REGULATORY SANDBOXES AND THE PUBLIC HEALTH

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Recently, administrative agencies around the world have engaged in a grand experiment to regulate new technologies: regulatory sandboxes. Regulatory sandboxes allow developers, in cooperation with an agency, to conduct limited tests of new technologies in real-world settings for the purpose of generating and sharing information about them. Thus far, however, "regulatory sandboxes"—as named—appear almost exclusively in the context of financial technologies, or FinTech. Whether regulatory sandboxes, in fact, exist elsewhere in administrative law would be a significant finding for both regulators and scholars; it would blunt criticisms that agencies are slow to respond to new technologies, provide regulators with an additional tool for governing new technologies, and suggest that lessons learned from current regulatory sandboxes are applicable elsewhere.

This Article is the first to explore this broader view of regulatory sandboxes and develop a synoptic theory of them. To do so, it uses one of the most radical programs to introduce new technologies in U.S. history: the U.S. Food and Drug Administration's ("FDA")'s Emergency Use Authorization ("EUA") program for COVID-19 treatments and vaccines. EUAs—like regulatory sandboxes but in stark contrast to typical FDA approval processes—focus on real-world deployment as a means for information gathering. EUAs are also technologically flexible and crafted with close input from the developer, among other features. Generalizing FDA's experience with EUAs also provides lessons about the intersection of regulatory sandboxes with public trust in the agency, political interference, and the maintenance of regulatory standards. At the same time, FDA's COVID-19 EUAs are exceptional in two senses: they touch upon the public health, widely considered to be exceptional subject matter in administrative law;

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and arose in the context of an unprecedented global pandemic. Nonetheless, FDA's experience with EUAs suggest regulatory sandboxes may be an underexplored and undertheorized feature of administrative governance of new technologies. Future work in the area should assess whether regulatory sandboxes exist under the rubric identified here, which technologies they regulate, and how those sandboxes operate.

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I. INTRODUCTION

Recently, administrative agencies around the world have engaged in a grand experiment in regulating and fostering the development of new technologies: regulatory sandboxes.[1] Regulatory sandboxes operate outside of agencies' typical approval paradigms and allow developers to "conduct limited tests of their innovations with fewer regulatory constraints, real customers, less risk of enforcement action, and ongoing guidance from regulators."[2] But this experiment has been limited: so far, regulatory sandboxes—and scholarship assessing them—appear directed almost entirely to new financial technologies, or "FinTech."[3] A broader view of regulatory sandboxes, however, presents the possibility that regulatory sandboxes do, indeed, exist elsewhere in administrative law. If so, this would blunt common criticisms that administrative agencies are slow to respond to new technologies, suggest that lessons learned from existing regulatory sandboxes are applicable elsewhere, and provide regulators with an additional tool for evaluating and encouraging new technologies. This Article explores this broader view of regulatory sandboxes with one of the most radical programs to introduce new technologies in U.S. history: the U.S. Food and Drug Administration's ("FDA")'s emergency authorization of COVID-19 diagnostics, treatments, and vaccines.[4] Assessing whether these authorizations constitute a regulatory sandbox has significant implications for FDA and the public health—and scholarship on the regulation of new technologies.

First proposed in 2015 by the UK's Financial Conduct Authority ("FCA"), regulatory sandboxes provide developers "a 'safe space' in which businesses can test innovative products, services, business models and delivery mechanisms without immediately incurring all the normal regulatory consequences of engaging in the activity in question."[5] The immediate impetus for the FCA's program

1. Dirk A. Zetzsche, Ross P. Buckley, Janos N. Barberis & Douglas W. Arner, *Regulating a Revolution: From Regulatory Sandboxes to Smart Regulation*, 23 FORDHAM J. CORP. & FIN. L. 31, 64–68 (2017); *see also* Hilary J. Allen, *Regulatory Sandboxes*, 87 GEO. WASH. L. REV. 579, 592 (2019); Lawrence G. Baxter, *Adaptive Financial Regulation and RegTech: A Concept Article on Realistic Protection for Victims of Bank Failures*, 66 DUKE L.J. 567, 600–01 (2016); Wolf-Georg Ringe & Christopher Ruof, *The DLT Pilot Regime: An EU Sandbox, at Last!*, OXFORD BUS. L. BLOG (Nov. 19, 2020), https://www.law.ox.ac.uk/business-law-blog/blog/2020/11/dlt-pilot-regime-eu-sandbox-last [https://perma.cc/BAE8-QUB2].

