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COVID-19: A Crisis and an Opportunity to Improve the Emergency Use Authorization Process

*Daniel Walsh, Ph.D**

The pandemic caused by the SARS-CoV-2 virus has thrown the world into chaos. The virus has necessitated the use of the emergency use authorization (EUA) process by the FDA to speed public access to vaccines. This Note reviews the EUA process as codified in 21 U.S.C. § 360bbb-3 and presents research on the history of § 360bbb-3. This Note argues that this historical context highlights how § 360bbb-3 as written is ill suited to the challenges posed by public health in the context of authorizing a vaccine for an emerging infectious disease. This Note discusses how the EUA process functioned in the context of SARS-CoV-2, in particular examining the events surrounding hydroxychloroquine. This Note argues that these events demonstrate that the process as codified in § 360bbb-3 is unsuited for authorizing vaccines for emerging infectious diseases. In particular this Note argues that the EUA process as codified fails to account for the social benefits afforded by vaccine induced herd immunity which is predicated on public trust in the safety of authorized vaccines. Finally, this Note proposes an alternative framework for emerging infectious disease vaccine EUAs based on the FDA's regulatory actions in approving vaccines during the SARS-CoV-2 pandemic.

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I. INTRODUCTION

The Food and Drug Administration (FDA) is currently experiencing a crisis of legitimacy.¹ The SARS-CoV-2 pandemic has made it necessary for the agency to approve therapies via emergency use authorizations (EUAs),² but the agency is also publicly perceived to be acting politically.³ FDA's mission is twofold: it must "promote the public health" by approving new therapies in a "timely manner" but it must also "protect the public health" by "ensuring . . . drugs are safe and effective."⁴ Right or wrong, FDA's actions to satisfy its dual mandate have come to be perceived by some as political maneuvering.⁵ Public confidence in vaccines is paramount to achieving widespread immunization, which in turn is necessary to the ultimate aim of achieving vaccine-induced herd immunity.⁶ At the same time, pandemic infectious disease outbreaks are expected to become more and more

1. See Lindsey R. Baden, et al., *The FDA and the Importance of Trust*, 384 N. ENG. J. MED. e148(1), e148(2) (2020) ("[T]he trust the FDA has built and maintained over the past century is eroding."); see also Kyle Thomson & Herschel Nachlis, *Emergency Use Authorizations During the COVID-19 Pandemic: Lessons From Hydroxychloroquine for Vaccine Authorization and Approval*, 324 JAMA 1282, 1282 (2020) ("[P]roblems include the authorization of potentially ineffective or unsafe therapeutics, the appearance of nonexpert political advocacy generating public pressure for product authorizations with questionable safety and efficacy, and the imposition of significant costs on the health of the public and on the credibility and influence of . . . the FDA.").

2. See FOOD & DRUG ADMIN., EMERGENCY USE AUTHORIZATION FOR VACCINES TO PREVENT COVID-19: GUIDANCE FOR INDUSTRY (Oct. 2020), <https://www.fda.gov/media/142749/download> [hereinafter OCTOBER FDA GUIDANCE] (expressing the FDA's vaccine EUA guidance position in October 2020); see also FOOD & DRUG ADMIN., DEVELOPMENT AND LICENSURE OF VACCINES TO PREVENT COVID-19: GUIDANCE FOR INDUSTRY (June 2020), <https://www.fda.gov/media/139638/download> [hereinafter JUNE FDA GUIDANCE] (expressing the FDA's vaccine EUA guidance position in June 2020).

3. E.g., Nathaniel Weixel, *Government Watchdog to Investigate Allegations of Trump Interference at CDC, FDA*, HILL (Oct. 19, 2020 2:15 PM), <https://thehill.com/policy/healthcare/521716-government-watchdog-to-investigate-allegations-of-trump-interference-at-cdc> (reporting a Senate request for investigation into "political interference with public health agencies").

4. 21 U.S.C. § 393.

5. *National Tracking Poll #2008114: (Aug. 26–28 2020)*, MORNING CONSULT (Sept. 3, 2021), https://assets.morningconsult.com/wp-uploads/2020/09/03131941/2008114_crosstabs_FDA_Adults_v1_LM-1.pdf (showing 28% of respondents think FDA approval decisions relating to SARS-CoV-2 treatments and vaccines are based on political pressure as opposed to science (49%) or don't know / no opinion (23%)).

6. See Haley E. Randolph & Luis B. Barreiro, *Herd Immunity: Understanding COVID-19*, 52 IMMUNITY 737, 737 (2020) ("[Herd Immunity] refers to

common in the future and, by implication, the FDA will be called on to issue more and more EUAs.⁷ In particular, the FDA will need to issue EUAs for vaccines, as they are one of the most effective public health interventions ever invented.⁸

The events of the COVID-19 crisis at the FDA are revealing. The EUA process⁹ was not created with emerging diseases in mind, and a different balance of safety and efficacy is necessary to address this threat.¹⁰ The EUA process is also heavily reliant on executive branch norms that have already been breached and, to this end, the broad administrative fiat conferred to the FDA to issue EUAs for vaccines should be restricted in the context of

the indirect protection from infection conferred to susceptible individuals when a sufficiently large proportion of immune individuals exist in a population.”).

7. See Juliet Bedford, et al., *A New Twenty-First Century Science for Effective Epidemic Response*, 575 NATURE 130, 130 (2019) (arguing that “[w]ith rapidly changing ecology, urbanization, climate change, increased travel and fragile public health systems, epidemics will become more frequent, more complex and harder to prevent and contain.”); see also WORLD ECON. FORUM, *OUTBREAK READINESS AND BUSINESS IMPACT PROTECTING LIVES AND LIVELIHOODS ACROSS THE GLOBAL ECONOMY* 7 (2019), http://www3.weforum.org/docs/WEF%20HGH_I_Outbreak_Readiness_Business_Impact.pdf [hereinafter: WEF WHITE PAPER] (citing factors such as “growth in travel, trade and connectivity,” human expansion into previously uninhabited spaces, and climate change as increasing the risk of infectious disease outbreaks).

8. While this Note touches on issues of vaccine safety readers should not draw the conclusion that modern vaccines are not safe and effective. Vaccines are one of the safest and most effective public health interventions ever invented. See generally Vanessa Rémy, York Zöllner & Ulrike Heckmann, *Vaccination: The Cornerstone of an Efficient Healthcare System*, 3 J. MKT. ACCESS & HEALTH POL’Y 27041, 27041 (2015) (“During the 20th century, improved sanitation, nutrition, and the widespread use of antibiotics as well as vaccines have all contributed to the decreased incidence of numerous diseases and associated mortality. Vaccination was one of the public health measures that had the greatest impact on the reduction of the burden from infectious diseases and associated mortality, especially in children. It is estimated that, each year worldwide, vaccines prevent up to 3 million deaths.”) (citations omitted); Paul A. Offit, Robert L. Davis & Deborah Gust, *Vaccine safety*, in VACCINES 1629, 1629–1650 (Stanley A. Plotkin, Walter A. Orenstein, Paul A. Offit eds., 2008) (reviewing procedures in place to ensure vaccine safety); Matthew Z. Dudley, et al., *The State of Vaccine Safety Science: Systematic Reviews of the Evidence*, 20 LANCET INFECTIOUS DISEASE e80, e80 (2020) (Concluding “[v]accines have an excellent safety profile overall and provide protection against infectious diseases to individuals and the general population.”). This Note addresses only whether the EUA process contains the appropriate statutory guardrails to ensure that future hypothetical vaccines are safe and therefore effective.

9. See 21 U.S.C. § 360bbb-3 (enabling the EUA process).

10. *Infra* Part II.C (describing the origins of the EUA process).

pandemic diseases.¹¹ An alternative emerging infectious disease vaccine EUA pathway should be created that retains the EUA standards for efficacy, but which raises the bar on safety to be similar to traditional FDA vaccine approval. This change is not intended to hamstring the agency's ability to employ sound scientific judgment, but rather, to support it. A formalized framework could support the FDA's legitimacy, promote regulatory expediency in crisis, and ensure scientific rigor in the context of an expedited approval process that necessarily rebalances speed, safety, and efficacy.

This Note will begin by reviewing scientific information on SARS-CoV-2 (the causative virus of the disease COVID-19) and the role of vaccination in ending the COVID-19 crisis. Then, it will explain FDA's role in vaccine development and approval via the EUA process and the legislative developments that lead to the EUA process as it exists today. Finally, this Note will summarize the implementation of the EUA process in response to COVID-19 and explain why it has led to a perception of political interference with agency decision making.

This Note will argue that the hydroxychloroquine EUA demonstrates the failings of the current EUA process and that a distinct EUA process for emerging infectious disease vaccines should be codified with a higher standard of safety.¹² The standard this Note advocates is inspired by the level of review employed by the FDA to authorize vaccines in the SARS-CoV-2 pandemic.¹³ This Note argues that regulatory actions of the FDA relating to the emergency authorization of the Pfizer-BioNTech¹⁴ and Moderna SARS-CoV-2 vaccines had appropriate scientific

11. *Infra* Part II.D–E (describing the implementation of the EUA process generally and in the context of COVID-19).

12. Specifically, the safety standard codified by 21 U.S.C. § 355(d), which indicates approval should be denied if “[1] submissions to the FDA] do not include adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof; [2] the results of such tests show that such drug is unsafe for use under such conditions or do not show that such drug is safe for use under such conditions; . . . [or] [4] upon the basis of the information submitted to him as part of the application, or upon the basis of any other information before him with respect to such drug, he has insufficient information to determine whether such drug is safe for use under such conditions”

13. *Infra* Part II.E (describing the FDA's guidance on the COVID-19 EUA process).

14. This Note will refer to this as the Pfizer vaccine, for brevity.

support, but were the result of institutional inertia rather than a sound statutory framework. This Note does not argue that the FDA should use the same regulatory process for emerging infectious disease vaccine EUAs as is used for a typical New Drug Application (NDA)¹⁵ but rather that the current statutory EUA standard for safety is inappropriate in the context of vaccines intended for emerging infectious diseases.

II. BACKGROUND

A. THE VIRUS SARS-CoV-2

In 2019 a novel virus, eventually named SARS-CoV-2, emerged in the area around Wuhan, China.¹⁶ The SARS-CoV-2 virus causes the disease COVID-19.¹⁷ This virus spread quickly and was declared a pandemic illness by the World Health Organization in March of 2020.¹⁸ While the majority of COVID-19 cases are mild, a subset of patients experience a life threatening form of the disease that requires hospitalization.¹⁹ A smaller fraction of cases are fatal.²⁰ The burden of COVID-19 is not

15. This Note suggests adopting §355(d)'s legal standard for safety. It does not argue that this new regulatory pathway should mirror the NDA process as implemented by the FDA in practice (requiring complete phase I, II, and III clinical trials to obtain approval).

16. See Ben Hu, et al., *Characteristics of SARS-CoV-2 and COVID-19*, 19 NAT'L REV. MICROBIOLOGY 141, 141 (2020) ("At the end of 2019, a novel coronavirus designated as SARS-CoV-2 emerged in the city of Wuhan, China, and caused an outbreak of unusual viral pneumonia. Being highly transmissible, this novel coronavirus disease, also known as coronavirus disease 2019 (COVID-19), has spread fast all over the world.") (citations omitted).

17. See *id.*

18. See Tedros Adhanom, World Health Organization Director-General, Opening Remarks at the Media Briefing on COVID-19 (Mar. 11, 2020), in WORLD HEALTH ORG., <https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19-11-march-2020> ("We have therefore made the assessment that COVID-19 can be characterized as a pandemic.").

19. See Hu, *supra* note 16 at 148 ("In a report of 72,314 cases in China, 81% of the cases were classified as mild, 14% were severe cases that required ventilation in an intensive care unit (ICU) and a 5% were critical (that is, the patients had respiratory failure, septic shock and/or multiple organ dysfunction or failure).") (citations omitted).

20. Two different metrics of fatality are presented. Case Fatality Rate (CFR) measures deaths in those diagnosed with SARS-CoV-2 infection. Infection Fatality rate (IFR) is an estimate of deaths among anyone who was infected with SARS-CoV-2. Because many SARS-CoV-2 infections are asymptomatic,

evenly distributed through the population: severe disease is more common in the elderly²¹ and disadvantaged communities²² due to a variety of factors, including preexisting disparities in medical care²³ and socioeconomic disadvantage.²⁴ In every population, symptoms of COVID-19 can persist for months after initial symptom onset.²⁵ Long-term issues associated with SARS-CoV-2 infection include damage to the cardiovascular, pulmonary, and nervous systems including brain tissue.²⁶

IFR is necessary lower. See Gideon Meyerowitz-Katz & Lea Merone, *A Systematic Review and Meta-Analysis of Published Research Data on COVID-19 Infection Fatality Rates*, 101 INT. J. INFECT. DIS. 138, 138 (2020) (“The meta-analysis demonstrated a point estimate of IFR of 0.68% (0.53%–0.82%) with high heterogeneity ($p < 0.001$).”); see also Wan Yang, et al., *Estimating the Infection-Fatality Risk of SARS-CoV-2 in New York City During the Spring 2020 Pandemic Wave: a Model-Based Analysis*, 21 LANCET INFECTIOUS DISEASE 203, 203 (2020) (“We estimated an overall infection-fatality risk of 1.39% (95% credible interval 1.04–1.77) in New York City.”).

21. See Yang et al., *supra* note 20, at 203 (“[C]umulative estimated infection-fatality risk of 0.116% (0.0729–0.148) for those aged 25–44 years and 0.939% (0.729–1.19) for those aged 45–64 years versus 4.87% (3.37–6.89) for those aged 65–74 years and 14.2% (10.2–18.1) for those aged 75 years and older.”).

22. See Donald J. Alcendor, *Racial Disparities-Associated COVID-19 Mortality Among Minority Populations in the US*, 9 J. CLIN. MED. 2442, 2444 (2020) (“An examination of 131 predominantly [African American (AA)] counties shows a COVID-19 infection rate of 137.5 per 100,000 and a death rate of 6.3 per 100,000, which is three times higher than the predominant [non-Hispanic White] counties. Moreover, the death rate for the AA counties were found to be six times higher than the rate observed in predominant white counties.”).

23. See *id.* at 2452 (“Longstanding health disparities such as diabetes, hypertension, CVD, and pulmonary disease among minority populations in the US may serve to predispose these communities to SARS-CoV-2 infection and increased risk for clinically severe COVID-19.”).

24. See Matthew A. Raifman & Julia R. Raifman, *Disparities in the Population at Risk of Severe Illness From COVID-19 by Race/Ethnicity and Income*, 59 AM. J. PREV. MED. 137, 137 (2020) (“Among those aged <65 years, 40% of low-income people were at higher risk (PR=1.63, 95% CI=1.59, 1.67) relative to 24% of those with higher income”); see also J. A. Patel, et al., *Poverty, Inequality and COVID-19: the Forgotten Vulnerable*, 183 PUBLIC HEALTH 110, 110 (2020) (highlighting potential mechanisms that translate economic disadvantage into a higher risk of COVID-19).

25. See Michael Marshall, *The Lasting Misery of Coronavirus Long-Haulers*, 585 NATURE 339, 339 (2020) (“Months after infection with SARS-CoV-2, some people are still battling crushing fatigue, lung damage and other symptoms of ‘long COVID.’”).

26. See Carlos del Rio, Lauren F. Collins & Preeti Malani, *Long-term Health Consequences of COVID-19*, 324 JAMA 1723, 1723–1724 (2020) (reviewing evidence of chronic symptoms post COVID-19).

The emergence of SARS-CoV-2 is not unexpected.²⁷ Respiratory viral pandemics are a recurring occurrence in human history.²⁸ SARS-CoV-2 is closely related to other respiratory viruses known to infect humans such as SARS-CoV-1 and MERS-CoV (which cause serious disease in human hosts) but also endemic viruses including HCoV-NL63, HCoV-229E, HCoV-OC43, and HCoV-HKU1 (which typically cause mild disease states similar to the common cold).²⁹ Epidemics and pandemics are predicted to become more common in the future, driven by factors such as increasing interconnectedness and climate change.³⁰

B. DEVELOPING A VACCINE

A safe and effective vaccine is the clearest path out of the SARS-CoV-2 pandemic.³¹ Vaccines are a crowning achievement of modern medicine.³² Emerging technologies such as RNA and

27. In 2018 Bill Gates spoke about the likelihood of emerging pandemic diseases in 2018 and advocated for a “coordinated global approach” to confronting them. *See* Bill Gates, Shattuck Lecture (Apr. 27, 2018), *in* Press Room, BILL & MELINDA GATES FOUND., <https://www.gatesfoundation.org/Media-Center/Speeches/2018/04/Shattuck-Lecture-Innovation-for-Pandemics>.

28. *See generally* Rashed Noor & Syeda Muntaka Maniha, A Brief Outline of Respiratory Viral Disease Outbreaks: 1889–Till Date on the Public Health Perspectives, 31 *VIRUSDISEASE* 441 (2020) (reviewing history of respiratory pandemics).

29. *See* Vivaldo Gomes da Costa, Marcos Lázaro Moreli & Marielena Vogel Saivish, *The Emergence of SARS, MERS and Novel SARS-2 Coronaviruses in the 21st Century*, 165 *ARCHIVES VIROLOGY* 1517, 1517–1524 (2020) (reviewing the emergence of SARS-CoV-1, SARS-CoV-2, and MERS-CoV); *see also* Victor M Corman, et al., *Hosts and Sources of Endemic Human Coronaviruses*, 100 *ADVANCES VIRUS RES.* 163, 163–179 (2018) (reviewing research on endemic human coronaviruses).

30. *See supra* note 7 and accompanying text.

