SYMPOSIUM ARTICLE

Southern Economic Journal WILEY

The FDA and the COVID-19: A political economy perspective

Raymond J. March

Center for the Study of Public Choice and Private Enterprise, North Dakota State University, Fargo, North Dakota, USA

Correspondence
Raymond J. March, Center for the Study of Public Choice and Private Enterprise, North Dakota State University, Fargo, ND.
Email: raymond.j.march@ndsu.edu

Abstract

This article utilizes a political economy framework to examine how FDA regulations impacted the U.S. healthcare sector's ability to address COVID-19. I specifically examine the developing COVID-19 testing, the approval of the medication remdesivir, and COVID-19 vaccines. By examining periods before and after the FDA issued Emergency Use Authorizations (EUAs), my analysis finds that the FDA's regulations enacted before the COVID-19 pandemic began strongly restricted clinician and patient access to COVID-19 testing, remdesivir treatment, and approving vaccines. After the FDA issued EUAs, the healthcare sector quickly adopted COVID-19 testing and remdesivir with little evidence of negative consequences. These findings contribute to the economics literature examining the FDA and contemporary COVID-19 policy research.

KEYWORDS

bureaucracy, COVID economics, Food and Drug Administration, health economics, healthcare regulation, pandemics

JEL CLASSIFICATION

I18; N31; N32

1 | INTRODUCTION

When the COVID-19 pandemic emerged in late 2019, researchers across disciplines employed various techniques to estimate its impact. For example, some research estimates the expected

number of infections (Jung *et al.*, 2020), hospitalizations (Sussman, 2020), mortality (Jung *et al.*, 2020; Sussman, 2020), and broader economic consequences (Borgonovi and Andrieu, 2020; Coibion *et al.*, 2020a; 2020b; Cachanosky *et al.*, 2020; Nicola *et al.*, 2020). Hoping to implement effective policy responses to COVID-19, other literature examines the effectiveness of various voluntary and involuntary measures to prevent healthcare systems from becoming overwhelmed (Chudik *et al.*, 2020; Gupta *et al.*, 2020; Hornstein, 2020; Mongey *et al.*, 2020; Piguillem and Shi, 2020).[1]

As the COVID-19 pandemic continued into 2020, health policy and medical literature began examining how the US healthcare sector might adjust to provide treatment for COVID-19 patients and treat patients with other conditions. This literature includes policy recommendations for technology adoption and expanded access to telemedicine (Hollander and Carr, 2020; Kandel *et al.*, 2020; Keesara *et al.*, 2020; Portnoy *et al.*, 2020). However, many of the recommended policy changes face regulatory obstacles issued by the Food and Drug Administration (FDA). Consequently, much of the literature examining how to expand healthcare capacity during the pandemic notes how existing FDA regulations prevent or delay recommended policy changes (Atluri *et al.*, 2020; Chen and Mao, 2020; March, 2020; Ravi *et al.*, 2020).

Much of the analysis examining the FDA's impact during the COVID-19 pandemic is found in medical and public health journals. However, a considerable body of economics research finds that FDA regulations have hindered the U.S. healthcare sector's ability to treat patients long before COVID-19 (Higgs, 1995; Philipson and Sun, 2008). Previous literature specifically finds FDA regulations of approving pharmaceuticals, medical devices, and other forms of treatment prolong or prevent their adoption within the US to the detriment of patients and healthcare providers (Evans and Watson, 2015; Higgs, 1995; Peltzman, 1973; Ward, 1992).

Curiously, previous economic literature examining the FDA has not examined the agency's impact during public health crises, including pandemics. Given the impact of COVID-19 on the U.S. economy and healthcare sector, a more robust understanding of how FDA regulation impacted the United States' response to the COVID-19 pandemic is vital to developing effective policy responses to better help the healthcare sector serve patients.

This article examines this question by employing a political economy framework to examine how FDA regulations have impacted COVID-19 testing, the utilization of remdesivir, and COVID-19 vaccines. I specifically examine these components of addressing the pandemic because they were issued Emergency Use Authorization (EUA) by the FDA, allowing them to reach clinicians and patients without undergoing the agency's regulatory approval process. Comparing the healthcare sector's adoption of COVID testing and treatment before and after the EUAs provides insight into the impact of the FDA's regulations restricting access to testing and treatment. My analysis finds that the FDA's regulations enacted before the COVID-19 pandemic began strongly restricted clinician and patient access to COVID-19 testing, remdesivir, and vaccines. After the FDA issued EUAs, the healthcare sector quickly adopted COVID-19 testing and remdesivir with little evidence of negative consequences. These findings contribute to the economics literature examining the FDA and contemporary COVID-19 policy research.

This article proceeds as follows. Section 2 reviews the economic literature assessing the FDA's regulatory impact on the healthcare sector. Section 3 develops a political economy framework to examine the FDA's incentives when determining whether to approve goods. Section 4 applies this framework to examine the development of COVID-19 testing, remdesivir treatment,

---

[1]In the United States, these efforts are often referred to as "flattening the curve."

and vaccination before and after the FDA issued EUAs. Section 5 concludes and provides implications for future research.

2 | LITERATURE REVIEW

Most economic analysis of the FDA occurs after the Kefauver-Harris Amendments of 1962.[2] These legislative acts granted the FDA the authority to determine both efficacy and safety standards for drugs before entering the market. The amendments also allowed the agency to set clinical trial standards and designs (Hanson, 1995). In the first economic analysis of the FDA and the 1962 Amendments, Peltzman (1973) finds that the increased regulatory stringency resulted in an estimated 5–10% tax on drug purchases. The author also noted the high cost of compliance "engendered a marked reduction in drug innovation" (p. 1049).

Much of the literature following Petlzman's analysis concludes increased regulatory stringency into the drug market resulted in considerable increases in drug prices. Examining a sample of 93 randomly selected new chemical entities, DiMasi *et al.* (1991) estimate the cost of developing a new drug in 1991 was approximately $114 million ($260 million in 2020 dollars). Nearly a decade after, DiMasi *et al.* (2003) estimate the cost of new drug approval to be approximately $804 million in 2003 ($1.2 billion in 2020 dollars). Adams and Branter (2006) similarly estimated the cost to be between $500 and $2 billion in 2000 dollars (between $752 million and $3 billion in 2020 dollars).

FDA authority to set drug approval standards also lengthened the time required for drugs to reach patients. Grabowski *et al.* (1978) find the average time required to approve new drugs from 1962 to 1967 increased from an average of approximately 7–30 months. Pharmaceuticals' time to complete FDA approval continued to increase throughout the 1980s and mid-1990s. From 1980 to 1989, the average time from the synthesis of a new drug to marketing approval averaged 14.1 years, rising to 15.2 years from 1990 to 1996 (Miller, 1988). These long approval times exceeded those found in other developed nations. Over mostly the same period, Wardell (1973) notes the time required to have new drugs approved in the United States exceeded those in the United Kingdom by an average of 2 years. Kaitin *et al.* (1989) find a similar two-year difference between drug approval times between the United States and the United Kingdom from 1977 to 1987. From 1970 to 1993, approval times for drugs and medical devices in the United States trailed those in the United Kingdom, Germany, France, and Spain (Kaitin and Brown, 1995). Longer approval times for many drugs can be lethal. Gieringer (1985) estimates that a one-year delay in drug benefits can result in approximately 37,000–76,000 patient deaths.

Economic analysis of the FDA's drug approval process frequently finds increased costs to develop new drugs and longer times required to reach the market deters producers from introducing new drugs and engaging in pharmacological innovation. Faust (1985) writes, "since the passage of the New Drug Amendments of 1962, the influence of regulation on the drug development process and biomedical research, in general, has resulted in considerable negative fall-out highlighted by a decline in drug innovation" (p. 201). The author also finds that other advanced nations "where regulatory stringencies have not been as significant a deterrent to research productivity" did not experience a similar decrease in new drug introductions (p. 201). Case studies

---

[2]A noteworthy exception is Sobel (2008), who employs a public choice framework to examine the special interests involved in lobbying for the 1906 Pure Food and Drug Act.

and empirical analyses support these claims. Grabowski *et al.* (2002) note that R&D for beta-blockers, anxiolytics, anti-depressants, and the first birth control drugs constituted a large component of drug producers' R&D before the 1962 amendments. Wiggins (1981) estimates the 1962 amendments reduced the introduction of new medicines by approximately 60%. More recently, Evans and Watson (2015) and Tabarrok (2017) find that the FDA's approval process has delayed genomic medicine advancement within the United States.[3] Economic literature examining the FDA's medical device regulation through legislative acts in 1976, 1988, and 1990 (Munsey, 1995) reaches similar conclusions. From 1983 to 1990, the FDA received about 80 premarket approvals a year but only approved approximately 45 (Higgs, 1995).[4] By 1992, the FDA had only approved 12 (Higgs, 1995). Miller (1988) similarly finds that the FDA's oversight of medical devices restricts new product development and innovation.

