Regulatory Reactivity: FDA and the Response to COVID-19

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ABSTRACT

The immense pressures created by the COVID-19 pandemic have exposed ingrained shortcomings in the regulatory and administrative apparatus for addressing public health crises, shortcomings that are particularly salient in the context of FDA's emergency response. Political and public pressure, along with more subtle pressures exerted by private sector stakeholders, have combined with the sheer urgency to respond quickly to push agencies like FDA into emergency modes of decision-making that are at odds with long-held scientific and professional standards that have been the bedrock of their work.

In this Article, we provide a novel way of understanding emerging modes of decision-making at FDA in the context of highly disruptive public health crises such as COVID-19. We develop and apply the concept of "regulatory reactivity" to capture the ways in which agencies—specifically FDA—have departed from evidence-based decision-making frameworks in response to external pressures. We illustrate regulatory reactivity at work through the use of two examples drawn from FDA's response to COVID-19: the adoption of emergency use authorizations (EUAs) and the evolution of the Coronavirus Treatment Action Plan (CTAP), an emergency program for accelerating the development of therapeutics for COVID-19. These examples illustrate how reactive modes of decision-making at FDA fail to meet both the short-term and the long-term public health mission of the agency.

I. INTRODUCTION

Public health-oriented agencies and institutions have long played a critical role in responding to public health emergencies in the United States, particularly in the face of outbreaks of infectious disease. We have leaned heavily upon them in the midst of the current COVID-19 outbreak to fashion an emergency response to rapidly changing and worsening conditions. The dependence on therapeutics and vaccines as the

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ultimate way of overcoming the pandemic has created an extreme stress test for the U.S. Food and Drug Administration (FDA) in particular, placing it at the forefront of emergency response. This Article argues that the immense pressures created by the COVID-19 pandemic have exposed ingrained shortcomings in the regulatory and administrative apparatus for addressing public health crises, shortcomings that are particularly salient in the context of FDA's emergency response. Political and public pressure, along with more subtle pressures exerted by private sector stakeholders, have combined with the sheer urgency to respond quickly to push agencies like FDA into emergency modes of decision-making that are at odds with long-held scientific and professional standards that have been the bedrock of their work.

In this Article, we provide a novel way of understanding emerging modes of decision-making at FDA in the context of highly disruptive public health crises. We develop and apply the concept of "regulatory reactivity" to capture the ways in which agencies—specifically FDA[1]—have departed from evidence-based decision-making frameworks in response to external pressures. We use two main areas of FDA's response to COVID-19 as case studies of regulatory reactivity. The first is the adoption of emergency use authorizations (EUAs) in certain cases as a mechanism to authorize the administration of unapproved drugs, vaccines, and other types of medical products needed in situations of emergency.[2] The second is the evolution of the Coronavirus Treatment Action Plan (CTAP), an emergency program for accelerating the development of therapeutics for COVID-19. The Article shows how reactive modes of decision-making at FDA fail to meet both the short-term and the long-term public health mission of the agency.

The Article proceeds as follows. In Part II, we develop the concept of regulatory reactivity and delineate the conceptual and practical differences between what we term "reactive modes" of decision-making and non-reactive decision-making modes that keep the agency anchored in evidence-based procedures. In Part III, we use two short case studies of FDA decision-making to illustrate regulatory reactivity and its consequences. In Part IV, we argue that the existing administrative law framework is ill-equipped to redress the departures from evidence-based decision-making that occur in a state of regulatory reactivity. We conclude by suggesting that greater agency accountability and independence are essential to curtail reactivity in response to public health emergencies. This Article shows why achieving this goal is critical, leaving the debate over how to achieve it, or at least move closer towards it, for further discussion.

II. REGULATORY REACTIVITY

An effective response to public health emergencies in the United States is dependent on regulatory agencies like FDA or Centers for Disease Control and Prevention (CDC) making evidence-based public health decisions even in the midst of a crisis. By making decisions that reflect a careful, scientifically grounded balancing of short and long-

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[1] We explore further embodiments of regulatory reactivity in other agency settings in forthcoming work.

[2] *See Emergency Use Authorization*, U.S. FOOD & DRUG ADMIN. (May 5, 2021), https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization [perma.cc/6QBB-J3FJ]; *Emergency Use Authorization for Vaccines Explained*, U.S. FOOD & DRUG ADMIN. (Nov. 20, 2020), https://www.fda.gov/vaccines-blood-biologics/vaccines/emergency-use-authorization-vaccines-explained [perma.cc/2UEP-FJ85].

term public health risks and benefits based on reliable data, these agencies give us some measure of trust that the outcomes will further public health goals. When this decision-making process is affected by external interests or political and public pressures, there is no guarantee that the resulting agency decisions will yield net public health benefits. The concept of regulatory reactivity is intended to capture a shift in agency decision-making processes that appear as formally compliant with both legal frameworks and long-held regulatory postures while at the same time departing from these regulatory standards. In the context of emergency decision-making at FDA, it captures a departure from data-driven and evidence-based criteria that is at odds with the public health-oriented mission of the agency.

As a general proposition, regulatory agencies that have been tasked with various facets of protecting public health often operate at the intersection of precautionary frameworks designed to minimize risks and public benefit frameworks designed to support and encourage innovative public health solutions. A large legal and administrative structure has evolved over time to enable these agencies to arrive at scientifically informed decisions about public health responses through pre-established and routinely applied decision-making principles and procedural channels. Expected costs, risks, and benefits of advancing a particular guideline or new technology are carefully considered and balanced within a principle-based framework designed to meet both short- and long-term public health needs. These decision-making mechanisms are not monolithic, but rather encapsulate different risk-benefit approaches across the administrative state. They evolve over time in response to technological and scientific developments.[3] They have built-in structures that bring flexibility into regulatory review processes and allow regulators to expedite these processes when exceptional circumstances justify a departure from standard review. While the standards that emerge from this principle-based framework will shift to reflect the exigencies of each situation, the principles themselves are not subject to change. The unchanging foundation of public health principles protects the integrity of the decision-making process and its attachment to evidence-based reasoning.

When acting in its role as gatekeeper for the approval of new drugs and vaccines, FDA operates squarely at this intersection of precautionary frameworks designed to minimize risk and innovation frameworks designed to support the expeditious development of welfare-enhancing technologies to meet public health needs. As the COVID-19 pandemic has illustrated, speeding up the development and approval of drugs or other products for which there is an immediate need can constitute an important tool to improve public health and promote other public interest goals, but only where safety and efficacy are adequately addressed.

Expedited regulatory decisions can further the public interest. In the case of agencies like FDA, they can further public health goals by making certain regulated products available to patients sooner than under standard review. But expedited regulatory decisions come at a cost: they typically use data sets that are less robust

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[3] For instance, the Kefauver-Harris Amendments, also known as the 1962 Drug Amendments to the Federal Food, Drug, and Cosmetic Act, were introduced in response to shortcomings detected in the drug review process, introducing, inter alia, a requirement that drug sponsors submit "substantial evidence" of the efficacy of their product before bringing them to market. *See generally* Drug Amendments of 1962, Pub. L. No. 87-781, 76 Stat. 781 (codified at 21 U.S.C. § 355(d)). Elsewhere in the administrative state, the National Environmental Policy Act of 1969 introduced a requirement that federal agencies submit environmental assessments and environmental impact statements before undertaking certain types of actions. *See* Pub. L. No. 91-190, 83 Stat. 852 (codified at 42 U.S.C. § 4321 *et seq*.).

than data submitted at the end of standard studies or research and development (R&D) processes. Under standard modes of agency decision-making, expedited regulatory pathways weigh the costs of less robust evidence against the benefits of speed, producing expedited decisions that are based on a risk-benefit analysis performed in light of available data.[4] While standards of review are lowered,[5] the law continues to place stringent obligations on regulators: even under a lesser standard of review. Agencies must rely on scientifically sound data as they perform a risk-benefit analysis, demand and monitor the ongoing production of additional data, and revoke any authorizations or approvals if necessary.[6] In this way, under situations of extraordinary need, regulatory agencies can depart from standard regulatory modes of review to respond nimbly to pressing circumstances without departing from their basic principles of decision-making. When agencies are operating in ways that are consistent with their missions, decisions entailing a departure from usual standards constitute principled departures, consistent with the gatekeeping and/or public health mission of these agencies.