31. *See* Debby van Riel & Emmie de Wit, *Next-Generation Vaccine Platforms for COVID-19*, 19 *NAT. MATERIALS* 810, 810 (2020) (“Consensus among experts is that only an effective COVID-19 vaccine will end the pandemic.”); *see also* Nsikan Akpan, *A ‘Herd Mentality’ Can’t Stop the COVID-19 Pandemic. Neither Can a Weak vaccine*, *NAT’L GEOGRAPHIC* (Oct. 2, 2020), <https://www.nationalgeographic.com/science/2020/10/natural-herd-immunity-mentality-cannot-stop-coronavirus-weak-vaccine-cvd/> (“It’s very unlikely that we’re going to see elimination of COVID-19 altogether from the population simply through the buildup of natural immunity,” says Pitzer. But if we add a highly effective vaccine on top of that, Pitzer says, “then it is theoretically possible that we could eliminate the virus” or at least control it.”) (quoting Virginia Pitzer, Associate Professor of Epidemiology, Yale School of Public Health).

32. *See generally* Brian Greenwood, *The Contribution of Vaccination to Global Health: Past, Present and Future*, 369 *PHIL. TRANSACTIONS ROYAL SOC. LONDON BIOLOGY* 20130433 (2014) (“[I]t is indisputable that vaccination has

viral vector vaccines have increased the pace of vaccine development considerably.³³ This resulted in an unprecedented number of SARS-CoV-2 vaccines entering development and clinical trials.³⁴ Vaccines can act to either prevent infection (sterilizing immunity) or to prevent disease (partially protective immunity).³⁵ Both sterilizing and partially protective immunity have the secondary benefit of reducing the ability of the virus to spread in the local community via vaccine-induced herd immunity.³⁶ However, achieving vaccine-induced herd immunity requires immunizing a significant share of the population, enough that the virus

made an enormous contribution to human and animal health, especially in the developing world. Mortality from smallpox and measles was massive in the pre-vaccination period with up to a half of the population dying from the former during epidemics and measles was only a little less lethal in susceptible populations.”).

33. See van Riel & de Wit, *supra* note 31, at 810 (“The main advantage of next-generation vaccines is that they can be developed based on sequence information alone. If the viral protein(s) important to provide protection from infection or disease, and thus for inclusion in a vaccine (that is, the vaccine antigen), is known the availability of coding sequences for this viral protein(s) suffices to start vaccine development, rather than having to depend on the ability to culture the virus. This makes these platforms highly adaptable and speeds up vaccine development considerably”); see also Susanne Rauch, et al., *New Vaccine Technologies to Combat Outbreak Situations.*, 9 FRONTIERS IMMUNOLOGY 1963 (2018) (reviewing new vaccine technologies immediately prior to the pandemic).

34. Jeff Craven, *COVID-19 Vaccine Tracker*, REG. FOCUS (Mar. 18, 2021), <https://www.raps.org/news-and-articles/news-articles/2020/3/covid-19-vaccine-tracker> (last visited Mar. 19, 2021) (listing all SARS-CoV-2 vaccines currently in clinical trials).

35. Heidi Ledford, *What the Immune Response to the Coronavirus Says About the Prospects for a Vaccine*, 585 NATURE 20, 21–22 (2020) (explaining sterilizing immunity: “response, typically mediated by antibodies, that can rapidly prevent a returning virus from gaining ground in the body” and protective immunity: “immunity could be strong enough to reduce or even eliminate symptoms . . . a vaccine that could reduce mortality would likely still be helpful”). See generally Angela Choi, et al., *Non-Sterilizing, Infection-Permissive Vaccination With Inactivated Influenza Virus Vaccine Reshapes Subsequent Virus Infection-Induced Protective Heterosubtypic Immunity From Cellular to Humoral Cross-Reactive Immune Responses*, 11 FRONTIERS IMMUNOLOGY 1166 (2020) (applying the concepts of sterilizing and protective immunity to influenza vaccines).

36. See Michael L Mallory, Lisa C Lindesmith & Ralph S Baric, *Vaccination-Induced Herd Immunity: Successes and Challenges*, 142 J. ALLERGY CLINICAL IMMUNOLOGY 64, 64 (2018) (“In addition to individual protection, vaccination programs also rely on population or ‘herd’ immunity: immunization of large portions of the population to protect the unvaccinated, immunocompromised, and immunologically naive by reducing the number of susceptible hosts to a level less than the threshold needed for transmission.”).

runs out of potential hosts susceptible to infection.³⁷ Experts estimate that 60–75% of people must be immune to achieve herd immunity to SARS-CoV-2.³⁸ However, these estimates rely on assumptions about the virus and immune response that may not hold true in practice.³⁹ The bottom line is that a herculean public

37. See Randolph & Barreiro, *supra* note 6, at 737 (“In a completely naive population, a pathogen will propagate through susceptible hosts in an unchecked manner following effective exposure of susceptible hosts to infected individuals. However, if a fraction of the population has immunity to that same pathogen, the likelihood of an effective contact between infected and susceptible hosts is reduced, since many hosts are immune and, therefore, cannot transmit the pathogen. If the fraction of susceptible individuals in a population is too few, then the pathogen cannot successfully spread, and its prevalence will decline. The point at which the proportion of susceptible individuals falls below the threshold needed for transmission is known as the herd immunity threshold.”).

38. See Christie Aschwanden, *The False Promise of Herd Immunity for COVID-19*, 587 NATURE 26, 26–28 (2020) (reviewing expert estimates on herd immunity); see also Lewis F. Buss et al., *Three-quarters Attack Rate of SARS-CoV-2 in the Brazilian Amazon During a Largely Unmitigated Epidemic*, 371 SCIENCE 288, 292 (2021) (“Our data show that >70% of the population had been infected in Manaus about 7 months after the virus first arrived in the city. This is above the theoretical herd immunity threshold. However, prior infection may not confer long-lasting immunity.”).

39. See Aschwanden, *supra* note 38, at 27–28 (“Although plugging numbers into the formula spits out a theoretical number for herd immunity, in reality, it isn’t achieved at an exact point. Instead, it’s better to think of it as a gradient, says Gypsyamber D’Souza, an epidemiologist at Johns Hopkins University in Baltimore, Maryland. And because variables can change, including R_0 and the number of people susceptible to a virus, herd immunity is not a steady state.”); Roy M. Anderson et al., *Challenges in Creating Herd Immunity to SARS-CoV-2 Infection by Mass Vaccination*, 396 LANCET 1614, 1615 (2020) (“Given an R_0 value before lockdowns in most countries of between 2.5 to 3.5, we estimate the herd immunity required is about 60–72%. If the proportional vaccine efficacy, ϵ , is considered, the simple expression for p_c becomes $[1 - 1/R_0] / \epsilon$. If we assume ϵ is 0.8 (80%), then the herd immunity required becomes 75–90% for the defined range of R_0 values. For lower efficacies, the entire population would have to be immunised. These overall estimates ignore heterogeneities that can make these figures lower or higher in specific locations.”)

health effort will be necessary to vaccinate enough people to control the spread of the SARS-CoV-2 virus.⁴⁰ Anything that dissuades individuals from getting vaccinated⁴¹ will negatively impact the health of the larger population,⁴² especially the well-being of individuals who cannot effectively be vaccinated due to underlying health conditions.⁴³

C. FDA'S ROLE IN VACCINE DEVELOPMENT

The FDA regulates the safety and approval of vaccines in the United States.⁴⁴ Under normal circumstances, vaccines must

40. See Kenneth Gorelick, *Here's How Hard it Will Be to Distribute a Coronavirus Vaccine*, WASH. POST (Sept. 25, 2020, 6:00 AM), <https://www.washingtonpost.com/outlook/2020/09/25/covid-vaccine-distribution-logistics/> (“Rapidly distributing a safe and effective vaccine across the nation is likely to be one of the most significant logistical challenges ever undertaken by the government within our borders.”).

41. See Sarah Kreps et al., *Factors Associated with US Adults' Likelihood of Accepting COVID-19 Vaccination*, JAMA NETWORK OPEN, Oct. 2020, at 1, 1–13 (surveying Americans on different factors that affect their decision whether or not to receive a hypothetical SARS-CoV-2 vaccine); see also Jeanine P. D. Guidry et al., *Willingness to Get the COVID-19 Vaccine with and Without Emergency Use Authorization*, 49 AM. J. INFECT. CONTROL 137, 137–42 (2020) (surveying Americans on “demographics and psychosocial predictors of intent to get a future COVID-19 vaccine as well as willingness to get such a vaccine under EUA.”).

42. See Lynne Peeples, *Rethinking Herd Immunity*, 25 NAT. MED. 1178, 1178–80 (2019) (explaining the effects of “vaccine hesitancy” on the larger population).

43. See, e.g., Jan Smetana et al., *Influenza Vaccination in the Elderly.*, 14 HUM. VACCINE IMMUNOTHERAPEUTICS 540, 540 (2018) (“[P]rimary prevention via immunization is effective in reducing the burden of influenza illness among the elderly. However, the elderly may be insufficiently protected by vaccination due to the immunosenescence which accompanies aging. In addition, vaccine hesitancy among the younger populations increases the likelihood of circulating infectious diseases, and thus concomitant exposure.”).

44. See *Vaccines*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/vaccines-blood-biologics/vaccines> (last visited Nov. 16, 2020) (“The Center for Biologics Evaluation and Research (CBER) [a division of FDA] regulates vaccine products.”).

utilize the Investigational New Drug (IND)⁴⁵ and Biologics License Application (BLA)⁴⁶ processes to obtain FDA approval.⁴⁷ However, in an emergency the FDA gains access to the Emergency Use Authorization (EUA) process codified at 21 U.S.C. § 360bbb-3.⁴⁸ The EUA process originated as § 1603 of the National Defense Authorization Act for Fiscal Year 2004.⁴⁹ Originally, emergency use could only be authorized in response to “a military emergency, or a significant potential for a military emergency, involving a heightened risk to United States military forces of attack with a specified biological, chemical, radiological, or nuclear agent or agents.”⁵⁰ The process was amended by the Project BioShield Act of 2004 to permit authorization in response to “a public health emergency . . . that affects, or has a significant potential to affect, national security, and that involves a specified biological . . . agent or agents, or a specified disease or

45. See *Investigational New Drug (IND) or Device Exemption (IDE) Process (CBER)*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/vaccines-blood-biologics/development-approval-process-cber/investigational-new-drug-ind-or-device-exemption-ide-process-cber> (last visited Nov. 16, 2020) (“An Investigational New Drug Application (IND) is a request for authorization from the Food and Drug Administration (FDA) to administer an investigational drug or biological product to humans. Such authorization must be secured prior to interstate shipment and administration of any new drug or biological product . . .”).

46. See *Biologics License Applications (BLA) Process (CBER)*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/vaccines-blood-biologics/development-approval-process-cber/biologics-license-applications-bla-process-cber> (last visited Nov. 16, 2020) (“The Biologics License Application (BLA) is a request for permission to introduce, or deliver for introduction, a biologic product into interstate commerce.”).

47. See 42 U.S.C. § 262(a) (2021) (prohibiting introduction of biologics into interstate commerce without an approved BLA).

48. 21 U.S.C. § 360bbb-3 (2021).

49. National Defense Authorization Act for Fiscal Year 2004, Pub. L. No. 108-136, § 1603, 117 Stat. 1392, 1684 (2003) (prior to 2004 amendment).

50. National Defense Authorization Act for Fiscal Year 2004 § 1603; see H.R. REP. NO. 108-354, at 782 (2003) (Conf. Rep.) (discussing a rejected senate amendment that would “authorize the President to waive the right of service members to refuse administration of a product . . .” under EUA); H.R. REP. NO. 108-106, pt. 1, at 361 (2003) (“The conditions under which the countermeasures could be used are identical to those current in effect under section 731(a) of the Strom Thurmond National Defense Authorization Act for Fiscal year 1999 for the use of investigational new drugs.”); see also Strom Thurmond National Defense Authorization Act for Fiscal Year 1999, Pub. L. No. 105-261 § 731(a), 112 Stat. 1920, 2070–71 (establishing a “Process for Waiving Informed Consent Requirement for Administration of Certain Drugs to Members of Armed Forces for Purposes of a Particular Military Operation”).

condition that may be attributable to such agent or agents.”⁵¹ The Pandemic and All-Hazards Preparedness Reauthorization Act of 2013 added the possibility of an authorization in the event of “a significant potential for a public health emergency” as previously defined.⁵² More minor changes followed in 2016⁵³ and 2017.⁵⁴ The EUA process emerged in the shadow of terrorism;⁵⁵ an early case even endorsed the EUA process permitting administration of an anthrax vaccine “on a voluntary basis, pursuant to the terms of a lawful [EUA]”⁵⁶

D. THE EMERGENCY USE AUTHORIZATION PROCESS AS CODIFIED IN 21 U.S.C. § 360BBB-3

The current version of the EUA process⁵⁷ is reliant on the formal declaration of an emergency made by the Secretary of Health and Human Services (HHS).⁵⁸ In some instances, the dec-

51. Project Bioshield Act of 2004, Pub. L. No. 108-276, § 4, 118 Stat. 835, 854 (2004) (prior to 2013 amendment).

52. The Pandemic and All-Hazards Preparedness Reauthorization Act of 2013, Pub. L. No. 113-5 § 302, 127 Stat. 161, 180 (2013) (prior to 2016 amendments).

53. See 21st Century Cures Act of 2016, Pub. L. No. 114-255 § 3088, 130 Stat. 1033, 1148–49 (2016) (“Clarifying Food and Drug Administration emergency use authorization”) (prior to 2017 amendments).

54. See Pub. L. No. 115-92, 131 Stat. 2023, 2023–25 (2017) (“authoriz[ing] additional emergency uses for medical products to reduce deaths and severity of injuries caused by agents of war . . .”).

55. See Matthew W. McCarthy et al., *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/> (“[E]mergency use authorization . . . was actually designed for counterterrorism measures to address chemical, biological, radiological, and nuclear hazards—not necessarily a pandemic.”).

56. *Doe v. Rumsfeld*, No. 03-707 (EGS), 2005 U.S. Dist. LEXIS 5573, at *3 (D.D.C. Apr. 6, 2005).

57. See *generally Summary of Process for EUA Issuance*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/summary-process-eua-issuance> (last visited Nov. 16, 2020) (summarizing the EUA process).

58. See 21 U.S.C. § 360bbb-3(b) (2021) (describing the process by which a “[d]eclaration of emergency or threat justifying emergency authorized use” is made). This authority has been delegated to the FDA Commissioner. See FOOD AND DRUG ADMIN., SMG 1410.10, FDA STAFF MANUAL GUIDES, VOLUME II – DELEGATIONS OF AUTHORITY (2016), <https://www.fda.gov/media/81983/download> (delegating EUA authority from Secretary of HHS to FDA Commissioner); see also FOOD AND DRUG ADMIN., OMB Control No. 0910-0595, EMERGENCY USE AUTHORIZATION OF MEDICAL PRODUCTS AND RELATED AUTHORITIES:

laration may be made based on an initial determination by either the Secretary of Homeland Security⁵⁹ or Defense⁶⁰ that there is a national security-related emergency or threat. More relevant to emerging diseases, the declaration may also be based on an initial determination by the Secretary of HHS themselves “that there is a public health emergency, or a significant potential for a public health emergency . . . that involves a biological . . . agent or agents, or a disease or condition that may be attributable to such agent or agents”⁶¹ Regardless of the source of the initial determination, the Secretary of HHS must then make a subsequent formal declaration “that the circumstances exist justifying the authorization”⁶²

The FDA commissioner⁶³ is thereafter empowered to actually issue an EUA if the criteria defined by 21 U.S.C. § 360bbb-3(c) are met.⁶⁴ These criteria include firstly: that the agent in question “can cause a serious or life-threatening disease or condition”⁶⁵ Secondly, that “based on the totality of scientific

GUIDANCE FOR INDUSTRY AND OTHER STAKEHOLDERS (2017), <https://www.fda.gov/media/97321/download> (expressing FDA’s view of the legal authority undergirding EUAs).

59. See 21 U.S.C. § 360bbb-3(b)(1)(A), (D) (describing a determination by the Secretary of Homeland Security that there is a domestic emergency “involving a heightened risk of attack with a biological, chemical, radiological, or nuclear agent or agents” or that there was a material threat identified pursuant to 42 U.S.C. § 247d-6b); see also 42 U.S.C. § 247d-6b(c)(2)(A) (2021) (“The Homeland Security Secretary, in consultation with the Secretary [of HHS] and the heads of other agencies as appropriate, shall on an ongoing basis . . . assess current and emerging threats of chemical, biological, radiological, and nuclear agents; and . . . determine which of such agents present a material threat against the United States population sufficient to affect national security.”).

60. See 21 U.S.C. § 360bbb-3(b)(1)(B) (describing a determination by the Secretary of Defense “that there is a military emergency . . . involving a heightened risk . . . of attack with . . . a biological, chemical, radiological, or nuclear agent or agents . . .”).

61. 21 U.S.C. § 360bbb-3(b)(1)(C). The 2004 version of the law referenced 42 U.S.C. § 247d for this public health emergency declaration, but this reference was removed when the law was amended in 2013. See Project Bioshield Act of 2004, Pub. L. No. 108-276, § 4, 118 Stat. 835, 854 (2004) (prior to 2013 amendment); see also The Pandemic and All-Hazards Preparedness Reauthorization Act of 2013, Pub. L. No. 113-5 § 302, 127 Stat. 161, 180 (2013) (prior to 2016 amendments).

62. 21 U.S.C. § 360bbb-3(b)(1).

63. See FOOD AND DRUG ADMIN., SMG 1410.10, *supra* note 58 (delegating EUA authority from Secretary of HHS to FDA Commissioner).

64. 21 U.S.C. § 360bbb-3(c).

65. *Id.* at § 360bbb-3(c)(1).

evidence available to the Secretary [of HHS], including data from adequate and well-controlled clinical trials, if available, it is reasonable to believe that . . . the product may be effective in diagnosing, treating or preventing” the subject of the emergency declaration and that “the known and potential benefits of the product . . . outweigh the known and potential risks . . .” when used to treat the subject of the emergency declaration.⁶⁶ Thirdly, that “there is no adequate, approved, and available alternative to the product . . .”⁶⁷ Finally, “that such other criteria as the Secretary may by regulation prescribe are satisfied.”⁶⁸ These determinations are made “after consultation with the Assistant Secretary for Preparedness and Response, the Director of the National Institutes of Health, and the Director of the Centers for Disease Control and Prevention (to the extent feasible and appropriate given the applicable circumstances . . .).”⁶⁹

If an EUA is granted, notice must be published in the Federal Register.⁷⁰ The EUA must state “each disease or condition that the product may be used to diagnose, prevent, or treat,” the FDA commissioner’s conclusions regarding the risk benefit tradeoff, and the conclusions as to safety and efficacy including, if possible, “an assessment of the available scientific evidence.”⁷¹ The secretary is permitted to place additional “[c]onditions of [a]uthorization” upon an EUA “as the Secretary finds necessary or appropriate to protect the public health . . .”⁷² Conditions in-

66. *Id.* at § 360bbb-3(c)(2). Note that this section also allows for an EUA for a product that treats a disease or condition “caused by a product authorized under this section . . .” *Id.* at § 360bbb-3(c)(2)(A)(ii).