Consistent findings that the FDA regulatory barriers delay drug development, increase the cost of development, and prolong approval times have resulted in economists' widespread agreement that they are on net harmful to patients (Klein, 2000). With few exceptions, the FDA's regulatory scope continued to expand into the early 2000s (FDA, 2018a). Philipson *et al.* (2008) estimate the FDA's regulatory scope encompasses approximately 20% of all consumer spending in the United States. However, considerably less economic research has examined the FDA's impact on and its regulatory impact on the U.S. healthcare industry since the early 2000s (Philipson and Sun, 2008). What research has been produced continues to find that the agency's regulation continues to stifle innovation. Chorniy *et al.* (2021) find that three additional months of delayed approval time result in one less drug developed by drug producers.

Although a considerable body of research finds that FDA regulations are harmful, the agency does provide avenues for patients to experimental treatments under certain circumstances. For example, the FDA's expanded access allows patients with terminal illnesses to access experimental treatments with the agency's approval (FDA, 2020a). Dranvoe and Meltzer (1994) find that the FDA approves "more important drugs" comparatively more quickly.[5] However, the author's estimates for drug importance do not account for medicinal urgency and broader public health considerations. Because addressing the impact of COVID-19 requires assessing tradeoffs of evaluating the safety and effectiveness of goods used to treat a novel virus with a need to quickly disseminate treatments due to medical urgency, further research into contemporary FDA regulatory actions are necessary to bolster our understanding of the agency's impact on the healthcare sector's ability to treat patients during pandemics.

3 | THE FDA, POLITICAL ECONOMY, AND PANDEMICS

Although the FDA's regulatory scope includes a variety of products, Higgs (2004) notes the agency's primary authority is "banning existing products from the market until their manufacturers adduce satisfactory evidence of efficacy and safety" (p. 60). Because the FDA is a federal agency, it follows the incentive structure of a bureaucracy, mainly that of maximizing its revenue (Tullock, 1965; Mises, 1944). The FDA, as well as other regulatory bodies, typically obtains

---

[3]Takahashi *et al.* (2020) review several genomic treatments which could potentially benefit COVID-19 patients.

[4]Premarket approvals are the approval required for phase three medical devices to receive FDA approval.

[5]The authors measure drug importance by examining drug citations in medical textbooks, medical journals, and patent applications, as well as total sales and number of countries introducing a drug.

more revenue through expanding its number of operations, increasing the regulatory stringency over the products it oversees, and expanding its regulatory scope (Tullock, 1965).

The incentive to obtain more personnel, federal funding, and other resources while expanding its regulatory stringency and scope works to elongate and complicate the FDA's approval process for the goods it oversees (Higgs, 2004). The agency's incentives also influence its willingness to approve potentially harmful treatments and other goods.[6] Because the FDA faces the threat of public backlash or political disapproval by approving a product which could potentially harm a patient, it has little incentive to approve the product despite its potential benefits. Instead, the agency either fails to approve the product or requires the producer to conduct more clinical research to further demonstrate it is safe (Higgs, 1995). The agency also faces little threat of repercussions from failing to approve a safe and effective product because the harms of denying patients a safe treatment option are rarely observable (Tabarrok, 2000).

Both considerations create a disincentive for the FDA to weigh the risks of harm against the benefits, providing overly stringent regulation (March, 2016; Tabarrok, 2000, 2017). A pandemic caused by a novel disease creates a demand to provide novel products to treat, detect, or deter a disease. Novelty combined with the FDA's motivation to approve products conservatively could motivate the agency to exercise harmfully stringent standards for goods created to address a pandemic. Recent analysis finds evidence for this. Using a Bayesian decision analysis, Isakov *et al.* (2019) find the FDA is overly conservative in designing clinical studies for drugs designed to treat terminal illnesses with no existing therapies.

Philipson and Sun (2008) note that the FDA's incentive to provide overly stringent regulation generates "dynamic considerations," which hinder the agency's ability to provide effective regulation (p. 96). Consequently, the agency's approval process results in higher costs to develop products and longer times to reach patients, but with potentially little additional assurance of product safety (p. 96).[7] Higgs (2004) notes that side effects from FDA medications deemed safe for use constitute the fourth leading cause of death in the United States.[8] While these findings could be interpreted as a need for more regulatory stringency, further research finds deregulatory processes occurring in the early 2000s provided faster approvals with sacrificing safety. Philipson *et al.* (2008) examine the Prescription Drug User Fee Acts, which allowed for prescription drugs to undergo an expedited review by the FDA for a fee. The authors find little safety was sacrificed with expedited reviews for drugs. Grabowski and Wang (2008) reach similar conclusions. Even when treatments pose knowable risks, March (2017) finds that physicians and drug producers can provide more effective risk-management than the FDA.

The effectiveness of FDA regulations to prevent unsafe products from entering the market can also be negatively impacted by rent-seeking activity from the private sector. Chu (2008) finds lobbying expenditures from the top 10 pharmaceutical companies listed in the Fortune 500 exceeded their total R&D spending from 1998 to 2006. Drug producers also frequently hire former FDA employees who know the regulatory process to increase their likelihood of having their products approved. Ruwart (2018) notes that the number of FDA officials that left for the

---

[6]Higgs (1995), Klein (2000), and Tabarrok (2000) dichotomize the FDA's incentives to withhold risky, although potentially beneficial, treatments or devices into type 1 and type 2 errors. Type 1 errors constitute failing to approve products that are safe and effective. Type 2 errors constitute erroneously approving a product that is unsafe and/or ineffective.

[7]The authors also note "static" concerns including that alternative establishments and legal institutions, including private sector testing of products and product liability laws, create regulatory redundancies for many products.

[8]FDA approved drugs only trailing heart disease, stroke, and cancer.

pharmaceutical industry increased from 10 to 76% after the adoption of the Kefauver Harris Amendments.[9]

Despite the FDA's history of harmful regulation, the agency has historically gained additional oversight and resources during periods of perceived public health crises. Higgs (2004, 1995) notes that the Kefauver Harris Amendments of 1962, Medical Device Amendments of 1976, and Safer Medical Devices Act of 1990 followed periods of public fear following the use of unsafe and faulty drugs and medical devices. More recently, the FDA gained regulatory jurisdiction over tobacco products through the Family Smoking Prevention and Tobacco Control Act due to public concerns of increased smoking rates among young users (Deyton *et al.*, 2010). The FDA also increased its regulatory stringency over the prescription and distribution of opioids to address the opioid epidemic (Cobin *et al.*, 2017).

However, these legislative changes stemmed from the public perception that medical goods were not sufficiently regulated. These concerns provided an avenue for more political action and an expanded role for the FDA (Higgs, 1995). Public concerns during a pandemic could create different incentives for politicians and health-related regulators. If the FDA prevents or delays goods that help diagnose, treat, or prevent disease spread, it could face similar public and political backlash for preventing healthcare providers from addressing a crisis. Research finds portions of the U.S. population expressed frustration with governmental actions taken during the COVID-19 pandemic. Mello *et al.* (2020) find, "Across the United States, health officers have been subject to doxing (publishing private information to facilitate harassment), angry and armed protesters at their personal residences, vandalism, and harassing telephone calls and social media posts, some threatening bodily harm and necessitating private security details" (p. 741). These and other hostilities from the public and political figures directed at the FDA could motivate the agency to relax its regulatory stringency.

From the standpoint of developing effective pandemic-response policies, reduced FDA regulatory stringency authority allows for greater decision-making capability for state health agencies, physicians, and other decentralized units (Higgs, 2004). Decentralization during public health crises have provided numerous examples of state-level and private action finding effective ways to address public health crises. Trosken (2015) finds that federalism and secured property rights provided much of the United States with effective infrastructure to mitigate the spread of yellow fever, typhoid fever, and smallpox from 1850 to 1950. Similarly, Carson (2016) notes private firms underwent various efforts to prevent malaria spread during the early 1900s when state-efforts were either poorly provided or unprovided. Candela and Geloso (2021) and Geloso and Pavlik (2019) find comparatively higher amounts of economic freedom are associated with quicker economic recovery after pandemics.