In stark contrast, the phenomenon we document in this Article, and which we term regulatory reactivity, occurs when there is a setting-aside of agency procedures, expertise, and priorities, often under the guise of regulatory nimbleness. Instead of applying the appropriate standard, an agency is driven by a particular result it seeks to achieve, often in pursuit of short-term goals. Rather than reaching a decision on the basis of a pre-established standard, the agency uses the standard as a shield to protect its choice. In some cases, it uses the flexibility afforded by an expedited pathway to issue an authorization or approval when, in light of available data and guiding principles, such authorization or approval should not be issued.

We define regulatory reactivity as a mode of agency decision-making that occurs: 1) when an agency does not adhere to predetermined principles, standards, and/or operative procedures in reaching its decision; 2) in direct reaction to pressure, whether internal or external, political or non-political;[7] 3) resulting in the furtherance of short-term agendas rather than public health goals. Essentially, regulatory reactivity occurs when some form of pressure drives the decision-making process, with agency standards and evidence used ex post to justify the adoption of a particular decision.

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[4] Outside the context of situations of emergency, FDA has four pathways through which it may speed up regulatory review of qualifying drugs. *See Fast Track, Breakthrough Therapy, Accelerated Approval, Priority Review*, U.S. FOOD & DRUG ADMIN. (Feb. 23, 2018), https://www.fda.gov/patients/learn-about-drug-and-device-approvals/fast-track-breakthrough-therapy-accelerated-approval-priority-review [perma.cc/7RP5-MTTP]. The agency attempts to take action for drugs qualifying for "priority review" within six months from application, as opposed to the average twelve months it normally takes to complete drug review. *Id.; see also* Milena Lolic, Professional Affairs and Stakeholder Engagement, U.S. Food & Drug Admin., Presentation on NDA at the FDA, https://www.fda.gov/media/105012/download [https://perma.cc/TP66-X675]. "Fast track" designation is available for "drugs [that] treat serious conditions and fill an unmet medical need." *Fast Track*, *supra*. "Breakthrough therapy" designation is available for drugs that "may demonstrate substantial improvement over available therapy," and "accelerated approval" designation is available for drugs treating "serious conditions that filled an unmet medical need to be approved based on a surrogate endpoint." *Id.*

[5] *See infra* Section III.B.

[6] *See, e.g.*, 21 U.SC. § 360bbb-3 (establishing the standard for authorization of unapproved drugs and vaccines, which constitutes a lower standard than the one applicable to full FDA approval of a drug or vaccine).

[7] External, non-political sources of pressure may include, for example, patients and patient groups and industry stakeholders.

Factors extraneous to the mission of the agency displace evidence-based reasoning in reaching a decision, and evidence is used selectively ex post to justify the decision reached—or even, as in one case document below, data is overstated in support of a regulatory decision.[8]

There are two basic problems with reactive modes of regulatory decision-making within our current administrative law framework, the first relating to an undermining of public health goals in the decision-making process, and the second highlighting limitations of the existing legal framework to address reactivity.

First, when external pressures replace scientific evidence-based decision-making, the resulting decisions often undermine both short- and long-term public health goals. The term "reactivity" captures what is often an abrupt departure from standard agency procedures, priorities, and norms in response to external pressures in a manner that deemphasizes, undermines, or sets aside agency discretion and expertise. In so doing, reactivity undermines the bedrock of the justification for having administrative agencies in the first place. In the context of health-oriented agencies, we argue that such a departure is particularly problematic because it unmoors the decision from its likely consequences for public health, aligning decisions with special interests rather than with likely health outcomes. Reactive modes of decision-making translate into decisions that fail to capture the true costs, risks, and benefits (or lack thereof) of a given marketing authorization or approval. These decisions may result in potentially detrimental effects to public health and, as observed during the COVID-19 pandemic, risk of alienating public trust in the decision-making processes adopted by the agency.

Second, while this potential unmooring of decisions from evidence-based assessment of consequences might appear balanced by the existence of corrective mechanisms in administrative law, we further argue that reactive modes of decision-making fall through the cracks of existing legal frameworks. Existing review frameworks allow for agency discretion in fashioning urgent responses to rapidly changing problems. While recognizing the need for flexibility, we argue that the existing body of administrative law does not account for gray areas in actual responses during emergency situations when complex areas of science and law are involved. Reactive decisions generally do not rise to the level that would prompt a court to set them aside—as is the case of decisions covered by the application of the arbitrary and capricious standard[9]—because the agency can provide seemingly credible justifications for the adoption of a given measure.[10] Finding ex post justifications is particularly easy in the context of a public health emergency, where agencies are afforded more discretion and flexibility to meet emergency needs.

Reactivity is thus likely to fall within the gray zone in the spectrum of agency decision-making that escapes legal review, particularly in emergency contexts. When operating in reactivity mode, agency decisions and actions are lacking in evidentiary

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[8] *See infra* Section III.B (surveying the emergency authorization on COVID-19 convalescent plasma).

[9] 5. U.S.C. § 706(2)(A). *See, e.g.*, Nat. Res. Def. Council v. EPA, 966 F.2d 1292, 1297 (1992).

[10] *See, e.g.*, U.S. FOOD & DRUG ADMIN., *FDA Issues Emergency Use Authorization for Convalescent Plasma as Potential Promising COVID–19 Treatment, Another Achievement in Administration's Fight Against Pandemic* (Aug. 23, 2020), https://www.fda.gov/news-events/press-announcements/fda-issues-emergency-use-authorization-convalescent-plasma-potential-promising-covid-19-treatment [perma.cc/Y3UW-ZFNW] (grounding the emergency use authorization for convalescent COVID-19 plasma on "extensive review of the science and data." The data used in this instance, as well as the significance of the data as presented by FDA, were quickly challenged by public health experts). *See also infra* Section III.B.

support, reliability, accountability, and fairness, and are easily prone to conflicts of interest. The concept of reactivity encompasses responses to problems—and in the case of FDA, public health problems—that are aligned with interests, agendas, or goals that are not the ones the agency should be pursuing. The resulting departure from public health goals is difficult to challenge and rectify, given the agency's ability to justify its decision ex post through selective use of reasoning that meets current legal standards of administrative review.

In the following section, the Article illustrates the concept of regulatory reactivity by providing short case studies of FDA's involvement in the response to the COVID-19 pandemic. While we focus on examples that have arisen during the current emergency, we suggest that reactivity is an ongoing challenge that is limited to neither pandemics nor emergencies.

III. REGULATORY REACTIVITY AT FDA

> *"FDA is a regulator. As a regulator, FDA's responsibility is to ensure the safety of consumers by rigorously evaluating the evidence about the benefits and risks of medical products. . . . Each action FDA has taken for COVID-19 is grounded in the Agency's commitment to scientific integrity and regulatory independence, to deliver on our mission of protecting and promoting the public health."*[11]

> *"At risk is the FDA's ability to make the independent, science-based decisions that are key to combating the pandemic and so much more."*[12]

COVID-19 has increased both the salience and the magnitude of regulatory reactivity at FDA. In addition, it has showcased how administrative law and the checks and balances traditionally placed on regulatory agencies do not redress instances of departures from long-established standards and procedures despite significant flaws in agency decision-making. The following two case studies of FDA decision-making illustrate regulatory reactivity and its consequences. They describe ways in which FDA, while appearing to respond in an expeditious fashion to the heightened public health challenges posed by the pandemic, has instead been reacting to highly idiosyncratic factors, instrumentalizing existing procedures in pursuit of extraneous agendas. We begin by examining the most prominent example of reactivity, exploring the different instances in which FDA has resorted or considered resorting to EUAs during the COVID-19 pandemic. We then examine a more subtle and difficult to detect form of reactivity evidenced in the establishment of the Coronavirus Treatment Action Plan (CTAP) and its relationship to the Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) Partnership.