67. 21 U.S.C. § 360bbb-3(c)(3).

68. *Id.* at § 360bbb-3(c)(5). There is one additional criteria that only applies when the determination leading to the formal declaration comes from subsection (b)(1)(B)(ii); in that case, the request for emergency use can only be made by the Secretary of Defense. *Id.* at § 360bbb-3(c)(4); *see id.* at § 360bbb-3(b)(1)(B)(ii) (describing a determination by the Secretary of Defense “that there is a military emergency . . . involving a heightened risk of attack with . . . an agent or agents that may cause, or are otherwise associated with, an imminently life-threatening and specific risk to the United States military forces.”).

69. 21 U.S.C. § 360bbb-3(c).

70. *See id.* at § 360bbb-3(h)(1) (“The Secretary shall promptly publish in the Federal Register a notice of each authorization, and each termination or revocation of an authorization under this section, and an explanation of the reasons therefor . . .”).

71. *Id.* at § 360bbb-3(d).

72. *Id.* at § 360bbb-3(e).

clude informed use assurance, reporting obligations, and distribution restrictions.⁷³ The EUA lasts until either it is revoked,⁷⁴ or the HHS secretary's declaration is terminated.⁷⁵ The FDA has broad discretion to revoke an EUA.⁷⁶ Finally, agency action on EUAs is exempt from normal Administrative Procedure Act (APA) review.⁷⁷

E. THE EMERGENCY USE AUTHORIZATION PROCESS IN PRACTICE

On February 4, 2020, the Secretary of HHS simultaneously made the initial declaration of a public health emergency in response to SARS-CoV-2⁷⁸ and secondary declaration that “circumstances exist justifying the authorization of emergency use of in vitro diagnostics.”⁷⁹ Additional secondary declarations followed: “personal respiratory protective devices” on March 2, 2020,⁸⁰

73. *Id.*

74. *Id.* at § 360bbb-3(g).

75. *Id.* at § 360bbb-3(f).

76. *Id.* at § 360bbb-3(g)(2) (“The Secretary may revise or revoke if . . . [among other reasons] other circumstances make such revision or revocation appropriate to protect the public health or safety.”).

77. *See* 21 U.S.C. § 360bbb-3(i) (“Actions under the authority of [§ 360bbb-3] by the Secretary, by the Secretary of Defense, or by the Secretary of Homeland Security are committed to agency discretion.”); *see also* Association of Am. Physicians & Surgeons v. United States FDA, No. 20-1784, 2020 U.S. App. LEXIS 30622, at *8 (6th Cir. Sep. 24, 2020) (“[E]mergency-use authorizations are exempt from review under the APA.”). This means the agency action is reviewed under the highly deferential “abuse of discretion” standard. *See generally* John C. Moore, *Judicial Review Under the APA of “Agency Action Committed to Agency Discretion by Law”*, 29 WASH. & LEE L. REV. 360, 360–72 (1972) (reviewing the procedural implications of Congress choosing to exempt agency action from APA review).

78. *See* Determination of Public Health Emergency, 85 Fed. Reg. 7316 (“[T]here is a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad and that involves a novel (new) coronavirus (nCoV) first detected in Wuhan City, Hubei Province, China in 2019 (2019-nCoV).”).

79. *Id.* (“[O]n the basis of my determination of a public health emergency . . . that involves the novel (new) coronavirus (2019-nCoV) . . . circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of the novel coronavirus (2019-nCoV) . . .”).

80. *See* Emergency Use Declaration, 85 Fed. Reg. 13907 (“[O]n the basis of my determination of a public health emergency . . . that involves the novel (new) coronavirus . . . circumstances exist justifying the authorization of emergency use of personal respiratory protective devices during the COVID-19 outbreak . . .”).

“medical devices” on March 24, 2020,⁸¹ and “drugs and biological products” on March 27, 2020.⁸² The FDA also issued nonbinding guidance in June⁸³ and October⁸⁴ to help vaccine manufacturers understand the scientific standards the FDA intended to employ in reviewing any potential EUA and to highlight scientific issues the FDA was particularly concerned with. The October guidance made it clear the FDA was willing to issue a vaccine EUA based on data derived from a partially completed phase III clinical trial, at the earliest.⁸⁵ The first EUA came into effect on February 4, 2020, authorizing the Center for Disease Control’s (CDC) RT-PCR diagnostic test for nucleic acids.⁸⁶ The CDC test soon become infamous for an issue with one of the reagents which impacted test results.⁸⁷

On March 19 then President Trump began advocating for the use of the drug hydroxychloroquine sulfate (commonly known as hydroxychloroquine, or HCQ) to treat COVID-19/SARS-CoV-2 infection.⁸⁸ At the time, scientific evidence of the

81. See Emergency Use Authorization Declaration, 85 Fed. Reg. 17335 (“[O]n the basis of my determination of a public health emergency . . . that involves the novel (new) coronavirus, SARS-CoV-2 . . . circumstances exist justifying the authorization of emergency use of medical devices . . .”).

82. See Notice of Emergency Use Authorization Declaration, 85 Fed. Reg. 18250 (“[O]n the basis of my determination of a public health emergency . . . that involves the novel (new) coronavirus . . . circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic . . .”).

83. See JUNE FDA GUIDANCE, *supra* note 2 (expressing the FDA’s vaccine EUA guidance position in June 2020).

84. See OCTOBER FDA GUIDANCE, *supra* note 2 (expressing the FDA’s vaccine EUA guidance position in October 2020).

85. *Id.* (“FDA acknowledges the potential to request an EUA for a COVID-19 vaccine based on an interim analysis of a clinical endpoint from a Phase 3 efficacy study.”).

86. See U.S. FOOD & DRUG ADMIN., LETTER AUTHORIZING EMERGENCY USE OF 2019-nCoV RT-PCR (Mar. 15, 2020) (reissuing the original Feb. 4, 2020 authorization with amendments).

87. See Jon Cohen, *The United States Badly Bungled Coronavirus Testing—But Things May Soon Improve*, SCIENCE (Feb. 28, 2020, 5:45 PM), <https://www.sciencemag.org/news/2020/02/united-states-badly-bungled-coronavirus-testing-things-may-soon-improve> (“CDC finally started to send kits to state and local health labs on 5 February. But on 12 February, it revealed that several labs had difficulty validating the test because of a problem with one of the reagents.”).

88. See Libby Cathey, *Timeline: Tracking Trump Alongside Scientific Developments on Hydroxychloroquine*, ABC NEWS (Aug. 8, 2020 7:12 AM), <https://abcnews.go.com/Health/timeline-tracking-trump-alongside-scientific->

safety and efficacy of HCQ and chloroquine phosphate (commonly known as chloroquine or CQ) was limited to an unblinded clinical trial⁸⁹ and in vitro studies.⁹⁰ An EUA issued on March 28, 2020 for CQ and HCQ.⁹¹ The CDC reported an approximately 1.85 fold increase in prescription dispensation of HCQ and CQ immediately following the EUA.⁹² The events surrounding this EUA received widespread media coverage, a media landscape review found that “stories discussing President Donald Trump and hydroxychloroquine are more numerous than all stories combined that cover companies and individual researchers working on COVID-19 vaccines.”⁹³ The decision to issue an EUA was criticized by former FDA executives⁹⁴ and the head of Biomedical

developments-hydroxychloroquine/story?id=72170553 (establishing a timeline of President Trump’s advocacy for HCQ).

89. See Philippe Gautret et al., *Hydroxychloroquine and Azithromycin as a Treatment of COVID-19: Results of an Open-Label Non-Randomized Clinical Trial*, 56 INT. J. ANTIMICROBIAL AGENTS, 2020, at 1 (“COVID-19 patients were included in a single arm protocol from early March to March 16th, to receive 600mg of hydroxychloroquine daily and their viral load in nasopharyngeal swabs was tested daily in a hospital setting Twenty cases were treated in this study and showed a significant reduction of the viral carriage at D6-post inclusion compared to controls . . .”).

90. See Xueting Yao et al., *In Vitro Antiviral Activity and Projection of Optimized Dosing Design of Hydroxychloroquine for the Treatment of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)*, 71 CLINICAL INFECTIOUS DISEASES 732, 732 (2020) (“The pharmacological activity of chloroquine and hydroxychloroquine was tested using SARS-CoV-2–infected Vero cells.”); see also Manli Wang et al., *Remdesivir and Chloroquine Effectively Inhibit the Recently Emerged Novel Coronavirus (2019-nCoV) in Vitro*, 30 CELL RESEARCH 269, 270 (2020) (“Vero E6 cells were infected with 2019-nCoV at an MOI of 0.05 in the treatment of different doses of the indicated antivirals for 48 h.”).

91. See U.S. Food & Drug Admin., *Letter of Authorization – Chloroquine Phosphate and Hydroxychloroquine Sulfate* (2020) (authorizing emergency use of HCQ and CQ).

92. 759,186 prescriptions in March 2020 compared to 407,959 in March 2019. Lara Bull-Otterson et al., *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, 1210–15 (2020) (tracking new and continuing prescriptions of HCQ and CQ).

93. Bruce Sacerdote, Ranjan Sehgal & Molly Cook, *Why Is All Covid-19 News Bad News?* 2 (Nat’l Bureau of Econ. Research, Working Paper No. 28110, 2020), <https://www.nber.org/papers/w28110>.

94. See Charles Piller, *Former FDA Leaders Decry Emergency Authorization of Malaria Drugs for Coronavirus*, SCIENCE (Apr. 7, 2020, 6:20 PM), <https://www.sciencemag.org/news/2020/04/former-fda-leaders-decry-emergency-authorization-malaria-drugs-coronavirus> (quoting Scott Gottlieb and Margaret Hamburg discussing how the “EUA for chloroquine phosphate and

Advanced Research and Development Authority (BARDA) claimed he was demoted and later fired because he opposed HCQ on scientific grounds.⁹⁵ On April 24, 2020 the FDA issued a statement warning that HCQ could cause heart problems when used in conjunction with azithromycin, a common antibiotic.⁹⁶ The President later claimed that he himself took HCQ on May 18, 2020.⁹⁷ However, on June 15, 2020 the FDA revoked HCQ's EUA citing the failure of a recent clinical trial.⁹⁸ Despite this, the

hydroxychloroquine sulfate undermines FDA's scientific authority because it appeared to be a response not to scientific evidence, but to fervent advocacy of the drugs by Trump and other political figures . . .").

95. See Michael D. Shear & Maggie Haberman, *Health Dept. Official Says Doubts on Hydroxychloroquine Led to His Ouster*, N. Y. TIMES (May 14, 2020), <https://www.nytimes.com/2020/04/22/us/politics/trick-bright-trump-hydroxychloroquine-coronavirus.html> ("Dr. Bright . . . assailed the leadership at the health department, saying he was pressured to direct money toward hydroxychloroquine, one of several 'potentially dangerous drugs promoted by those with political connections' and repeatedly described by the president as a potential 'game changer' in the fight against the virus.").

96. See *FDA Cautions Against Use of Hydroxychloroquine or Chloroquine for COVID-19 Outside of the Hospital Setting or a Clinical Trial Due to Risk of Heart Rhythm Problems*, FDA DRUG SAFETY PODCAST (Apr. 24, 2020), <https://www.fda.gov/drugs/fda-drug-safety-podcasts/fda-cautions-against-use-hydroxychloroquine-or-chloroquine-covid-19-outside-hospital-setting-or> (last visited Nov. 17, 2020) (warning HCQ and CQ "have not been shown to be safe and effective for treating or preventing COVID-19 . . . we authorized their temporary use . . . for treatment of the virus in hospitalized patients when clinical trials are not available . . ."); see also Sarah M. Lofgren et al., *Safety of Hydroxychloroquine Among Outpatient Clinical Trial Participants for COVID-19*, 7 OPEN FORUM INFECTIOUS DISEASE, Oct. 2020, at 1 (finding in November 2020 that "[d]ata from 3 outpatient COVID-19 trials demonstrated that gastrointestinal side effects were common but mild with the use of hydroxychloroquine while serious side effects were rare. No deaths occurred related to hydroxychloroquine. Randomized clinical trials, in cohorts of healthy outpatients, can safely investigate whether hydroxychloroquine is efficacious for COVID-19.").

97. See Nikki Carvajal & Kevin Liptak, *Trump Says He is Taking Hydroxychloroquine Though Health Experts Question its Effectiveness*, CNN (May 19, 2020, 4:58 AM), <https://www.cnn.com/2020/05/18/politics/donald-trump-hydroxychloroquine-coronavirus/index.html> ("A couple of weeks ago, I started taking it," Trump said. He later said he'd been taking it every day for a week and a half.").

98. See FDA, LETTER REVOKING EUA FOR CHLOROQUINE PHOSPHATE AND HYDROXYCHLOROQUINE SULFATE (June 15, 2020) ("Today's request to revoke is based on new information, including clinical trial data results, that have led BARDA to conclude that this drug may not be effective to treat COVID-19 [Coronavirus Disease 2019] and that the drug's potential benefits for such use do not outweigh its known and potential risks.") (alteration in original).

President continued to advocate for the drug, claiming the revocation was political.⁹⁹ Later studies published in the fall of 2020 confirmed that short term use of HCQ was safe, but long term use or use in conjunction with azithromycin could lead to heart issues.¹⁰⁰

The antiviral drug remdesivir was issued EUA on May 1, 2020.¹⁰¹ Despite scientific controversy about its efficacy in a subset of patients,¹⁰² remdesivir received full FDA approval on October 22, 2020.¹⁰³ Actual approval of remdesivir was subject to

99. See Cathey, *supra* note 88 (“Hydroxy has tremendous support, but politically it is toxic, because I supported it. If I would have said, “Do not use hydroxychloroquine under any circumstances,” they would have come out and they would have said it’s a great thing,’ Trump tells White House reporters.”).

100. See Jennifer C E Lane et al., Risk of Hydroxychloroquine Alone and in Combination With Azithromycin in the Treatment of Rheumatoid Arthritis: A Multinational, Retrospective Study, 2 LANCET RHEUMATOL, 698, 698 (2020) (“No excess risk of severe adverse events was identified when 30-day hydroxychloroquine and sulfasalazine use were compared. Self controlled case series confirmed these findings. However, long-term use of hydroxychloroquine appeared to be associated with increased cardiovascular mortality (calibrated HR 1.65 [95% CI 1.12–2.44]). Addition of azithromycin appeared to be associated with an increased risk of 30-day cardiovascular mortality (calibrated HR 2.19 [95% CI 1.22–3.95]), chest pain or angina (1.15 [1.05–1.26]), and heart failure (1.22 [1.02–1.45]).”); see also Lofgren et al., *supra* note 96, at 1 (“Data from 3 outpatient COVID-19 trials demonstrated that gastrointestinal side effects were common but mild with the use of hydroxychloroquine, while serious side effects were rare. No deaths occurred related to hydroxychloroquine. Randomized clinical trials, in cohorts of healthy outpatients, can safely investigate whether hydroxychloroquine is efficacious for COVID-19.”).

101. See U.S. FOOD & DRUG ADMIN., VEKLURY (REMDESIVIR) EUA LETTER OF APPROVAL (2020) (reissuing EUA for remdesivir, which originally issued on May 1, 2020).

102. See Pauline Vetter et al., *Dexamethasone and Remdesivir: Finding Method in the COVID-19 Madness*, THE LANCET MICROBE 309 (2020) (“Although remdesivir was shown to have an effect in shortening time to hospital discharge in patients with severe pneumonia, data are conflicting in patients without hypoxaemia.”) (citations omitted).

103. See FDA Approves First Treatment for COVID-19, U.S. FOOD & DRUG ADMIN. (Oct. 22, 2020), <https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-covid-19> (“Today, the U.S. Food and Drug Administration approved the antiviral drug Veklury (remdesivir) for use in adult and pediatric patients 12 years of age and older and weighing at least 40 kilograms (about 88 pounds) for the treatment of COVID-19 requiring hospitalization.”) (last visited Nov. 17, 2020).

further controversy because the sponsor, Gilead, received a priority review voucher,¹⁰⁴ a valuable, transferrable incentive worth a considerable sum on the private market.¹⁰⁵

Finally, in September 2020, the President suggested that a vaccine might be available prior to the 2020 Presidential election.¹⁰⁶ Scientists associated with the administration downplayed this statement¹⁰⁷ and no vaccine received authorization before the election.¹⁰⁸ In response to fears that an unsafe vaccine would be approved for political reasons, a number of states formed expert panels to review safety and efficacy data prior to distributing any vaccine.¹⁰⁹ Polling across the United States re-

104. See *id.* (“The Agency also granted this application a Material Threat Medical Countermeasure Priority Review Voucher, which provides additional incentives for certain medical products intended to treat or prevent harm from specific chemical, biological, radiological and nuclear threats.”).

105. See Zachary Brennan, *FDA Approves remdesivir as First Coronavirus Drug*, POLITICO (Oct. 22, 2020, 5:18 PM), <https://www.politico.com/news/2020/10/22/fda-approves-remdesivir-coronavirus-431336> (“The voucher is potentially worth about \$100 million.”).

106. See Charles Schmidt, *Don't Expect a COVID Vaccine Before the Election*, SCIENTIFIC AMERICAN (Oct. 16, 2020), <https://www.scientificamerican.com/article/dont-expect-a-covid-vaccine-before-the-election/> (“We’re going to have a vaccine very soon,’ Trump said. ‘Maybe even before a very special day—you know what day I’m talking about.’”).