Research examining contemporary public health crises find decentralized policy responses demonstrate similar success. For example, the off-label uses of prescription drugs are self-regulated among physicians and drug producers. A pharmaceutical is used off-label when it is prescribed to treat a condition that it was not approved for by the FDA. As of 2003, the off-label prescription of pharmaceuticals accounts for approximately 25% of all U.S. prescriptions (Leibman, 2003). Previous research examining the governance of off-label drug prescription within the healthcare finds it frequently establishes safe and effective uses for drugs before the FDA (Klein and Tabarrok, 2004; March, 2016; Tabarrok, 2000). During the first 10 months of the COVID-19 pandemic, any treatment offered for COVID-19 was off-label (Shojaei and Salari, 2020).

---

[9]Pharmaceutical companies hiring FDA agencies remains common (Piller, 2018).

South Korea provides an example of effective reduced regulatory stringency's benefits in addressing the COVID-19 pandemic. After experiencing an outbreak of the Middle East Respiratory virus in 2005, the South Korean government implemented emergency approval measures to quickly approve testing kits for emerging infectious diseases (Wang *et al*., 2020). These measures allowed South Korean biotechnology companies to have their COVID-19 testing kits approved by the Korean Centers Disease Control and Prevention within 2 weeks of South Korea's first confirmed COVID-19 infection (Kim and Denyer, 2020).

Although reduced regulatory stringency by the FDA and other public health agencies during a pandemic provides comparatively faster access to medical goods, it also creates a potential for less safe or effective products to enter the market. Maintaining safety standards, even during a pandemic, is still vital to avoid misdiagnosing and erroneously treating patients. Because the FDA faces backlash for approving ineffective or harmful products, the FDA maintains an incentive to reduce regulatory standards as little as possible, yielding only to avoid public and political backlash (Rome and Avorn, 2020).

However, the typical amount of regulatory stringency may not allow for the healthcare sector to effectively address a health crisis. The FDA's tendency to increase its regulatory scope and stringency despite widespread evidence of the harms caused by regulation provide enough reason to examine the agency's impact during pandemics. Because pandemics constitute some of the deadliest events in human history (Lina, 2008), barriers preventing the approval and adoption of medical goods and services that can help address them are especially harmful.

4 | COVID-19 AND FDA REGULATION

In late January 2020, a middle-aged man in Washington State became the first known U.S. patient to test positive for COVID-19 (Holshue *et al*., 2020). The virus quickly spread across the country through traveling and community spread, reaching national emergency status on March 13, 2020 (AJMC Staff, 2020a; WHO, 2020). To prevent overwhelming the healthcare sector with infected patients, the federal and state governments enacted travel restrictions and lockdown measures to varying degrees of restrictiveness, beginning with California on March 19, 2020 (AJMC Staff, 2020b). Secon (2020) notes that state-level lockdown measures at their peak affected approximately 94% of the U.S. population.

The United States still struggled to contain the pandemic 8 months after receiving its first confirmed infection. By August 2020, approximately 25% of all COVID-19 infections and fatalities globally occurred in the United States. As of late October 2020, the Coronavirus Research Center at John's Hopkins University (2020) estimated over 8.6 million U.S. COVID-19 infections, resulting in approximately 225,000 fatalities. Much of its early failures to address the COVID-19 pandemic stem from its healthcare sector's inability to overcome FDA regulations to develop and provide COVID-19 testing as well as provide COVID-19 treatment. After the FDA issued EUAs for these products, the healthcare sector could utilize them to better address the pandemic.

4.1 | COVID-19 testing

In 1976, congress granted the FDA the authority to establish rules for developing laboratory-developed tests (LDTs). LDTs, as defined by the FDA, include any test, "designed,

manufactured, and used within a single laboratory" (FDA, 2018b, pp. 1). Although the agency provided little regulatory oversight initially, the proliferation of LDTs by independent laboratories to diagnose a variety of ailments and conditions prompted the FDA to establish guidelines in the early 2010s (FDA, 2018b).

In 2014, the FDA drafted guidance for a rigorous regulatory review process. The process included requirements for laboratories to notify the FDA when LDTs were developed, a process to report adverse events, a premarket review process, a channel to submit clinical literature demonstrating the LDT's validity, and a risk-based phase-in approach to implementing premarket reviews (FDA, 2014, p. 15). The degree of stringency for these guidelines varied depending on whether the FDA considered the LDT to be considered the tests to be low, moderate, or high risk.

The FDA began enforcing these guidelines in 2017 despite never formally adopting them (Shapiro, 2019). Shapiro (2019) likened the agency's oversight of LDT's to, "jump[ing] the fence and...roaming free" (pp. 10). Enforcing LDT guidelines without clearly establishing what was required for approval left laboratories unsure how to achieve compliance with the FDA and financially strapped to complete the approval processes (Genzen, 2019). As Dr. Duane Newton, Director of clinical microbiology at the University of Michigan, notes, LDT regulations "hamper the willingness and ability of manufacturers and laboratories to invest resources into developing and implementing new tests" (Patel, 2020a, pp. 8).

Because COVID-19 tests require testing for a novel virus, any laboratory-developed test-kit is considered an LDT. Consequently, private laboratories were largely unable to create COVID-19 tests promptly as the virus began to spread across the United States. Laboratories that developed and administered Coivd-19 tests without the FDA's approval were ordered to discontinue testing even when evidence of communal spread was available (CDC, 2020; Fink and Baker, 2020). By March 5, 2020, about 5 weeks after the first confirmed case of COVID-19 in the United States, only 1,235 patients nationwide were tested for COVID-19 (Patel, 2020a). Other countries were able to administer millions of tests over a similar period (Patel, 2020a).

The FDA also prevented laboratories from administering COVID-19 tests without a clinical laboratory certificate, which can require months to complete (Fink and Baker, 2020).[10] Consequently, only 40 public health laboratories and a small group of commercial laboratories had access to COVID-19 test-kits 2 months after the first reported COVID-19 infection (Soucheray, 2020). Hospitals that did not have approved laboratories were required to submit patients' COVID-19 tests to certified laboratories to receive a diagnosis. Lag times between administering a test and receiving a diagnosis could be considerable depending on the distance between hospitals and processing laboratories, which hindered hospitals' ability to treat patients severely affected by the virus (Johnson, 2020).

As the pandemic spread across the United States in February 2020, politicians, state health agencies, clinical organizations, and other medical professionals began publicly criticizing the FDA for delaying the approval COVID-19 tests (Khazan, 2020; AACC, 2020). Facing criticisms and a critical shortage of COVID-19 testing-kits and laboratories permitted to process tests, the FDA established new procedures, "enabling laboratories to immediately use tests they developed and validated" on February 29, 2020 (FDA, 2020b, pp. 6). The new procedures permitted laboratories to develop and offer COVID-19 testing after applying for a EUA from the FDA

---

[10]Receiving a clinical laboratory certificate from the FDA required laboratories to first receive approval from the Center for Disease Control and the center for Medicare and Medicaid Services, and to meet state-level requirements.

while later submitting clinical evidence of effectiveness. The agency also eliminated requirements for clinical laboratory certification to process COVID-19 tests (FDA, 2020c).

Testing capacity expanded rapidly after the agency issued EUAs. By April 21 2020, less than 2 months after reducing its regulatory barriers, the FDA approved 50 separate COVID-19 test kits (FDA, 2020d). Writing in June 2020, Patel (2020b) finds laboratories were able to administer and process thousands of tests per day, and the United States, "has more COVID-19 tests than it knows what to do with" (pp.1). March (2020) notes that after EUAs were provided, test developers also improved the quality of COVID-19 tests by developing test-kits, which provided significantly faster diagnoses and could be performed with saliva samples rather than nasal swabs. The rapid proliferation and innovation of COVID-19 tests following the FDA's EUAs also did not sacrifice efficacy for expediency. As of August 20th, 2020, the FDA issued EUA for 140 COVID-19 diagnostic tests, with two having their EUA removed as of the same date (FDA 2020e; 2020f).

Although the FDA reduced its regulatory stringency for LDTs, it only did so after receiving mounting evidence that its regulatory barriers created a critical shortage of test kits. COVID-19 test-kits and their proliferation after the FDA began granting EUAs provide an example of the agency's incentives to without beneficial products unless presented with sufficient backlash for its failures to adjust regulatory standards appropriate for a pandemic.