2. Allen, *supra* note 1, at 580.

3. In the US, the seemingly lone exception appears to be the State of Utah's Office of Legal Services Innovation, which is "authorized to oversee the Utah legal Sandbox for new and innovative legal business models and services." *The Office of Legal Services Innovation*, STATE OF UTAH SUPREME COURT, https://utahinnovation-office.org (last visited Nov. 22, 2021) [https://perma.cc/WB6Z-2TLS]; *see also* Deno G. Himonas & Tyler J. Hubbard, *Democratizing the Rule of Law*, 26 STAN. J. C.R. & C.L. 261, 273 (2020) (reviewing the Utah legal services regulatory sandbox). In Europe, the European Commission recently proposed the creation of a regulatory sandbox for certain artificial intelligence-based technologies, but whether and how such a sandbox will function remains, as of this writing, unclear. EUROPEAN COMMISSION, PROPOSAL FOR A REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL: LAYING DOWN HARMONISED RULES ON ARTIFICIAL INTELLIGENCE (ARTIFICIAL INTELLIGENCE ACT) AND AMENDING CERTAIN UNION LEGISLATIVE ACTS 69–70 (Apr. 21, 2021) [hereinafter EC AI PROPOSAL], https://ec.europa.eu/newsroom/dae/redirection/document/75788 [https://perma.cc/3LEK-CFBM].

4. *See* discussion *infra* Section III.B.

5. FIN. CONDUCT AUTH., REGULATORY SANDBOX 2 (Nov. 2015), https://www.fca.org.uk/publication/research/regulatory-sandbox.pdf [https://perma.cc/7DMQ-JN38].

was the rapid expansion of—and hyperbolic demand for—various financial technologies, including Bitcoin.[6] Regulatory sandboxes, under FCA's approach and those later adopted by agencies in numerous other countries, allowed FinTech developers to test their wares under real-world conditions while requiring developers to report data from their experiments back to the governing agency.[7] Viewed as a whole, regulatory sandboxes comprise several elements: the collection of experimental data; structure based on industry input; flexibility for different iterations of a broader technology; deployment in real-world settings; and limits on scope, use, and duration.[8] In this way, regulatory sandboxes are like their childhood namesakes: a dedicated space for free experimentation without the usual risk of harm.

This mode of regulation is quite different from traditional command-and-control models of agency oversight, as typified, perhaps, by FDA's approval processes for new therapies and medical devices.[9] In those, FDA requires developers of new therapeutic technologies to first demonstrate their safety and efficacy before making their products available to the public.[10] Satisfying this requirement often takes years to complete and includes robust clinical trials costing as much as hundreds of millions of dollars.[11] Such stringency has been criticized—rightly or wrongly—as doing more harm than good, especially when confronted with a public health crisis: patients die waiting for the data to come in.[12] But as of 2013, FDA also has the power to *temporarily authorize* rather than *approve* new technologies under its Emergency Use Authorization ("EUA") program in the event of a public health emergency.[13] When a public health emergency is declared,

6. *See id.* at 9–10; *see also* Allen, *supra* note 1, at 587 (mentioning Coinbase); Baxter, *supra* note 1, at 602 (mentioning Bitcoin).

7. DELOITTE, REGULATORY SANDBOX: MAKING INDIA A GLOBAL FINTECH HUB 6 (July 2017), https://www2.deloitte.com/content/dam/Deloitte/in/Documents/technology-media-telecommunications/in-tmt-fintech-regulatory-sandbox-web.pdf [https://perma.cc/7E5Q-7G2M] ("The sandbox is an experimental environment where the regulator may tweak regulations, assess impact of regulatory changes and then use this data for final policy making.").

8. *See* discussion *infra* Section II.C.