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[11] Anand Shah, Deputy Comm'r for Med. & Sci. Affairs, *Remarks on FDA Leadership to Accelerate the Recovery from COVID-19 to the Alliance for Health Policy*, U.S. FOOD & DRUG ADMIN. (Aug. 20, 2020), https://www.fda.gov/news-events/speeches-fda-officials/remarks-fda-leadership-accelerate-recovery-covid-19-alliance-health-policy-08202020-08202020 [perma.cc/ZDJ6-ZHEN].

[12] Robert Califf, Scott Gottlieb, Margaret Hamburg, Jane Henney, David Kessler, Mark McClellan & Andy von Eschenbach, Opinion, *7 Former FDA Commissioners: The Trump Administration is Undermining the Credibility of the FDA*, WASH. POST, Sept. 29, 2020.

A. Emergency Use Authorizations (EUAs)

The EUA pathway was established in the aftermath of 9/11 as a mechanism for FDA to authorize the use of unapproved FDA-regulated products, as well as unapproved uses of approved products, during public health emergencies.[13] Rather than waiting for comprehensive data supporting an application for full approval, EUA legislation gives the agency the authority to examine earlier datasets indicative of the likelihood of efficacy of a product and, if FDA concludes that existing data demonstrates that such a likelihood exists and that the potential benefits of use of the product outweigh the potential and known risks, authorize the use of the product in limited contexts while the emergency is ongoing, while continuing the evaluation of the product.[14] The EUA pathway thus seeks to balance the need to respond to extraordinary challenges posed by public health crises with the core gatekeeping functions of FDA as a regulator of drugs and other medical products.

FDA first used the EUA pathway in 2005 during the anthrax scare,[15] and has revisited it during other public health crises, most recently in connection with the Ebola, Zika, and COVID-19 outbreaks.[16] The temporary authorization triggered by an EUA is based on a standard of review that is different from the one applicable to the review of products being considered for full approval. Typically, the sponsor of a drug or vaccine being considered for full approval must submit "substantial evidence" that the product is both safe and effective.[17] By contrast, in order to gain authorization under the EUA pathway, the data submitted by the sponsor need only show that "it is reasonable to believe" that the product "may be effective."[18] Importantly, even though the approval standard for EUAs is significantly lower than for full approval, it is a standard nonetheless. Moreover, the EUA pathway was established in primary legislation which insisted on the need for data-driven decision-making—the touchstone of every regulatory pathway for bringing drugs and other medical products to market.[19] While it is possible to argue that the standard itself can be too easily misused,[20] it is important to recognize that this lesser standard still binds FDA to a data-driven decision-making process. FDA has nonetheless departed from that

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[13] 21 U.S.C. § 360bbb-3; *see also* Stuart L. Nightingale, Joanna M. Prasher & Stewart Simonson, *Emergency Use Authorization (EUA) to Enable Use of Needed Products in Civilian and Military Emergencies, United States*, 13 EMERGING INFECTIOUS DISEASES 1046 (2007), https://pubmed.ncbi.nlm.nih.gov/18214177/ [https://perma.cc/5B38-MGUF].

[14] *Id.*; *see also Emergency Use Authorization*, U.S. FOOD & DRUG ADMIN. (July 9, 2021), https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization [https://perma.cc/L44V-FWY9].

[15] *See* Authorization of Emergency Use of Anthrax Vaccine Adsorbed for Prevention of Inhalation Anthrax by Individuals at Heightened Risk of Exposure Due to Attack With Anthrax, 70 Fed. Reg. 5452 (Feb. 2, 2005), https://www.federalregister.gov/documents/2005/02/02/05-2028/authorization-of-emergency-use-of-anthrax-vaccine-adsorbed-for-prevention-of-inhalation-anthrax-by [https://perma.cc/R3CB-LEE7].

[16] *See* Nightingale et al., *supra* note 13, at 1050.

[17] *See* 21 U.S.C. § 351(a)(2); 42 U.S.C. § 262(a)(2)(C)(i)(I).

[18] 21 U.S.C. § 360bbb–3.

[19] 21 U.S.C. § 360bbb–3(c) (listing the criteria for the issuance of an emergency use authorization).

[20] *See, e.g.*, Sarah Zhang, *What the 'Emergency' Blood-Plasma Debacle Reveals*, THE ATLANTIC (Aug. 26, 2020), https://www.theatlantic.com/health/archive/2020/08/the-emergency-use-loophole/615679/ [perma.cc/77NA-UKVX].

standard when issuing certain EUAs during the COVID-19 pandemic, as illustrated by the examples discussed below.[21] Formally, the agency appeared to be reacting to the time-sensitive challenges posed by the pandemic, seemingly invoking data to justify its decisions.[22] In practice, however, FDA used data in a way that led many commentators to question their significance and suitability.[23]

The first case involved the anti-viral drug remdesivir,[24] for which FDA issued an EUA in May 2020.[25] The EUA, which restricted authorized uses of remdesivir to severe cases of COVID-19 in hospitalized patients, was reissued on two occasions: first in August 2020 and then again in October 2020, maintaining remdesivir's status as an authorized investigational drug.[26] While some public health experts criticized the remdesivir EUA—asserting that the data in support of the EUA was insufficient to meet even the lower standard for EUAs[27]—others noted that FDA used "at least one

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[21] FDA issued hundreds of EUAs during the COVID-19 pandemic. *See, e.g.*, *Coronavirus Disease 2019 (COVID-19) Emergency Use Authorizations for Medical Devices*, U.S. FOOD & DRUG ADMIN. (Aug. 3, 2020), https://www.fda.gov/medical-devices/emergency-use-authorizations-medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices [https://perma.cc/Y69H-9FB6] (listing EUAs issued for medical devices); *In Vitro Diagnostics EUAs*, U.S. FOOD & DRUG ADMIN. (Apr. 20, 2021), https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas [https://perma.cc/4TTH-ZYP2] (listing EUAs issued for in vitro diagnostics). Our analysis focuses on the cases in which the agency's decision-making process was not properly supported by scientific evidence, even under the lower review standard that is applicable under the EUA pathways.

[22] *See Frequently Asked Questions on the Emergency Use Authorization (EUA) for Chloroquine Phosphate and Hydroxychloroquine Sulfate for Certain Hospitalized COVID-19 Patients*, U.S. FOOD & DRUG ADMIN. (Jun. 15, 2020), https://www.fda.gov/media/136784/download [perma.cc/DQ2X-YN6Z] (citing lab evidence in support of the EUAs issued by FDA for chloroquine phosphate and hydroxychloroquine sulfate).

[23] *See, e.g.*, Michael S. Saag, *Misguided Use of Hydroxychloroquine for COVID-19: The Infusion of Politics into Science*, 324 JAMA 2161 (2020), https://jamanetwork.com/journals/jama/fullarticle/2772921?widget=personalizedcontent&previousarticle=2770243 [perma.cc/75GU-SQR9]; Lindsey R. Baden, Caren G. Solomon, Michael F. Greene, Ralph B. D'Agostino & David Harrington, *The FDA and the Importance of Trust*, NEW ENG. J. MED. (Sept. 30, 2020), https://www.nejm.org/doi/full/10.1056/NEJMe2030687?query=health-policy [perma.cc/QTZ5-MY9S]; Kyle Thomson & Herschel Nachlis, *Emergency Use Authorizations During the COVID-19 Pandemic: Lessons from Hydroxychloroquine for Vaccine Authorization and Approval*, 324 JAMA 1282 (2020), https://jamanetwork.com/journals/jama/fullarticle/2770243 [perma.cc/5N8K-N3U6]; Kevin J. Tracey & Christina Brennan, *Emergency Use Authorizations Are a Threat to Science*, SCIENTIST (Dec. 1, 2020), https://www.the-scientist.com/news-opinion/opinion-emergency-use-authorizations-are-a-threat-to-science-68220 [perma.cc/Y2WW-K3NN].