4.2 | COVID-19 treatment with remdesivir

Although there is no cure for COVID-19, physicians and healthcare professionals can provide treatments to patients to recover from the infection and to mitigate side effects. One of the most established and used treatments for COVID-19 is remdesivir. Spinner *et al.* (2020) find remdesivir can help treat severe cases of COVID-19 and help patients recover more rapidly. Beigel *et al.* (2020) find that patients hospitalized with COVID-19 treated with remdesivir exhibited lower mortality rates, lower rates of respiratory infection, and faster recovery times. Williamson *et al.* (2020) find that remdesivir may decrease the chances of COVID-19 patients contracting pneumonia.

Despite being described as the "standard of care" for COVID-19 (Lovelace, 2020), remdesivir faced considerable obstacles to reaching the public by falling short of FDA regulatory requirements (Eastman *et al.*, 2020). In 2014, remdesivir was included in a randomized, controlled trial to treat patients in the Democratic Republic of the Congo infected with the Ebola virus. As Pardo *et al.* (2020) note, "although remdesivir performed well in preclinical studies, it did not meet efficacy endpoints [established by the FDA] in a randomized trial conducted during an Ebola outbreak" (p. 4). Early analysis of this data generated concern that remdesivir would fail to obtain FDA approval, leading its producer to remove it from the clinical trial (Pardo *et al.*, 2020).

Remdesivir's promising preclinical results later prompted a collaborative effort from the University of Alabama at Birmingham, Vanderbilt University, and the University of North Carolina to examine the drug's effectiveness in treating SARS and MERS in 2016 (Gilead Sciences, 2020a; 2020b). Lo *et al.* (2017) note that preclinical results from studies on remdesivir," providing evidence to support new indications for this compound against human viruses of significant public health concern" (p. 1). However, remdesivir again failed to advance to clinical development and apply for FDA approval due to an inadequate number of patients to complete the necessary studies (Gilead Sciences, 2020a; 2020b).

As COVID-19 began spreading through the United States, clinicians were only able to access remdesivir through the FDA's expanded access program, which required applications for individual patients and the agency's approval before treatment could be administered (Grien *et al*., 2020). Consequently, few patients received remdesivir during the early stages of the pandemic. Grien *et al*. (2020) find that from January 25 to March 1, 2020, 22 patients in the United States were treated with remdesivir through the expanded access program. Over the same period, 39 patients in Canada, Italy, Austria, France, Germany, Netherlands, Spain, and Canada received remdesivir despite Gilead Sciences, remdesivir's producer, being in the United States. The authors find that these patients demonstrated improvement in oxygen class, and most patients placed on ventilators receiving remdesivir survived infection.

These successful results motivated several large-scale clinical trials organized and funded by the National Institute of Health and Gilead Sciences in March, 2020, distributing the drug to 70 countries severely impacted by the pandemic (Gilead Sciences, 2020a; 2020b). This includes two clinical trials at Capital Medical University in China (Eastman *et al*., 2020). Afterward, an additional clinical trial was established in Nebraska for hospitalized COVID-19 patients in late February 2020 (National Institute of Health, 2020). Summarizing the findings of large clinical trials for remdesivir, Lamb (2020) finds, "Phase III evaluation of remdesivir in the treatment of COVID-19 commenced in early 2020 and has thus far yielded promising results" (p. 1).

Remdesivir received a EUA from the FDA on May 1, 2020, to treat those with severe COVID-19 infections (Lamb, 2020).[11] Two months after receiving a EUA, the Department of Health and Human Services secured more than 500,000 remdesivir treatment courses, consisting of most of the projected supply for July–August (Health and Human Services, 2020). In August, the FDA extended its EUA for remdesivir to include any patient infected with COVID-19 (FDA, 2020g). Most recently, the FDA fully approved remdesivir to treatment of COVID-19, despite failing to undergo the FDA's approval process (Gilead Sciences, 2020a; 2020b).[12]

Remdesivir's transition from withdrawing from clinical trial fearing it would not meet efficacy standards to receiving one of the only FDA approvals to treat COVID-19 provides another example of how the agency failed to adapt its standards for pandemic conditions. The use of remdesivir across the globe and for compassionate use in the United States further suggest that the FDA's hesitancy to approve the drug stemmed from its incentive to prolong approval despite providing a benefit well understood by the medical community.

4.3 | COVID-19 vaccine development

The FDA began regulating vaccines in 1972. The authority was transferred from the National Institute of Health (NIH), which faced criticism from politicians and the public for failing to provide enough regulatory stringency while approving a vaccine to address the 1958 pandemic. Under the regulatory guidelines set by the NIH during the 1958 pandemic, private producers developed a vaccine before the influenza responsible for the pandemic reached the United States. These producers also manufactured 60 million doses (for a population of approximately

---

[11]The agency defined severe COVID-19 infections as, "patients with oxygen saturation (SpO2) ≤94% on room air or requiring supplemental oxygen or requiring mechanical ventilation or requiring extracorporeal membrane oxygenation" (FDA[7] 2020g, footnote 2).

[12]The FDA also issued EUA for the rheumatoid arthritis drug named baricitinib (FDA,[8] 2020h) and for blood transfusion treatments from previously infected patients to currently infected patients (FDA,[9] 2020i). The agency also issued an EUA for the malaria drugs cloroquine hydroxychloroquine, but later revoked its authorization (FDA,[10] 2020j).

180 million people) during the first 4 months of the pandemic (US Department of Health, Education, and Welfare, 1958). However, analyses performed after the pandemic indicated the vaccine was relatively ineffective in preventing infection (Greene, 1958).[13]

Under the FDA's vaccine approval process, vaccine producers are required to submit a biologics licensure application to the agency's Center for Biologics Evaluation and Research (CBER). CBER requires vaccines to undergo three stages of clinical trials, ranging in size from dozens to thousands of participants (CDC, 2014). Johns Hopkins University's Coronavirus Research Center (2020) estimates that the vaccine approval process requires an average of 5–10 years to complete. Darrow *et al*. (2020) find that the FDA approved an average of two vaccines per year from 1998 to 2018.

During the COVID-19 pandemic, the FDA instituted an accelerated timeline to provide an EUA for COVID-19 vaccines quickly (Coronavirus Research Center, 2020). To reduce the time required for a COVID-19 vaccine to receive an EUA, the FDA allowed clinical trial phases for experimental vaccines to be combined (Coronavirus Research Center, 2020). Federally funded programs also provided some vaccine producers with resources to conduct trails more quickly. On March 15th, 2020, the White House instituted Operation Warp Speed. "Warp Speed" provided vaccine producers selected by the program with federal subsidies to conduct clinical trials to advance vaccine approval more quickly (Department of Health and Human Services; HHS, 2020). The federal government also pre-emptively purchased vaccine doses before clinical trials were completed to reduce the time needed to distribute and produce a vaccine if it received an EUA (HHS, 2020).

On December 11, 2020, the FDA granted its first COVID-19 vaccine EUA to partnering drug producers Pfizer and BioNTech (FDA, 2020k). One week later, the FDA granted another EUA to Moderna's COVID-19 vaccine (FDA, 2020l). Both producers were able to quickly manufacture large quantities of vaccines receiving EUA. Slotkin (2020) finds that 7.9 million doses of both vaccines were available to distribute by December 19. Pfizer contracted with the federal government to provide an additional 100 million doses by July 2021 (Pfizer, 2020a). Both vaccines' clinical trial results indicated effectiveness rates exceeding 90% (Balfour, 2020; Pfizer, 2020b).

Although the FDA's expedited approval process successfully brought two effective COVID-19 vaccines to the US healthcare market within a year, the agency's regulatory barriers still provided noteworthy delays that prevented a COVID-19 vaccine from reaching patients sooner. Pfizer applied for a vaccine EUA on November 20 (Chandler, 2020). Moderna applied for a vaccine EUA on November 30 (Wientraub, 2020). The several week delay from the FDA issuing an EUA was caused by the agency electing to assemble and receive council from an additional advisory panel (FDA, 2020). Seeking additional input came at a high cost. The COVID Tracking Project (2020) finds an average of approximately 2,200 patients died from COVID-19 daily from November 22 to December 18.

Further analysis indicates the development of COVID-19 vaccines significantly earlier in the pandemic than previously thought. Wallace-Wells (2020) finds that Moderna's vaccine was designed on January 13, 2020, and was developed over a two-day period. Even with an expedited process developed to approve and distribute a vaccine to address the pandemic, the FDA prevented Moderna's vaccine from reaching patients (outside of a clinical trial) by approximately 11 months.

