administration in March 2020.[314] These broad legal safeguards, when coupled with the low statutory standard for the EUA pathway (even though FDA ultimately imposed a higher standard than statutorily required for COVID-19 vaccine EUAs), increased public concerns that unsafe or ineffective vaccines would come to market.[315] These perceived risks, in turn, drastically increased vaccine hesitancy across the country.[316] At the end of August 2020, one study found that 78% of the American public believed that the COVID-19 vaccine "approval" process was being driven by politics, rather than science.[317]

By mid-September 2020, several experts expressed concern that vaccine trials were not properly structured and that the vaccines were on course to be authorized without essential data on critically important endpoints.[318] For example, for three leading vaccine candidates at the time—from Moderna, Pfizer, and AstraZeneca—FDA authorized a study goal whereby a positive endpoint is achieved if the vaccine can lower the risk of mild COVID-19, even if the vaccine does not reduce moderate or severe COVID-19 cases, the risk of hospitalization, admission to intensive care, or death.[319]

This structure was criticized for several reasons. First, there is no guarantee that a vaccine that reduces the risk of mild cases will also reduce the risk of moderate or severe cases.[320] Similarly, a reduction in mild cases does not necessarily translate to a reduction in hospitalizations or deaths.[321] Moreover, many vaccine candidates are

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meaningful benefit to patients beyond that already offered by expanded access, have expressed similar views. *See, e.g.*, Steven Joffe & Holly Fernandez Lynch, *Federal Right-to-Try Legislation—Threatening the FDA's Public Health Mission*, 378 NEW ENG. J. MED. 695 (2018).

[314] U.S. DEP'T HEALTH & HUM. SERVS., OFF. OF THE SEC'Y, DECLARATION UNDER PUBLIC READINESS AND EMERGENCY PREPAREDNESS ACT FOR MEDICAL COUNTERMEASURES AGAINST COVID-19, 85 Fed. Reg. 15,198, 15,198 (Mar. 17, 2020).

[315] *See, e.g.*, Ed Silverman, *Poll: Most Americans Believe the Covid-19 Vaccine Approval Process is Driven by Politics, Not Science*, STAT NEWS (Aug. 31, 2020), https://www.statnews.com/pharmalot/2020/08/31/most-americans-believe-the-covid-19-vaccine-approval-process-is-driven-by-politics-not-science/ [https://perma.cc/WK59-D8EL].

[316] *See, e.g.*, *id.*

[317] *See id.* In August 2020, it was not only people whose political affiliation did not align with the Trump Administration's that had such concerns. For individuals who identified as Democrats or Republicans, the number was over 70%. *See id.* The public's lack of confidence led vaccine manufacturers to take the unusual step of announcing that they would abide by high standards of premarket research, though many viewed this announcement as a public relations ploy without a legally binding mandate. *See, e.g.*, Parasidis, *supra* note 76.

[318] *See* Peter Doshi & Eric Topol, *These Coronavirus Trials Don't Answer the One Question We Need to Know*, N.Y. TIMES (Sept. 22, 2020), https://www.nytimes.com/2020/09/22/opinion/covid-vaccine-coronavirus.html [https://perma.cc/E2P6-9FEW].

[319] *See id.*

[320] *See id.*

[321] *See id.*

associated with adverse effects that are analogous to COVID-19 symptoms for mild cases.[322] For Pfizer's vaccine, for example, more than half of research participants experienced headache, muscle pain, and chills—in other words, the adverse effects may be more severe than mild COVID-19 cases.[323] Additionally, a vaccine that does not prevent COVID-19 transmission does little to help stop the spread of the disease. And, vaccination may motivate large segments of the public to ignore or limit adherence to important public health tools such as physical distancing and masks, because individuals may wrongly believe that a vaccine means they are immune and cannot spread the virus.

Although many of these concerns were not borne out, they were expressed at the time FDA was evaluating the vaccine candidates. Consistent with the concerns, at a Senate Health, Education, Labor, and Pensions (HELP) Committee hearing in late September 2020, the FDA Commissioner described new and more exacting expectations for the scientific evidence that would support an agency decision to issue an EUA for a COVID-19 vaccine.[324] The new guidance, which the agency spent weeks calibrating, was intended to come close to matching the standards utilized during vaccine approvals (an intent the agency realized when it issued the vaccine EUAs).[325] Within hours of the FDA Commissioner's testimony, the White House challenged the agency's position, asking FDA to justify its standards for vaccine authorization.[326] President Trump also indicated that the White House could override FDA if the agency updated its standards.[327] Meanwhile, HHS Secretary Azar made a blanket statement on President Trump's challenges to FDA's updated guidance, stating that "[t]here's no political influence."[328]

Days later—with less than a month before Election Day 2020—the White House issued a statement that it was overruling FDA and calling for a shortened window of

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[322] *See id.*; Smriti Mallapaty & Heidi Ledford, *COVID-Vaccine Results Are on the Way—And Scientists' Concerns are Growing*, NATURE (Sept. 25, 2020), https://www.nature.com/articles/d41586-020-02706-6 [https://perma.cc/9E44-986W]; Thomas M. Burton, *White House Takes Issue with FDA's Plans for Authorizing a Covid-19 Vaccine*, WALL ST. J. (Oct. 2, 2020), https://www.wsj.com/articles/white-house-takes-issue-with-fdas-plans-for-authorizing-a-covid-19-vaccine-11601663139 [https://perma.cc/E7UR-GEGA].

[323] *See* Adam Cancryn, *How Trump is Undermining his Own Vaccine Race*, POLITICO (Sept. 24, 2020), https://www.politico.com/news/2020/09/24/trump-undermining-vaccine-race-421487 [https://perma.cc/G7J3-JA55]; Jon Cohen, *On the Road with Operation Warp Speed, the U.S. COVID-19 Vaccine Effort*, SCIENCE (Sept. 29, 2020), https://www.science.org/news/2020/09/road-operation-warp-speed-us-covid-19-vaccine-effort [https://perma.cc/6QBW-4CLT].

[324] *See* Cancryn, *supra* note 323.

[325] *See id.*; Mallapaty & Ledford, *supra* note 322; Burton, *supra* note 322.

[326] *See* Cancryn, *supra* note 323; Cohen, *supra* note 323.

[327] *See* Paul LeBlanc, *Trump Claims White House Can Overrule FDA's Attempt to Toughen Guidelines for Coronavirus Vaccine*, CNN (Sept. 24, 2020), https://www.cnn.com/2020/09/23/politics/trump-fda-coronavirus-vaccine/index.html [https://perma.cc/838J-52HP].

[328] Cancryn, *supra* note 323.

review for vaccine safety and effectiveness.[329] According to the Trump Administration, there was "no clinical or medical reason" for FDA's position on what evidence would be needed to issue an EUA for a COVID-19 vaccine.[330] At the same time, the White House indicated that industry objections to FDA's position contributed to the Trump Administration's decision to overrule FDA.[331] FDA pushed back,[332] and the White House changed its position and indicated it would not block the new guidance document.[333] That same day, FDA published its guidance document,[334] which President Trump characterized as "just another political hit job!"[335] Notably, the October 2020 FDA guidance did not indicate that vaccine candidates submitted for emergency authorization must have data that demonstrate that the vaccine reduces moderate or severe COVID-19 cases, the risk of hospitalization, admission to intensive care, or death.[336] Rather, there was no specific information on required clinical endpoints.[337] This back-and-forth between the President and FDA may have contributed to vaccine hesitancy across the country at the time.[338] To combat this troubling trend, in fall 2020, several experts called for more transparency and scientific

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[329] *See* Oliver Milman, *White House Overruled FDA to Shorten Period for Covid-19 Vaccine*, THE GUARDIAN (Oct. 6, 2020), https://www.theguardian.com/world/2020/oct/06/coronavirus-vaccine-trump-administration-fda [https://perma.cc/QQW2-HSKU].