9. *See* Jordan Paradise, *21st Century Citizen Pharma: The FDA & Patient-Focused Product Development*, 44 AM. J.L. & MED. 309, 311–312 (2018).

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

11. Arti K. Rai, *The Information Revolution Reaches Pharmaceuticals: Balancing Innovation Incentives, Cost, and Access in the Post-Genomics Era*, 2001 U. ILL. L. REV. 173, 181 ("As a consequence, the process of discovering and developing a drug typically takes eleven or twelve years and can cost hundreds of millions of dollars per successful drug that makes it to market.").

12. *See, e.g.*, Lewis A. Grossman, *AIDS Activists, FDA Regulation, and the Amendment of America's Drug Constitution*, 42 AM. J.L. & MED. 687, 708–709 (2016) (exploring these criticisms with respect to the AIDS crisis in the 1980s).

13. Pandemic and All-Hazards Preparedness Reauthorization Act of 2013, Pub. L. 113-5, 127 Stat. 179–80 (2013); *see also* discussion *infra* Section III.D (comparing EUAs to other FDA programs). To be clear, the EUA program has formally existed since the Project BioShield Act of 2004, Pub. L. 108-276, 118 Stat. 835 (2004). But the Project BioShield Act was largely focused on national security, and rarely used—only twice—prior to the Pandemic and All-Hazards Preparedness Reauthorization Act of 2013. And EUAs prior to 2009 were used for military purposes only. *See* FORUM ON MEDICAL AND PUBLIC HEALTH PREPAREDNESS FOR CATASTROPHIC EVENTS, INSTITUTE OF MEDICINE, MEDICAL COUNTERMEASURES DISPENSING: EMERGENCY USE AUTHORIZATION AND THE POSTAL MODEL WORKSHOP SUMMARY 4 (Clare Stroud, Lori Nadig & Bruce M. Altevogt, *rapporteurs*, 2010).

FDA can quickly authorize new technologies under an EUA for distribution to the public under a "totality of the scientific evidence" standard, so long as the developer continually reports experimental data back to the agency.[14] By lowering FDA's usual regulatory barriers, even temporarily, EUAs are designed to encourage the development of new technologies directed to the crisis at hand.[15] This is the framework under which, as of this writing, three new vaccines directed against COVID-19 have been developed and distributed in the United States in less than a year.[16]

EUAs may therefore constitute regulatory sandboxes. As with their analogs in FinTech, EUAs focus on the development of new technology, imbued with requirements on experimentation and data-sharing.[17] EUAs are also structured with robust input from developers in dialogue with the Agency.[18] They're technologically flexible.[19] Perhaps most dramatically for FDA, products tested under an EUA are not limited to laboratory-controlled environments like clinical testing grounds but are deployed in the real world.[20] And, like other regulatory sandboxes, EUAs have limits—limits on scope, duration, the identity of developers,

14. 21 U.S.C.A. § 360bbb-3(c)(2) (West 2020); *id.* § (e)(1)(B)(iii).

15. *See* U.S. GOV'T ACCOUNTABILITY OFF., GAO-21-207, COVID-19: FEDERAL EFFORTS ACCELERATE VACCINE AND THERAPEUTIC DEVELOPMENT, BUT MORE TRANSPARENCY NEEDED ON EMERGENCY USE AUTHORIZATIONS 20 (Nov. 2020), https://www.gao.gov/assets/720/710691.pdf [https://perma.cc/D48R-EUMU] ("EUAs are an important tool for quickly making vaccines and therapeutics available in time of emergency, when speed and flexibility are needed.").

16. Letter from Denise M. Hinton, Chief Scientist, FDA to Ruta Walawalkar, Janssen Biotech, Inc. 2 (Feb. 27, 2021) [hereinafter J&J EUA], https://www.fda.gov/media/146303/download [https://perma.cc/S59M-7LA2]; Letter from Denise M. Hinton, Chief Scientist, FDA to Carlota Vinals, ModernaTX, Inc. 3 (Dec. 18, 2020) [hereinafter Moderna EUA], https://www.fda.gov/media/144636/download [https://perma.cc/B9BE-BMDC]; Letter from Denise M. Hinton, Chief Scientist, FDA to Elisa Harkins, Pfizer, Inc. 3 (Dec. 11, 2020) [hereinafter Pfizer EUA], https://www.fda.gov/media/144412/download [https://perma.cc/XPW9-3CSL].