[24] *See* Yaniv Heled, Ana Santos Rutschman & Liza Vertinsky, *The Problem with Relying on Profit-Driven Models to Produce Pandemic Drugs*, J. L. BIOSCIENCES, Jan.–June 2020 (surveying the development of remdesivir).

[25] *Coronavirus (COVID-19) Update: FDA Issues Emergency Use Authorization for Potential COVID-19 Treatment*, U.S. FOOD & DRUG ADMIN. (May 1, 2020), https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-issues-emergency-use-authorization-potential-covid-19-treatment [perma.cc/WQ6P-H47S].

[26] Letter from Denise M. Hinton, Chief Scientist, U.S. Food & Drug Admin., to Ashley Rhoades, Manager, Regulatory Affairs, Gilead Sciences (Oct. 1, 2020), https://www.fda.gov/media/137564/download [perma.cc/56QY-Z3YW].

[27] Karen Weintraub, *'Without Evidence': Once Again, FDA Expands Use of COVID-19 Treatment Without Research to Back It Up*, USA TODAY (Aug. 28, 2020), https://www.usatoday.com/story/news/2020/08/28/fda-ignores-science-expanding-remdesivir-treat-covid-19/5662305002/ [perma.cc/UCU2-38N7] (arguing that the data used to support the EUA, especially under the August authorization, which expanded access to remdesivir, was insufficient).

high-quality randomized, placebo-controlled trial."[28] However, experts have agreed that the agency has departed from the data-driven standard imposed by the EUA pathway in at least two other EUAs involving three purported treatments for COVID-19.[29]

In March 2020, FDA issued an EUA for hydroxychloroquine and chloroquine.[30] These drugs, which before COVID-19 had been studied in the context of malaria and autoimmune diseases, were authorized as treatments for COVID-19 early on in the outbreak after a very public endorsement by the White House, including a forceful endorsement directly from the President.[31] Similarly, in August 2020, FDA issued an EUA for COVID-19 convalescent plasma, a form of passive immunotherapy,[32] and took the highly unusual step of announcing the EUA from the White House on a Sunday afternoon—incidentally, or not, on the eve of the Republican National Convention.[33] FDA's decisions to issue the EUAs for these three products were quickly decried by public health experts as lacking scientific basis.[34]

The criticism of these EUAs was based on strong consensus among public health experts that there was a near complete lack of adequate data to justify issuing an EUA in connection with any of these drugs.[35] In particular, there was no clinical trial data available to FDA showing that any of these drugs would likely be efficacious in the treatment or prevention of COVID-19.[36] In the case of hydroxychloroquine and chloroquine, FDA itself arrived at that conclusion shortly after issuing the EUA, noting that the drugs were "unlikely to produce an antiviral effect,"[37] revoking the EUA after

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[28] *See* Baden et al., *supra* note 23.

[29] *See* Saag, *supra* note 23; Baden et al., *supra* note 23; Thomson & Nachlis, *supra* note 23; Tracey & Brennan, *supra* note 23.

[30] FOOD & DRUG ADMIN., *supra* note 21.

[31] *See* Elyse Samuels & Meg Kelly, *How False Hope Spread About Hydroxychloroquine to Treat Covid-19—And the Consequences That Followed*, WASH. POST (Apr. 13, 2020), https://www.washingtonpost.com/politics/2020/04/13/how-false-hope-spread-about-hydroxychloroquine-its-consequences/ [perma.cc/QLU3-HZR8].

[32] *FDA Issues Emergency Use Authorization for Convalescent Plasma as Potential Promising COVID–19 Treatment, Another Achievement in Administration's Fight Against Pandemic*, U.S. FOOD & DRUG ADMIN. (Aug. 23, 2020), https://www.fda.gov/news-events/press-announcements/fda-issues-emergency-use-authorization-convalescent-plasma-potential-promising-covid-19-treatment [perma.cc/KF5M-6DSX].

[33] *Id. See also* Paige Winfield Cunningham, *The Health 202: Trump Played Up a Coronavirus Treatment on the Eve of the Republican Convention*, WASH. POST (Aug. 24, 2020), https://www.washingtonpost.com/politics/2020/08/24/health-202-trump-played-up-coronavirus-treatment-eve-republican-convention/ [perma.cc/84M4-T5FC].

[34] Saag, *supra* note 23; Baden et al., *supra* note 23; Thomson & Nachlis, *supra* note 23; Tracey & Brennan, *supra* note 23.

[35] Saag, *supra,* note 23; Baden et al., *supra* note 23; Thomson & Nachlis, *supra* note 23; Tracey & Brennan, *supra* note 23.

[36] Saag, *supra,* note 23; Baden et al., *supra* note 23; Thomson & Nachlis, *supra* note 23; Tracey & Brennan, *supra* note 23.

[37] Letter from Denise Hinton, Chief Scientist, U.S. Food & Drug Admin. to Gary L. Disbrow, Deputy Assistant Sec'y, Director, Med. Countermeasure Programs, Off. Of Assistant Sec'y for Preparedness & Response, U.S. Dep't of Health & Hum. Servs. (June 15, 2020), https://www.fda.gov/media/138945/download [https://perma.cc/MZ4L-PF3J]; *see also FDA In Brief: FDA Updates Emergency Use Authorization for COVID-19 Convalescent Plasma to Reflect New Data*, U.S. FOOD & DRUG ADMIN. (Feb.

only three months.[38] While the decision to revoke the EUA was supported by evidenced-based reasoning, this revocation did not completely displace the permissive regulatory gesture that allowed it in the first place, one that hinged on watered down data standards.

Similarly, in the case of convalescent plasma, studies conducted outside the context of COVID-19 had produced mixed efficacy results of the therapeutic value of such treatment,[39] and there was no clinical study performed in connection with COVID-19.[40]

As many commentators and experts have observed, the conduct of FDA in approving the convalescent plasma EUA seemed to be, primarily, a response to political pressure.[41] It did not meet even the lower established regulatory standard for EUAs, which FDA has continuously applied to less politicized products even during the COVID-19 pandemic.[42] This particular EUA process included a highly unusual intervention from FDA Commissioner Stephen Hahn, who not only announced the EUA from the White House, but in doing so grossly overstated (and arguably misrepresented) the data used by FDA to support the authorization.[43] During this announcement, both President Trump and Commissioner Hahn stated that "35 more people out of 100 would survive the coronavirus if they were treated with [COVID-19 convalescent] plasma."[44] As numerous experts were quick to point out, the statements were misleading and significantly overstated the findings on which FDA had based its decision.[45] Commissioner Hahn retracted the claim and apologized for its inaccuracy the following day.[46]

A number of concerned public health experts, including former and current advisors serving on FDA external committees, summed up the agency decision-making processes in issuing these EUAs as follows: "[T]he EUAs granted for

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4, 2021), https://www.fda.gov/news-events/fda-brief/fda-brief-fda-updates-emergency-use-authorization-covid-19-convalescent-plasma-reflect-new-data [perma.cc/PXW2-X724].

[38] *See Coronavirus (COVID-19) Update: FDA Revokes Emergency Use Authorization for Chloroquine and Hydroxychloroquine*, U.S. FOOD & DRUG ADMIN. (June 15, 2020), https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-revokes-emergency-use-authorization-chloroquine-and [https://perma.cc/B6UD-ADSF].

[39] Jonathan Abraham, *Passive Antibody Therapy in COVID-19*, 20 NAT. REVS. IMMUNOLOGY 401 (2020), https://www.nature.com/articles/s41577-020-0365-7 [perma.cc/V6KH-XTG9].