[330] *See id.*

[331] *See* Adam Cancryn, *White House Cited Drug Companies' Objections in Overruling FDA's Vaccine Standards*, POLITICO (Oct. 6, 2020), https://www.politico.com/news/2020/10/05/white-house-fda-vaccine-standards-426605 [https://perma.cc/7GR5-BVQV].

[332] Among other things, the agency made use of the transparency required by the Federal Advisory Committee Act, publishing what it described as a "Summary of Advice Provided to Individual Sponsors in Response to Questions Regarding Emergency Use Authorization of Vaccines to Prevent COVID-19" as part of its publicly available materials for the October 22 meeting of the Vaccines and Related Biological Products Advisory Committee, effectively making public much of its thinking that was ultimately described in guidance. *See* U.S. FOOD & DRUG ADMIN., BRIEFING DOCUMENT: VACCINES AND RELATED BIOLOGICAL PRODUCTS ADVISORY COMMITTEE MEETING (Oct. 22, 2020), https://www.fda.gov/media/142723/download [https://perma.cc/J8T8-MG4C].

[333] *See* Zachary Brennan, *White House Lifts Block on FDA's Stricter Vaccine Requirements*, POLITICO (Oct. 6, 2020), https://www.politico.com/news/2020/10/06/fda-vaccine-guidelines-white-house-426764 [https://perma.cc/VYB9-CB85].

[334] *See* U.S. FOOD & DRUG ADMIN., EMERGENCY USE AUTHORIZATION FOR VACCINES TO PREVENT COVID-19: GUIDANCE FOR INDUSTRY (Oct. 2020).

[335] *See* Brennan, *supra* note 333.

[336] *See id.*

[337] *See id.*

[338] *See, e.g.*, Silverman, *supra* note 315.

rigor in vaccine evaluation,[339] while others called for limiting or eliminating the broad legal immunities afforded to vaccine manufacturers.[340]

Thereafter, FDA took numerous steps in an apparent effort to reassure the public and rebuild trust. As noted in Section III.B, *supra*, the agency held a VRBPAC meeting in October 2020 to discuss COVID-19 vaccine development and committed to transparency around its EUA decisions. During the meeting, Marion Gruber, director of FDA's Office of Vaccines Research and Review, discussed the possibility that FDA would not issue an EUA for a COVID-19 vaccine, but rather would expand premarket access to vaccine candidates under the agency's expanded access program.[341] The impetus for the proposal was a desire to ensure that research in vaccine safety and efficacy would not be compromised by allowing widespread public access to a vaccine, as might be available under an EUA.[342] As Gruber detailed, "We are concerned about the risk that use of a vaccine under an EUA would interfere with long-term assessment of safety and efficacy in ongoing trials and potentially even jeopardize product approval. And not only the first vaccine, but maybe even follow-on vaccines."[343] The acting chair of the committee echoed Gruber's concerns, and a separate committee member urged FDA not to grant an EUA for any COVID-19 vaccine.[344] In the event FDA decided to issue an EUA, several committee members urged FDA to not permit the vaccine manufacturers to halt their clinical trials, so that the agency could continue to evaluate long-term safety and effectiveness.[345]

In November 2020, Pfizer and Moderna announced results from their respective clinical trials—reporting that their vaccine candidates reduced infections by 95% and 94.5%, respectively.[346] But questions remained about the safety and efficacy profiles of the vaccine candidates.[347] For each of the vaccine candidates, conclusions about effectiveness were based on fewer than 200 cases of COVID-19.[348] These small

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339 *See, e.g.*, Jason Schwartz, *Evaluating and Deploying Covid-19 Vaccines—The Importance of Transparency, Scientific Integrity, and Public Trust*, 383 NEW ENG. J. MED. 1703 (2020).

340 *See, e.g.*, Hals, *supra* note 84; Lerner, *supra* note 84; Parasidis, *supra* note 76.

341 *See* Helen Branswell, *FDA Shows Signs of Cold Feet Over Emergency Authorization of Covid-19 Vaccines*, STAT NEWS (Oct. 23, 2020), https://www.statnews.com/2020/10/23/fda-shows-signs-of-cold-feet-over-emergency-authorization-of-covid-19-vaccines/ [https://perma.cc/4ZGS-GQFV].

342 *See id.*

343 *Id.*

344 *See id.*

345 *See id.*

346 *See, e.g.*, Damian Garde & Matthew Herper, *Pfizer and BioNTech to Submit Covid-19 Vaccine Data to FDA as Full Results Show 95% Efficacy*, STAT NEWS (Nov. 18, 2020), https://www.statnews.com/2020/11/18/pfizer-biontech-covid19-vaccine-fda-data/#:~:text=Pfizer%20and%20BioNTech%20to%20submit,full%20results%20show%2095%25%20efficacy&text=Pfizer%20and%20BioNTech%20announced,of%20cases%20of%20the%20disease. [https://perma.cc/SBH8-CC52].

347 *See* Heidi Ledford, David Cyranoski & Richard Van Noorden, *Covid Vaccines: What Scientists Now Want to Know*, 588 NATURE 205, 205–06 (2020).

348 *See id.*

numbers made it difficult to parse out details about effectiveness in sub-populations such as the elderly or those with preexisting health conditions.[349] Moreover, for both vaccine candidates, the data at the time were inconclusive on effectiveness for individuals aged 65 and over, a key demographic that has suffered disproportionally from serious COVID-19 complications and death.[350]

Coupled with the aforementioned limitations, neither Pfizer nor Moderna demonstrated that their respective vaccine candidate prevented asymptomatic SARS-CoV-2 infection, nor did the companies demonstrate that their vaccine candidate reduced the spread of the virus in a population.[351] During clinical trials, the companies did not conduct asymptomatic testing of clinical trial participants, but rather only performed symptomatic tests.[352] Thus, at the time the vaccine candidates were being evaluated for issuance of an EUA, it was not clear if the vaccine candidates prevented or reduced the chance for asymptomatic cases.[353] This was significant because asymptomatic individuals can pass the virus to a person who then might contract a serious or life-threatening COVID-19 infection.[354] At the time, studies found that asymptomatic cases represented approximately 40% of SARS-CoV-2 infections and were responsible for nearly 50% of transmissions.[355]

The trials at that time also were not designed to evaluate the vaccines in pregnant women and children under 16.[356] There likewise were no data on how long vaccine-induced immunity lasted.[357] Although the Pfizer and Moderna vaccine candidates both utilize mRNA technology, there are subtle differences in the vaccines that may affect relative safety and effectiveness.[358] Safety data was only collected for a period of two months, and no data were then available on long-term safety concerns.[359]

Notwithstanding such concerns about the data, on December 2, 2020, the United Kingdom issued an emergency authorization for the Pfizer vaccine, becoming the first

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[349] *See id.*

[350] *See id.*

[351] *See id.* Even if these, and other vaccines issued EUAs like Janssen's, ultimately are shown effective for these endpoints, it is important to recognize the limitations of what could be learned from the trials supporting the initial authorization and the implications of those limitations. *See, e.g.*, Smriti Mallapaty, *Can COVID Vaccines Stop Transmission? Scientists Race to Find Answers*, NATURE (Feb. 19, 2021), https://www.nature.com/articles/d41586-021-00450-z (describing ongoing research on whether vaccinated people transmit disease) [https://perma.cc/A3QL-2TGF].

[352] *See* Ledford et al., *supra* note 347.