17. *Coronavirus Treatment Acceleration Program (CTAP)*, FDA, https://www.fda.gov/drugs/coronavirus-covid-19-drugs/coronavirus-treatment-acceleration-program-ctap [https://perma.cc/V6SH-7VSW] (last visited Nov. 18, 2021); *see also* FDA, EMERGENCY USE AUTHORIZATION OF MEDICAL PRODUCTS AND RELATED AUTHORITIES: GUIDANCE FOR INDUSTRY AND OTHER STAKEHOLDERS 26 (Jan. 2017) [hereinafter FDA EUA Guidance], https://www.fda.gov/media/97321/download [https://perma.cc/CE3G-5V78] (discussing data sharing requirements); *COVID-19 Update: FDA's Ongoing Commitment to Transparency for COVID-19 EUAs*, FDA (Nov. 17, 2020)] [hereinafter FDA EUA Transparency Commitment], https://www.fda.gov/news-events/press-announcements/covid-19-update-fdas-ongoing-commitment-transparency-covid-19-euas [https://perma.cc/UA5J-Z97S] (announcing data transparency requirements).

18. FDA EUA Transparency Commitment, *supra* note 17 ("We work with sponsors so that additional data about the product's safety and effectiveness continue to be collected and reviewed. If the available scientific evidence changes or if new information becomes available, we can pivot and potentially adapt the EUA, including revising the authorized use or revoking the EUA.").

19. *See, e.g.*, Letter from Denise M. Hinton, Chief Scientist, FDA to Laboratories Who Have Developed a Molecular-Based Test (LDTs) for Coronavirus Disease 2019 (COVID-19) 4 (Mar. 31, 2020) [hereinafter Umbrella EUA], https://www.fda.gov/media/136598/download [https://perma.cc/9PJ9-MP8Z] (providing an "umbrella" EUA with technological templates).

20. *See* Hershcel Nachlis, *The FDA's Evolving COVID-19 Emergency Use Authorizations: How The Convalescent Plasma Authorization Can Inform Future Vaccine And Therapeutic EUAs*, HEALTH AFFAIRS BLOG (Oct. 20, 2020), https://www.healthaffairs.org/do/10.1377/hblog20201016.659416/full/ [https://perma.cc/K8BY-YS97] ("Through the EUA process . . . the FDA may grant expedited market access to unapproved products or for unapproved indications of approved products.").

and recipients of the experimental product.[21] This makes EUAs significantly different from other FDA approval programs, even those focused on experimental products and rapid development of new technologies.[22]

Whether, how, and to what extent FDA's EUA program constitutes a regulatory sandbox has important implications about this movement in regulatory science, writ large. If FDA's EUA program is characteristic of regulatory sandboxes, it has much to teach regulators and administrative law scholars about the intersection of regulatory sandboxes with issues such as the public trust, political interference, the decay of regulatory standards, and regulation's effect on the speed of innovation.[23] Alternatively, FDA's experience with EUAs may simply be a form of public health exceptionalism, an admission that FDA's oversight of public health is "somehow unique in the realm of administrative law."[24] Or, the more so for the COVID–19 pandemic, specifically, the single most exceptional public health crisis in modern U.S. administrative history.[25]

This Article is the first to explore regulatory sandboxes outside the FinTech context and develop a broader theory of what regulatory sandboxes are. The Article provides ways of assessing whether regulatory sandboxes in fact exist in other places in administrative law and proposes directions for future research in the area. Part II of the Article reviews the genesis of regulatory sandboxes, develops a theory of them, and examines risks and criticisms of this move in regulatory science. Part III explores EUAs as forms of regulatory sandboxes. It compares EUAs to FDA's typical procedures for approving new therapies and devices, provides examples of several EUAs, and discusses issues specific to the COVID-19 EUAs during the pandemic. Part IV then attempts to generalize its analysis of these issues to regulatory sandboxes as a whole, while acknowledging some limits on their instructive potential. Ultimately, this Article uses FDA's experience with EUAs in the COVID-19 pandemic as a lens to examine regulatory sandboxes in the public health, and concludes by offering areas for future explorations to test this paper's descriptive account.