[40] *See* Baden et al., *supra* note 23.

[41] Saag, *supra,* note 23; Baden et al., *supra* note 23; Thomson & Nachlis, s*upra* note 23; Tracey & Brennan, s*upra* note 23; *see also* Editorial, Louis M. Katz, *(A Little) Clarity on Convalescent Plasma for Covid-19*, 384 NEW. ENG. J. MED. 666 (2021), https://www.nejm.org/doi/full/10.1056/NEJMe2035678 [https://perma.cc/Z9GQ-CTMV]; Nicholas Florko, *FDA, Under Pressure From Trump, Authorizes Blood Plasma as Covid-19 Treatment*, STAT (Aug. 23, 2020), https://www.statnews.com/2020/08/23/fda-under-pressure-from-trump-expected-to-authorize-blood-plasma-as-covid-19-treatment/ [https://perma.cc/8FRR-LSTQ].

[42] *See* Saag, *supra* note 23; Baden et al., *supra* note 23; Thomson & Nachlis, *supra* note 23; Tracey & Brennan, *supra* note 23.

[43] *See* Matthew Perrone & Deb Riechmann, *FDA Chief Apologizes for Overstating Plasma Effect on Virus*, AP NEWS (Aug. 25, 2020), https://apnews.com/article/a7f0e8aac34a860ad502912564681b7c [https://perma.cc/DB3E-8VDT].

[44] *Id.*

[45] *Id.*

[46] *Id.*

hydroxychloroquine and chloroquine and, more recently, for convalescent plasma have raised the troubling concern that political pressure rather than a data-driven process influenced the FDA's decision making. . . . Without a clear, transparent, and scientifically sound decision-making process, the trust the FDA has built and maintained over the past century is eroding."[47]

FDA's departure from its typical data-driven procedures in the context of certain COVID-19 EUAs exhibits the hallmarks of regulatory reactivity. First, there was inadequate consideration of data (or the absence thereof) reflecting the most up-to-date scientific knowledge. As a result, the agency partly abdicated its gatekeeping function and public health mission. Second, FDA appears to have instrumentalized existing data and information as an ex post rationalization of its behavior. The outcome that the agency set out to achieve drove the interpretation of scientific evidence. And third, this instrumentalization of data—and of the agency itself—was a result of external pressure (in this case, of political nature), in ways that overpowered the agency's own inclination to adhere to statutorily set procedures and standards, as well as long-term policies.

At the time of writing, there are three COVID-19 vaccine candidates that have received FDA authorization through the EUA pathway.[48] Before the COVID-19 pandemic, EUAs had never been used for newly developed vaccines targeting new pathogens.[49] This prompted some public health experts to caution against use of the EUA pathway during the COVID-19 pandemic.[50] While we do not take issue with the use of the EUA pathway for the authorization of vaccines per se,[51] we note here that the agency's regulatory behavior in this area is not perceived by the public in isolation from the broader EUA context. The recent developments at FDA in connection with the EUA pathway cast some doubts on whether it can escape the reactivity that has

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47 *See* Baden et al., *supra* note 23.

48 Letter from Denise M. Hinton, Chief Scientist, U.S. Food & Drug Admin., to Elisa Harkins, Pfizer Inc. (May 10, 2021), https://www.fda.gov/media/144412/download [https://perma.cc/B9HK-7FVP]; Letter from Denise M. Hinton, Chief Scientist, U.S. Food & Drug Admin., to Carlota Vinals, ModernaTX, Inc. (Feb. 25, 2021), https://www.fda.gov/media/144636/download [https://perma.cc/8439-6RG5]; Letter from Denise M. Hinton, Chief Scientist, U.S. Food & Drug Admin., to Ruta Walawalkar, Janssen Biotech, Inc. (June 10, 2021), https://www.fda.gov/media/146303/download [https://perma.cc/HP3W-X3FK].

49 We note that no event of a magnitude approaching that of the COVID-19 pandemic has taken place between the inception of the EUA pathway and the current pandemic, or even in the decades leading up to the creation of the EUA pathway. As such, the adequateness of the EUA pathway for the authorization of vaccines targeting emerging pathogens had not been explored before.

50 *See* Derek Staahl, *Why An 'Emergency Use Authorization' Worries Experts When It Comes to a Vaccine*, ABC NEWS (Sept. 18, 2020), https://www.10news.com/news/coronavirus/why-an-emergency-use-authorization-worries-experts-when-it-comes-to-a-vaccine.

51 Several drug regulators elsewhere greenlighted the emergency use of the same vaccines authorized by FDA through the EUA pathway, which seems to indicate that—unlike the cases of hydroxychloroquine, chloroquine, and convalescent plasma—there was not regulatory exceptionalism on the part of FDA here. *See, e.g.*, *EMA Recommends First COVID-19 Vaccine for Authorization in the EU*, EUR. MEDS. AGENCY (Dec. 21, 2020), https://www.ema.europa.eu/en/news/ema-recommends-first-covid-19-vaccine-authorisation-eu [https://perma.cc/4BHR-EWT3]; *EMA Recommends COVID-19 Vaccine Moderna for Authorisation in the EU*, EUR. MEDS. AGENCY (Jan. 6, 2021), https://www.ema.europa.eu/en/news/ema-recommends-covid-19-vaccine-moderna-authorisation-eu [https://perma.cc/E66K-2CAH]; Marco Cavaleri, Harald Enzmann, Sabine Straus & Emer Cooke, *The European Medicines Agency's EU Conditional Marketing Authorisations for COVID-19 Vaccines*, 397 LANCET 355 (Jan. 30, 2021), https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00085-4/fulltext [https://perma.cc/6QJG-SRSQ].

plagued the earlier uses discussed above. If nothing else, such doubts are bound to contribute to the ongoing polarization of the debate surrounding vaccine development and policy, and they may negatively affect the levels of public trust in COVID-19 vaccine(s) authorized or approved in the United States.

B. The Coronavirus Treatment Acceleration Plan (CTAP)

On January 31, 2020, following an earlier declaration by the World Health Organization (WHO) recognizing COVID-19 as a public health emergency of international concern, Secretary of Health and Human Services (HHS), Alex Azar, declared a public health emergency in the United States.[52] At the end of March, the first COVID-19 Emergency Relief Bill was enacted, providing $2 trillion in relief money, of which $80 million were designated to FDA.[53] Almost immediately thereafter, on March 31, 2020, FDA announced its plan to establish a Coronavirus Treatment Acceleration Plan (CTAP).[54] CTAP was hailed by FDA as the "path forward" in responding to COVID-19.[55] The stated goal of CTAP was to advance treatments to patients as quickly as possible, while at the same time finding out "whether they are helpful or harmful."[56] This goal seems to be largely the same as FDA's general mission of advancing safe and effective biomedical innovations to the market as quickly as possible, however, raising the question of what this "new" program was designed to change.

While the internal structure and operations of CTAP remain opaque, the announced focus of the program is accelerating the regulatory process for potential COVID-19 therapies by 1) increasing the speed of review, and 2) reducing barriers in the review process.[57] To date, FDA has not expressed exactly what it meant by its promise that CTAP would "use every available method to move new treatments to patients as

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[52] *See* Press Release, Secretary Azar Declares Public Health Emergency for United States for 2019 Novel Coronavirus, U.S. Dep't Health & Hum. Servs. (Jan. 31, 2020), https://www.hhs.gov/about/news/2020/01/31/secretary-azar-declares-public-health-emergency-us-2019-novel-coronavirus.html [https://perma.cc/N89C-XBNB].

[53] Coronavirus Aid, Relief and Economic Security Act (CARES Act), Pub. L. No. 116-136 (2021), https://www.congress.gov/116/bills/hr748/BILLS-116hr748enr.pdf [https://perma.cc/FK6G-2LDZ]; *see also* Press Release, FDA On Signing of the COVID-19 Emergency Relief Bill, U.S. Food & Drug Admin. (Mar. 30, 2020), https://www.fda.gov/news-events/press-announcements/fda-signing-covid-19-emergency-relief-bill-including-landmark-over-counter-drug-reform-and-user-fee [https://perma.cc/Y84E-AMYY].