[353] *See id.*

[354] *See id.*

[355] *See* Yasmin Rafiei & Michelle M. Mello, *The Missing Piece—SARS-CoV-2 Testing and School Reopening*, 383 NEW ENG. J. MED. e126 (2020).

[356] *See* Ledford et al., *supra* note 347.

[357] *See id.*

[358] *See id.* Moreover, comparison studies were not conducted. *See id.*

[359] *See id.*

nation in the world to do so.[360] The approval was criticized by public health officials in the United States and Europe. Anthony Fauci said that the U.K. "really rushed through that approval" and that the British regulators "just took the data from the Pfizer company. And instead of scrutinizing it really, really carefully, they said 'Ok, let's approve it.'"[361] The European Medicines Agency (EMA) issued a statement that criticized the U.K. for granting a hasty approval, noting that the EMA requires a more robust review of safety and efficacy data.[362] U.K. leaders dismissed the claims, alleging that their review was adequate and appropriate and citing as a matter of national pride that U.K. citizens would be the first in the world to receive the Pfizer vaccine.[363] The U.K. authorization also raised questions in the United States about whether FDA was moving too slowly.[364]

On the first day that British officials administered the vaccine to the public, two health care workers with documented allergies of different types suffered unexpected, severe allergic reactions that required hospitalization.[365] These life-threatening adverse effects prompted U.K. regulators to exclude from immunization those individuals with "a significant history of allergic reactions."[366]

On December 10, 2020, approximately one week after the U.K. emergency authorization, VRBPAC met to discuss Pfizer's vaccine candidate and voted 17-4 to recommend that FDA issue an EUA.[367] Although the committee favored authorization, during its discussions, members of the advisory committee raised various concerns. Some members raised concerns about vaccinating people with severe allergies, and others questioned whether adolescents aged 16–17 should be included given very

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[360] *See id.*

[361] Quint Forgey, *Fauci: U.K. 'Really Rushed Through That Approval of Pfizer Vaccine*, POLITICO (Dec. 3, 2020), https://www.politico.com/news/2020/12/03/fauci-uk-pfizer-vaccine-rush-442588 [https://perma.cc/U3EA-STYG]. In light of the upcoming review of Pfizer's vaccine in the United States, Fauci's remarks caused great controversy, and he later apologized for his comments on the U.K. approval. *See* Estelle Shirbon, *Fauci Apologizes for Casting Doubt Over UK's Approval of Pfizer Vaccine*, REUTERS (Dec. 3, 2020), https://www.reuters.com/article/us-health-coronavirus-britain-fauci/fauci-apologizes-for-casting-doubt-over-uks-approval-of-pfizer-vaccine-idUSKBN28D31J [https://perma.cc/K5Z3-CZUU].

[362] *See* Fracesco Guarascio, *EU Criticises 'Hasty' UK Approval of Covid-19 Vaccine*, REUTERS (Dec. 2, 2020), https://www.reuters.com/article/us-health-coronavirus-britain-eu/eu-criticises-hasty-uk-approval-of-covid-19-vaccine-idUSKBN28C1B9 [https://perma.cc/7VF8-CXBT].

[363] *See id.*

[364] *See* Matthew Herper & Nicholas Florko, *How Key Decisions Slowed FDA's Review of a Covid-19 Vaccine—But Also Gave It Important Data*, STAT NEWS (Dec. 4, 2020), https://www.statnews.com/2020/12/04/how-key-decisions-slowed-fdas-review-of-covid-19-vaccine-but-also-gave-it-important-data/ [https://perma.cc/6AU5-GFL7].

[365] *See* Emma Reynolds, Sharon Braithwaite & Amy Cassidy, *Allergy Warning for Pfizer/BioNTech Vaccine After UK Health Workers with Allergy History Suffer Reaction*, CNN (Dec. 10, 2020), https://www.cnn.com/2020/12/09/health/covid-vaccine-allergies-health-workers-uk-intl-gbr/index.html [https://perma.cc/YCT2-TVWM].

[366] *See id.*

[367] *See FDA Advisory Panel Endorses Pfizer/BioNTech Covid-19 Vaccine*, STAT NEWS (Dec. 10, 2020), https://www.statnews.com/2020/12/10/tracking-the-fda-advisory-panel-meeting-on-the-pfizer-biontech-covid-19-vaccine/ [https://perma.cc/SDR2-TNDD].

limited premarket data on vaccine safety and effectiveness in children under 18.[368] Of the more than 40,000 individuals enrolled in Pfizer's clinical trials, only 153 were between the ages of 16–17.[369] Another question raised during the meeting was whether one dose would be sufficient to confer immunity because eliminating the two-dose regimen, assuming no significant decrease in effectiveness, would double the number of people who could be immunized and cut the cost of vaccine administration in half.[370] The trials, however, were not designed to study a one-dose regimen and, accordingly, without evidence supporting the safety and effectiveness of such dosing, it was not recommended.

The morning after the VRBPAC meeting, there were reports that the White House told FDA Commissioner Hahn that he should tender his resignation if FDA did not issue an EUA for the Pfizer vaccine by the end of the day.[371] Contemporaneously, President Trump characterized FDA as "a big, old, slow turtle" and urged the agency to "get the dam [sic] vaccines out NOW."[372] In turn, the agency reportedly accelerated its review, and, by the end of the day, FDA issued the EUA.[373] Thereafter, FDA denied that political pressure impacted its analysis or review timeline.[374]

Within days, VRBPAC met again, this time to evaluate Moderna's COVID-19 vaccine candidate.[375] The committee again voted overwhelmingly in favor of issuing the EUA, and the following day, December 18, 2020, FDA issued an EUA for the vaccine.[376] The EUA for the Moderna vaccine, as with Pfizer's vaccine, contained a warning that people with severe allergies to components of the product should not receive the vaccine.[377]

Upon issuance of the two EUAs, Moderna and Pfizer supported unblinding their studies and allowing trial participants to receive a COVID-19 vaccine.[378] Many experts

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[368] *See id.*

[369] *See id.*

[370] *See id.* To be sure, a reduction may also cut the company's profits in half.

[371] *See* Josh Dawsey & Laurie McGinley, *White House Orders FDA Chief to Authorize Pfizer-BioNTech Vaccine Friday or Submit his Resignation*, WASH. POST (Dec. 11, 2020), https://www.washingtonpost.com/health/2020/12/11/trump-stephen-hahn-fda-covid-vaccine/ [https://perma.cc/J88H-LAJU].

[372] *See id.*

[373] *See* Maria Carrasco, *FDA's Hahn: Covid-19 Vaccine Authorization Based in 'Science and Data'*, POLITICO (Dec. 13, 2020), https://www.politico.com/news/2020/12/13/fdas-hahn-coronavirus-vaccine-approval-science-data-444854 [https://perma.cc/NWN7-ZQT6].

[374] *See id.*

[375] *See* Alice Park, *Moderna's Covid-19 Vaccine Becomes Second Shot Authorized for Emergency Use in the U.S.*, TIME (Dec. 18, 2020), https://time.com/5922752/moderna-covid-19-vaccine-approved-fda-emergency-use/ [https://perma.cc/DV7X-MSUM].