---

[13]The Department of Health, Education, and Welfare (1958) notes that the 1958 pandemic constituted, at the time, the most contagious influenza pandemic in the past 40 years.

Prolonging issuing an EUA for a COVID-19 vaccine despite availability and promising clinical trial results further demonstrates the FDA's incentive to delay the approval of potentially risky products even when the risks are comparatively low. Requiring Moderna's vaccine to complete the full approval process instead of allowing it to be accessed as an experimental medication outside of clinical trials significantly curtailed patient access. Establishing additional advisory boards after each of the COVID-19 vaccines completed clinical trials designed by the same agency provides further evidence that, despite willingness to expedite an EUA, the FDA still faces bureaucratic incentives.

5 | CONCLUSION AND IMPLICATIONS

As the pandemic persists, public health and medical literature frequently find regulations enacted by the FDA prevents US healthcare from making urgently needed adjustments to provide treatment to patients. Economics literature examining the impact of the FDA often finds it increases the cost of development, prolongs approval times, and reduces innovation for the products it regulates. However, previous literature examining the FDA has not examined the impact of the agency's regulation on the healthcare sector during pandemics. This article contributes to the FDA's economic research by examining the agency's impact during the COVID-19 pandemic, specifically on the development of testing and adoption of treatment for the virus. Because the FDA issued EUAs for both kinds of medical goods, the COVID-19 pandemic provides a unique case study to examine the impact of regulatory structure and deregulation during the same pandemic.

FDA regulations implemented on developing LDTs to test for novel conditions, including COVID-19, strongly restricted laboratories and COVID-19 test developers from providing adequate testing while initial outbreaks began in the United States. Further FDA regulations requiring laboratories to obtain a clinical laboratory certificate to perform COVID-19 tests also prevented many laboratories from diagnosing patients. Consequently, the US healthcare sector lagged considerably behind other developed nations in providing COVID-19 testing to assess the advancement of the pandemic.

The development of the only FDA-approved treatment for COVID-19 treatment, remdesivir, was also prevented from reaching patients because of FDA regulations. Despite exhibiting promise in preclinical trials to treat Ebola, MERS, and SARS, regulations set forth by the FDA left remdesivir unlikely to earn the agency's approval. The only access patients had to receive remdesivir as the pandemic reached the United States was through the FDA's expanded access program. Conversely, other countries were able to provide remdesivir for patients through clinical trials organized without the FDA and through other means. The FDA's delays in issuing an EUA for both COVID-19 vaccines further demonstrates the agency's bureaucratic incentives to provide high degrees of regulatory stringency despite being presented with strong evidence of the vaccine's effectiveness and concurrent rising mortality figures from the pandemic.

The FDA's EUAs issued for laboratories to develop and administer COVID-19 tests and treat patients with remdesivir rapidly expanded patient and clinician access to both products. COVID-19 test-kits also witnessed reductions in the time required to diagnose and develop saliva-based tests with little reduction in efficacy. These findings suggest that previously enacted FDA regulations hindered the healthcare sector's ability to address the COVID-19 pandemic. In contrast, the proliferation and development of COVID-19 testing and rapid adoption of remdesivir to treat patients after the FDA issued EUAs strongly indicate that the healthcare

sector might have better adjusted to the pandemic more quickly with less FDA oversight. Considering the FDA's incentive to provide high degrees of regulatory stringency and the urgent need for the healthcare sector to adjust to meet the pandemic's demands, this manuscript's findings strongly suggest that standard FDA approval processes are ill-suited for pandemics can significantly undercut the adoption of new treatments and other medical goods during health care crises.

Although this manuscript contributes to contemporary COVID-19 policy literature and research examining the impact of FDA regulation, it has several limitations. First, this manuscript cannot provide a full picture of which changes in treatment, testing, and other efforts were ultimately successful in addressing the COVID-19 pandemic.[14] With additional medical discovery and changes to regulation, other means to treat and detect COVID-19 may become more prevalent as the healthcare sector adjusts to the pandemic. Second, it evaluates regulatory changes that occurred while pandemic conditions worsened, which does not allow comparisons to how effective such regulatory changes would be if they occurred earlier.

Additional research is needed to examine the FDA's full impact on the COVID-19 pandemic and other public health crises. Further research examining how the US healthcare sector adapted when the FDA held comparatively less regulatory authority would provide critical insight into the healthcare sector's adaptability during public health emergencies. Lastly, evaluating FDA programs allowing medical goods to bypass its normal approval process such as EUAs, expanded access, and the recently enacted Coronavirus Treatment Acceleration Program would also provide fruitful implications for evaluating the role of the FDA during public health emergencies.

REFERENCES

Adams, C.P. & Branter, V.V. (2006) Estimating the cost of drug development: is it really $802 million? *Health Affairs*, 25, 420–428.

American Association of Clinical Chemistry. 2020 *AACC calls on FDA to allow clinical labs to develop their own tests for the coronavirus*. Available at: https://www.aacc.org/advocacy-and-outreach/comment-letters/2020/aacc-calls-on-fda-to-allow-clinical-labs-to-develop-their-own-tests-for-the-coronavirus.

American Journal of Managed Care. (2020a) *COVID-19 Roundup: coronavirus now a national emergency, with plans to increase testing*. Available at: https://www.ajmc.com/view/COVID19-roundup2.

American Journal of Managed Care. (2020b) *A timeline of COVID-19 developments in 2020*. Available at: https://www.ajmc.com/view/a-timeline-of-COVID19-developments-in-2020.

Atluri, S., Manchikanti, L. & Hirsch, J.A. (2020) Expanded umbilical cord mesenchymal stem cells (UC-MSCs) as a therapeutic strategy in managing critically ill COVID-19 patients: the case for compassionate use. *Pain Physician*, 23, 71–83.

Balfour, Hannah. (2020) *Moderna's COVID-19 vaccine is 94.5 percent effective, according to interim analysis*. Available at: https://www.europeanpharmaceuticalreview.com/news/133520/modernas-COVID-19-vaccine-is-94-5-percent-effective-according-to-interim-analysis/.

Beigel, J.H., Tomashek, K.M., Dodd, L.E., Mehta, A.K., Zingman, B.S., Kalil, A.C., Hohmann, E., Chu, H.Y., Luetkemeyer, A., Kline, S., Lopez de Castilla, D., Finberg, R.W., Dierberg, K., Tapson, V., Hsieh, L., Patterson, T.F., Paredes, R., Sweeney, D.A., Short, W.R., Touloumi, G., Chien, D., Ohmagari, N., Oh, M., Ruiz-Palacios, G.M., Benfield, T., Fätkenheuer, G., Kortepeter, M.G., Atmar, R.L., Creech, B., Lundgren, J., Babiker, A.G., Pett, S., Neaton, J.D., Burgess, T.H., Bonnett, T., Green, M., Makowski, M., Osinusi, A., Nayak, Seema & Lane, H.C. (2020) Remdesivir for the treatment of COVID-19-final report. *The New England Journal of Medicine*, 383, 1813–1826.

---

[14]This manuscript was written in early January 2021, before the end of the COVID-19 pandemic.

Borgonovi, F. & Andrieu, E. (2020) Bowling together by bowling alone: social capital and COVID-19. *COVID Economics*, 17, 73–96.

Candela, R. & Geloso, V. (2021) Economic freedom, pandemics, and robust political economy. *Southern Economic Journal*, 87(4), 1250–1266.

Carson, B. (2016) Firm-led malaria prevention in the United States, 1910-1920. *American Journal of Law and Medicine*, 42, 310–332.

Cachanosky, N., Cutsinger, B.J., Hogan, T.P., Luther, W.J., & Salter, A.W. (2021) The Federal Reserve's response to the COVID-19 contraction: an initial appraisal. *Southern Economic Journal*, 87(4), 1152–1174.

Centers for Disease Control. (2014) *The journey of your child's vaccine.* Available at: https://www.cdc.gov/vaccines/parents/infographics/journey-of-child.

Centers for Disease Control. (2020) *Public health response to the initiation and spread of pandemic COVID-19 in the united states.* Available at: https://www.cdc.gov/mmwr/volumes/69/wr/mm6918e2.htm.

Chandler, Vishwadha. (2020) Pfizer files COVID-19 vaccine application to U.S. FDA. Available at: https://www.reuters.com/article/health-coronavirus-vaccines-pfizer/pfizer-files-COVID-19-vaccine-application-to-u-s-fda-idUSKBN2801D8.