[54] *See* Press Release, FDA Continues to Accelerate the Development of Novel Therapies for COVID-19, U.S. Food & Drug Admin. (Mar. 31, 2020), https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-continues-accelerate-development-novel-therapies-covid-19 [https://perma.cc/3WTS-ZQ6T].

[55] *See, e.g.*, Stephen Hahn, Peter Marks & Janet Woodcock, *The Path Forward: Coronavirus Treatment Acceleration Program*, U.S. FOOD & DRUG ADMIN. (Apr. 20, 2020), https://www.fda.gov/news-events/fda-voices/path-forward-coronavirus-treatment-acceleration-program [https://perma.cc/45AU-XWF7].

[56] *See id.*

[57] News Release, Coronavirus (COVID-19) Update: FDA Continues to Accelerate Development of Novel Therapies for COVID-19, U.S. Food & Drug Admin. (Mar. 31, 2020), https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-continues-accelerate-development-novel-therapies-covid-19 [https://perma.cc/K45U-4NSN]. For a description of CTAP and its focus on accelerating the development of therapeutics, see also Anand Shah, Kushal T. Kadakia, Peter Marks, Patrizia Cavazzoni & Stephen Hahn, *FDA Initiatives to Accelerate the Development of COVID-19 Therapeutics*, HEALTH AFF. BLOG (Aug. 18, 2020), https://www.healthaffairs.org/do/10.1377/hblog20200814.351515/full/ [https://perma.cc/BW26-7974].

quickly as possible" apart from increased private access to FDA personnel and FDA support in moving more quickly through the approval process.[58] In order to expedite the review process for potential new therapies, CTAP announced that it would employ an around the clock regulatory response to submissions of new clinical study protocols,[59] that it would redeploy staff from other tasks within FDA to focus on review of COVID-19 proposals and protocols,[60] and that it would mount an effort to remove "bureaucratic impediments" to the review process.[61] However, the inside mechanics of how CTAP programs would operate and what "bureaucratic impediments" were targeted have not been made public.

While the jury is still out on CTAP's functioning and overall performance, what is already known about CTAP suggests at least three areas of possible regulatory reactivity.

First, given the speed of implementation and the limited resources available to FDA, there are few assurances that CTAP procedures are adequate and that its personnel have the necessary expertise and time to provide adequate review. The dearth of transparency regarding CTAP's inner workings has further exacerbated concerns that the quality of review offered by CTAP might be inadequate.[62] Under standard agency decision-making processes, there are typically robust measures that are aimed at ensuring a principled, evidence-based evaluation in the face (and sometimes in spite) of conflicting pressures, allowing for compromises on higher risk levels and lower data requirements where the benefit of significant public health value outweighs the risks attached to speed. Where too much pressure is placed on speed, the careful balancing of these risks is undermined. CTAP's overriding goal of speeding up the regulatory review process specifically for COVID-19 treatments increases the tension already inherent in all FDA decision-making processes between speed, on the one

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[58] *See Coronavirus Treatment Acceleration Program (CTAP)*, U.S. FOOD & DRUG ADMIN., https://www.fda.gov/drugs/coronavirus-covid-19-drugs/coronavirus-treatment-acceleration-program-ctap (last updated July 16, 2021) [https://perma.cc/7BZR-ZLRK].

[59] *See, e.g.*, Thomas Sullivan, *FDA Covid-19 Special Emergency Program for Accelerating Research and Development,* POLICY & MEDICINE (Apr. 30, 2020), https://www.policymed.com/2020/05/fda-covid-19-special-emergency-program-for-accelerating-research-and-development.html [https://perma.cc/54JV-L9JU].

[60] *See, e.g.*, Leigh Turner, *Could Pressure for COVID-19 Drugs Lead the FDA to Lower Its Standards*, WGBH NEWS (June 10, 2020), https://www.wgbh.org/news/science-and-technology/2020/06/10/could-pressure-for-covid-19-drugs-lead-the-fda-to-lower-its-standards [https://perma.cc/4KCN-NKK9]; *see also* Coronavirus (COVID-19) Update: FDA Continues to Accelerate Development of Novel Therapies for COVID-19, *supra* note 57.

[61] Turner, *supra* note 60.

[62] *Id. See also id.*; Leigh Turner, *Could Pressure for COVID-19 Drugs Lead the FDA to Lower Its Standards?*, YAHOO NEWS (June 11, 2020), https://news.yahoo.com/coronavirus-pressure-drugs-lead-fda-030000963.html [https://perma.cc/N75R-6U87] ("Because of how little information has been disclosed about CTAP's operation, the inner workings of CTAP seem beyond public scrutiny. No information is available on why some trials were cleared to proceed despite what many researchers would consider glaring shortcomings. This includes poor study design, small sample size, substantial overlap with other studies, or as in case of the stem cell study, a lack of a control group."); Sarah Owermohle, *FDA Moves to Speed Coronavirus Reviews Could Stick*, POLITICO (June 12, 2020), https://www.politico.com/newsletters/prescription-pulse/2020/06/12/fda-moves-to-speed-coronavirus-reviews-could-stick-around-489507 [https://perma.cc/5RJZ-36ZJ] ("Turner points to CTAP in particular, noting that the FDA has not disclosed how many staff members have been moved to those review teams and that it's not certain if those reassigned staff have the background and training to review Covid-19 studies. He also pointed to the quick turnaround on hydroxychloroquine despite thin evidence.").

hand, and safety and efficacy, on the other hand, with possible long-term negative repercussions on public health. The departure from standard operating procedures in response to pressure to speed review is an illustration of agency reactivity at work.

CTAP's focus on accelerating regulatory review and supporting the rapid development of new treatments also appears to have been done without ensuring adequate, commensurate capacity to handle the pace and volume of proposed treatments.[63] In so doing, CTAP effectively invites additional pressure on FDA's already strained resources to act quickly, opening the door for agency decisions based on inadequate data.[64]

Second, one of the less discussed aspects of CTAP, but one that is in some ways a more concerning sign of reactivity, is the expanded role of the private sector in shaping the data generation and submission process. In addition to speed, CTAP's goal is to make it easier for private companies to communicate directly with FDA personnel and obtain permission to conduct clinical studies more quickly and without delay.[65] The immense pressure on FDA to demonstrate progress towards an approved therapy leads to a greater agency emphasis on facilitating private sector studies and protocols.[66] While on their face these goals of speed and ease of communication and processes of approval appear desirable—even commendable—they pose risks to FDA's carefully crafted procedures and evidence-based weighing of risks versus benefits because of the danger that private sector interests may unduly influence the review process. While there is always private sector involvement in clinical studies and testing, this involvement traditionally takes place within a decision-making framework that is not itself the result of private sector involvement and innovation. In this example of reactivity, external pressures and expanded private sector involvement in the review process may well lead to a divergence from pre-determined standards of review in furtherance of short-term metrics that demonstrate speed and volume of drug development efforts.

The expanded role of the private sector can also be seen in the emphasis within the CTAP program on facilitating public-private partnerships to identify and accelerate

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63 *See, e.g.*, Turner, *supra* note 60.

64 *See* discussion *infra* Section III.A.

65 *See* Stephen M. Hahn, Patrizia Cavazzoni & Peter Marks, *An Update and Behind the Scenes: FDA's Coronavirus Acceleration Treatment Program*, U.S. FOOD & DRUG ADMIN, https://www.fda.gov/news-events/fda-voices/update-and-behind-scenes-fdas-coronavirus-treatment-acceleration-program (last updated July 14, 2020) [https://perma.cc/HCP8-US2L] [hereinafter Hahn et al., *An Update and Behind the Scenes*].