[376] *See id.*

[377] *See id.*

[378] *See id.*; Matthew Herper, *Pfizer and BioNTech Speed Up Timeline for Offering Covid-19 Vaccine to Placebo Volunteers*, STAT NEWS (Jan. 1, 2021), https://www.statnews.com/2021/01/01/pfizer-and-biontech-speed-up-timeline-for-offering-covid-19-to-placebo-volunteers/ [https://perma.cc/8A36-CS7J].

cautioned against this approach because it would preclude long-term study of vaccine adverse events.[379] On the other hand, ethical concerns were raised about precluding study participants access to a vaccine that might help them.[380]

Thereafter, in light of the increase of COVID-19 variants of concern, on February 22, 2021, FDA updated its vaccine guidance, originally issued in October 2020, to provide recommendations to manufacturers seeking to amend their EUA to address the new variants.[381] The updated guidance also explored clinical and manufacturing issues related to modified vaccines that are formulated to counter new variants.[382]

On February 27, 2021, FDA issued its third vaccine EUA—for a single dose inoculation developed by Janssen Biotech, a division of Johnson & Johnson.[383] Unlike the Pfizer and Moderna vaccines, which use mRNA technology, the Janssen vaccine utilizes a genetically engineered adenovirus as a viral vector to stimulate an immune response to protect against SARS-CoV-2.[384] In clinical trials the vaccine was deemed to be 66% effective in preventing moderate-to-severe/critical COVID-19.[385] The efficacy rate varied depending on the type of virus variant found in a population, with protection ranging from 57% in trials conducted in South Africa to 72% in trials conducted in the United States.[386] At the time the EUA was issued, similar to the Pfizer and Moderna products, there were no data on how well the vaccine prevented SARS-CoV-2 transmission, nor were there any data on the duration of vaccine-induced immunity.[387]

For the authorized vaccines, the CDC is coordinating efforts to track vaccine-induced adverse events.[388] This includes reliance on legacy adverse event reporting

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379 *See* Park, *supra* note 375.

380 *See id.*

381 *See* U.S. FOOD & DRUG ADMIN., EMERGENCY USE AUTHORIZATION FOR VACCINES TO PREVENT COVID-19: GUIDANCE FOR INDUSTRY (Feb. 22, 2021); Press Release, U.S. Food & Drug Admin., FDA Issues Policies to Guide Medical Product Developers Addressing Virus Variants (Feb. 22, 2021), https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-issues-policies-guide-medical-product-developers-addressing-virus [https://perma.cc/AL3D-PFVY].

382 *See id.*

383 U.S. FOOD & DRUG ADMIN., FDA ISSUES EMERGENCY USE AUTHORIZATION FOR THIRD COVID-19 VACCINE (2021).

384 *See id.*

385 *See id.*

386 *See, e.g.*, Berkeley Lovelace, Jr., *FDA Panel Unanimously Recommends Third Covid Vaccine as J&J Wins Key Vote in Path to Emergency Use*, CNBC (Feb. 26, 2021), https://www.cnbc.com/2021/02/26/johnson-and-johnson-covid-vaccine-fda-panel-recommends-emergency-use.html [https://perma.cc/A6CS-MYT6].

387 U.S. FOOD & DRUG ADMIN., *supra* note 381.

388 See *FDA Advisory Panel Endorses Pfizer/BioNTech Covid-19 Vaccine*, STAT NEWS (Dec. 10, 2020), https://www.statnews.com/2020/12/10/tracking-the-fda-advisory-panel-meeting-on-the-pfizer-biontech-covid-19-vaccine/ [https://perma.cc/UCH6-DXQ8].

systems,[389] many of which are known to inadequately capture vaccine adverse events.[390] As of March 8, 2021, the CDC had not created a nationwide COVID-19 vaccine database to track vaccine doses, adverse events, and whether a person vaccinated has contracted COVID-19. Serious gaps also remained in the context of compensation for vaccine-induced injuries.[391]

Although the above-discussed concerns about the clinical trial design and adverse event surveillance remained, FDA's decisions to issue the EUAs for the three authorized vaccines, while also requiring more than the bare minimum evidence of safety and effectiveness, allowed for quicker access, ultimately saving lives—consistent, perhaps, with the purpose of the EUA provision. Following issuance of the EUAs, public debate quickly shifted to vaccine distribution, administration, and supply concerns.[392] Equity and other concerns included whether vaccine mandates could or should be utilized,[393] and whether individuals should have a choice of which vaccine they are administered.[394] For example, following issuance of the EUA for the Janssen vaccine, U.S. Catholic Church leaders recommended against acceptance of the vaccine due to use of cell lines derived from aborted fetuses during vaccine development.[395] Others expressed fears that the "inferior" Janssen vaccine would be over-utilized in poor and marginalized communities, or that vaccine distribution would exacerbate existing health inequities.[396] Despite the concerns, as of March 2021, the American public was trending towards greater acceptance of COVID-19 vaccines

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[389] *See id.*

[390] *See, e.g.*, Parasidis, *supra* note 84.

[391] *See* Katherine Van Tassel, Carmel Shachar & Sharona Hoffman, *Covid-19 Vaccine Injuries: Preventing Inequities in Compensation*, 384 NEW ENG. J. MED. e34(1) (Jan. 21, 2021).

[392] Laurie McGinley, Yasmeen Abutaleb & Carolyn Y. Johnson, *Pfizer Tells U.S. Officials It Cannot Supply Substantial Additional Vaccine Until Late June or July*, WASH. POST. (Dec. 8, 2020), https://www.washingtonpost.com/health/2020/12/07/pfizer-vaccine-doses-trump/ [https://perma.cc/G8DH-28GQ].

[393] *See, e.g.*, Efthimios Parasidis & Aaron S. Kesselheim, *Assessing the Legality of Mandates for Vaccines Authorized Via an Emergency Use Authorization*, HEALTH AFFS. BLOG (Feb. 16, 2021), https://www.healthaffairs.org/do/10.1377/hblog20210212.410237/full/ [https://perma.cc/37HM-5CUU].

[394] *See, e.g.*, Daniel B. Kramer, Douglas J. Opel, Efthimios Parasidis & Michelle M. Mello, *Choices in a Crisis: Individual Preferences Among SARS-CoV-2 Vaccines*, 384 NEW ENG. J. MED. e62(1) (Mar. 3, 2021).

[395] *See, e.g.*, Lisa Zengarini, *U.S. Bishops Express Moral Concern Over 'Johnson & Johnson' Vaccine*, VATICAN NEWS (Mar. 4, 2021), https://www.vaticannews.va/en/church/news/2021-03/us-bishops-moral-concern-johnson-vaccine-covid.html [https://perma.cc/CG76-3RRK].

[396] *See, e.g.*, Ruth R. Faden & Ruth A. Karron, *Using the New Johnson & Johnson Vaccine to Create Equity and Trust*, STAT NEWS (Mar. 5, 2021), https://www.statnews.com/2021/03/05/use-johnson-johnson-covid-19-vaccine-create-equity-trust/ [https://perma.cc/NBP6-PPR4]; Simar S. Bajaj & Fatima C. Stanford, *Beyond Tuskegee: Vaccine Distrust and Everyday Racism*, 384 NEW ENG. J. MED. e12 (Jan. 21, 2021). In part, the distribution concerns stem from the cold storage capacity needs for the two mRNA vaccines; the Janssen vaccine can be stored in standard refrigerator temperatures. *See id.*

upon witnessing that the EUA vaccines were effective in preventing severe COVID-19 and that serious vaccine-induced adverse events were rare.[397]

IV. RECALIBRATING THE EUA FRAMEWORK

EUAs have been central to the health and public health response to COVID-19. As of March 8, 2021, several drugs and therapeutic biological products for COVID-19—including some with dubious effectiveness—had been marketed under EUAs.[398] Access to PPE and other key medical devices and supplies had expanded because of EUAs. Hundreds of COVID-19 diagnostic and antibody tests had been authorized via an EUA.[399] And, FDA had issued three vaccine EUAs.[400] Concurrently, throughout the pandemic, FDA had been subjected to relentless pressure from a diverse set of stakeholders, including the White House, state and federal lawmakers, pharmaceutical and medical device companies, advocacy groups, public health officials, and the public.