Chen, K.Z. & Mao, R. (2020) Fire lines as fault lines: increased trade barriers during the COVID-19 pandemic further shatter the global food system. *Food System*, 12, 375–378.

Chorniy, A., Bailey, J., Civan, A. & Maloney, M. (2021) Regulatory review time and pharmaceutical research and development. *Health Economics*, 30(1), 113–128.

Chu, A.C. (2008) Special interest politics and intellectual property rights: an economic analysis of strengthening patent protection in the pharmaceutical industry. *Economics and Politics*, 20, 185–215.

Chudik, A., Hashem Pesaran, M. & Rebucci, A. (2020) Voluntary and mandatory social distancing: evidence on COVID-19 exposure rates from chinese provinces and selected countries. *COVID Economics*, 7, 26–62.

Cobin, S., Brown Jr, R.E., Du Vivier, D. & Ramachandran, B.K. (2017) The US opioid crisis: current federal and state legal issues. *Chronic Pain Medicine*, 125, 1675–1681.

Coibion, O., Gorodnichenko, Y. & Weber, M. (2020a) The cost of the COVID-19 crisis: lockdowns, macroeconomic expectations, and consumer spending. *COVID Economics*, 20, 1–51.

Coibion, O., Gorodnichenko, Y. & Weber, M. (2020b) Catastrophic declines in the employment in the US. *COVID Economics*, 21, 40–58.

Coronavirus Research Center at Johns Hopkins University (2020). Vaccine research & Development: How can COVID-19 vaccine development be done quickly and safely? Available at: https://coronavirus.jhu.edu/vaccines/timeline#:∼:text=A%20typical%20vaccine%20development%20timeline,vaccine%20doses%20for%20widespread%20distribution.

Darrow, J.J., Avorn, J. & Kesselheim, A.S. (2020) FDA approval and regulation of pharmaceuticals, 1983-2018. *Journal of the American Medical Association*, 323, 164–176.

Deyton, L., Sharfstein, J. & Hamburg, M. (2010) Tobacco product regulation — a public health approach. *The New England Journal of Medicine*, 362, 1753–1756.

DiMasi, J.A., Hansen, R.W. & Grabowski, H.G. (2003) The price of innovation: new estimates of drug development costs. *Journal of Health Economics*, 22, 151–185.

DiMasi, J.A., Hansen, R.W., Grabowski, H.G. & Lasagna, L. (1991) Cost of innovation in the pharmaceutical industry. *Journal of Health Economics*, 10, 107–142.

Dranvoe, D. & Meltzer, D. (1994) Do important drugs reach the market sooner? *RAND Journal of Economics*, 25, 402–423.

Eastman, R.T., Roth, J.S., Brimacombe, K.R., Simeonov, A., Shen, M., Patnaik, S. & Hall, M.D. (2020) Remdesivir a review of its discovery and development leading to emergency use authorization for treatment of COVID-19. *ACS Central Science*, 6, 672–683.

Evans, J.P. & Watson, M.S. (2015) Genetic testing and FDA regulation: overregulation threatens the emergence of genomic medicine. *Journal of the American Medical Association*, 313, 669–670.

Faust, R.E. (1985) The impact of the 1962 drug amendments on the research process. *Managerial and Decision Economics*, 1, 201–203.

Fink, S. & Baker, M. (2020). It's just everywhere already': how delays in testing set back the US coronavirus response. *New York Times*. Available at: https://www.nytimes.com/2020/03/10/us/coronavirus-testing-delays.html?searchResultPosition=6.

Food and Drug Administration. (2014) *Draft guidance for industry, food and drug administration staff, and clinical laboratories.* Available at: https://www.fda.gov/media/89841/download

Food and Drug Administration. (2018a) *The history of FDA's fight for consumer protection and public health.* Available at: https://www.fda.gov/about-fda/history-fdas-fight-consumer-protection-and-public-health#:∼:text=Although%20it%20was%20not%20known,force%20behind%20this%20law%20and.

Food and Drug Administration. (2018b) Laboratory developed tests. Available at: https://www.fda.gov/medical-devices/vitro-diagnostics/laboratory-developed-tests#:∼:text=A%20laboratory%20developed%20test%20 (LDT,used%20within%20a%20single%20laboratory.

Food and Drug Administration. (2020a) Expanded access. Available at: https://www.fda.gov/news-events/public-health-focus/expanded-access.

Food and Drug Administration. (2020b) Policy for coronavirus disease-2019 tests during the public health emergency (revised). Available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/policy-coronavirus-disease-2019-tests-during-public-health-emergency-revised.

Food and Drug Administration. (2020c) *Coronavirus (COVID-19) update: fda issues new policy to help expedite availability of diagnostics.* Available at: https://www.fda.gov/news-events/press-announcements/corona virus-COVID-19-update-fda-issues-new-policy-help-expedite-availability-diagnostics.

Food and Drug Administration. (2020d) *Coronavirus (COVID-19) update: fda issues new policy to help expedite availability of diagnostics.* Available at: https://www.fda.gov/news-events/press-announcements/corona virus-COVID-19-update-fda-issues-new-policy-help-expedite-availability-diagnostics.

Food and Drug Administration. (2020e) *Invtro diagnostic eua.* Available at: https://www.fda.gov/medical-devices/coronavirus-disease-2019-COVID-19-emergency-use-authorizations-medical-devices/vitro-diagnostics.

Food and Drug Administration. (2020f) *FAQs on testing for SARS-CoV-2.* Available at: https://www.fda.gov/medical-devices/coronavirus-COVID-19-and-medical-devices/faqs-testing-sars-cov-2.

Food and Drug Administration. (2020g) Available at: https://www.fda.gov/media/137564/download.

Food and Drug Administration. (2020h) Available at: https://www.fda.gov/media/143822/download.

Food and Drug Administration. (2020i) *Recommendations for investigational COVID-19 convalescent plasma.* Available at: https://www.fda.gov/vaccines-blood-biologics/investigational-new-drug-ind-or-device-exemp tion-ide-process-cber/recommendations-investigational-COVID-19-convalescent-plasma.

Food and Drug Administration. (2020j) *Coronavirus (COVID-19) update: FDA revokes emergency use authorization for chloroquine and hydroxychloroquine.* Available at: https://www.fda.gov/news-events/press-announce ments/coronavirus-COVID-19-update-fda-revokes-emergency-use-authorization-chloroquine-and.

Food and Drug Administration. (2020k) Available at: https://www.fda.gov/media/144412/download.

Food and Drug Administration. (2020l) Available at: https://www.fda.gov/media/144636/download.

Food and Drug Administration. (2020m). *Vaccines and related biological products advisory committee December 10, 2020 meeting announcement.* Available at: https://www.fda.gov/advisory-committees/advisory-commit tee-calendar/vaccines-and-related-biological-products-advisory-committee-december-10-2020-meeting-annou ncement.

Geloso, V. & Pavlik, J.B. (2019) Economic freedom and the economic consequences of the 1918 pandemic. *Contemporary Economic Policy* TBD.

Genzen, J.R. (2019) Regulation of laboratory-developed tests: a clinical laboratory perspective. *American Journal of Clinical Pathology*, 152(2), 122–131.

Gieringer, D.H. (1985) The safety and efficacy of new drug approval. *Cato Journal*, 5, 177–201.

Gilead Sciences (2020a) Development of remdesivr. Available at: https://www.gilead.com/-/media/gilead-corpor ate/files/pdfs/COVID-19/gilead_rdv-development-fact-sheet-2020.pdf.

Gilead Sciences. (2020b) *U.S. food and drug administration approves gilead's antiviral veklury (remdesivir) for treatment of COVID-19.* Available at: https://www.gilead.com/news-and-press/press-room/press-releases/2020b/10/us-food-and-drug-administration-approves-gileads-antiviral-veklury-remdesivir-for-treatment-of-COVID19.

Grabowski, H. & Richard Wang, Y. (2008) Do faster drug administration drug reviews adversely affect patient safety? An analysis of the 1992 prescription drug user fee act. *Journal of Law and Economics*, 51, 377–405.

Grabowski, H., Vernon, J. & DeMasi, J.A. (2002) Returns on research and development for 1990s new drug introductions. *PharmacoEconomics*, 20, 11–29.

Grabowski, H., Vernon, J.M. & Thomas, L.G. (1978) Estimating the effects of regulation on innovation: an international comparative analysis of the pharmaceutical industry. *Journal of Law and Economics*, 21, 133–163.