66 We acknowledge that the private sector has been central to the design and completion of clinical trials, and the limitations of the public sector, which has historically lacked the ability to play a more substantial role in this area. We also acknowledge that existing calls for greater involvement of the public sector in this area cannot be implemented without major changes to the drug development status quo and political economy. Our primary concern here is the potential instrumentalization of the CTAP model to further tilt the balance in favor of the representation of private-sector interests. On the topic of the roles of the public and private sectors in clinical trials, see, e.g., Tracy R. Lewis, Jerome H. Reichman & Anthony D. So, *The Case for Public Funding and Public Oversight of Clinical Trials*, ECONOMISTS' VOICE (Jan. 2007), https://static1.squarespace.com/static/562094dee4b0d00c1a3ef761/t/56d8d18286db43ab864f316c/1457049986629/Lewis+Tracy-Economists+Voice.pdf [https://perma.cc/FY5F-VCRK]. On the complex set of issues arising out of the many interplays between FDA and industry—which greatly exceed the scope of this paper, but which nonetheless inform our analysis—see, e.g., DANIEL CARPENTER, REPUTATION AND POWER: ORGANIZATIONAL IMAGE AND PHARMACEUTICAL REGULATION AT THE FDA (2010); Charles Piller, *Is FDA's Revolving Door Open Too Wide?*, 6 SCIENCE 361 (July 6, 2018), https://pubmed.ncbi.nlm.nih.gov/29976809/ [https://perma.cc/NJ4K-6FB2].

the development of leading drug candidates.[67] CTAP's relationship to another program in which FDA is involved, Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) Partnership,[68] raises additional concerns about the ability of FDA to perform its gatekeeping role as regulator of the safety and efficacy of drugs while it is simultaneously acting to collaborate in drug development.

While the expanded role of the private sector in the regulatory process is a more subtle form of reactivity than that evident in the EUA case studies discussed above, it is likely to have long term consequences for FDA's drug and vaccine review processes. The efforts to facilitate private sector drug and vaccine development are a natural response to the immense pressure on FDA to deliver an approved treatment for COVID-19. But once new patterns of private sector access and involvement in FDA approval process are established, they will be difficult to reverse. Rather than identifying and responding to specific barriers within the existing FDA framework, CTAP aims more generally at "streamlining" FDA review and advice, with the "overriding objective . . . [of finding] . . . effective medicines that don't cause more harm than good as soon as possible."[69] This seems to lower the standard that FDA uses to review proposed studies in response to pressures for speed and access.

Further, private sector participants in these efforts operate with vested interests in their own drug development programs to encourage modes of data submission and use that to facilitate their own approval processes. Thus, the public–private initiatives, while creating opportunities for new and more rapid ways of obtaining data on drug efficacy, also run the risk of blurring the boundaries between different types of data generating processes and different levels of data integrity.[70]

Third, for CTAP, "success" seems to be measured in terms of accelerating the speed and volume of therapeutic development.[71] With a CTAP dashboard that, as of July

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[67] *See, e.g.*, Anand Shah et al., *supra* note 57 ("[T]o help accelerate the development of therapeutics for other unmet medical needs, we can draw lessons from efforts such as the development of a COVID-19 Natural History Master Protocol through the Sentinel Initiative and the use of the CURE ID platform in partnership with the Critical Path Institute to aggregate real world data to support further research.").

[68] ACTIV involves a public–private collaboration to select and speed the development of promising drug candidates for COVID-19. As described by FDA, "[u]nder the CTAP program, FDA can better ensure that critical focus is placed on reviewing those therapies prioritized by the ACTIV partnership. The involvement of FDA in the ACTIV partnership will also help ensure these reviews are more efficient, particularly in evaluating proposed preclinical and clinical studies that received ACTIV input." *Coronavirus Treatment Acceleration Program Dashboard*, U.S. FOOD & DRUG ADMIN., https://www.fda.gov/drugs/coronavirus-covid-19-drugs/coronavirus-treatment-acceleration-program-ctap#dashboard (last updated July 16, 2021) [https://perma.cc/G9ET-EF5D].

[69] *See, e.g.*, Hahn et al., *An Update and Behind the Scenes*, *supra* note 55.

[70] *See, e.g.*, Liza Vertinsky, *Patents, Partnerships, and the Pre-Competitive Collaboration Myth in Pharmaceutical Innovation*, 48 U.C. DAVIS L. REV.1509 (2015) (discussing the challenges of protecting the public interest in public private partnerships in drug development); Matthew Goldstein & Patricia Cohen, *Public Private Projects Where the Public Pays and Pays*, N.Y. TIMES (June 6, 2017), https://www.nytimes.com/2017/06/06/business/dealbook/trump-infrastructure-plan-privatized-taxpayers.html [https://perma.cc/XZ4F-HZT5] (analyzing public-private partnerships outside the drug development space and finding several cases "in which local governments essentially guarantee their private partners substantial payments"); Jonathan H. Marks, *What's the Big Deal? The Ethics of Public-Private Partnerships Related to Food and Health* (Penn. State Univ., Working Paper, No. 11), https://papers.ssrn.com/sol3/papers.cfm?abstract_id=2268079 [https://perma.cc/H4CX-NSQE] (noting that the structure of public-private partnerships "can have serious implications for the integrity and trustworthiness of public officials and institutions, and for trust and confidence in those officials and institutions").

[71] *See Coronavirus Treatment Acceleration Plan Dashboard*, *supra* note 68.

2021, highlights more than 620 drug development programs in progress, 460 trials being reviewed, ten treatments authorized for emergency use, and one treatment (remdesivir) already approved,[72] CTAP's measure of success seems to focus largely on metrics that are meant to appeal to a public desperate for a treatment and a political constituency that wants to highlight progress in combatting the pandemic.

In this vein, the recent FDA approval of Veklury (the brand name for remdesivir) under the auspices of CTAP is very likely an example of reactivity at work. On October 22, 2020, FDA announced the approval of Veklury pursuant to the CTAP program as the first approved drug to treat COVID-19.[73] But FDA's approval of Veklury has since been called into question in ways that cast it as an example of regulatory reactivity. Scientists have criticized FDA's approval of Veklury and WHO now specifically recommends against the use of remdesivir for COVID-19 patients on the grounds that there is currently no evidence that it improves survival and other outcomes in these patients.[74]

Overall, CTAP's focus on accelerating regulatory review and supporting the speedy development of new treatments promises speed without adequate attention to (indeed, perhaps even at the expense of) safety and efficacy. From the start, the roll-out of CTAP has been a product of reactivity, involving 1) a departure from established processes for working with the private sector 2) in direct response to political and public pressures,[75] as well as private sector interests in reducing the requirements for approval of clinical studies 3) resulting in an extreme emphasis on speed and volume of private sector protocols and studies under review at FDA. Thus, not only are CTAP's actions and procedures prone to reactivity, but, arguably, CTAP itself is an example of FDA reactivity in the face of political and public pressure.

IV. MOVING AWAY FROM REGULATORY REACTIVITY

Reactive modes of agency decision-making can be understood as falling into a gray area difficult to scrutinize under existing administrative law frameworks. Reactivity occurs in areas in which agencies are used to wielding their authority and in which agencies are held to have particular expertise, making specific occurrences of reactivity subject to legal scrutiny, as well as being difficult to identify and prove.

The law seemingly provides ample mechanisms for evaluating and setting aside:

> actions, findings, and conclusions [that] are found to be . . . (A) arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with the

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[72] *See id.*

[73] *See FDA's Approval of Veklury (Remdesivir) for the Treatment of Covid-19—The Science of Safety and Effectiveness*, U.S FOOD & DRUG ADMIN. (Nov. 22, 2020), https://www.fda.gov/drugs/drug-safety-and-availability/fdas-approval-veklury-remdesivir-treatment-covid-19-science-safety-and-effectiveness [https://perma.cc/6DCJ-BYTD].