107. See Berkeley Lovelace Jr., *Fauci Says a Coronavirus Vaccine Is ‘Unlikely’ by U.S. Election*, CNBC (Sept. 8, 2020, 2:53 PM), <https://www.cnbc.com/2020/09/08/coronavirus-vaccine-dr-fauci-says-its-unlikely-it-will-be-ready-by-us-election.html> (“Fauci said it’s more likely a vaccine will be ready by ‘the end of the year’”).

108. See *FDA Takes Key Action in Fight Against COVID-19 By Issuing Emergency Use Authorization for First COVID-19 Vaccine*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/news-events/press-announcements/fda-takes-key-action-fight-against-covid-19-issuing-emergency-use-authorization-first-covid-19> (last updated Dec. 12, 2020) (“For Immediate Release: December 11, 2020 Today, the U.S. Food and Drug Administration issued the first emergency use authorization (EUA) for a vaccine for the prevention of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. The emergency use authorization allows the Pfizer-BioNTech COVID-19 Vaccine to be distributed in the U.S.”).

109. See, e.g., Berkeley Lovelace Jr. & Noah Higgins-Dunn, *Trump Says Coronavirus Vaccine Won't Be Delivered to New York Right Away*, CNBC (Nov. 13, 2020 4:31 PM), <https://www.cnbc.com/2020/11/13/trump-says-coronavirus-vaccine-wont-be-delivered-to-new-york.html> (“The governor [of New York] said the state would independently review the vaccines after many questioned whether the White House was attempting to rush the approval process ahead of Election Day for political reasons.”).

flected acute concern about the vaccine with only 51% of Americans saying they “definitely” or “probably” “would get the vaccine” in September 2020 following the administration’s statements, a sharp decline from 72% indicating intention to get a hypothetical vaccine in May 2020.¹¹⁰ By December 2020 poll numbers had recovered with 71% indicating they would “definitely or probably get a vaccine.”¹¹¹ In September, nine vaccine manufacturers took the unusual step of pledging to “make the safety and well-being of vaccinated individuals our top priority” and that they would “[o]nly submit for approval or emergency use authorization after demonstrating safety and efficacy through a Phase 3 clinical study that is designed and conducted to meet requirements of expert regulatory authorities such as FDA.”¹¹² In October, the Government Accountability Office accepted a request from a handful of United States Senators to “review whether the CDC and FDA’s scientific integrity and communications policies have been violated and whether those policies are being implemented as intended to assure scientific integrity throughout the agency.”¹¹³ Finally, in December, things came to a head when the President threatened to fire the

110. See Alec Tyson, Courtney Johnson & Cary Funk, *U.S. Public Now Divided Over Whether To Get COVID-19 Vaccine*, PEW RES. CTR. (Sept. 17, 2020), <https://www.pewresearch.org/science/2020/09/17/u-s-public-now-divided-over-whether-to-get-covid-19-vaccine/> (showing a decline in individuals who said they would get the vaccine from May to September 2020); see also Shannon Mullen O’Keefe, *One in Three Americans Would Not Get COVID-19 Vaccine*, GALLUP (Aug. 7, 2020), <https://news.gallup.com/poll/317018/one-three-americans-not-covid-vaccine.aspx> (“35% of Americans would not get free, FDA-approved vaccine if ready today”). See generally Tara C Smith, *Vaccine Rejection and Hesitancy: A Review and Call to Action*, 4 OPEN FORUM INFECT. DIS. (Jul. 18, 2017), <https://pubmed.ncbi.nlm.nih.gov/28948177> (reviewing factors contributing to vaccine hesitancy prior to SARS-CoV-2).

111. See Liz Hamel, Ashley Kirzinger, Cailey Muñana & Mollyann Brodie, *KFF COVID-19 Vaccine Monitor: December 2020*, KAISER FAM. FOUND. (Dec. 15, 2020), <https://www.kff.org/coronavirus-covid-19/report/kff-covid-19-vaccine-monitor-december-2020/> (“a new KFF survey finds an increase in the share of the public saying they would definitely or probably get a vaccine for COVID-19 if it was determined to be safe by scientists and available for free to everyone who wanted it. This share now stands at 71%, up from 63% in a September survey . . .”).

112. *Biopharma Leaders Unite to Stand With Science*, BUS. WIRE (Sept. 8, 2020 6:30 AM), <https://www.businesswire.com/news/home/20200908005498/en/>.

113. Letter from Gov’t Accountability Off. to Elizabeth Warren, U.S. Senator (Oct. 16, 2020), <https://www.warren.senate.gov/imo/media/doc/21-0015%20Warren.pdf>.

head of the FDA if Pfizer's vaccine did not receive an EUA by the end of the day.¹¹⁴ The Pfizer vaccine received an EUA the same day as these threats.¹¹⁵ A vaccine made by Moderna received an EUA a week later.¹¹⁶

The FDA began working with regulated entities early in the pandemic, issuing guidance documents in June and October indicating what kinds of clinical trials the FDA expected to see in order to grant an EUA.¹¹⁷ In these guidance documents, the FDA "acknowledge[d] the potential to request an EUA for a COVID-19 vaccine based on an interim analysis of a clinical endpoint from a Phase 3 efficacy study."¹¹⁸ Such interim analyses were submitted to the FDA¹¹⁹ and included data supporting both

114. See Jonathan Lemire, Darlene Superville & Matthew Perrone, *White House Threatens FDA Chief's Job Over Vaccine Approval*, ASSOCIATED PRESS (Dec. 11, 2020), <https://apnews.com/article/donald-trump-business-mark-meadows-coronavirus-pandemic-0902fbb041b0459e55da86be75b1457a> ("Hours before the Food and Drug Administration authorized the first COVID-19 vaccine late Friday, a high-ranking White House official told the agency's chief he could face firing if the vaccine was not cleared by day's end, two administration officials said.").

115. See COVID-19 Vaccine EUA Letter of Authorization Letter from Food & Drug Admin. to Pfizer (Dec. 23, 2020), <https://www.fda.gov/media/144412/download> (reissuing EUA for Pfizer vaccine first issued on December 11, 2020).

116. See COVID-19 Vaccine EUA Letter of Authorization Letter from Food & Drug Admin. to Moderna (Dec. 18, 2020), <https://www.fda.gov/media/144636/download> (authorizing emergency use of Moderna vaccine).

117. See JUNE FDA GUIDANCE, *supra* note 2, at 1–19 (laying out the FDA's expectations for preclinical data and clinical trial design); see also OCTOBER FDA GUIDANCE, *supra* note 2, at 1–11 (providing more specifics on data expected to obtain an EUA, logistical considerations, and information on the VRBPAC).

118. October FDA Guidance, *supra* note 2, at 9.

119. See FDA, Pfizer-Biontech Covid-19 Vaccine (Bnt162, Pf-07302048) Vaccines And Related Biological Products Advisory Committee Briefing Document (Dec. 10, 2020), <https://www.fda.gov/media/144246/download> [hereinafter Pfizer-Biontech Briefing] (containing Pfizer's submission to the FDA advisory committee presenting clinical trial results); see also FDA, FDA Briefing Document Moderna COVID-19 Vaccine (Dec. 17, 2020), <https://www.fda.gov/media/144434/download> [hereinafter Moderna Briefing] (containing Moderna's submission to the FDA advisory committee presenting clinical trial results).

safety and efficacy for Pfizer¹²⁰ and Moderna¹²¹ vaccines. The FDA also stated it intended to consult with the Vaccines and Related Biological Products Advisory Committee (VRBPAC)¹²² to

120. See PFIZER-BIONTECH BRIEFING, *supra* note 119, at 53 (“Based on Phase 3 data from approximately 38,000 participants with a median of 2 months of follow-up after Dose 2 in Study C4591001, BNT162b2 at 30 µg was safe and well-tolerated in participants ≥16 years of age. Reactogenicity and AEs were generally milder and less frequent in participants in the older group (≥56 years of age) compared with the younger group (≤55 years of age). Reactogenicity was mostly mild to moderate and short-lived after dosing for both adult age groups and for younger adolescents 12 to 15 years of age (whose preliminary data provide support to ≥16 years of age indication), and the AE profile did not suggest any serious safety concerns. The incidence of SAEs and deaths were low in the context of the number of participants enrolled and comparable for BNT162b2 and placebo. The incidence of discontinuations due to AEs was also generally low and similar between BNT162b2 and placebo groups. This profile was consistent for the subset of approximately 19,000 participants who had at least 2 months of follow-up after Dose 2.”); *id.* at 54 (“VE [efficacy] of BNT162b2 was 95.5% with a 99.99% posterior probability for the true VE being >30% conditioning on available data, to overwhelmingly meet the prespecified interim analysis success criterion (>99.5%). The 95% credible interval for the VE was 88.8% to 98.4%, indicating that given these observed data there was a 95% probability that the true VE lies in this interval. Also, note that the posterior probability that true VE >86.0% is 99.5% and VE >88.8% is 97.5%.”). See generally Fernando P. Polack et al., *Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine*, 383 N. ENG. J. MED. 2603, 2603–2615 (2020), <https://doi.org/10.1056/NEJMoa2034577> (reviewing Pfizer clinical trial data in a publication).

121. See MODERNA BRIEFING, *supra* note 119, at 50 (“The vaccine elicited increased local and systemic adverse reactions as compared to those in the placebo arm, usually lasting a few days. The most common solicited adverse reactions were pain at injection site (91.6%), fatigue (68.5%), headache (63.0%), muscle pain (59.6%), joint pain (44.8%), and chills (43.4%). Adverse reactions characterized as reactogenicity were generally mild to moderate; 0.2% to 9.7% of these events were reported as severe, with severe solicited adverse reactions being more frequent after dose 2 than after dose 1 and generally less frequent in older adults (≥65 years of age) as compared to younger participants Serious adverse events, while uncommon (1.0% in both treatment groups), represented medical events that occur in the general population at similar frequency as observed in the study.”); *id.* at 23 (“[I]n participants ≥18 years of age, there were 5 COVID-19 cases in the vaccine group and 90 COVID-19 cases in the placebo group, with a VE of 94.5%, a lower bound of the 95% CI of 86.5%, and a one-sided p-value of <0.0001 for testing H0: VE ≤30%, which met the pre-specified success criterion. In participants ≥65 years of age in the Per-Protocol Set, there were no COVID-19 cases in the vaccine group and 15 COVID-19 cases in the placebo group.”).

122. *Charter of the Vaccines and Related Biological Products Advisory Committee*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/advisory-committees/vaccines-and-related-biological-products-advisory-committee/charter-vaccines-and-related-biological-products-advisory-committee> (last visited Jan. 6,

discuss safety and efficacy prior to issuing any EUA.¹²³ Prior to the issuance of either EUA, VRBPAC met and voted to advise the FDA to authorize both the Pfizer¹²⁴ and Moderna¹²⁵ vaccines after reviewing sponsor submissions.¹²⁶ A CDC advisory committee, the Advisory Committee on Immunization Practices (ACIP)¹²⁷ also reviewed available data and recommended the use of both the Pfizer¹²⁸ and Moderna¹²⁹ vaccines.

2021) (establishing the CRBPAC as a committee of independent scientific experts who “review[] and evaluate[] data concerning the safety, effectiveness, and appropriate use of vaccines and related biological products which are intended for use in the prevention, treatment, or diagnosis of human diseases, and, as required, any other products for which the (FDA) has regulatory responsibility . . .” in order to give recommendations to the FDA Commissioner).

123. See OCTOBER FDA GUIDANCE, *supra* note 2, at 11 (“FDA expects to convene an open session of FDA’s VRBPAC prior to the issuance of any EUA for a COVID-19 vaccine, to discuss whether the available safety and effectiveness data support authorization of an EUA for the specific request under review.”).

124. FDA, *Vaccines and Related Biological Products Advisory Committee*, YOUTUBE (Dec. 10, 2020), <https://youtu.be/owveMJBTC2I?t=31168> (voting 17-4-1 to authorize the Pfizer vaccine for those sixteen and older and discussing concerns whether there was sufficient data to authorize for those under age eighteen).

125. FDA, *Vaccines and Related Biological Products Advisory Committee*, YouTube (Dec. 17, 2020), <https://youtu.be/l4psAfbUtCO?t=29075> (voting 20-0-1 to authorize the Moderna vaccine for those eighteen and older).

126. See PFIZER-BIONTECH BRIEFING, *supra* note 119; see also MODERNA BRIEFING, *supra* note 119.

127. See *ACIP Charter*, CENTERS FOR DISEASE CONTROL AND PREVENTION, <https://www.cdc.gov/vaccines/acip/committee/charter.html> (last visited Jan. 6, 2021) (“The ACIP shall provide advice and guidance to the Director of the CDC regarding use of vaccines and related agents for effective control of vaccine-preventable diseases in the civilian population of the United States. Recommendations made by the ACIP are reviewed by the CDC Director, and if adopted, are published as official CDC/HHS recommendations in the Morbidity and Mortality Weekly Report (MMWR).”).

128. See Sara E. Oliver et al., U.S. Ctrs. for Disease Control & Prevention, *The Advisory Committee on Immunization Practices’ Interim Recommendation for Use of Pfizer-BioNTech COVID-19 Vaccine — United States*, December 2020, 69 *Morbidity & Mortality Wkly. Rep.*, 1922, 1922–1924 (2020) <http://dx.doi.org/10.15585/mmwr.mm6950e2> (“On December 12, 2020, after an explicit, evidence-based review of all available data, the Advisory Committee on Immunization Practices (ACIP) issued an interim recommendation for use of the Pfizer-BioNTech COVID-19 vaccine in persons aged ≥16 years for the prevention of COVID-19.”).

129. See Sara E. Oliver et al., U.S. Ctrs. for Disease Control & Prevention, *The Advisory Committee on Immunization Practices’ Interim Recommendation for Use of Moderna COVID-19 Vaccine — United States*, December 2020, 69 *Morbidity & Mortality Wkly. Rep.*, 1653, 1653–1656 (2021) <http://dx.doi.org/10.15585/mmwr.mm695152e1> (“On December 19, 2020, after a

Underserved communities have expressed concerns that they may be used as test subjects for a vaccine not yet proven safe.¹³⁰ Commentators have begun to ring alarm bells: “[w]ithout a clear, transparent, and scientifically sound decision-making process, the trust the FDA has built and maintained over the past century is eroding.”¹³¹ Scientists and the public at large expressed concern that a vaccine would be approved for political, rather than scientific reasons.¹³² The perception that a SARS-CoV-2 vaccine was approved for political reasons might increase vaccine hesitancy for the instant vaccine,¹³³ but also for vaccines

transparent, evidence-based review of available data, the Advisory Committee on Immunization Practices (ACIP) issued an interim recommendation for use of the Moderna COVID-19 vaccine in persons aged ≥ 18 years for the prevention of COVID-19.”).

130. See Laurel Wamsley, *Researchers Find Doubts About COVID-19 Vaccine Among People of Color*, NPR (Oct. 22, 2020 5:07 PM), <https://www.npr.org/sections/coronavirus-live-updates/2020/10/22/926813331/researchers-find-doubts-about-covid-19-vaccine-among-people-of-color> (“Participants [in listening sessions] also expressed fears based on past experiences. One person expressed a worry that ‘this is another Tuskegee experiment.’”).

131. Baden et al., *supra* note 1; see also Thomson & Nachlis, *supra* note 1, at 1282 (“[P]roblems include the authorization of potentially ineffective or unsafe therapeutics, the appearance of nonexpert political advocacy generating public pressure for product authorizations with questionable safety and efficacy, and the imposition of significant costs on the health of the public and on the credibility and influence of . . . FDA.”).

132. See Smriti Mallapaty & Heidi Ledford, *COVID-Vaccine Results Are on the Way — and Scientists’ Concerns Are Growing*, 586 NATURE, 16, 16–17 (2020), <https://doi.org/10.1038/d41586-020-02706-6> (“Researchers warn that vaccines could stumble on safety trials, be fast-tracked because of politics or fail to meet the public’s expectations.”); see also Jan Hoffman, *Mistrust of a Coronavirus Vaccine Could Imperil Widespread Immunity*, N.Y. TIMES (July 18, 2020), <https://www.nytimes.com/2020/07/18/health/coronavirus-anti-vaccine.html> (“Billions are being poured into developing a shot, but the rapid timetable and President Trump’s cheerleading are creating a whole new group of vaccine-hesitant patients.”); Albert Ko & Jeffrey Sonnenfeld, *Amid Vaccine Trials, the FDA is on Trial Itself*, FORTUNE (Sept. 24, 2020 3:01 PM), <https://fortune.com/2020/09/24/fda-covid-vaccine-trump-meddling/> (“[O]ur country’s core health institutions have suffered repeated controversies, reversals, and misinterpretation of evidence, which, in turn, have eroded the public’s confidence.”). But see Scott Gottlieb & Mark McClellan, *You Can Trust the FDA’s Vaccine Process*, WALL ST. J. (Sept. 20, 2020 4:22 PM), <https://www.wsj.com/articles/you-can-trust-the-fdas-vaccine-process-11600633351> (“We reject the claim that a vaccine EUA inherently falls short of FDA’s gold standard review, or that the process will be hijacked.”).

133. Cf. Roy M. Anderson et al., *Challenges in Creating Herd Immunity to SARS-CoV-2 Infection by Mass Vaccination*, 396 LANCET 1614, 1614–1616

more broadly.¹³⁴ Some have suggested that the FDA should be disentangled from the political thicket by making it an independent agency.¹³⁵ Others have argued the FDA should avoid the EUA process entirely in the context of SARS-CoV-2 to preserve intuitional credibility and ensure the vaccines are fully vetted.¹³⁶

The events of the COVID-19 crisis demonstrate how ill-suited the current EUA structure is at responding to emerging diseases in the modern era. The EUA process is reliant on executive branch norms that have already been broken.¹³⁷ In the context of vaccines for emerging disease, a lack of trust in the FDA

(2020), [https://doi.org/10.1016/S0140-6736\(20\)32318-7](https://doi.org/10.1016/S0140-6736(20)32318-7) (“Given vaccine hesitancy, the creation of herd immunity by vaccination is likely to be challenging in many countries.”); see also Patrick Peretti-Watel et al., *A Future Vaccination Campaign Against COVID-19 at Risk of Vaccine Hesitancy and Politicisation*, 20 LANCET INFECT. DIS. 769, 769–770 (2020), [https://doi.org/10.1016/S1473-3099\(20\)30426-6](https://doi.org/10.1016/S1473-3099(20)30426-6) (arguing that politics becoming intertwined with vaccination reduces vaccination rates).