21. FDA EUA Guidance, *supra* note 17, at 22–29.

22. *See* discussion *infra* Section III.D.

23. *See* discussion *infra* Section IV.A–D.

24. DANIEL CARPENTER, REPUTATION AND POWER 361 (2010).

25. That is, from about the 1940s in conjunction with the rise—and deference to—agency authority. *See, e.g.*, DANIEL R. ERNST, TOCQUEVILLE'S NIGHTMARE: THE ADMINISTRATIVE STATE EMERGES IN AMERICA, 1900-1940 (2014); *see also* COMM. EQUITABLE ALLOCATION OF VACCINE FOR THE NOVEL CORONAVIRUS, NAT'L ACAD. SCI., ENG'G & MED., FRAMEWORK FOR EQUITABLE ALLOCATION OF COVID-19 VACCINES 91 (Helene Gayle, William Foege, Lisa Brown & Benjamin Kahn, eds., 2020) (describing the COVID-19 crisis as "a pandemic of a magnitude not seen in a century").

II. REGULATORY SANDBOXES

A. The Impetus Behind Sandboxes

"A common complaint regarding the regulation of new technologies is that the law is slow to react to technological change."[26] While the complaint is often directed at a variety of private law regimes,[27] its full ire seems reserved for public regulatory law in particular.[28] As condemned by Jonathan H. Adler, "Government regulation of new technology inevitably slows its development and adoption."[29] Cass R. Sunstein declared the regulation of new technologies to be "counterproductive, ineffective, overly costly, or nonexistent."[30] In addition, where public regulation is especially burdensome, this appears to encourage gamesmanship, cheating, and even anticompetitive conduct "by which existing industries use regulation to prevent new competition. . . . [or] slow down regulation" itself.[31] Whether such criticisms are warranted is unclear; some of these complaints rest on empirical assessments for which data is absent or hard to come by.[32] Nonetheless, a regulatory system so ponderous that it thwarts its own advance and encourages its charges to circumvent it seems, well, bad.[33]

Yet some of this lack of speed is for good reason. New technologies frequently present safety concerns different from older counterparts in degree or kind.[34] Agencies responsible for overseeing such technologies may lack the

26. Gaia Bernstein, *When New Technologies Are Still New: Windows of Opportunity for Privacy Protection*, 51 VILL. L. REV. 921, 926 (2006).

27. *E.g.*, *id.* (privacy law and the internet); Jeffrey M. Hirsch, *Future Work*, 2020 U. ILL. L. REV. 889 (workplace liability and robotics); Gary E. Marchant & Rachel A. Lindor, *Genomic Malpractice: An Emerging Tide or Gentle Ripple?*, 73 FOOD & DRUG L.J. 1 (2018) (medical malpractice and genomics).

28. *E.g.*, Jonathan H. Adler, *More Sorry Than Safe: Assessing the Precautionary Principle and the Proposed International Biosafety Protocol*, 35 TEX. INT'L L.J. 173, 195 (2000) ("[T]he precautionary principle biases regulatory decisions against the introduction of any new technology . . . [which] may well leave us more sorry and less safe."); Lynn E. Blais & Wendy E. Wagner, *Emerging Science, Adaptive Regulation, and the Problem of Rulemaking Ruts*, 86 TEX. L. REV. 1701, 1702 (2008) ("[L]egal institutions can impede the assimilation of new information into regulatory requirements . . . ."); Cass R. Sunstein, *Administrative Substance*, 1991 DUKE L.J. 607, 631 ("[R]egulation [of new technologies] has been counterproductive, ineffective, overly costly, or nonexistent.").