FDA has been under the public microscope from the beginning of the pandemic. Several former FDA Commissioners and Deputy Commissioners have scrutinized FDA decision-making, at times questioning the agency's EUA decisions.[401] The public also has doubted FDA in several instances; for example, at some points in the pandemic, studies found that a majority of the public maintained skepticism about whether politics, not science, was driving the COVID-19 vaccine authorization process.[402] FDA and HHS leaders have sought to alleviate these concerns with statements, sometimes terse, professing an allegiance to science over politics.[403]

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[397] *See, e.g.*, Cary Funk & Alec Tyson, *Growing Share of Americans Say they Plan to Get a COVID-19 Vaccine—or Already Have*, PEW RSCH. CTR. (Mar. 5, 2021).

[398] To be sure, some interventions, such as remdesivir and convalescent plasma, were made available via FDA's expanded access program. Nevertheless, for these products, issuance of an EUA likely increased access, increased the likelihood that payors would cover all or part of the cost of treatments, and permitted manufacturers to profit off the products' sale.

[399] FDA COVID-19 EUA LIST, *supra* note 5.

[400] *See id.*

[401] *See, e.g.*, Charles Piller, *Former FDA Leaders Decry Emergency Authorization of Malaria Drugs for Coronavirus*, SCIENCE (Apr. 7, 2020), https://www.science.org/news/2020/04/former-fda-leaders-decry-emergency-authorization-malaria-drugs-coronavirus [https://perma.cc/WKC6-KUUU].

[402] *See* Silverman, *supra* note 315.

[403] *See* Dan Diamond, Adam Cancryn & Sarah Owermohle, *'It Just Created a Public Relations Nightmare': Inside Michael Caputo's Time at HHS*, POLITICO (Sept. 16, 2020), https://www.politico.com/news/2020/09/16/how-michael-caputo-shook-up-hhs-416632 [https://perma.cc/4XJT-5JB8]; Brianna Ehley & Rachel Roubein, *Azar Says HHS Reviewing $300M Pandemic Ad Campaign Amidst Scrutiny*, POLITICO (Oct. 2, 2020), https://www.politico.com/news/2020/10/02/azar-hhs-pandemic-ad-campaign-425371 [https://perma.cc/J86Q-Y4NK]. The public relations effort is also tainted by troubling conflicts of interest. Dan Diamond, *HHS Ad Blitz Sputters as Celebrities Back Away*, POLITICO (Sept. 29, 2020), https://www.politico.com/news/2020/09/29/hhs-ad-blitz-sputters-as-celebrities-back-away-423274 [https://perma.cc/L8Q2-S5MZ]. At one point, HHS allocated hundreds of millions of dollars to a public relations campaign to help alleviate the public concerns. *Id.* The public outreach efforts have done little to alleviate public fears, and the vast expenditures for media outreach came under intense scrutiny given funding shortfalls for a variety of pandemic-related health and public health initiatives. The advertising campaign was ultimately cancelled after the 2020 presidential election. Cameron Jenkins, *HHS Scraps*

This Article was drafted and edited in the midst of the COVID-19 pandemic, during the first thirteen months that FDA issued COVID-19 EUAs. In this section, we build off lessons learned in that time period and offer suggestions for recalibrating the EUA framework. In some cases, the suggested changes can be accomplished pursuant to FDA's existing authority, while for other recommendations congressional action is needed. Importantly, because of the varying questions posed by different kinds of medical products, different changes may be needed for drugs and therapeutic biologic products, medical devices, and vaccines. Across all categories, however, FDA must be more transparent with the public on EUA decisions and must afford the public with clear justifications for its actions that acknowledge known facts on safety and effectiveness, data gaps, and steps that the agency is undertaking to address the gaps and ensure that marketed medical products maintain an accurate risk-benefit profile.

A. Drugs and Therapeutic Biologic Products

EUAs are intended to provide patients with access to promising, but unproven, products for serious or life-threatening conditions where there are no adequate, approved, and available existing alternatives, and where there is some evidence that suggests the treatments may be safe or effective for the intended use.[404] One of the biggest challenges FDA has faced during the COVID-19 pandemic has been determining the type and amount of safety and effectiveness data that are sufficient in light of the lax statutory standard for issuing an EUA.

The flexible EUA standard that Congress afforded FDA during times of public health emergency is arguably appropriate because FDA scientists are highly trained experts in medical product review. At the same time, FDA is an agency within the Executive Branch.[405] The FDA Commissioner is appointed by the President, and the agency falls under the umbrella of HHS.[406] Although some political influence over FDA's policies is both inevitable and appropriate,[407] FDA acts within a political economy where government and industry often have very close ties, and FDA leaders and staff are prone to the pitfalls of regulatory capture, and other pressures, as with any governmental agency. Taken together, it is not surprising that FDA's decisions may at times be influenced by politicians, industry executives, and other stakeholders, particularly when the statutory bar for issuing an EUA is low and EUAs are considered within the politically charged context of a public health emergency.[408] As several

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Celebrity COVID-19 Ad Campaign Aimed at 'Defeating Despair', THE HILL (Nov. 18, 2020), https://thehill.com/homenews/news/526461-hhs-scraps-celebrity-covid-19-ad-campaign-aimed-at-defeating-despair [https://perma.cc/6KTX-6G2Z].

[404] 21 U.S.C. § 360bbb-3.

[405] U.S. FOOD & DRUG ADMIN., FDA ORGANIZATION (2020), https://www.fda.gov/about-fda/fda-organization [https://perma.cc/2AMH-GJMR].

[406] *See id.*

[407] *See, e.g.*, Lynch et al., *supra* note 96 (arguing that general policy choices that involve value judgements, as opposed to specific scientific decisions requiring relevant expertise, are legitimately politically influenced).

[408] *See* Benjamin N. Rome & Jerry Avorn, *Drug Evaluating During the COVID-19 Pandemic*, 382 NEW ENG. J. MED. 2282, 2284 (2020) ("During a pandemic that is causing morbidity and mortality to grow

policy scholars have noted, this political influence is a common feature of the neoliberal American political economy.[409]

This synthesis of factors shadows FDA leaders and decision-making. FDA's decisions often are subjected to intense scrutiny and debate, but particularly so during a global pandemic like COVID-19, which has disrupted the social fabric and imposed a massive toll on the health and welfare of individuals and society. The poor and people of color have borne disproportionate harms, as COVID-19 has exacerbated existing health and social inequities.[410] Society views countermeasures to prevent or treat COVID-19 as essential to overcoming the far-reaching health and societal carnage caused by the pandemic. In turn, FDA has sought to utilize every available regulatory tool to fulfill its public health mission to promote the health and safety of individuals and society.

One manifestation of this regulatory philosophy has been to issue EUAs for products absent convincing evidence of safety and effectiveness. Another has been to issue EUAs quickly—as clinical trials and observational studies were ongoing—even when it is predictable that allowing access under the EUAs would stymie ongoing research or new studies. As a practical matter, providing large numbers of patients with expedited access to products can severely hinder FDA's ability to determine whether the products are, in fact, safe and effective.

This conundrum was particularly evident with remdesivir and COVID-19 convalescent plasma. Yet, in both instances, FDA opted to grant the EUA rather than wait to gather more insightful data. Moreover, FDA did not structure or revise the EUAs to impose conditions that would address concerns about the ability to continue to conduct research.

In other words, FDA adopted a regulatory philosophy whereby the patients of tomorrow may be exposed to undue risks and uncertainty about effectiveness so that the patients of today can be administered an intervention that has the promise, albeit unproven, of benefit. Indeed, nearly ten months into the pandemic, several physicians pondered whether COVID-19 patients were faring better because physicians were using fewer EUA-authorized products.[411] Some went as far as to characterize COVID-19 products as "a graveyard for therapeutic interventions."[412] For example, American doctors wrote nearly 500,000 prescriptions for HQ, despite the lack of evidence of effectiveness.[413] But the issue extends beyond the widely criticized HQ EUA—for

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exponentially, there is an understandable temptation to make unproven therapies widely available and not wait for rigorous clinical trial data.").