134. See Brit Trogen, David Oshinsky & Arthur Caplan, *Adverse Consequences of Rushing a SARS-CoV-2 Vaccine: Implications for Public Trust*, 323 JAMA 2460, 2461 (2020), <https://doi.org/10.1001/jama.2020.8917> (“Failing to abide by standards of safety and scientific rigor during the COVID-19 crisis will fuel the argument that physicians and scientists cannot be trusted. Vaccination rates, which are declining due to widespread concern about visiting clinicians’ offices, could further decrease. The US could see resurgences of many vaccine-preventable illnesses, and inevitably, massive increases in avoidable deaths and irreversible outcomes.”).

135. See Dorit Rubinstein Reiss, *Is It Time for the FDA to Be Independent?*, STAT (Nov. 3, 2020), <https://www.statnews.com/2020/11/03/should-fda-be-independent/> (“To create an FDA independent of the HHS secretary, the public’s representatives in Congress—and the president—need to change the governance of the FDA. As a first step, the laws governing the FDA’s authorization of drugs and vaccines could be changed to make the FDA commissioner the decision maker, rather than the HHS secretary. Congress could also add more specific criteria for issuing an emergency use authorization for a vaccine or drug—criteria already exist for approval of both drugs (which must be ‘safe and effective’) and vaccines (which must be ‘safe, pure, potent and effective’).”).

136. See Matthew W. McCarthy et al., *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/> (arguing “an emergency use authorization for Covid-19 vaccines at this stage of development would not require careful reporting of adverse events and could potentially undermine ongoing and future clinical trials that are still necessary to determine safety and efficacy” among other concerns).

137. The Trump presidency put a glaring spotlight on outsized political influence in decisions of great national importance, but this is not a modern phenomenon. The historian Rick Atkinson argues that in July 1942 President Roosevelt pressured his generals to bring “U.S. ground troops . . . into action

threatens to fundamentally undermine the FDA's public health mandate. Congress and the FDA need to formalize the emerging infectious disease vaccine EUA process to more accurately reflect the regulatory reality, but also to restore public trust in the agency and future vaccines.

III. ANALYSIS

A. THE EVENTS SURROUNDING HCQ DEMONSTRATE THE FAILURE OF THE EUA PROCESS

The EUA issued for chloroquine phosphate (CQ) and hydroxychloroquine sulfate (HCQ)¹³⁸ and subsequent revocation¹³⁹ were marred by scandal with the unproven therapies being initially touted as a cure by the President on Twitter¹⁴⁰ followed by apparent direct interference in the regulatory process.¹⁴¹ It is critical to note that the HCQ and CQ EUA met the minimal legal bar set by 21 U.S.C. § 360bbb-3(c):

(1) [SARS-CoV-2] can cause a serious or life-threatening disease or condition; (2) that, based on the totality of scientific evidence available to the Secretary, including data from adequate and well-controlled clinical trials, if available, it is reasonable to believe that— (A) the product *may* be effective in diagnosing, treating, or preventing . . . [SARS-CoV-2 and] (B) the known and potential benefits of the product when used to . . . treat [SARS-CoV-2] outweigh the known and potential risks of the product . . . (3) that there is no adequate, approved, and available

against the enemy in 1942” partly in response to an upcoming midterm election in which Roosevelt expected to fare poorly. RICK ATKINSON, *AN ARMY AT DAWN: THE WAR IN NORTH AFRICA, 1942-1943* 15 (2002) (quoting Franklin D. Roosevelt). Atkinson goes on to argue that this pressure contributed to an Allied invasion of North Africa. *See id.* at 16. A president could take a less conspicuous approach to pressuring the FDA—applying the same amount of politically-motivated pressure, but in a less public manner—and such an approach arguably would have been much more damaging to public health.

138. *See* U.S. FOOD & DRUG ADMIN., *supra* note 91 (authorizing emergency use of HCQ and CQ).

139. *See* U.S. FOOD & DRUG ADMIN., *supra* note 98 (revoking emergency use of HCQ and CQ).

140. *See* Cathey, *supra* note 88 (“Trump tweets to his roughly 84 million followers that hydroxychloroquine taken with the antibiotic azithromycin could be ‘one of the biggest game changers in the history of medicine’ and should ‘be put in use immediately.’”).

141. *See* Michael D. Shear & Maggie Haberman, *supra* note 95 (describing the firing of Dr. Rick Bright who claimed to have been fired in part because he opposed the approval of HCQ and CQ).

alternative to the product for diagnosing, preventing, or treating such disease or condition¹⁴²

There is no dispute that SARS-CoV-2 “*can* cause a serious disease or condition” and there was no “adequate, approved, and available alternative” treatment.¹⁴³ After meeting these two requirements, the authorization threshold set by § 360bbb-3(c)(2) is effectively nonexistent: “the product *may* be effective in diagnosing, treating, or preventing” the disease “based on the totality of scientific evidence available to the Secretary”¹⁴⁴ In the context of an emerging infectious disease there may never be sufficient scientific evidence to make a considered approval decision, implying that an EUA could issue in light of minimal scientific evidence. That is precisely what happened with HCQ and CQ; the available evidence was a low-power, unblinded preliminary clinical trial¹⁴⁵ and in vitro experiments.¹⁴⁶

142. 21 U.S.C. § 360bbb-3(c) (emphasis added); *see also* U.S. FOOD & DRUG ADMIN., *supra* note 91 at 3.

143. 21 U.S.C. § 360bbb-3(c) (emphasis added).

144. *Id.* (emphasis added).

145. *See* Gautret et al., *supra* note 89 (reporting an “open-label non-randomized clinical trial” with 20 total cases of SARS-CoV-2 infection).

146. *See* Yao et al., *supra* note 90 at 732 (measuring the pharmacokinetics of HCQ and CQ in SARS-CoV-2 infected vero cells); *see also* Wang et al., *supra* note 90, at 270 (measuring viral replication in vero cells treated with CQ). Ironically as scientific understanding of the mechanism of HCQ in inhibiting SARS-CoV-2 replication in vitro progressed it became clear that HCQ might actually inhibit viral entry into host cells if combined with another drug, Camostat. Tianling Ou et al., *Hydroxychloroquine-Mediated Inhibition of SARS-CoV-2 Entry Is Attenuated by TMPRSS2*, 17 PLOS PATHOG. e1009212, 3 (2021) (showing that SARS-CoV-2 entry can be mediated by two distinct proteins; HCQ inhibits only one of these proteins but the other can be inhibited by the drug Camostat). This research implied that HCQ may have had potential as a SARS-CoV-2 therapy if used in conjunction with Camostat. *Id.* Clinical trials were started in 2020 to test this combination therapy, but they were cancelled prior to the publication of the aforementioned research in part because the control arm used HCQ alone and it became clear that HCQ alone had no clinical benefit. *See* COMBINATION THERAPY WITH CAMOSTAT MESILATE + HYDROXYCHLOROQUINE FOR COVID-19 (CLOCC), <https://clinicaltrials.gov/ct2/show/NCT04338906> (last updated Dec. 21, 2020) (“Withdrawn (lack of public funding; planned control arm with Hydroxychloroquine treatment showed out as not being standard of care anymore as time evolved.)”). *See generally* This Week in Virology, *Fauci Ouchy*, MICROBE.TV, at 3:58 (Feb. 4, 2021), <https://www.microbe.tv/twiv/twiv-715/> (reviewing and synthesizing this research on a hypothetical combination HCQ Camostat therapy). If the authorization of HCQ had not been so rushed perhaps there would have been time for the scientific understanding of its mechanism of action to mature to the point where it could have been used as a successful therapy. However, this seems unlikely now given the political baggage associated with the drug.

The events of the HCQ EUA lead to two distinct harms. Firstly, the March EUA was followed by a substantial increase in use of HCQ,¹⁴⁷ but a safety profile was not fully established until much later in the year.¹⁴⁸ Later evidence showed HCQ was unsafe in a subset of patients,¹⁴⁹ implying that medical harm was a real possibility. Secondly, and perhaps more pernicious, is the degree to which premature statements on a drug's effectiveness have undermined public faith in the FDA as an institution. The media have rightly highlighted these breaches of norms but have done so at the expense of informing the public about other public health information, such as the safety of vaccines in development.¹⁵⁰ Flagging public trust in the FDA has compounded fears that vaccine hesitancy¹⁵¹ will slow uptake of a vaccine which is safe and effective.¹⁵² If members of the public are unwilling to get a safe and effective vaccine it will be difficult or impossible to achieve vaccine-induced herd immunity and SARS-CoV-2 will continue exacting its toll on the public.¹⁵³

147. See Bull-Ottersson et al., *supra* note 92 (tracking new and continuing prescriptions of HCQ and CQ).

148. See Lofgren et al., *supra* note 96, at 1 (finding no evidence of safety issues with short term use of HCQ).

149. Lane et al., *supra* note 100, at 1 (finding a heart risk to long term use of HCQ or short-term use of HCQ in concert with azithromycin).

150. See Sacerdote et al., *supra* note 93, at 12 (“[W]e show results for mentions of COVID-19 vaccines and any names of the top ten institutions or companies working on a COVID-19 vaccine. The U.S. major outlets ran 1,371 such stories. During the same period they ran 8,756 stories involving Trump and mask wearing and 1,636 stories about Trump and hydroxychloroquine.”).

151. See generally Smith, *supra* note 110 (reviewing factors that contribute to vaccine hesitancy).

152. See Kreps et al., *supra* note 41, at 6 (“Political attributes were also associated with vaccine choice. An FDA EUA was associated with a lower probability of choosing a vaccine (coefficient, -0.03 ; 95% CI, -0.04 to -0.01) compared with a full FDA approval Compared with an endorsement from President Trump, Centers for Disease Control and Prevention and World Health Organization endorsements were associated with higher probabilities of choosing the vaccine (coefficient, 0.09 [95% CI, 0.07 - 0.11] vs 0.06 [95% CI, 0.04 - 0.08]).”); see also Hoffman, *supra* note 132 (“A growing number of polls find so many people saying they would not get a coronavirus vaccine that its potential to shut down the pandemic could be in jeopardy. Distrust of it is particularly pronounced in African-American communities, which have been disproportionately devastated by the virus. But even many staunch supporters of immunization say they are wary of this vaccine.”).

153. See Mallory et al., *supra* note 36, at 64 (explaining the concept of vaccination induced herd immunity); see also Aschwanden, *supra* note 38, at 26–28 (reviewing estimates of the vaccination rates necessary to achieve vaccination induced herd immunity).

The hypothetical where an untested vaccine receives an EUA is not unfounded. The statutory standard for a vaccine EUA is the standard that was employed for HCQ. This implies a vaccine EUA could theoretically have issued supported by comparably minimal scientific evidence. The only thing preventing a premature EUA from issuing in the context of SARS-CoV-2 vaccine was institutional inertia and norms, and these could have been overcome by a series of firings,¹⁵⁴ a real possibility in the context of the events surrounding SARS-CoV-2.¹⁵⁵ It is lucky that in this instance, the scientific consensus indicates that the Pfizer and Moderna vaccines are safe and effective.¹⁵⁶ In large part this is a result of the FDA using its institutional fiat to enforce a higher standard of safety review than is required by 35 U.S.C. § 360bbb-3.¹⁵⁷ The events surrounding HCQ EUA have severely undermined the institutional credibility of the FDA. Had similar events accompanied a vaccine EUA, the potential for harm could only have been magnified. Reform is therefore needed to allow the agency to rebuild public trust and withstand political pressure.

154. See Reiss, *supra* note 135 (“The HHS secretary oversees the FDA commissioner and is the one responsible (and, by implication, in charge). Both the FDA commissioner and the HHS secretary are removable at will by the president. Removing either because the president dislikes their policy choices is legal, if not always politically or substantively wise.”).

155. See Lemire et al., *supra* note 114 (“Hours before the Food and Drug Administration authorized the first COVID-19 vaccine late Friday, a high-ranking White House official told the agency’s chief he could face firing if the vaccine was not cleared by day’s end . . .”).

156. See PFIZER-BIONTECH BRIEFING, *supra* note 119 (providing data used by FDA to authorize Pfizer vaccine); see also MODERNA BRIEFING, *supra* note 119 (providing data used by FDA to authorize Moderna vaccine); Polack et al., *supra* note 120 (publishing Pfizer clinical trial data); Oliver et al., *supra* note 128 (providing ACIP’s endorsement of Pfizer vaccine); Oliver et al., *supra* note 129 (providing ACIP’s endorsement of Moderna vaccine).

157. See OCTOBER FDA GUIDANCE, *supra* note 2 (indicating that the FDA was willing to issue an authorization following an interim analysis of a phase III clinical trial at the earliest). Phase I and II vaccine clinical trials typically focus on obtaining safety data while phase III trials are more focused on efficacy data. See Michael G Hudgens et al., *Endpoints in vaccine trials.*, 13 STAT. METHODS MED. RES. 89, 89 (2004) <https://doi.org/10.1191/0962280204sm356ra> (“For vaccine candidates that are safe and immunogenic in Phase I and II trials, Phase III trials (n ~ 1000–100 000) are employed to evaluate efficacy of the vaccine within the population of interest. Vaccines that prove to be safe and efficacious in Phase III trials may be licensed by the appropriate regulatory agency.”).

B. A NEW EUA PATHWAY FOR VACCINES

i. The Origins of the Existing EUA Standard Make it Unsuitable for Public Health

The fundamental balance of safety and efficacy underlying the EUA process was codified in response to national security concerns,¹⁵⁸ and originally intended to be used only in the context of military operations.¹⁵⁹ The legal standards for authorization¹⁶⁰ remain unchanged and the legislature has simply added provisions allowing EUAs to be used in the context of public health emergencies tacked on.¹⁶¹

The legal standard for approval of a vaccine developed in response to a public health crisis should be higher than the standard for a product intended for emergency use in the context of a military operation. While one can draw colorable analogies between the pandemic and a state of war,¹⁶² the public health response to an emerging disease presents fundamentally different challenge than a military adversary. Military adversaries

158. See National Defense Authorization Act for Fiscal Year 2004, *supra* note 49 at § 1603 (permitting an EUA only after a declaration by the “Secretary of Defense that there is a military emergency, or a significant potential for a military emergency, involving a heightened risk to United States military forces of attack with a specified biological, chemical, radiological, or nuclear agent or agents.”).

159. See H.R. REP. NO. 108-106, at 361 (contending that this EUAs are meant to be used in conditions “identical to those current in effect under section 731(a) of the Strom Thurmond National Defense Authorization Act”); see also Strom Thurmond National Defense Authorization Act for Fiscal Year 1999, *supra* note 50, at § 731(a) (establishing a “Process for Waiving Informed Consent Requirement for Administration of Certain Drugs to Members of Armed Forces for Purposes of a Particular Military Operation”).

160. “[B]ased on the totality of scientific evidence available to the Secretary, including data from adequate and well-controlled clinical trials, if available, it is reasonable to believe that— (A) the product may be effective in diagnosing, treating, or preventing— (i) such disease or condition . . . [and] (B) the known and potential benefits of the product, when used to diagnose, prevent, or treat such disease or condition, outweigh the known and potential risks of the product” National Defense Authorization Act for Fiscal Year 2004, *supra* note 49 at § 1603; see also 21 U.S.C. §360bbb-3(e) (containing the same language).

161. See Project Bioshield Act of 2004, *supra* note 51, at § 4 (adding public health emergency declarations to 21 U.S.C. § 360bbb-3).

162. *E.g.*, Taylor Swift, Folklore (Republic Records 2020) (analogizing a medical worker in the SARS-CoV-2 pandemic to a soldier storming the beach in the track “epiphany”).

are responsive to persuasion and politics.¹⁶³ By contrast a virus obeys an evolutionary imperative; a virus cannot be bargained with or convinced to take a different course of action.¹⁶⁴ Unlike the traditional conception of a war, public health does not have a beginning and an end.¹⁶⁵ In the context of the SARS-CoV-2 pandemic a solution such as a vaccine mandate might seem compelling to a politician if it appears that the politician is directly addressing the problem in the short term.¹⁶⁶ Scientists and physicians are divided on whether such a mandate would be helpful, however, or whether a more nuanced solution would be more effective for public health both in the short and long term.¹⁶⁷ The

163. The military theorist Carl von Clausewitz famously argued “War is nothing but a continuation of political intercourse, with a mixture of other means. We say mixed with other means in order thereby to maintain at the same time that this political intercourse does not cease by the War itself, is not changed into something quite different, but that, in its essence, it continues to exist, whatever may be the form of the means which it uses” CARL VON CLAUSEWITZ, *ON WAR* 123 (James John Graham trans., N. Trübner & Company 1873) (1832), https://www.google.com/books/edition/On_War/PQY4AQAA-MAAJ.

164. See CHARLES DARWIN, *THE ORIGIN OF SPECIES* 278 (Signet Classics 2003) (1859) (arguing that the instinctual actions of living organisms are “not . . . specially endowed or created instincts, but . . . small consequences of one general law leading to the advancement of all organic beings,—namely, multiply, vary, let the strongest live and the weakest die.”); see also Jeffery K Taubenberger & John C Kash, *Influenza Virus Evolution, Host Adaptation, and Pandemic Formation*, 7 *CELL HOST MICROBE* 440, 440–451 (2010), <https://pubmed.ncbi.nlm.nih.gov/20542248> (reviewing evolution in the context of influenza viruses).

165. For example, consider the yearly influenza vaccine. It is necessary to vaccinate as many people as possible every year to achieve the optimal public health outcome, and this will continue to be the case for the foreseeable future. See generally Greenwood, *supra* note 32 (reviewing the history and predictions for the future of vaccines). An action which yields short-term political benefits in an influenza outbreak such as a vaccine mandate or a temporary lockdown may do nothing to address the long-term issue of influenza vaccination rates in the future and may actually harm public health if the short-term political action is taken at the expense of public trust in public health institutions.