29. Adler, *supra* note 28, at 174.

30. Sunstein, *supra* note 28, at 631.

31. *Id.*; *see also* Stacey L. Dogan & Mark A. Lemley, *Antitrust Law and Regulatory Gaming*, 87 TEX. L. REV. 685, 687 (2009) (defining regulatory gamesmanship "as private behavior that harnesses procompetitive or neutral regulations and uses them for exclusionary purposes").

32. *Cf.* Daniel E. Ho & Lisa Larrimore Ouellette, *Improving Scientific Judgments in Law and Government: A Field Experiment of Patent Peer Review*, 17 J. EMPIRICAL L. STUD. 190, 204 (2020) (describing difficulties in obtaining empirical evidence to make such assessments part of the "longstanding problem of translating scientific expertise into law and policy").

33. *Cf.* Daniel Carpenter, *Confidence Games: How Does Regulation Constitute Markets?*, *in* GOVERNMENT AND MARKETS: TOWARD A NEW THEORY OF REGULATION 164, 188 (Edward J. Balleisen & David A. Moss eds., 2010) ("[T]he randomized, controlled trial (RCT) as a technology for quality assessment in pharmaceuticals did not merely intervene into an existing market, but created a new market altogether. It is difficult to imagine therapeutic markets today without the presence of an RCT standard . . . .").

34. *E.g.*, Nathan Cortez, *The Mobile Health Revolution?*, 47 U.C. DAVIS L. REV. 1173, 1210 (2014) (mobile health applications and GPS radios); Hirsch, *supra* note 27, at 938–45 (artificial intelligence in the workplace); Marchant & Lindor, *supra* note 27, at 31 (variants of unknown significance in genomics).

immediate expertise required to assess it.[35] And it is often unclear whether a new piece of technology adequately fits in an older regulatory model or—even if it is assumed to—whether older regulatory models can competently guard against new technologies' infirmities.[36]

As a consequence, developers of new technologies are often uncomfortable experimenting with their wares in the open under the fear that that they may incur unforeseeable regulatory penalties or—perhaps even more damningly—establish a precedent that an older, creakier regulatory model covers a pathbreaking product.[37] Furthermore, without the blessing of a regulator, public deployment of an early-stage technology would likely paint a fat target for products liability lawsuits.[38] While Silicon Valley technology developers are famous for skirting if not flouting regulation—to "move fast and break things"—most other fields without regulatory certainty fear to tread.[39] Product testing, consequently, often remains firmly in the laboratory even where data from real-world use would be particularly valuable.[40]

To combat these tensions, there has been a long history of trying to make regulation more amenable to rapid developments in technology. In 1980, David Collingridge explored using an anticipatory approach: adopting regulations for bleeding edge, and in some cases, yet-to-exist technologies.[41] While Collingridge's concern was mainly focused on biomedical advances, his "dilemma"—a technology's impacts cannot be predicted until it is widely used; controlling impacts are difficult once the technology has become entrenched—has become a touchstone for regulation in a variety of other fields.[42] Beyond anticipatory

35. *See* Allen, *supra* note 1, at 637 (describing a lack of technical expertise from agencies as a "key challenge"); Blais & Wagner, *supra* note 28, at 1713 ("A decade or more after the first standard-setting process, the industries' expertise will likely outstrip that of concerned public interest groups and agency officials to an even greater extent than it did the first time through the process . . . ."); Cortez, *supra* note 34, at 1206 ("FDA is well aware that it lacks technical expertise on mobile technologies.").

36. Nathan Cortez, *Regulating Disruptive Innovation*, 29 BERKELEY. TECH. L.J. 175, 176 (2014); *cf.* Google LLC v. Oracle Am., Inc., 141 S. Ct. 1183, 1208 (2021) (noting this difficulty in the copyright context for application programming interfaces (APIs)).

37. Cortez, *supra* note 36, at 191–99 (assessing this with respect to agency threats).

38. *See, e.g.*, Christopher Buccafusco, *Disability and Design*, 95 N.Y.U. L. REV. 952, 981–82 (2020) (discussing this in the context of wheelchair design).

39. *See* Jeremy A. Carp, *Autonomous Vehicles: Problems and Principles for Future Regulation*, 4 U. PA. J.L. & PUB. AFF. 81, 136 (2018) ("Where technology-neutral laws produce uncertainty with respect to the scope or effect of a regulation, market participants must expend additional resources on regulatory compliance and evaluating the risks of investment; some developers may even respond to this uncertainty by exiting the market or deferring investment.").