[409] *See, e.g.*, CARPENTER, *supra* note 105; MARCIA ANGELL, THE TRUTH ABOUT THE DRUG COMPANIES (2005); Parasidis, *supra* note 209.

[410] *See* Michele K. Evans, *Covid's Color Line—Infectious Disease, Inequity, and Racial Justice*, 383 NEW ENG. J. MED. 408 (2020); Merlin Chowkwanyun & Adolph L. Reed, *Racial Health Disparities and Covid-19—Caution and Context*, 383 NEW ENG. J. MED. 201 (2020).

[411] *See, e.g.*, Haider J. Warraich, *Are More People Surviving Covid-19 Because Doctors are Doing Less?*, STAT NEWS (Jan. 15, 2021), https://www.statnews.com/2021/01/15/are-more-people-surviving-covid-19-because-doctors-are-doing-less/ [https://perma.cc/XK3J-S9AX].

[412] *Id.*

[413] *See id.*

instance, data on the effectiveness of remdesivir and COVID-19 convalescent plasma were minimal at best.[414]

As FDA considers additional drug and biologic EUAs, it should be mindful of both short-term and long-term benefits and risks. In the first year of the COVID-19 pandemic, the agency emphasized the former over the latter. Looking ahead, FDA should consider requiring manufacturers to have completed more exacting clinical trials prior to issuing an EUA, with clinical endpoints that more precisely capture salient health and public health concerns. The EUA provision in the FDCA permits, but does not mandate, that FDA issue an EUA when the low statutory bar is met[415]—this affords FDA flexibility to determine that the public health would not be served by a particular EUA even when statutory criteria may be satisfied.

Furthermore, FDA should condition each EUA on robust post-market observational studies and employ a mandatory data reevaluation period both in the near term and with pre-set follow-up intervals. Although research has demonstrated that FDA often struggles to enforce such post-market requirements for *approved* products,[416] there might be reason to believe that there is more promise for relying on post-market requirements in the EUA context. For example, EUAs are, from the outset, temporary—they only last as long as the public health emergency declaration.[417] Additionally, FDA can more easily revoke an EUA than it can an approved application, and it can unilaterally revise EUAs.[418]

FDA can incorporate these measures under its existing authority. But Congress also should consider amending the FDCA to improve how FDA uses its broad authority to shape EUAs to help ensure that future FDA decisions adequately capture a regulatory philosophy that balances the patients of tomorrow with the patients of today.[419] For example, Congress could amend the FDCA to require that post-market studies of both safety and effectiveness, as well as timelines for sponsors to submit information to enable EUA revaluation, be conditions of EUAs, to supplement the existing requirement that FDA "periodically" review the EUA.[420] While these suggested

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[414] *See id.*

[415] 21 U.S.C. § 360bbb-3.

[416] *See, e.g.*, Matthew Herder, *Pharmaceutical Drugs of Uncertain Value, Lifecycle Regulation at the US Food and Drug Administration, and Institutional Incumbency*, MILBANK Q. (2019); Kevin Fail, Matthew Daubresse & G. Caleb Alexander, *The Food and Drug Administration Amendments Act and Postmarketing Commitments*, 310 JAMA 202 (2013); Joshua D. Wallach, Alexander C. Egilman, Sanket S. Dhruva, Margaret E. McCarthy, Jennifer E. Miller, Steven Woloshin, Lisa M. Schwartz & Joseph S. Ross, *Postmarket Studies Required by the US Food and Drug Administration for New Drugs and Biologics Approved Between 2009 and 2012: Cross Sectional Analysis*, 361 BRIT. MED. J. k2031 (2018); Jean-David Zeitoun, Joseph S. Ross, Ignacio Atal, Alexandre Vivot, Nicholas S. Downing, Gabriel Baron & Philippe Ravaud, *Postmarketing Studies for Novel Drugs Approved by Both the FDA and EMA Between 2005 and 2010: A Cross-Sectional Study*, 7 BRIT. MED. J. e018587 (2017).

[417] 21 U.S.C. § 360bbb-3.

[418] *Id.*

[419] Of course, the patients of today also may not be served by a regulatory approach that does not ensure adequate evidence of safety and effectiveness, and adequate incentives to study products.

[420] 21 U.S.C. § 360bbb-3(g).

measures may, at times, lead to a longer wait before products can be marketed and higher research costs after issuance of an EUA, the products that come to market, and stay on the market, are more likely to be beneficial, and it would be more likely that there would be sufficient evidence to understand whether such products are, in fact, safe and beneficial.[421]

B. Medical Devices

The hundreds of EUAs that FDA has issued for devices have sought to address several pain points in the COVID-19 pandemic. One key area involves insufficient supply of PPE, including, but not limited to, N95 respirator masks, surgical masks, and medical-grade gloves. In large part, the shortage was due to pandemic-related disruptions in supply chains and American over-reliance on importing PPE.[422] Although FDA was not a cause of these supply-chain failures, the agency was relied upon to take quick action to address the shortcomings.

To do so, in some instances FDA issued EUAs for PPE without conducting an inspection of the products or manufacturing facilities, many of which were located outside the country.[423] Rather, FDA relied on third-party certification and then conducted limited post-market testing to evaluate PPE utilized in hospitals and throughout the country.[424] In other instances—for example, with respect to N95 mask decontamination devices—FDA issued an EUA notwithstanding identified concerns that a device did not work as advertised.[425] These decisions were made during the early months of the pandemic, when a severe shortage of PPE was threatening the health and safety of Americans, most notably front-line health care workers.[426]

More serious issues have arisen in the context of COVID-19 diagnostic tests. Although the agency set a "general expectation" of requiring at least 95% accuracy as a baseline for issuance of an EUA for a test, at times FDA ignored its own guidelines.[427] Furthermore, FDA applied inconsistent standards on what data were sufficient to demonstrate accuracy.[428] For example, in some cases EUAs for diagnostic tests were issued solely based on studies that evaluated lab samples of COVID-19, rather than evaluating the tests on humans who were known to be COVID-19-positive or negative.[429] As with PPE, in large part FDA was tasked with helping to respond to

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[421] Moreover, patients could still gain preapproval access to unproven products in some instances without an EUA—via FDA's expanded access regulations or under the Federal Right to Try Act. As they have been in the past, these measures also should be used sparingly and judiciously.

[422] CONG. RSCH. SERV., R46304, COVID-19: CHINA MEDICAL SUPPLY CHAINS AND BROADER TRADE ISSUES (2020).

[423] *See supra* Section III.B.

[424] *See id.*

[425] *See id.*

[426] *See id.*

[427] *See* Pradhan, *supra* note 260.

[428] *See id.*

[429] *See supra* Section III.B.

a testing shortage during a raging pandemic where testing was an integral public health tool.

Taken together, although FDA is not responsible for supply chain economics and the lack of adequate pandemic preparedness, the agency was relied upon by the government, industry, and public to address these concerns. FDA decision-making must be understood in the context of this unenviable position, which may have encouraged the agency to err on the side of issuing EUAs rather than denying them.