Grien, J., Ohmagari, N., Shin, D., Diaz, G., Asperges, E., Castagna, A., Feldt, T., Green, G., Green, M.L., Lescure, F.X., Nicastri, E., Oda, R., Yo, K., Quiros-Roldan, E., Studemeister, A., Redinski, J., Ahmed, S., Bernett, J., Chelliah, D., Chen, D., Chihara, Shingo, Cohen, S.H., Cunningham, J., Monforte, A.D., Ismail, S., Kato, H., Lapadula, G., L'Her, E., Maeno, T., Majumder, S., Massari, Marco, Mora-Rillo, M., Mutoh, Y., Nguyen, D., Verweij, E., Zoufaly, A., Osinusi, A.O., DeZure, A., Zhao, Y., Zhong, L., Chokkalingam, A., Elboudwarej, E., Telep, L., Timbs, L., Henne, I., Sellers, S., Cao, H., Tan, S.K., Winterbourne, L., Desai, P., Mera, R., Gaggar, A., Myers, R.P., Brainard, D.M., Childs, R. & Flanigan, T. (2020) Compassionate use of remdesivir for patients with severe COVID-19. *The New England Journal of Medicine*, 382, 2327–2336.

Gupta, S., Nguyen, T.D., Rojas, F.L., Raman, S., Lee, B., Bento, A., Simon, K.I. & Wing, C. (2020) Tracking public and private responses to the COVID-19 epidemic: evidence from state and local government actions. NBER Working Paper. Available at: https://www.nber.org/papers/w27027.

Hanson, R.W. (1995) FDA regulation of the pharmaceutical market. In: Higgs, R. (Ed.) *Hazardous to our health? FDA regulation of healthcare products*. Oakland, CA: Independent Institute.

Health and Human Services. (2020) *Trump administration secures new supplies of remdesivir for the united states*. Available at: https://www.hhs.gov/about/news/2020/06/29/trump-administration-secures-new-supplies-remdesivir-united-states.html.

Higgs, R. (1995) *Hazardous to our health? FDA regulation of healthcare products*. Oakland, CA: Independent Institute.

Higgs, R. (2004) *Against leviathan: government power and a free society*. Oakland, CA: Independent Institute.

Hollander, J.E. & Carr, B.G. (2020) Virtually perfect? Telemedicine for COVID-19. *The New England Journal of Medicine*, 382, 1679–1681.

Holshue, M.L., DeBolt, C., Lindquist, S., Lofy, K.H., Wiesman, J., Bruce, H., Spitters, C., Ericson, K., Wilkerson, S., Tural, A., Diaz, G., Cohn, A., Fox, L., Patel, A., Gerber, S.I., Kim, L., Tong, S., Lu, X., Lindstrom, S., Pallansch, M.A., Weldon, W.C., Briggs, H.M., Uyeki, T.M. & Pillai, S.K. (2020) First case of 2019 novel coronavirus in the United States. *New England Journal of Medicine*, 382, 929–936.

Hornstein, A. (2020) Alternatives to lockdowns. *COVID Economics*, 18, 42–72.

Isakov, L., Lo, A. & Montazerhodjat, V. (2019) Is the FDA too conservative or too aggressive? A Bayesian decision analysis of clinical trail design. *Journal of Econometrics*, 211, 117–136.

Johns Hopkins University & Medicine Corona Virus Research Center. 2020. *COVID-19 dashboard by the center for systems science and engineering at johns hopkins university*. Available at: https://coronavirus.jhu.edu/map.html.

Johnson, S.R. (2020) Frustrated by slow results, more hospitals seek their own COVID-19 testing. *Modern Healthcare* Available at: https://www.modernhealthcare.com/providers/frustrated-slow-results-more-hospitals-seek-their-own-COVID-19-testing.

Jung, J., Manley, J. & Shrestha, V. (2020) Coronavirus infections and deaths by poverty status: time trends and patterns. *COVID Economics*, 31, 1–58.

Kaitin, K.I. & Brown, J. (1995) A Drug lag update. *Drug Information Journal*, 29, 361–373.

Kaitin, K.I., Mattison, N., Northington, F.K. & Lasagna, L. (1989) The drug lag: an update of new drug introductions in the United States and in the United Kingdom, 1977 through 1987. *Clinical Pharmacology & Therapeutics*, 46, 121–138.

Kandel, N. (2020) Health security capabilities in the context of COVID-19 outbreak: an analysis of international health regulations annual report data from 182 countries. *The Lancet*, 395, 1047–1053.

Keesara, S., Jonas, A. & Schulman, K. (2020) COVID-19 and health care's digital revolution. *The New England Journal of Medicine*, 382, 1–3.

Khazan, Olga. (2020) The 4 key reasons the US is so behind on coronavirus testing. The Atlantic. Available at: https://www.theatlantic.com/health/archive/2020/03/why-coronavirus-testing-us-so-delayed/607954/.

Kim, M.J., & Denyer, S.. (2020) South Korea is doing 10,000 coronavirus tests a day. The US is struggling for even a small fraction of that. *Washington Post* Available at: https://www.washingtonpost.com/world/asia_pacific/coronavirus-test-kits-south-korea-us/2020/03/13/007f14fc-64a1-11ea-8a8e-5c5336b32760_story.html.

Klein, D.B. (2000) *Economists against the FDA*. Oakland, CA: Independent Institute. Available at: https://www.independent.org/publications/article.asp?id=279.

Klien, D.B. & Tabarrok, A. (2004) Who certifies off-label? *Regulation Summer*, 2004, 60–64.

Lamb, Y.N. (2020) Remdesivir: first approval. *Drugs*, 80, 1355–1363.

Leibman, M. (2003) Off-label, in bounds. Medical Marketing and Media. Available at: https://www.highbeam.com/doc/1P3-501142641.html.

Lina, B. (2008) History of influenza pandemics. In: Raoult, D. & Drancourt, M. (Eds.) *Paleomicrobiology: past human infections*. New York City, NY: Springer, pp. 199–211.

Lo, M.K., Jordan, R., Avery, A., Sudhamsu, J., Shrivastava-Ranjan, P., Hotard, R.L., Flint, M., McMullan, L.K., Seigel, D., Clarke, M.O., Mackman, R.L., Hui, H.C., Perron, M., Ray, A.S., Cihlar, T., Nichol, S.T. & Spiropoulou, C.F. (2017) GS-5734 and its parent nucleoside analog inhibit filo-, pneumo-, and paramyxoviruses. *Scientific Reports*, 7, 1–7.

Lovelace, B.. (2020) Dr. Anthony Fauci says Gilead's remdesivir will set a new 'standard of care' for coronavirus treatment. *CNBC*. Available at: https://www.cnbc.com/2020/04/29/dr-anthony-fauci-says-data-from-remdesivir-coronavirus-drug-trial-shows-quite-good-news.html.

March, R.J. (2016) Entrepreneurship in off-label drug prescription: just what the doctor ordered! *Journal of Private Enterprise*, 32, 75–92.

March, R.J. (2017) Skin in the game: comparing the public and private regulation of isotreninoin. *Journal of Institutional Economics*, 13, 649–672.

March, R.J. (2020) Flatten the bureaucracy: deregulation and COVID-19 testing. *Working Paper The Independent Review*. Available at: https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3668493&fbclid=IwAR3HDjL0C4_tklo9ga2XL1O3Q2N9xZZyKAuHND2aTF387jpEQc_OfNo4bIc

Mello, M.M., Greene, J.A. & Sharfstein, J.M. (2020) Attacks on public health officials during COVID-19. *Journal of the American Medical Association*, 324, 741–742.

Miller, H.I. (1988) Failed FDA reform. *Regulation*, 21, 24–30.

Mongey, S., Pilossoph, L., & Weinberg, A. (2020) Which workers bear the burden of social distancing policies? *NBER Working Paper*. Available at: https://www.nber.org/papers/w27085?sy=085.

Munsey, R.R. (1995) Trends and events in FDA regulation of medical devices over the last fifty years. *Food and Drug Law Journal*, 50, 163–177.

National Institute of Health. (2020) *NIH clinical trail of remdesivir to treat COVID-19 begins*. Available at: https://www.nih.gov/news-events/news-releases/nih-clinical-trial-remdesivir-treat-COVID-19-begins.

Nicola, M., Zaid, A., Catrin, S., Kerwan, A., Al-Jabir, A., Iosifidis, C., Agha, M. & Agha, R. (2020) The socio-economic implications of the coronavirus pandemic: a systematic review. *International Journal of Surgery*, 78, 185–193.–.