166. See generally BRYDEN SPURLING, *THE PERIL OF MODERN DEMOCRACY: SHORT-TERM THINKING IN A LONG-TERM WORLD*, 1–9 (United States Studies Centre, 2020), <https://www.ussc.edu.au/analysis/the-peril-of-modern-democracy-short-term-thinking-in-a-long-term-world> (discussing the issue of short-term incentives in liberal democracies).

167. See Liam Drew, *The Case for Mandatory Vaccination* 575 *NATURE* S58, S58–S60 (2019), <https://doi.org/10.1038/d41586-019-03642-w> (reporting on the scientific debate around mandatory vaccination). The example of mandatory vaccination is presented as an illustrative example, but resolution of this issue is beyond the scope of this Note.

incentives structure of war is fundamentally political,¹⁶⁸ and political incentives structures do not produce optimal public health outcomes because public health must necessarily prioritize long term solutions. Another concrete example of the distinction between warfare and public health is the value of transparency.¹⁶⁹ In national security, secrecy is often paramount to achieving a favorable policy outcome.¹⁷⁰ By contrast, secrecy is often counterproductive in public health. There is no reason not to publish the ingredients in an authorized vaccine and clinical trial data; viruses cannot read. In practice secrecy can undermine trust in public health and by implication policy outcomes, such as achieving a high vaccination rate.¹⁷¹

Because achieving vaccine-induced herd immunity¹⁷² represents the clearest resolution to a pandemic disease¹⁷³ convincing people to get the vaccine remains the keystone component to the response to an emerging infectious disease.¹⁷⁴ Vaccine hesitancy already represents a challenge to achieving vaccine-induced herd immunity¹⁷⁵ and a statutory standard that does not adopt a rigorous safety standard will only reinforce vaccine hesitancy. First, the current standard has already contributed to a deficit of trust in the FDA as an institution. The highly deferential standard for obtaining an EUA certainly contributed to the events surrounding HCQ and the subsequent loss of faith in the

168. See VON CLAUSEWITZ, *supra* note 163, at 123 (theorizing war is fundamentally a political action).

169. See Alan Z. Rozenshtein, *Digital Disease Surveillance* 70 AM. U. L. REV. (forthcoming 2021), https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3698431 (discussing the implication of transparency in a pandemic as opposed to national security).

170. See *id.*

171. See *id.*

172. See generally Randolph & Barreiro, *supra* note 6, at 737 (explaining the concept of herd immunity in the context of SARS-CoV-2).

173. See van Riel & de Wit, *supra* note 31, at 810 (“Consensus among experts is that only an effective COVID-19 vaccine will end the pandemic.”).

174. See Anderson et al., *supra* note 133, at 1616 (“Given vaccine hesitancy, the creation of herd immunity by vaccination is likely to be challenging in many countries.”); see also Peretti-Watel et al., *supra* note 133, at 769–770 (arguing that politics becoming intertwined with vaccination reduces vaccination rates).

175. See Smith, *supra* note 110 (explaining vaccine hesitancy).

FDA.¹⁷⁶ Second, the current standard can support misinformation. Skeptics of a vaccine could cite the text of 21 U.S.C. § 360bbb-3 to argue that the standard for authorization was minimal to nonexistent and that such a vaccine was therefore not proven safe. People who look to the statutory standard therefore may hesitate to trust the vaccines, even though the FDA adopted a more rigorous standard for each of the SARS-CoV-2 vaccines that received EUAs.¹⁷⁷ Third, legal standards should reflect social norms.¹⁷⁸ The actions of vaccine manufacturers¹⁷⁹ and the public at large¹⁸⁰ in the course of the SARS-CoV-2 pandemic reflect a social norm that vaccines be proven safe prior to being employed by the public. While it is true that in the course of the SARS-CoV-2 pandemic the FDA used its own institutional clout to ensure that the standard for authorization reflected these norms,¹⁸¹ as the events surrounding HCQ demonstrate there is no guarantee that scientific judgment, rather than politics, will always win the day. Fourth and finally, the cost paid in institutional trust by the FDA does not only affect the instant

176. See Baden et al., *supra* note 1 (discussing erosion of trust at the FDA) *see also* Thomson & Nachlis, *supra* note 1, at 1282 (citing events surrounding HCQ as one reason for loss of trust in the FDA).

177. See OCTOBER FDA GUIDANCE, *supra* note 2 (indicating that the FDA was willing to issue an authorization following an interim analysis of a phase III clinical trial at the earliest).

178. See generally Amir N. Licht, *Social Norms and the Law: Why Peoples Obey the Law*, 4 REV. LAW & ECON. 715 (2008) (analyzing the impact of social norms on legal compliance).

179. See *Biopharma Leaders Unite To Stand With Science*, *supra* note 112 (reporting on the vaccine manufacturer pledge to “[o]nly submit for approval or emergency use authorization after demonstrating safety and efficacy through a Phase 3 clinical study that is designed and conducted to meet requirements of expert regulatory authorities such as FDA.”).

180. See Tyson et al., *supra* note 110 (polling a decline in individuals who would get a hypothetical vaccine after concerns about an expedited vaccine approval process emerged); *see also* O’Keefe, *supra* note 110 (polling finding the same decline in individuals willing to receive a hypothetical vaccine).

181. The FDA stuck to requiring the level of evidence and process it indicated it would require following its initial process. See OCTOBER FDA GUIDANCE, *supra* note 2 (indicating the FDA was willing to issue an EUA following an interim analysis of a phase III clinical trial at the earliest); *see also* PFIZER-BIONTECH BRIEFING, *supra* note 119 (containing the aforementioned phase III interim analysis for the Pfizer vaccine); MODERNA BRIEFING, *supra* note 119 (containing the aforementioned phase III interim analysis for the Moderna vaccine). This was despite repeated instances of political pressure on the agency to approve a vaccine sooner. *See, e.g.*, Schmidt, *supra* note 106 (reporting on the administration’s statements that a vaccine would be approved before the 2020 Presidential election).

vaccine, but also public trust in vaccinations more broadly which adversely affects public health outcomes.¹⁸²

ii. The Proposed Emergency Infectious Diseases Vaccine EUA Pathway

Congress should therefore codify a distinct emergency approval pathway for vaccines developed in response to emerging infectious diseases.¹⁸³ The proposed emerging infectious disease vaccine EUA would parallel the existing EUA structure but would be entirely independent of the existing statutory framework of 21 U.S.C. § 360bbb-3. The proposed framework is presented in Appendix I of this Note. The language presented borrows heavily from the existing text of title 21 but is intended as a framework, not proposed statutory text.¹⁸⁴

The proposed emerging infectious disease vaccine EUA should be reliant on an emergency declaration distinct from the traditional EUA process while leaving the traditional EUA process fundamentally intact. One could argue that an emerging disease pandemic does not meet the legal standard set by § 360bbb-3(b)(1)(C).¹⁸⁵ The creation of a separate authorization

182. Cf. Peebles, *supra* note 42 (“In January, the World Health Organization (WHO) listed ‘vaccine hesitancy’, which describes the reluctance or refusal to vaccinate despite the availability of vaccines, among the top ten global health threats in 2019.”).

183. There is an argument that such a distinct emergency approval pathway should apply to any therapeutic developed in response to a pandemic, but this Note will be limited to arguing for a pathway for vaccines in particular because concerns about safety are fundamentally linked to the public health outcomes for vaccines in a unique way in light of vaccine hesitancy and the widespread use of vaccines in healthy individuals.

184. For instance the framework presented in Appendix I does not discuss a mechanism for terminating the emerging infectious disease vaccine EUA. For the sake of clarity and focus this Note focuses only on the legal standards for the initial authorization, but the existing EUA framework provides a roadmap that would be informative for many other situations, including how EUAs are to terminate. See 21 U.S.C. § 360bbb-3(b)(2) (“Termination of declaration”).

185. “[D]etermination by the Secretary that there is a public health emergency, or a significant potential for a public health emergency, *that affects, or has a significant potential to affect, national security or the health and security of United States citizens living abroad*, and that involves a biological, chemical, radiological, or nuclear agent or agents, or a disease or condition that may be attributable to such agent or agents . . .” 21 U.S.C. § 360bbb-3(b)(1)(C) (emphasis added). A hypothetical argument could be that in light of the legislative history of § 360bbb-3 such national security concerns are limited to active troop deployments and EUAs should therefore be limited to military personal. See H.R. REP. NO. 108-106, at 361 (contending that this EUAs are meant to be used

pathway would make it clear that the current EUA process is meant to be reserved for traditional national security threats while simultaneously preserving the current deferential EUA process if such circumstances arise.¹⁸⁶ This presumption will be reinforced by modifying the initial 21 U.S.C. § 360bbb-3(b)(1)(A-D) emergency declaration to require a finding that the emergency cannot be addressed under the proposed emerging infectious disease vaccine EUA, to ensure that the proposed pathway

in conditions “identical to those current in effect under section 731(a) of the Strom Thurmond National Defense Authorization Act”); *see also* Strom Thurmond National Defense Authorization Act for Fiscal Year 1999, *supra* note 50, at § 731(a) (establishing a “Process for Waiving Informed Consent Requirement for Administration of Certain Drugs to Members of Armed Forces for Purposes of a Particular Military Operation”); McCarthy et al., *supra* note 55 (arguing that EUA should not be used for pandemics as a policy matter). This argument does not seem particularly convincing because § 360bbb-3(b)(1)(C) was added as a distinct emergency declaration from § 360bbb-3(b)(1)(B) which concerns military emergencies, but congress could endorse a reading where the traditional EUA pathway was reserved only for the most serious emergencies by slightly amending §360bbb-3(b)(1)(C) to make this clear.

186. For instance, the traditional EUA process would undoubtedly be more appropriate in the event of a bioterrorism attack. The 1918 influenza pandemic presents another circumstance where a traditional EUA might be appropriate, given that the United States was participating in World War I. *See generally* Carol R Byerly, *The U.S. Military and the Influenza Pandemic of 1918–1919*, 125 *Suppl 3 PUBLIC HEALTH REP.* 82, 82–91 (2010), <https://pubmed.ncbi.nlm.nih.gov/20568570> (discussing the intersection of the 1918 pandemic and the war). There is a more difficult question of whether existing emerging infectious diseases that present with at least an order of magnitude higher mortality burden such as Ebola, Marburg, and Nipah. *See* Adam J. Kucharski & W. John Edmunds, *Case Fatality Rate for Ebola Virus Disease in West Africa*, 384 *LANCET* 1260, 1260 (2014), [https://doi.org/10.1016/S0140-6736\(14\)61706-2](https://doi.org/10.1016/S0140-6736(14)61706-2) (reporting Ebola case fatality rates ranging from 50 to 70% depending on the outbreak and methodology); *see also* Kyle Shifflett & Andrea Marzi, *Marburg Virus Pathogenesis – Differences and Dimilarities in Humans and Animal Models*, 16 *VIROLOGY J.* 165 (2019), <https://doi.org/10.1186/s12985-019-1272-z> (reporting Marburg “case fatality rate ranging from 23 to 90%, depending on the outbreak . . .”); Aditi & Malini Shariff, *Nipah Virus Infection: A Review*, 147 *EPIDEMIOLOGY INFECTION* 1, 2 (2019), <https://doi.org/10.1017/s0950268819000086> (reporting Nipah morality ranging from 40 to 70% depending on the outbreak). These dwarf the mortality rate for SARS-CoV-2. *See* Meyerowitz-Katz & Merone, *supra* note 20 (estimating an IFR of 0.68%); *see also* Yang et al., *supra* note 20 (estimating a CFR of 1.39%). It is likely if there was a widespread outbreak of Ebola, Marburg, or Nipah the high mortality rate would necessitate the use of a traditional EUA, another reason to leave the traditional EUA process relatively intact. Emerging infectious disease with a mortality rates over 50% are also more amicable to characterization as national security threats.

is explicitly deemed unacceptable prior to invoking the more expansive powers codified by 21 U.S.C. § 360bbb-3.

The fundamental reform needed for this vaccine EUA pathway is a rebalancing of the fundamental regulatory concerns of safety and efficacy. The traditional EUA pathway's requirement is minimal for both safety and efficacy.¹⁸⁷ An emerging infectious disease vaccine EUA should retain the current standard for efficacy but look to the normal FDA approval process for its safety standards.

iii. The Proposed Emergency Infectious Diseases Vaccine EUA Standard for Efficacy

The traditional EUA standard for efficacy¹⁸⁸ is appropriate in the context of emerging infectious diseases. When a therapy has a large or clear benefit it will generally be possible to ascertain this quickly.¹⁸⁹ However, when the efficacy is smaller a larger sample size will be necessary to obtain the same level of certainty with regards to efficacy.¹⁹⁰ In the context of an emerging infectious disease, it is desirable that the FDA approve vaccines that have passed a rigorous safety threshold where there is a preponderance of evidence that they are also efficacious, but where it will take significantly more time to determine this for certain due to the logistical challenges of running long-term clinical trials necessary to ascertain the real world effectiveness of a vaccine.¹⁹¹ Often the size of the effect on an individual's immunity will be small, and it would require a very large clinical trial

187. See 21 U.S.C. § 360bbb-3(c) (requiring only that the product may be effective, and that its "known and potential benefits" outweigh the "known and potential risks").

188. See 21 U.S.C. §360bbb-3(c)(2) ("[B]ased on the totality of scientific evidence available to the Secretary, including data from adequate and well-controlled clinical trials, if available, it is reasonable to believe that— (A) the product may be effective in diagnosing, treating, or preventing— (i) such disease or condition . . .").

189. See Biau et al., *Statistics in Brief: The Importance of Sample Size in the Planning and Interpretation of Medical Research*, 466 *Clinical Orthopaedics Related Res.* 2282, 2286 fig.2 (2008) (showing the relationship between confidence interval and sample size).

190. *Id.*

191. There are a variety of logistical challenges to running clinical trials in areas with outbreaks of emerging infectious diseases. See Jon Cohen & Martin Enserink, *Updated: Past Failures Shadow Current Hopes of Testing Drugs Dur-*

to properly quantify the effect in order to reach a finding of effectiveness, which might take years. However, even marginal increases in immunity compound when vaccination is widespread, resulting in vaccine-induced herd immunity.¹⁹² A vaccine with 50% efficacy is better than no vaccine at all¹⁹³ and a small effect size compounds to protect many as a result of vaccine-induced herd immunity.

There are compelling scientific arguments to embrace a marginally lower standard of efficacy in the context of an emerging infectious disease. In the context of the SARS-CoV-2 pandemic variants of concern have emerged.¹⁹⁴ There is some evidence that these variants spread faster,¹⁹⁵ and some have

ing an Ebola Outbreak, SCI. (June 4, 2018, 3:00 PM), <https://www.sciencemag.org/news/2015/12/special-report-ebolas-thin-harvest> (explaining how logistical issues have impaired the completion of clinical trials for Ebola).

192. See generally Randolph & Barreiro, *supra* note 6 (explaining the concept of herd immunity in the context of the SARS-CoV-2 pandemic). By way of example, the effectiveness of the yearly flu vaccine in individuals is not particularly impressive, ranging from 40-60% effective depending on the year. *How Effective Is the Flu Vaccine?*, CTRS. FOR DISEASE CONTROL & PREVENTION (Dec. 16, 2020) <https://www.cdc.gov/flu/vaccines-work/vaccineeffect.htm>.

193. In the context of the SARS-CoV-2 pandemic the FDA announced it would consider vaccines that met a 50% efficacy threshold for an EUA. See JUNE FDA GUIDANCE, *supra* note 2 at 14 (“To ensure that a widely deployed COVID-19 vaccine is effective, the primary efficacy endpoint point estimate for a placebo-controlled efficacy trial should be at least 50%, and the statistical success criterion should be that the lower bound of the appropriately alpha-adjusted confidence interval around the primary efficacy endpoint point estimate is >30%.”).

194. See *SARS-CoV-2 Variants*, U.S. CTRS. FOR DISEASE CONTROL & PREVENTION (Jan. 31, 2021) <https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/variant-surveillance/variant-info.html> (last visited Feb. 23, 2021) (discussing evidence of variants of concern, commonly referred to as mutants); see generally Rochelle P. Walensky, et al., *SARS-CoV-2 Variants of Concern in the United States—Challenges and Opportunities*, J. AM. MED. ASS’N (2021), <https://doi.org/10.1001/jama.2021.2294> (discussing the prevalence of these variants at the time and the United States’ planned response).

195. See *SARS-CoV-2 Variants*, *supra* note 194 (reporting a 50% increase in transmissibility in the variant of concern B.1.1.7 based on preprint studies).

suggested the variants could render vaccines and other therapeutics less efficacious,¹⁹⁶ though it is premature to reach conclusions about either assertion.¹⁹⁷ Regardless it is certainly true that when a previously zoonotic illness becomes endemic in the human population it will be subjected to selection pressure.¹⁹⁸ Further, the faster the virus spreads, the more opportunities there will be for mutation.¹⁹⁹ Effectively this means that the virus will evolve faster if it is allowed to spread unchecked and infect a greater number of hosts.²⁰⁰ The first line of defense against this must necessarily be nonpharmaceutical interventions.²⁰¹ Still, getting access to a vaccine marginally faster, even

196. See Zijun Wang et al., *mRNA Vaccine-Elicited Antibodies to SARS-CoV-2 and Circulating Variants*, NATURE (2021), <https://doi.org/10.1038/s41586-021-03324-6> (“Taken together the results suggest that the monoclonal antibodies in clinical use should be tested against newly arising variants, and that mRNA vaccines may need to be updated periodically to avoid potential loss of clinical efficacy.”).

197. See Adam S. Lauring & Emma B. Hodcroft, *Genetic Variants of SARS-CoV-2—What Do They Mean?*, 325 J. AM. MED. ASS’N 529, 531 (2021), <https://doi.org/10.1001/jama.2020.27124> (discussing why it will take time to determine what impact, if any, the variants of concern will have).