Looking ahead, FDA should issue guidance that identifies a risk-based framework for evaluating device EUAs, similar to what the agency employs in its standard medical device review. Although FDA, of course, cannot anticipate all scientific and other considerations likely to be relevant for all future emergencies in which EUAs will be issued, general guidance documents would help the agency communicate the lessons it has learned and encourage sponsors to develop appropriate evidence, while also giving industry stakeholders more certainty about available paths to market in times of emergency. For example, for diagnostic testing, a guidance document could generally discuss levels of specificity and sensitivity expected to support an EUA.[430] Given the experience with COVID-19 devices marketed under EUAs, FDA should also consider generally issuing EUAs for products manufactured outside the United States only when facilities can be inspected (which may not be feasible in the context of a global pandemic) *or* a robust inspection of the product can be conducted when it enters the United States. Reliance on third-party certification—particularly in time of crisis—can create undue risks for patients and the public in certain circumstances. Furthermore, for all device EUAs, as with drugs and therapeutic biological products, FDA should condition the EUA on robust post-market observational studies and employ a mandatory data reevaluation period in the near term. Again, although these suggested measures may lead to a longer wait before devices can be marketed, the devices that come to market, and stay on the market, are more likely to be beneficial. Similarly, these are measures that FDA can institute under its existing statutory authority, though Congress could also amend the FDCA to require these measures.

C. Vaccines

Recall that a key motivating factor underlying enactment of the EUA mechanism was DoD's desire to continue its anthrax vaccine immunization program after a court halted the program because the vaccine was not an FDA-approved prophylaxis against weaponized anthrax.[431] Although military contingencies influenced enactment of legislation that created EUAs, the new law was drafted to encompass military and civilian uses of medical countermeasures during national security or public health

[430] On March 16, 2021, more than thirteen months into the pandemic, FDA issued a template and other guidance for manufacturers seeking an EUA for certain tests utilized for serial testing, which involves testing the same person multiple times within a few days in order to increase the likelihood that a person has an accurate picture of whether they are SARS-CoV-2 positive or not. *See* U.S FOOD & DRUG ADMIN., FDA TAKES STEPS TO STREAMLINE PATH FOR COVID-19 SCREENING TOOLS, PROVIDES INFORMATION TO HELP GROUPS ESTABLISHING TESTING PROGRAMS (Mar. 16, 2021).

[431] *See supra* Section II.

emergencies.[432] The anthrax vaccine was the first EUA issued by FDA, and, prior to COVID-19, the only time that FDA had issued an EUA for a vaccine.[433]

Vaccine EUAs pose unique clinical and ethical concerns. Unlike EUAs for drugs and biologics—which are administered to sick individuals who may be hospitalized and at serious risk for death from COVID-19—vaccines that come to market via the EUA mechanism are intended for use in healthy individuals. Accordingly, in the context of vaccines, it is particularly critical to ensure: a) appropriate clinical trial designs; b) appropriate standards for demonstrated safety and effectiveness before EUA issuance; and c) safeguards to keep EUAs from preventing the generation of evidence necessary to understand products' safety and effectiveness.

Clinical trials with COVID-19 vaccine candidates revealed vaccine-related adverse effects in many inoculated individuals. For example, in studies for vaccine candidates from Pfizer and AstraZeneca, more than half of research participants experienced vaccine-induced adverse effects such as fever, headaches, muscle pain, and soreness.[434] Serious adverse events, on the other hand, have been rare, though clinical trials for AstraZeneca's vaccine (which, as of this writing, has not received EUA authorization, though the vaccine has been approved for use in other countries) were halted twice to investigate reports of serious adverse reactions, including spinal cord damage.[435] Death or serious adverse effects from a COVID-19 vaccine issued an EUA, even if rare, risk mass panic amongst the public and driving people away from vaccination—particularly if the COVID-19 vaccine were not supported by robust evidence demonstrating its safety and effectiveness.

From a public health standpoint, however, vaccines have helped stop the spread of COVID-19 and have decreased morbidity and mortality associated with COVID-19. As detailed above, however, before issuing vaccine EUAs, FDA authorized vaccine study goals whereby a positive endpoint was achieved if the vaccine candidate lowered the risk of mild COVID-19 cases, and did not require that the vaccine trials determine that the vaccine candidate prevented the disease altogether, reduced moderate or severe COVID-19 cases, reduced the risk of hospitalization, reduced admission to intensive care, or reduced death.[436] In October 2020, some scientists called for animal studies that might help fill these gaps.[437] Even if concerns about the clinical trial design

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[432] *See id.*

[433] *See id.*

[434] *See* Rebecca Robbins, Adam Feuerstein & Helen Branswell, *AstraZeneca Covid-19 Vaccine Study Put on Hold Due to Suspected Adverse Reaction Participant in the U.K.*, STAT NEWS (Sept. 8, 2020), https://www.statnews.com/2020/09/08/astrazeneca-covid-19-vaccine-study-put-on-hold-due-to-suspected-adverse-reaction-in-participant-in-the-u-k/ [https://perma.cc/SE9W-ACP7]; Arthur Allen & Liz Szabo, *NIH 'Very Concerned' About Serious Side Effects in Coronavirus Vaccine Trial*, KAISER HEALTH NEWS (Sept. 14, 2020), https://khn.org/news/nih-and-fda-examine-serious-side-effect-that-surfaced-in-covid-vaccine-trial/ [https://perma.cc/9XKT-ZM4Z]; Doshi & Topol, *supra* note 318.

[435] *See* Robbins et al., *supra* note 434; Allen & Szabo, *supra* note 434.

[436] *See supra* Section III.C.

[437] *See* Jon Cohen, *Saying Human Trials Aren't Enough, Researchers Call for Comparison of COVID-19 Vaccines in Monkeys*, SCIENCE (Oct. 7, 2020), https://www.science.org/content/article/saying-human-trials-arent-enough-researchers-call-comparison-covid-19-vaccines-monkeys [https://perma.cc/LPK6-C4BB].

were ultimately addressed by post-EUA studies in the case of COVID-19, it is important to recognize the limitations of that research design. In future pandemics, with a different FDA or less good fortune in vaccine development, for example, this approach may risk a large-scale immunization program conducted with a low-quality vaccine, which in turn may call into question the massive time, money, and resources dedicated to vaccine development, procurement, and administration.[438]

Vaccine research and development takes time. The quickest vaccine to come to market before the COVID-19 vaccines was the mumps vaccine, which took four years from the time virus samples were collected to FDA approval.[439] Most vaccines take a decade or longer to develop, due to the intricacies in honing the vaccine formula to assess safety and effectiveness, and to ensure that the vaccine provides sufficient antibodies to protect against the virus over time.[440] The COVID vaccines built on decades of prior vaccine research and public investments focused on other coronaviruses (e.g., MERS and SARS), which allowed for more rapid progress.[441] But consistent with experience in other contexts, several COVID-19 vaccine candidates were abandoned after lackluster clinical trials.[442]

For all these reasons, developing rigorous evidence of safety and effectiveness—and developing such evidence across all sub-populations for which a vaccine is intended—is particularly critical before authorizing distribution of a COVID-19 vaccine via an EUA or otherwise. Yet, for the first three vaccine EUAs issued by FDA, many of the aforementioned data points went unanswered. Looking ahead, insofar as FDA considers additional vaccine EUAs, the agency should require sponsors to use more precise clinical trial endpoints that capture salient aspects of disease transmission and disease burden, while remaining cognizant of the need to move as quickly as possible in an urgent, pandemic setting. Although data from the first months of vaccine administration showed that the vaccines authorized via the EUA protocol appeared to be as safe and effective as revealed during pre-authorization clinical trials, experience-to-date also shows diminished effectiveness over time (particularly with virus variants) and a small rate of serious adverse events.[443]

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[438] The catastrophic federal swine flu vaccine program from 1976 provides an apt example. Although not perfectly analogous for various reasons, the 1976 vaccination program should be examined closely. The swine flu vaccine was rushed to market to address a public health emergency. Although an outbreak of swine flu did not materialize, the vaccine itself caused dozens of deaths and thousands of vaccine-induced injuries, including paralysis. For discussion of the 1976 swine flu vaccine program, see generally Parasidis, *supra* note 84.