Pardo, J., Shukla, A.M., Chamarthi, G. & Gupte, A. (2020) The journey of remdesivir: from ebola to COVID-19. *Drugs in Context*, 9, 4–14.

Patel, N.V. (2020a) Why the CDC botched its coronavirus testing. *MIT Technology Review* Available at: https://www.technologyreview.com/2020/03/05/905484/why-the-cdc-botched-its-coronavirus-testing/.

Patel, N.V. (2020b) The US now has more COVID-19 tests than it knows what to do with. *MIT Technology Review* Available at: https://www.technologyreview.com/2020b/06/27/1004545/us-COVID-19-coronavirus-test-capacity-unused-available-reopening/.

Peltzman, S. (1973) An evaluation of consumer protection legislation: the 1962 drug amendments. *Journal of Political Economy*, 81, 1049–1091.

Pfizer. (2020a) *Pfizer and BioNTech to supply the US with 100 million additional doses of COVID-19 vaccine*. Available at: https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-supply-us-100-million-additional-doses.

Pfizer. (2020b) *Pfizer and BioNTech announce vaccine adiate against COVID-19 achieved success in first interim analysis from phase 3 study*. Available at: https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-announce-vaccine-candidate-against.

Philipson, T.J. & Sun, E. (2008) Is the food and drug administration safe and effective? *Journal of Economic Perspectives*, 22, 85–102.

Philipson, T.J., Berndt, E.R., Gottschalk, A.H.B. & Sun, E. (2008) Cost-benefit analysis of the FDA: the case of the prescription drug user fee act. *Journal of Public Economics*, 92, 1306–1325.

Piguillem, F. & Shi, L. (2020) Optimal COVID-19 quarantine and testing policies. *COVID Economics*, 27, 123–165.

Piller, C. (2018) FDA's revolving door: companies often hire agency staffers who manage their successful drug reviews. *Science Magazine* Available at: https://www.sciencemag.org/news/2018/07/fda-s-revolving-door-companies-often-hire-agency-staffers-who-managed-their-successful.

Portnoy, J., Waller, M. & Elliott, T. (2020) Telemedicine in the era of COVID-19. *The Journal of Allergy and Clinical Immunology: In Practice*, 8, 1489–1491.

Ravi, N., Cortade, D.L., Ng, E. & Wang, S.X. (2020) Diagnostics for SARS-CoV-2 detection: a comprehensive review of the FDA-EUA COVID-19 testing landscape. *Biosensors and Bioelectronics*, 165, 1–13.

Rome, B.N. & Avorn, J. (2020) Drug evaluation during the COVID-19 pandemic. *The New England Journal of Medicine*, 382, 2282–2284.

Ruwart, M.J. (2018) *Death by regulation: how we were robbed of a golden age of health and how we can reclaim*. Bangalore: SunStar Press.

Secon, H. (2020) An interactive map of the US cties and states still under lockdown — and those that are reopening. *Business Insider*. Available at: https://www.businessinsider.com/us-map-stay-at-home-orders-lockdowns-2020-3.

Shapiro, J.K. (2019) Regulation of laboratory developed tests by FDA: time for the agency to cease and desist until congress enacts legislation. *FDA Law Blog* Available at: http://www.fdalawblog.net/2019/10/regulation-of-laboratory-developed-tests-by-fda-time-for-the-agency-to-cease-and-desist-until-congress-enacts-legislation/.

Shojaei, A. & Salari, P. (2020) COVID-19 and off label use of drugs: an ethical viewpoint DARU. *Journal of Pharmaceutical Science*, 8, 1–5.

Slotkin, J. (2020) Warp speed official: 7.9 Million doses of vaccine ready for distribution next week NPR. Available at: https://www.npr.org/sections/coronavirus-live-updates/2020/12/19/948349851/warp-speed-official-7-9-million-doses-of-vaccine-ready-for-distribution-next-week.

Sobel, R.S. (2008) Public health and the placebo: the legacy of the 1906 pure food and drug act. *Cato Journal*, 21, 463–479.

Soucheray, S. (2020) Feds to allow state public health labs to test for COVID-19. *CIDRAP News* Available at: https://www.cidrap.umn.edu/news-perspective/2020/02/feds-allow-state-public-health-labs-to-test-for-COVID-19.

Spinner, C.D., Gottlieb, R.L., Criner, G.J., Arribas López, J.R., Cattelan, A.M., Viladomiu, A.S., Ogbuagu, O., Malhotra, P., Mullane, K.M., Castagna, A., Chai, L.Y.A., Roestenberg, M., Tsang, O.T.Y., Bernasconi, E., Turnier, P.L., Chang, S.C., SenGupta, S., Hyland, R.H., Osinusi, A.O., Cao, H., Blair, C., Wang, H., Gaggar, H., Brainard, D.M., McPhail, M.J., Bhagani, S., Ahn, M.Y., Sanyal, A.J., Huhn, G. & Marty, F.M. (2020) Effect of remdesivir vs standard care on clinical status at 11days in patients with moderate COVID-19. *Journal of the American Medical Association*, 324, 1048–1057.

Sussman, N. (2020) Time for bed(s): hospital capacity and mortality from COVID-19. *COVID Economics*, 11, 116–131.

Tabarrok, A. (2017) Discussion: the FDA is unprepared for personalized medicine. *Biostatistics*, 18, 403–404.

Tabarrok, A.T. (2000) Assessing the FDA via the anomaly of off-label drug prescribing. *Independent Review* Summer, 2000, 25–53.

Takahashi, T., Luzum, J.A., Nicol, M.R. & Jacobson, P.A. (2020) Pharmacogenomics of COVID-19 therapies. *Genomic Medicine*, 35, 1–7.

Tracking public and private responses to the COVID-19 epidemic: evidence from state and local government actions. NBER Working Paper. Available at: https://www.nber.org/papers/w27027.

Trosken, W. (2015) *The pox of liberty: how the constitution left americans rich, free, and prone to infection*. Chicago, IL: University of Chicago Press.

Tullock, G. (1965) *The politics of bureaucracy*. New York City, NY: Public Affairs Press.

US Department of Health and Human Services. Fact sheet: Operation Warp Speed. Available at: https://www.hhs.gov/coronavirus/explaining-operation-warp-speed/index.html.

US Department of Health, Education, and Welfare. (1958) Report 1955/1956–1957/1958. US Government Printing Office.

von Mises, L. (1944) *Bureaucracy*. New Haven, CT: Yale University Press.

Wallace-Wells, D. (2020) We had the vaccine the whole time. *New York Inquirer*. Available at: https://nymag.com/intelligencer/2020/12/moderna-COVID-19-vaccine-design.html.

Wang, X., Yoo, C.K., Han, M.G., Lee, S.W., Lee, H., Chun, S., Lee, W.G. & Min, W.K. (2020) Preparedness and rapid implementation of external quality assessment helped quickly increase COVID-19 testing capacity in the Republic of Korea. *Clinical Chemistry*, 66, 979–981.

Ward, M.R. (1992) Drug approval overregulation. *Regulation*, 15(2), 47–53.

Wardell, W.M. (1973) Introduction of new therapeutic drugs in the United States and Great Britain: an international comparison. *Clinical Pharmacology & Therapeutics*, 14, 773–790.

Wientraub, K. (2020) *Moderna becomes second company to request emergency FDA authorization for COVID-19 vaccine candidate*. Available at: https://www.usatoday.com/story/news/health/2020/11/30/moderna-emergency-fda-authorization-COVID-19-vaccine-pfizer/6376336002/.

Wiggins, S.N. (1981) Product quality regulation and new drug introductions: some new evidence from the 1970s. *Review of Economics and Statistics*, 63, 615–619.

Williamson, B.N., Feldmann, F., Schwarz, B., Meade-White, K., Porter, D.P., Schulz, J., van Doremalen, N., Leighton, I., Yinda, C.K., Pérez-Pérez, L., Okumura, A., Lovaglio, J., Hanley, P.W., Saturday, G., Bosio, C.M., Anzick, S., Barbian, K., Cihlar, T., Martens, C., Scott, D.P., Munster, V.J. & de Witt, E. (2020) Clinical benefits of remdesivir in rhesus macaques infected with SARS-COV-2. *Nature*, 585, 273–276.

World Health Organization. (2020) *Coronavirus disease 2019 (COVID-19) situation report – 80*. Available at: https://apps.who.int/iris/bitstream/handle/10665/331778/nCoVsitrep09Apr2020-eng.pdf.