198. See generally Colin R. Parrish et al., *Cross-Species Virus Transmission and the Emergence of New Epidemic Diseases*, 72 MICROBIOLOGY MOLECULAR BIOLOGY REVS. 457, 457–470 (2008), <https://pubmed.ncbi.nlm.nih.gov/18772285> (“Here we review what is known about host switching leading to viral emergence from known examples, considering the evolutionary mechanisms, virus-host interactions, host range barriers to infection, and processes that allow efficient host-to-host transmission in the new host population.”).

199. This can be understood logically. If a virus has x opportunities to mutate when it infects a single host, it will have $2x$ opportunities to mutate after spreading to a second one. Consider that viral propagation in a naïve population is not linear, but exponential. This is a vastly oversimplified model of viral evolutionary dynamics. See Troy Day et al., *On the Evolutionary Epidemiology of SARS-CoV-2*, 30 CURRENT BIOLOGY R849, R854 Box 2 (2020) (presenting evolutionary modeling data on SARS-CoV-2; “reducing the total number of infections will reduce the input of SARS-CoV-2 mutations, and thus slow adaptation, especially if complex mutations underlie fitness gains.”). This is a complicated phenomenon and while it appears to apply to interventions which reduce the total number of infections, such as vaccines, it does not apply to interventions which redistribute infections over a greater stretch of time such as social distancing alone. *Id.*

200. *Id.*

201. See Nathan D. Grubaugh et al., *Public Health Actions to Control New SARS-CoV-2 Variants*, CELL (2021), <https://doi.org/10.1016/j.cell.2021.01.044> (“With potentially more transmissible SARS-CoV-2 variants circulating globally, public officials should communicate the known health risks and tighten the personal, procedural, engineering, and societal control measures that are

if it is not particularly effective, will reduce the total number of infections and thus reduce the opportunities for the virus to mutate, potentially limiting variants of concern.²⁰²

The traditional EUA standard for efficacy is also appropriate because it promotes personal choice and because traditional concerns about fraud are lessened in an emergency. People want access to therapies, and once the FDA is reasonably certain the therapies are safe there is no reason to hold back in an emergency. There is an argument that providing individuals with credible information and trusting them to make the correct medical decision results in higher levels of vaccination than government mandates.²⁰³ There is also a concern that otherwise safe therapies will be used to defraud²⁰⁴ and FDA authorization might be viewed as a tacit source of approval. However, the traditional EUA standard for efficacy still provides protection from facially fraudulent therapies.²⁰⁵ The proposed elevated safety standard compensates for the admittedly deferential efficacy standard because meeting the proposed safety standard will re-

known to be effective at decreasing transmission. These include the following: reducing social contacts, effective testing and tracing, robust outbreak identification and control, support to ensure effective isolation and quarantine, and population vaccination.”).

202. There is a subsequent question as to what statutory standard for safety is appropriate when testing ‘booster’ shots intended to address variants of concern. The scientific questions underlying the appropriate standard are complex and are beyond the scope of this Note.

203. See Drew, *supra* note 167 (“The problem highlighted by the WHO earlier this year was not vaccine refusal, but vaccine hesitancy. In most countries, the proportion of the population that staunchly opposes vaccines is less than 2%. The bigger problem, Salmon says, is the much larger group of people with some concerns about vaccination that might make them hesitant. He estimates that up to one-third of Americans have concerns about vaccines. ‘Making the laws stricter doesn’t address that,’ he says.”).

204. See *Beware of Fraudulent Coronavirus Tests, Vaccines and Treatments*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/consumers/consumer-updates/beware-fraudulent-coronavirus-tests-vaccines-and-treatments> (last visited Feb. 22, 2021) (providing consumers information on avoiding fraudulent SARS-CoV-2 therapies).

205. For example, if faced with a facially fraudulent vaccine it should be trivial for the FDA to refuse to conclude that “based on the totality of scientific evidence available to the Secretary . . . the product may be effective in diagnosing, treating, or preventing— (i) such disease or condition” when there is no possible mechanism or data to support a product sponsored for an EUA. 21 U.S.C. §360bbb-3(c)(2).

quire performing some clinical trials and doing so would generate sufficient efficacy data²⁰⁶ for the FDA to make a more informed final determination as to efficacy.²⁰⁷ At this point the decision must be left to physicians and individuals to decide whether the magnitude of the benefit outweighs any potential risks in an emergency.²⁰⁸ The FDA could still impose labeling requirements to ensure consumers are adequately informed of the evidence of efficacy.²⁰⁹ The FDA's role as a gatekeeper who protects from fraud²¹⁰ must necessarily give ground in an emergency.

206. Even phase I clinical trials include measurements of immunogenicity. See e.g., Edward E. Walsh et al., *Safety and Immunogenicity of Two RNA-Based Covid-19 Vaccine Candidates*, 383 N. ENG. J. MED. 2439, 2448–49 fig.4 (2020), <https://doi.org/10.1056/NEJMoa2027906> (reporting safety and immunogenicity of the vaccines including the Pfizer vaccine that went on to receive an EUA).

207. If there is still no data to support efficacy after performing a phase II clinical trial, it would seem appropriate that the FDA refuse to issue an authorization as a lack of data amounts to accepting the null hypothesis that the therapy does nothing.

208. There is a historical debate about whether the FDA can or does regulate the practice of medicine. See Wendy Teo, *FDA and the Practice of Medicine: Looking at Off-Label Drugs*, 41 SETON HALL LEGIS. J. 305, 305–306 (2017) (“The Food and Drug Administration (‘FDA’) has always taken a deferential stance with regard to the practice of medicine, and maintains that it will not interfere with the physicians’ autonomy in this regard. This is otherwise known as the ‘practice of medicine exception.’ However, the reality is that it is often difficult to draw a clear line between the role of FDA in safeguarding the public from unsafe drugs and the autonomy that physicians have in prescribing off-label medication in the practice of medicine.”)

209. 21 U.S.C. § 360bbb-3(a) only creates an exemption to the interstate commerce liability hooks in the Food Drug and Cosmetic Act. E.g., 21 U.S.C. § 355(a) (“No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) or (j) is effective with respect to such drug.”). A variety of provisions can define products as adulterated or misbranded for failing to meet labeling or general safety requirements. E.g., 21 U.S.C. § 352(a) (“A drug or device shall be deemed to be misbranded . . . [i]f its labeling is false or misleading in any particular.”). 21 U.S.C. § 331 still makes it a violation to introduce or receive an adulterated or misbranded product in interstate commerce. The most natural reading of § 360bbb-3(a) would leave § 331’s prohibitions intact, and the FDA could therefore still bring enforcement actions for general safety and labeling concerns. See 21 U.S.C. § 331 et seq (codifying the FDA’s enforcement mechanisms).

210. Cf. *United States v. 88 Cases, Bireley’s Orange Beverage*, 187 F.2d 967, 972 (3d Cir. 1951) (holding that the FDA can condemn a food product as adulterated if sufficient proof is provided that a consumer would confuse it for a superior product).

iv. The Proposed Emergency Infectious Diseases Vaccine EUA Standard for Safety

The most important distinction between the traditional EUA standard and this proposal is that the proposed emerging infectious disease vaccine EUA would use the standard of safety from 21 U.S.C. § 355(d)(1), (2), and (4).²¹¹ Notably this proposal excludes the safety provision of 21 U.S.C. § 355(d)(3) which prohibits approval if: “the methods used in, and the facilities and controls used for, the manufacture, processing, and packing . . . are inadequate to preserve its identity, strength, quality, and purity . . .” This Note’s proposal excludes 21 U.S.C. § 355(d)(3) because the FDA has redundant regulatory authority to prevent the introduction of products manufactured to undesirable settings from entering interstate commerce both in the proposed approval framework²¹² and elsewhere in title 21.²¹³ Requiring companies to demonstrate “identity, strength, quality, and purity” to the FDA before receiving an EUA in an emergency would therefore unnecessarily slow authorizations when the

211. These read in relevant part “If the Secretary finds . . . [(1) the submissions] do not include adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof; (2) the results of such tests show that such drug is unsafe for use under such conditions or do not show that such drug is safe for use under such conditions . . . (4) upon the basis of the information submitted to him as part of the application, or upon the basis of any other information before him with respect to such drug, he has insufficient information to determine whether such drug is safe for use under such conditions . . .” 21 U.S.C. § 355(d).

212. This proposal also explicitly calls for the adoption of 21 U.S.C. 360bbb-3(c)(5) into the emerging infectious disease vaccine EUA standard. It requires: “that such other criteria as the Secretary may by regulation prescribe are satisfied” be met prior to issuing an authorization. 21 U.S.C. 360bbb-3(c)(5). Given that the vaccines being discussed necessarily relate to emergencies, the FDA would also be within its rights to make use of ‘good cause’ authority codified at 5 U.S.C. § 553(b)(B) to expedite the process. *See generally* Babette E.L. Boliek, *Agencies in Crisis? An Examination of State and Federal Agency Emergency Powers*, 81 *FORDHAM L. REV.* 3339, 3353–71 (2013) (reviewing regulatory agency emergency rulemaking authority).

213. *E.g.*, 21 U.S.C. § 351 (which deems drugs adulterated if they meet a wide variety of standards including standards which relate to identity, strength, quality, and purity). This section is incorporated by 42 U.S.C. § 262(j) and therefore applies to vaccines.

FDA already has the authority to effectively regulate “identity, strength, quality, and purity.”²¹⁴

Under the proposed standard the burden is on the sponsor to provide enough evidence of safety to satisfy the FDA and approval can be denied if the FDA is not convinced the product is safe based on available data,²¹⁵ if adequate tests have not been performed to determine safety,²¹⁶ or if there is any indication that the FDA has inadequate information to make a determination of safety.²¹⁷ Adopting this standard would raise the burden of proof required to issue an EUA; this is desirable for vaccines developed to prevent emerging infectious diseases because public confidence in a vaccine’s safety is intrinsically tied to the vaccine’s ultimate aim of protecting public health. A public that does not trust that the vaccine is safe will not get the vaccine, and the population as a whole will not achieve vaccine-induced herd immunity. A higher standard of safety in this context is also desirable because unlike other therapies, vaccines are given prophylactically to individuals who are not yet sick and therefore necessarily are used on many more individuals than other kinds of therapeutics. A higher incidence of use implies a higher standard of safety is required.²¹⁸

214. If congress felt that a priori regulation was more desirable than the increase in speed obtained from excluding 21 U.S.C. § 355(d)(3) this would certainly be a valid and defensible position. This Note only argues that the regulatory oversight provided by § 355(d)(3) is marginal and slightly redundant, but the speed gained by excising this section might be equally marginal. If congress wishes to include the safety standard of § 355(d)(3) it should consider modifying this standard to indicate that this is meant to merely be a ‘paper review’ as in person inspections of manufacturing facilities are often impractical during an emerging infectious disease outbreak.

215. *See* 21 U.S.C. § 355(d).

216. *See id.*

217. *See id.*

218. Because vaccines are theoretically given to every healthy individual in order to achieve the desired outcome the risk of rare side effects is necessarily multiplied. *See* Offit et al., *supra* note 8, at 1629 (“Because vaccines are given to healthy children and adults, a higher standard of safety is generally expected of immunizations compared with other medical interventions.”).

C. CRITICISMS OF THE PROPOSAL AND RESPONSES

i. An Emerging Infectious Disease EUA Would Not Undermine Consumer Autonomy

One criticism of the proposed emerging infectious disease EUA could be that the traditional EUA system is still capable of maintaining consumer trust while also promoting personal liberty and earlier access to vaccines. A hypothetical informed consumer could rationally decide that they do not want to get a vaccine approved under the traditional EUA standard and wait for full approval. The traditional EUA approach thus maximizes personal choice for this hypothetical informed consumer.

This criticism is flawed for a number of reasons. First, it assumes that consumers are always intimately informed about the FDA authorization and subsequent approval of therapies. This is unlikely to be the case.²¹⁹ It is unlikely that consumers understand the distinction between an EUA and full FDA approval.²²⁰ However, under the proposed standard public health advocates would be able to argue that the law requires emerging infectious disease vaccines be proven safe, a simple and easy to digest message. Second, this argument ignores the lost institutional trust incurred from a single incorrect regulatory decision as demonstrated by the EUA issued for HCQ. In practice, consumers are disproportionately exposed to the FDA's regulatory failures rather than successes.²²¹ This may imply that the average consumer will have a negatively skewed perception of the FDA's actions, further undermining the premise that the hypothetical informed consumer even exists. Third, this argument ignores the

219. See Thaler, Richard H. & Will Tucker, *Smarter Information, Smarter Consumers*, Harv. Bus. Rev., Jan.–Feb. 2013, <https://hbr.org/2013/01/smarter-information-smarter-consumers> (arguing that even highly educated consumers do not make informed decisions); see also Daniel L. McFadden, *The New Science of Pleasure*, 1–37 (Nat'l Bureau of Econ. Rsch., Working Paper No. 18687, 2013), https://www.nber.org/system/files/working_papers/w18687/w18687.pdf (reviewing economic and historical evidence of irrational consumer behavior).

220. See Helen W. Sullivan et al., *Consumer Understanding of the Scope of FDA's Prescription Drug Regulatory Oversight: A Nationally Representative Survey*, 29 PHARMACOEPIDEMOLOGY & DRUG SAFETY 134, 138 (2020), (“The results from our survey are in line with results from previous studies and suggest that there is a consistent proportion of consumers who carry some misconceptions about prescription drugs, [and] what FDA approval of prescription drugs means . . .”).

221. See, e.g., Sacerdote et al., *supra* note 93 (analyzing the media landscape of SARS-CoV-2 media coverage).

FDA's actions in the instant crisis. The FDA has required a high standard of safety evidence to approve the Pfizer and Moderna vaccines,²²² in effect using the proposed elevated evidentiary standard while still paying the institutional credibility price of using the traditional EUA pathway.

Personal choice is desirable, but it is outweighed by ensuring institutional credibility which will promote the public good of population level immunity as a result of widespread vaccination. Attempting to maximize personal choice sounds good in theory, but practical concerns should prevail in the field of public health.

ii. An Emerging Infectious Disease EUA Would Not Undermine Regulatory Flexibility

Another criticism of a higher safety standard is that it undermines the FDA's regulatory flexibility.²²³ Regulatory flexibility is particularly desirable for EUAs because the circumstances that lead to an EUA are necessarily unique and unforeseeable. An emerging infectious disease with characteristics closer to Ebola requires a more extreme regulatory response in light of a

222. See OCTOBER FDA GUIDANCE, *supra* note 2 (indicating that the FDA was willing to issue an authorization following an interim analysis of a phase III clinical trial at the earliest). Phase I and II vaccine clinical trials typically focus on obtaining safety data while phase III trials are more focused on efficacy data. See Hudgens et al., *supra* note 157 at 89 ("For vaccine candidates that are safe and immunogenic in Phase I and II trials, Phase III trials (n ~ 1000–100 000) are employed to evaluate efficacy of the vaccine within the population of interest. Vaccines that prove to be safe and efficacious in Phase III trials may be licensed by the appropriate regulatory agency."). See also *Step 3: Clinical Research*, U.S. FOOD & DRUG ADMINISTRATION, <https://www.fda.gov/patients/drug-development-process/step-3-clinical-research> (last visited Jan. 8, 2021) (stating the purposes of phase I, II, and III are "[s]afety and dosage[.]" "[e]fficacy and side effects[.]" and "[e]fficacy and monitoring of adverse reactions" respectively).

223. Cf. Walter G Johnson & Gary E Marchant, *Legislating in the Time of a Pandemic: Window of Opportunity or Invitation for Recklessness?*, 7 J. L. & BIOSCIENCES 1, 8 (2020), ("Substantively, emergency policymaking may result in regulatory norms or programs poorly calibrated to the longer-term and complex set of stakeholder interests and policy concerns at play. Specifically in food and drug crisis decision-making, Peter Barton Hutt comments '[a]s is often true under those conditions, the legislation has been shaped as much by public emotion as rational policy design.' Accordingly, legislatures tend to underregulate a problem before a crisis occurs, but often overregulate after disaster strikes.") (citation omitted).

mortality rate in excess of 50%.²²⁴ However, the proposed approach does not abolish the traditional EUA pathway. To access the traditional EUA pathway, the proposal only requires a finding that the proposed pathway is inadequate to address the emergency, promoting accountability and discouraging inappropriate use of the traditional pathway. Thus, the proposed emerging infectious disease vaccine EUA does not undermine regulatory flexibility, but rather strengthens it. Undoubtedly, the FDA also wishes to exert its own sound scientific judgment rather than be subject to political influence in making regulatory decisions. A suitable statutory framework strengthens the FDA's hand by promoting accountability for political actors. The FDA would still be able to take extreme measures if it felt this was necessary while still being forced to explicitly find the powers granted under the proposed statute are insufficient. The institutional damage from a poor regulatory decision made because of the lower standard may legitimately be justified in the context of a war or an infectious disease outbreak with a mortality rate in the double digits. But this tradeoff seems normatively unwise in the context of the SARS-CoV-2 pandemic.²²⁵

iii. An Emerging Infectious Disease EUA Would Not Undermine Speed

There is an argument that a greater emphasis on safety would undermine the FDA's ability to quickly authorize necessary therapies. There is a recurring concern that if the FDA's standards for regulation are too high this will hinder access to potentially lifesaving therapies.²²⁶ This is a valid concern in the context of a pandemic, as there are unlikely to be any therapies

224. See Kucharski & Edmunds, *supra* note 186, at 1260 (reporting Ebola case fatality rates ranging from 50 to 70% depending on the outbreak and methodology).

225. There is no question that the SARS-CoV-2 pandemic has affected national security. The issue is one of magnitude. Widespread community transmission of Ebola would affect national security in a much more fundamental way than the SARS-CoV-2 pandemic has.

226. See, e.g., *Abigail All. for Better Access to Developmental Drugs v. Von Eschenbach*, 495 F.3d 695 (D.C. Cir. 2007) (holding that there is no constitutional "right to try" experimental therapies that have not been approved by the FDA); see also 21 U.S.C. § 360bbb-0a (creating said "right to try" under particular circumstances).

available and a speedy approval process is certainly desirable.²²⁷ However, this argument is less convincing when applied to vaccines for a number of reasons.