[439] *See, e.g.*, Nsikan Akpan, *Why a Coronavirus Vaccine Could Take Way Longer Than a Year*, NAT'L GEOGRAPHIC (Apr. 10, 2020), https://www.nationalgeographic.com/science/article/why-coronavirus-vaccine-could-take-way-longer-than-a-year [https://perma.cc/TK4U-PTWG].

[440] *See id.*

[441] *See, e.g.*, John P. Moore & Ian P. Wilson, *Decades of Basic Research Paved the Way for Today's 'Warp Speed' Covid-19 Vaccines*, STAT NEWS (Jan. 5, 2021), https://www.statnews.com/2021/01/05/basic-research-paved-way-for-warp-speed-covid-19-vaccines/ [https://perma.cc/6FRY-8STS].

[442] *See* Robbins et al., *supra* note 434; Doshi & Topol, *supra* note 318.

[443] There have also been some reports, with various degrees of reliability, of rare cases of more serious health complications, and sometimes death, following vaccine administration. *See, e.g.*, Ashley Collman, *A Virginia Man Who Got Johnson & Johnson's COVID-19 Vaccine Developed a Severe Rash that Spread Over His Entire Body*, BUS. INSIDER (Mar. 31, 2021), https://www.businessinsider.com/johnson-and-john

To be sure, these shortcomings may be unavoidable in the context of a pandemic involving a novel coronavirus. Indeed, given the circumstances, it appears as if FDA did a thorough job in evaluating the three authorized COVID-19 vaccines. Nevertheless, as FDA considers how best to use its EUA authority in the next pandemic, it would be wise to structure pre-EUA clinical trials that better elicit important information on a vaccine candidate's ability to prevent transmission, infection, and disease burden.[444] FDA can take these steps within its existing regulatory authority. Moreover, Congress should consider amending the FDCA to incorporate a more rigorous standard for vaccine EUAs. And, as with drugs and devices, FDA should also consider requiring post-market safety and effectiveness studies, including mandatory post-market adverse event surveillance,[445] and setting post-market reevaluation timelines as conditions on vaccine EUAs.

V. CONCLUSION

The law grants FDA broad discretion to apply its expertise when analyzing whether, for any given medical product, data on safety and effectiveness are sufficient to meet the low statutory standard for issuing an EUA. The flexibility afforded to FDA is both a blessing and a curse. It allows FDA to move quickly and be nimble in a public health emergency, but it also exposes FDA decisions and decision-makers to risks and

son-coronavirus-vaccine-man-develops-severe-rash-after-2021-3 [https://perma.cc/XR6S-8AGZ]; Helen Branswell, *'Real World' Study by CDC Shows Pfizer and Moderna Vaccines Were 90% Effective*, STAT NEWS (Mar. 29, 2021), https://www.statnews.com/2021/03/29/real-world-study-by-cdc-shows-pfizer-and-moderna-vaccines-were-90-effective/ [https://perma.cc/57PV-GFAD]; Bill Chappell, *Merck Stops Developing Both of Its COVID-19 Vaccine Candidates*, NPR (Jan. 25, 2021), https:// www.npr.org/ sections/coronavirus-live-updates/2021/01/25/960294852/merck-stops-developing-both-of-its-covid-19-vaccine-candidates [https://perma.cc/3WPB-3L9P]; Bill Chappell, *Moderna Finds COVID-19 Vaccine Still Protects Against Emerging Strains*, NPR (Jan. 25, 2021), https://www.npr.org/sections/coronavirus-live-updates/2021/01/25/960341384/moderna-finds-covid-19-vaccine-less-effective-against-variant-found-in-south-afr [https://perma.cc/HF49-T7U4]; Ingrid Torjesen, *Norway Investigates 23 Deaths in Frail Elderly Patients After Vaccination*, 372 BRIT. MED. J. n149 (Jan. 15, 2021) (noting that the individuals received Pfizer's vaccine); Karen Weintraub, *Death of Florida Doctor After Receiving COVID-19 Vaccine Under Investigation*, USA TODAY (Jan. 6, 2021), https://www.usatoday.com/story/news/health/2021/01/06/death-florida-doctor-following-pfizer-covid-19-vaccine-under-investigation-gregory-michael/6574414002/ [https://perma.cc/K6JL-TMPL]; Jop de Vrieze, *Suspicions Grow That Nanoparticles in Pfizer's COVID-19 Vaccine Trigger Rare Allergic Reaction*, SCIENCE (Dec. 21, 2020), https://www.science.org/news/2020/12/suspicions-grow-nanoparticles-pfizer-s-covid-19-vaccine-trigger-rare-allergic-reactions [https://perma.cc/JN8Q-FU9S]. Debate continues on whether the deaths were caused by vaccination. *See, e.g.*, Ed Browne, *Fact Check: Have 966 People Died After Receiving the COVID Vaccine?*, NEWSWEEK (Mar. 8, 2021), https://www.newsweek.com/covid-vaccine-deaths-cause-pfizer-moderna-fact-check-966-died-1574447 [https://perma.cc/6YSC-3VLS]. At the same time, some reports have detailed unintended benefits that may be linked to immunization, including amelioration of symptoms for Covid "long haulers," who are individuals that have endured COVID-19 symptoms for several months. *See, e.g.*, Will Stone, *Mysterious Ailment, Mysterious Relief: Vaccines Help Some COVID Long-Haulers*, NPR (Mar. 31, 2021), https://www.npr.org/sections/health-shots/2021/03/31/982799452/mysterious-ailment-mysterious-relief-vaccines-help-some-covid-long-haulers [https://perma.cc/NN68-AFL5].

[444] *See, e.g.*, WHO Ad Hoc Expert Group, *Placebo-Controlled Trials of Covid-19 Vaccines: Why We Still Need Them*, 384 NEW ENG. J. MED. e1 (Jan. 14, 2021) (outlining key data points in vaccine development).

[445] For a discussion of the need for active adverse event reporting, surveillance, and analysis, see, e.g., Efthimios Parasidis, *Patients Over Politics: Addressing Legislative Failure in the Regulation of Medical Products*, 2011 WISC. L. REV. 929 (2011).

pressures that are less present when the agency utilizes its standard pathways for review and approval. Although EUAs may grant patients and the public expedited access to promising medical products, the safety and efficacy profile of such products is less clear. Patients may be exposed to unknown and serious risks, while public health decision-making can be skewed by inaccurate or incomplete data, and clinical trial completion may be delayed or even become impossible. Uncertainties in the benefit-risk calculus always are problematic, but especially so during a pandemic like COVID-19 where little is known about the virus and disease.

As a public health agency that oversees several key sectors of the economy integral to the health and welfare of society, it is essential that FDA be widely viewed as a reliable and trustworthy authority. In the context of EUAs, to ensure as much as possible that authorized medical products are safe and effective, there are concrete areas where Congress could amend the EUA mechanism and FDA could recalibrate use of its existing authority. The many shortcomings of EUAs issued during the COVID-19 pandemic illustrate that FDA should employ more exacting premarket review and more comprehensive post-market surveillance and analysis.

The COVID-19 pandemic has unmasked regulatory grey zones where FDA maintains broad discretion. Although this discretion is a necessary component of medical product review, the very low evidentiary bar for EUAs set by the authorizing statute leaves ample space for political wrangling to infiltrate scientific decision-making. Despite the challenges, FDA remains the core gatekeeper to public access to medical products. The agency must exercise its authority carefully, as the health and welfare of an entire nation are at stake.