[74] *See, e.g.*, Michael Day, *Covid-19: Experts Criticise Claim That Remdesivir Cuts Death Rates*, 370 BRIT. MED. J. m2839 (July 14, 2020), https://www.bmj.com/content/370/bmj.m2839 [https://perma.cc/B7HL-5ANM]; Press Release, World Health Org., WHO Recommends Against the Use of Remdesivir in COVID-19 Patients (Nov. 20, 2020), https://www.who.int/news-room/feature-stories/detail/who-recommends-against-the-use-of-remdesivir-in-covid-19-patients [https://perma.cc/JY76-FMAH].

[75] *See, e.g.*, Veronica Stracqualursi, *Trump, Without Evidence, Accuses FDA of Delaying Coronavirus Vaccine Trials and Pressures Agency Chief*, CNN (Aug. 23, 2020), https://www.cnn.com/2020/08/22/politics/trump-fda-coronavirus-vaccine/index.html [https://perma.cc/FU3N-2J23].

> law; . . . (C) in excess of statutory jurisdiction, authority, or limitations, or short of statutory right; (D) without observance of procedure required by law; . . . [or] (F) unwarranted by the facts.[76]

However, the purported adherence by agencies, while in reactivity mode, to what may seem to non-experts as agency procedures, evidence-based standards, and expertise, makes it exceedingly difficult to actually establish that these actions (and potentially inaction) fall under any of these categories. The elusive nature of regulatory reactivity and its capacity to dodge scrutiny is primarily due to agencies' proficiency in using their own internal frameworks and unique jargon to portray their actions while in reactivity mode as consistent with long-held data-driven approaches. As shown by the case studies above, agencies operating in reactive mode can, and often do, produce ex post language, such as references to scientific data of dubious quality, that seemingly justifies a given decision. This is particularly true when agency decision-making requires a balancing of competing interests while considering complex subject matter in which the agency is held to have expertise.

The difficulty of holding agencies accountable for decisions and actions while in reactive mode is further exacerbated by well-established administrative law doctrines such as *Chevron* deference and the presumption against review of agency inaction under *Heckler v. Chaney*.[77] These doctrines make courts highly reluctant to step into an agency's shoes, leaving gray areas that are effectively beyond the reach of courts. While there are good reasons for according some measure of deference to agencies, this freedom from review without similar freedom from public and political pressure allows agencies to make reactive decisions that may undermine the foundations on which the authority to make these decisions is established: impartiality, objectivity, and expertise. Although these challenges to administrative decision-making may not be new or unique to regulatory reactivity, the COVID-19 pandemic has exposed the consequences of such decision-making to broader public scrutiny. Given the significant immediate ramifications of reactivity for public health, it is critical to find ways in which agency reactivity may be curtailed and, where prevention is impossible or unsuccessful, addressed.

One possible way of nipping regulatory reactivity in its bud would be to address its primary cause: outside pressure on the agencies—in this case, FDA—to act in ways that align with private interests rather than public health concerns. Insulating agencies from the pressures exerted by outside influences, while at the same time retaining external accountability, has long been considered the best way to maintain their independence and adherence to long-term policy goals, professionalism, and evidence-based standards. Yet, while calls to make FDA more independent from political and special interest pressures are not new, increased independence has remained elusive. Well before the current pandemic, a number of former FDA commissioners publicly advocated for making FDA an independent agency, rather than an agency under the direction of HHS, on the grounds that by making it less vulnerable to the broader political pressures and agendas of HHS, the agency could better focus on its public

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[76] 5 U.S.C. § 706(2).

[77] *See* Chevron U.S.A. v. Natural Res. Def. Council., 468 U.S. 837 (1984) (establishing the principle of judicial deference to agency interpretation of its statutory powers where Congress has not spoken directly to the issue); Heckler v. Chaney, 470 U.S. 821 (1985) (ruling that an agency's decision not to pursue discretionary enforcement action is unreviewable under the Administrative Procedure Act).

health mission.[78] But turning FDA into an independent agency depends entirely on the political will of the current administration and Congress, and remains unlikely to occur any time soon. As an intermediate step in moving towards greater independence, we have in other work proposed tasking an independent, trusted review body with the review of FDA decisions.[79] This would reduce departures from evidence-based decision-making and make the role of outside influences more transparent without any radical changes to the existing regulatory structure.

Another more easily and immediately attainable way of curbing regulatory reactivity would be to include strategies for precommitting to decision-making pathways in emergency settings that can retain the basic principles of evidence-based decision-making while allowing for necessary forms of flexibility. The goal would be to limit the effects of outside pressure by tethering agencies to predetermined standards and procedures in ways that make it harder to depart from them without clear, evidence-based justifications. In other words, by committing to a certain set of rules in advance, and stress testing these rules to see how they function in emergency settings, agencies may decrease the likelihood of reactivity. While FDA has engaged in efforts to improve emergency preparedness and has developed standards such as the EUA standards to guide emergency decision-making, significant discretion remains within this framework. The existing emergency approaches allow emergency responses through increased flexibility without also providing an adequate framework to guide the tradeoffs that are made. There is no predetermined framework to guide how this increased discretion is exercised, leaving open opportunities for further refinement and stress testing of emergency preparedness decision frameworks.

The last and, admittedly, most cumbersome (and, thus, least attainable) way of curbing reactivity is to change the standards for evaluation of agency decisions and actions so as to increase the level of scrutiny of agency decisions and actions made during an emergency. Courts may, for instance, practice a diminished level of *Chevron* deference or craft an exception to the *Chevron* doctrine when agency decisions and actions are made during a time of public health emergency. This last suggestion entails extended considerations within interrelated areas of administrative law that vastly exceed the scope of this Article. We mention it here, however, as a way to draw attention to the need for further scrutiny of seemingly justified regulatory decisions that, upon closer examination, may reveal a departure from long-held, science-driven regulatory frameworks.

The three approaches discussed above serve as the beginning, rather than the end, to a much-needed conversation about how to equip agencies such as FDA to avoid, or at least mitigate, the harms of reactivity.

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[78] Nicholas Forko, *Decrying Political Pressure at FDA, Former Commissioners Breakaway Plan*, STAT NEWS (Oct. 19, 2018), https://www.statnews.com/2018/10/19/seven-former-fda-commissioners-think-the-agency-faces-too-much-political-pressure/ [https://perma.cc/FC2S-5L7C] ("While FDA's mission has always been politicized, the issue is particularly salient now given President Trump's propensity for pressuring the agency to prioritize politically popular policies.").

[79] In other work, we have developed a proposal for re-funding the Office of Technology Assessment and tasking it with the role of reviewing decisions by FDA in a credible and transparent manner, limiting departures from evidence-based decision-making, and building public trust in the ultimate decisions made. *See* Yaniv Heled, Ana Santos Rutschman & Liza Vertinsky, *An Institutional Solution to Build Trust in Pandemic Vaccines*, HARVARD PUB. HEALTH REV. (last visited Aug. 10, 2021), https://harvardpublichealthreview.org/31-article-heled/ [https://perma.cc/9B3A-8J2C].

V. CONCLUSION

In this Article we have sought to provide a new framework to describe and assess emerging modes of decision-making at health-oriented agencies such as FDA in the context of highly disruptive public health crises, such as the COVID-19 pandemic. We focused on shifts in data-driven decision-making processes observed at FDA throughout the response to the pandemic, explaining how certain EUAs issued in connection with COVID-19 products and the creation of CTAP illustrate reactivity paradigms. We conclude with some ideas of how to mitigate reactivity within FDA and, possibly, other regulatory agencies, in order to protect the evidence-based, science-driven decision-making that is the gold standard of institutions charged with protecting the public health. We have proposed alternative avenues to pursue in the search for a better mode of agency decision-making in times of public health crises, yet we recognize that each avenue is fraught with political, legal, and institutional challenges, and that the real work of finding the right road map for institutional reform remains before us.