Firstly, the proposed emerging infectious disease vaccine pathway would leave the existing EUA pathway intact while making it clear that such a pathway is intended only for the most serious emergencies. The existence of a hypothetical pathway earmarked for emerging infectious diseases would be a strong signal that such a pathway should be used for this purpose. The FDA would also be forced to make an explicit finding that the proposed pathway was insufficient to invoke traditional EUA powers making the FDA more accountable for this act. Therefore, the proposed pathway does not undermine speed when speed is necessary, rather it promotes accountability for employing EUAs when they are unnecessary. If the public felt that a lower safety standard was warranted in light of the circumstances, there would be no (or a minimal) political cost to pay for using a traditional EUA.²²⁸

Secondly, speed is worthless if people do not get the vaccine. The metric by which we should measure public health is not whether an untested vaccine is available, but whether people use it. There is ample survey evidence that employing a vaccine perceived to be less tested increases vaccine refusal.²²⁹ There is

227. Faster access to therapies is always desirable; the trick is ensuring they are safe and efficacious while balancing these concerns in abnormal circumstances. See Tomas J. Philipson et al., *Assessing the Safety and Efficacy of the FDA: The Case of the Prescription Drug User Fee Acts 3–4* (Nat'l Bureau of Econ. Rsch., Working Paper No. 11724, 2005) (reviewing the perennial debate of safety, efficacy, and speed).

228. India, for instance has embraced a lower standard of evidence in approving a vaccine and is experiencing significant political backlash. See Aniruddha Ghosal & Sheikh Saaliq, *India's Quick Nod to Homegrown COVID-19 Vaccine Seeds Doubt*, ASSOCIATED PRESS (Jan. 11, 2021), <https://apnews.com/article/asia-pacific-clinical-trials-india-coronavirus-pandemic-coronavirus-vaccine-16a4c1cfb1b6b5def70812e638e5fc54> (reporting on issues with India's rapid rollout of an experimental vaccine); see also Emily Schmall & Karan Deep Singh, *A Mix of Pride and Doubts as Modi Launches India's Covid-19 Vaccine Drive*, N.Y. TIMES (Jan. 15, 2021), <https://www.nytimes.com/2021/01/15/world/asia/coronavirus-india-vaccine.html> (reporting on the same issues of trust with the experimental vaccine).

229. See Guidry et al., *supra* note 41, at 140–41 (reporting survey data in tables 4 & 5 showing “[c]oncern about side effects of [a hypothetical] vaccine” and the perception that “[d]evelopment [was] too rushed to test safety” both strongly correlate with vaccine refusal); see also Kreps et al., *supra* note 41, at

also evidence that individuals are much less likely to get a vaccine authorized via EUA than one that receives traditional FDA approval.²³⁰ Vaccines serve to protect individuals,²³¹ but a vaccination program's ultimate goal is to protect the population as a whole, including individuals who are unable to get vaccines due to underlying health conditions.²³² If an untested vaccine undermines widespread vaccination this undermines the most fundamental public health goal of vaccination, which is to protect the population as a whole from the disease, not just an individual.

Thirdly, there is no reason to think that the FDA could not quickly determine that a vaccine was safe even using a higher standard of safety. It is true that 21 U.S.C. § 355(d) lays out a higher standard of safety than 21 U.S.C. § 360bbb-3(c), but the standard of § 355(d) is still highly deferential to the FDA.²³³ Fur-

1 (reporting survey data showing that a “decrease in the incidence of major adverse effects from 1 in 10 000 to 1 in 1 000 000 was associated with a higher probability of choosing a [hypothetical SARS-CoV-2] vaccine (coefficient, 0.07; 95% CI, 0.05-0.08).”)

230. See Guidry et al., *supra* note 41, at 139 (“Of the total sample, 30.7% of respondents were *definitely planning*, 29.2% were *probably planning*, 18.8% were *neutral*, 9.4% *probably not planning* and 11.9% would *definitely not planning* [sic] to receive a future COVID-19 vaccine. When asked if they would get the vaccine under the EUA, 10.4% reported being *definitely willing* to do so, 14.2% *willing*, 22.3% *somewhat willing*, 14.3% *somewhat unwilling*, 16.4% *probably unwilling*, and 22.3% *definitely unwilling*.” (emphasis in original)); see also Kreps et al., *supra* note 41 at 1 (“An FDA emergency use authorization was associated with a lower probability of choosing a vaccine (coefficient, -0.03; 95% CI, -0.04 to -0.01) compared with full FDA approval.”)

231. See generally Rémy et al., *supra* note 8, at 1 (reviewing evidence of modern vaccine efficacy).

232. See Randolph & Barreiro, *supra* note 6, at 737 (explaining the concept of herd immunity).

233. 21 U.S.C. § 355(d) indicates that approval should be denied if “[1] submissions to the FDA] do not include adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof; (2) the results of such tests show that such drug is unsafe for use under such conditions or do not show that such drug is safe for use under such conditions . . . (4) upon the basis of the information submitted to him as part of the application, or upon the basis of any other information before him with respect to such drug, he has insufficient information to determine whether such drug is safe for use under such conditions . . .” The principal change is that this standard shifts the burden of proving safety to the sponsor. However the FDA still receives substantial deference in determining whether this standard has been met. See, e.g., Ubi-

thermore, in the context of vaccines the FDA can make a determination of safety using the standard from § 355(d) in a time frame similar to the EUA timeline for the Pfizer and Moderna vaccines.²³⁴ In a vaccine clinical trial, the phase III component must last years in order to assess the effectiveness of the vaccine at preventing disease long term.²³⁵ Trials can be performed much faster when safety is the sole concern, because in the context of vaccines adverse safety events are clustered around the administration of the vaccine itself.²³⁶ However, if Congress is

otica Corp. v. Food & Drug Admin., 427 F.2d 376, 378–79 (6th Cir. 1970) (affirming a denial of NDA pursuant to § 355(d)); cf. United States v. Article of Drug . . . Bacto-Unidisk, 394 U.S. 784 (1969) (demonstrating the significant deference the FDA receives in interpreting the FDCA).

234. While the Pfizer and Moderna vaccines were approved using an EUA, both vaccines underwent phase I, II and an interim analysis of phase III clinical trials pursuant to FDA guidance. See PFIZER-BIONTECH BRIEFING, *supra* note 119 (containing data supporting the EUA of the Pfizer vaccine); see also MODERNA BRIEFING, *supra* note 119 (containing data supporting the EUA of the Moderna vaccine). This amount of safety testing would seem to meet the proposed safety standard of 21 U.S.C. §355(d) which indicates in relevant part that approval should be denied if “[1] the submissions] do not include adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof; [2] the results of such tests show that such drug is unsafe for use under such conditions or do not show that such drug is safe for use under such conditions . . . [4] upon the basis of the information submitted to him as part of the application, or upon the basis of any other information before him with respect to such drug, he has insufficient information to determine whether such drug is safe for use under such conditions . . .” 21 U.S.C. § 355(d).

235. See generally Hudgens et al., *supra* note 157, at 89–114 (reviewing the purposes of the different phases for vaccine clinical trials and appropriate statistical methods).

236. It is true that in testing any new therapy it is difficult to predict when and what side effects will arise. However, vaccine side effects are logically linked to the immune system on which the vaccine acts. See COMMITTEE TO REVIEW ADVERSE EFFECTS OF VACCINES, *Evaluating Biological Mechanisms of Adverse Events*, in ADVERSE EFFECTS OF VACCINES: EVIDENCE AND CAUSALITY 57–101 (Kathleen Stratton et al., eds 2011), <https://www.ncbi.nlm.nih.gov/books/NBK190017/> (reviewing the causal mechanisms of vaccine side effects); see also Caroline Hervé et al., *The How’s and What’s of Vaccine Reactogenicity*, 4 NPJ VACCINES 39, 39–50 (2019), (reviewing the biology of vaccine side effects and making clinical recommendations). While vaccines make permanent changes to the immune system in the form of immune memory the most common side effects of vaccination appear and resolve relatively quickly after vaccination with the adaptive immune system returning to immune homeostasis within about a month of a challenge. See KENNETH MURPHY & CASEY WEAVER, *JANEWAY’S IMMUNOBIOLOGY* 24 fig.1.25 (9th ed. 2017)

worried that the safety standard from § 355(d) would slow approval, it might consider appending the safety standard with language that requires the FDA to consider safety in light of the circumstances that necessitate the use of an emergency authorization.²³⁷

Finally, it is important to remember that the proposed pathway is intended to be based on the standard employed in practice in issuing EUAs for the Pfizer and Moderna SARS-CoV-2 vaccines.²³⁸ This Note argues the statutory standard of safety codified by 21 U.S.C. 355(d)(1), (2), and (4) be adopted, not the practices of the FDA in satisfying these standards in the course of reviewing and NDA. Ultimately, a speedy approval process is desirable, but a desire for regulatory expediency cannot arrive at the expense of safety in the context of vaccines, because optimal

(showing the course of a typical antibody response to immunization). This hypothesis holds in practice, with the vast majority of vaccine side effects being observed soon after administration in clinical trials. See World Health Organization, *Module 3: Adverse Events Following Immunization*, VACCINE SAFETY BASICS, <https://vaccine-safety-training.org/vaccine-reactions.html> (last visited Feb. 21, 2021) (reviewing evidence of onset interval for serious adverse events post vaccination); see also G L D'alò et al., *Frequently Asked Questions on Seven Rare Adverse Events Following Immunization*, 58 J. PREV. MED. & HYGIENE. E13, E13–E26 (2017), (reviewing evidence of the association between adverse events and time post vaccination); Jerome H. Kim et al., *Looking Beyond COVID-19 Vaccine Phase 3 Trials*, 27 NATURE MED. 205, 208 (2021) (“There are certain safety-related events that, due to rarity or pathogenesis, might be detected only during longer-term surveillance for adverse events after immunization. The FDA guidance for Emergency Use Authorization suggests a median duration of follow-up of phase 3 vaccine trial volunteers of 2 months. Most events are expected to fall within that window after vaccination.”); This Week in Virology, *With Vaccines, Offit Is on it*, MICROBE.TV, at 18:20 (Feb. 14, 2021), microbe.tv/twiv/twiv-720/ (discussing the FDA’s process of determining vaccine safety and experiences participating in vaccine clinical trials with Dr. Paul Offit in the context of the SARS-CoV-2 pandemic). In light of these immunological precepts, it seems likely that phase I, II, and an interim analysis of phase III clinical trials are “adequate tests . . . to show whether or not such drug is safe for use . . .” because such trials will follow patients for more than a month, and thus will be capable of detecting side effects if they are adequately powered. 21 U.S.C. § 355(d).

237. 21 U.S.C. § 360bbb-3(c)(2)(B) provides language that could serve as a model: “taking into consideration the material threat posed by the agent or agents identified [in the initial emergency declaration] . . .” This would ensure that the FDA considers not only the safety and efficacy any hypothetical vaccine in isolation, but also that it balances the need for safety and efficacy against the magnitude of the “material threat.” *Id.*

238. See *supra* note 174 and accompanying text.

public health outcomes for vaccines rely on safety in a way that other therapies do not.

IV. CONCLUSION

The crisis of legitimacy at the FDA was not caused by any single factor. The emergence of a respiratory pandemic disease was not a regular occurrence, but it was also not entirely unexpected.²³⁹ There will be respiratory pandemic diseases in the future.²⁴⁰ America has a history of populist Presidents pushing the boundaries of norms²⁴¹ and it will likely have norm pushing Presidents in the future. Rebuilding trust in the FDA as an institution will require strengthening the regulatory guardrails and rethinking the policy tradeoffs that lead to the development of the EUA process as currently codified in 21 U.S.C. § 360bbb-3.

The fundamental balance of safety and efficacy for vaccine EUAs that issue for emerging infectious diseases should be based on a statutory and regulatory framework grounded in public health outcomes, not a statute that was intended to allow the emergency approval of therapies for troops engaged in “[m]ilitary [o]peration[s] . . .”²⁴² Public health concerns unique to vaccines demand safety. Widespread use on healthy individuals requires a balance of safety and efficacy, but necessarily favors

239. See Gates, *supra* note 27 (predicting future viral respiratory pandemics).

240. See Bedford et al., *supra* note 7, at 130 (“With rapidly changing ecology, urbanization, climate change, increased travel and fragile public health systems, epidemics will become more frequent, more complex and harder to prevent and contain.”).

241. See Martin Eiermann, *How Donald Trump Fits into the History of American Populism*, 33 NEW PERSP. Q. 29, 29–34 (2016), (reviewing the history of American populism and placing the Trump presidency in this context) see also Yascha Mounk & Jordan Kyle, *What Populists Do to Democracies*, THE ATLANTIC (Dec. 26, 2018), <https://www.theatlantic.com/ideas/archive/2018/12/hard-data-populism-bolsonaro-trump/578878/> (arguing populists harm democratic institutions).

242. See Strom Thurmond National Defense Authorization Act for Fiscal Year 1999 Pub. L. No. 105-261 § 731(a), 112 Stat. 1920, (establishing a “Process for Waiving Informed Consent Requirement for Administration of Certain Drugs to Members of Armed Forces for Purposes of a Particular Military Operation”).

safety.²⁴³ Further, because widespread use is a necessary predicate to realizing the ultimate goal of vaccination-induced herd immunity²⁴⁴ the public must trust that any vaccine is safe. Thus, an emphasis on safety is doubly important in the context of vaccines. Finally, a lack of institutional trust in the safety of FDA approved vaccines affects public health through reduced uptake of the instant vaccine, but also through reduced uptake of vaccines more broadly as a result of vaccine hesitancy.²⁴⁵ An emphasis on safety is therefore paramount and the regulatory framework for emergency vaccines should reflect this.

It is true that the Pfizer and Moderna vaccines produced in the context of the SARS-CoV-2 pandemic appear to be safe, but the FDA was forced to resist significant political pressure to ensure that this was the case.²⁴⁶ The FDA may not be able to do so in the future. An alternative regulatory pathway will not undermine the FDA's regulatory flexibility, but rather promote accountability. It will not slow the regulatory approval of effective therapies, because vaccine efficacy is largely dependent on vaccination uptake. A vaccine the public trusts that arrives a hypothetical month later (if that) is worth ten times a vaccine that no one elects to receive. Formally rebalancing the statutory framework for emerging infectious disease vaccine EUAs will restore institutional trust in the FDA, allowing it to better carry out its public health mandate.

243. See Offit et al, *supra* note 8, at 1629 (“Because vaccines are given to healthy children and adults, a higher standard of safety is generally expected of immunizations compared with other medical interventions.”).

244. See Randolph & Barreiro, *supra* note 6, at 737 (explaining how widespread immunity in a population slows the spread of an infectious agent).

245. See Trogen et al., *supra* note 134, at 2461 (“Failing to abide by standards of safety and scientific rigor during the COVID-19 crisis will fuel the argument that physicians and scientists cannot be trusted. Vaccination rates, which are declining due to widespread concern about visiting clinicians’ offices, could further decrease. The US could see resurgences of many vaccine-preventable illnesses, and inevitably, massive increases in avoidable deaths and irreversible outcomes.”).

246. See *supra* note 185 and accompanying text.

Appendix I

EUA Pursuant to 21 U.S.C. § 360bbb-3

Emergency Declaration by Secretary of Homeland Security, Secretary of Defense, Secretary of HHS or identification of material threat pursuant to 42 U.S.C. § 247d-6b by Secretary of HHS.

Any of the above emergency declarations must include a finding that this emergency cannot be addressed under 21 U.S.C. § XXX.

Declaration that the circumstances exist justifying the authorization by Secretary of HHS including findings:

- (1) The agent in question can cause a serious or life-threatening disease or condition.
- (2) Based on the totality of scientific evidence available to the Secretary of HHS including data from adequate and well-controlled clinical trials, if available:
 - (a) it is reasonable to believe that the product may be effective in diagnosing, treating or preventing the subject of the emergency declaration; and
 - (b) the known and potential benefits of the product outweigh the known and potential risks when used to treat the subject of the emergency declaration taking into consideration the material threat posed by the subject of the declaration.
- (3) There is no adequate, approved, and available alternative to the product.
- (4) That such other criteria as the Secretary may by regulation prescribe are satisfied.

Amend 21 U.S.C. §360bbb-3(c)(2)(A)(ii) to permit normal EUAs to issue to treat conditions caused by products authorized pursuant to 21 U.S.C. § XXX.

Note: Large parts of the text in these proposed statutes are taken from the current version of 21 U.S.C. §§ 360bbb-3 and 355(d). Quotation marks have been removed to ensure readability. What is presented here should be treated as a guide to what is proposed, not as proposed language. Aspects that would be necessary in a final version of either of these statutes have been omitted for clarity of the proposal. Proposed additions indicated with a black box, additions of interest are indicated with underline.

Proposed 21 U.S.C. § XXX

Emergency Declaration by Secretary of HHS that there is a public health emergency, or a significant potential for a public health emergency, that affects, or has a significant potential to affect, national security or the health and security of United States citizens living abroad which involves an emerging infectious disease in humans.

Declaration that the circumstances exist justifying the authorization by Secretary of HHS including findings:

- (1) The agent in question can cause a serious or life-threatening disease or condition.
- (2) Based on the totality of scientific evidence available to the Secretary of HHS including data from adequate and well-controlled clinical trials, if available, it is reasonable to believe that the vaccine product may be effective in diagnosing, treating or preventing the subject of the emergency declaration
- (3) There is no adequate, approved, and available alternative to the vaccine product.
- (4) That such other criteria as the Secretary may by regulation prescribe are satisfied.
- (5) Authorization shall not issue:
 - (a) if submissions to the FDA do not include adequate tests by all methods reasonably applicable to show whether or not such vaccine is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof; and
 - (b) the results of such tests show that such vaccine is unsafe for use under such conditions or do not show that such vaccine is safe for use under such conditions; and
 - (c) upon the basis of the information submitted to the FDA as part of the application, or upon the basis of any other information before the FDA with respect to such vaccine, the FDA has insufficient information to determine whether such vaccine is safe for use under such conditions.*

*This standard is taken in large part from 21 U.S.C. § 355(d)(1), (2), (4).