40. *Cf.* Gerald F. Tietz, *Strict Products Liability, Design Defects and Corporate Decision-Making: Greater Deterrence Through Stricter Process*, 38 VILL. L. REV. 1361, 1370–75 (1993) (discussing premarket product testing).

41. *See generally* DAVID COLLINGRIDGE, THE SOCIAL CONTROL OF TECHNOLOGY (1981).

42. *See, e.g.*, Olya Kudina & Peter Paul Verbeek, *Ethics from Within: Google Glass, the Collingridge Dilemma, and the Mediated Value of Privacy*, 44 SCI. TECH. & HUM. VALUES 291, 292–94 (2019) (augmented reality); Richard M. Re & Alicia Solow-Niederman, *Developing Artificially Intelligent Justice*, 22 STAN. TECH. L. REV. 242, 286 (2019) (artificial intelligence); NUFFIELD COUNCIL ON BIOETHICS, GENOME EDITING AND HUMAN REPRODUCTION: SOCIAL AND ETHICAL ISSUES 51 n.164 (2018), https://www.nuffieldbioethics.org/assets/pdfs/Genome-editing-and-human-reproduction-report.pdf [https://perma.cc/NFM4-JKQP] (human genome editing).

regulation, regulators have also experimented with narrow exemptions or waivers for cutting-edge technologies. The Environmental Protection Agency ("EPA"), for example, can grant air pollution waivers for new power sources "to encourage the use of an innovative technological system or systems of continuous emission reduction."[43]

Keeping regulations honest, apace, and, at the same time, friendly to new technologies has been a particular challenge for FDA, which seems to be continually faced with major challenges in implementing its own regulations to cover new developments in biomedical science. Gene therapy—the "modifi[cation] of a person's genes to treat or cure disease"[44]—has been a particular challenge to the Agency since the therapy was first conceptually proposed in 1972.[45] While the Agency has claimed jurisdiction over the technique since at least 1986, it has routinely settled on definitions of the term that have either been too constrictive, rapidly outmoded by new technologies, or are "so broad as to be essentially meaningless."[46] In a similar vein, FDA has recently been challenged with how to characterize, as a regulatory matter, fecal microbial transplants ("FMT")—stool donations—after the procedure was recently, and shockingly, found to be effective in some cases.[47] While the Agency has jurisdiction over "human tissue," the nature of the technology has rendered such a regulatory locus undesirable. Instead, FDA—in a way only FDA lawyers could love—regulates FMT as a "drug."[48] And the Agency is currently faced with difficulties in regulating certain precision medicines specific to a single patient's defective genes, "N-of-1" therapies.[49] For FDA, in particular, "[a]s long as speed and safety are seen as opposing forces in drug development and approval, progress will be halting"[50]—and regulation will be complex.

B. The Origin of Regulatory Sandboxes

"Regulatory sandboxes," as that term has come to be known, appear to have been first proposed in 2015 by the UK's Financial Conduct Authority ("FCA"), a government agency tasked with regulating the conduct of financial services

43. 42 U.S.C.A. § 7411 (West 2020). Whether this system is, itself, better characterized as a regulatory sandbox or a blank waiver would be worth exploring under the framework set out in this Article.

44. FDA, *What Is Gene Therapy?* (Jan. 9, 2018), https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTher-apyProducts/ucm573960.htm [https://perma.cc/WY6A-CNTM]. FDA's official definition is more complex: "the administration of genetic material to modify or manipulate the expression of a gene product or to alter the biological properties of living cells for therapeutic use." *Id.* For a criticism of this definition, see Jacob S. Sherkow, Patricia J. Zettler & Henry T. Greely, *Is it "Gene Therapy"?*, 5 J.L. BIOSCIENCES 786 (2018).

45. *See* Theodore Friedmann & Richard Roblin, *Gene Therapy for Human Genetic Disease?*, 175 SCIENCE 949 (1972); *see also* Sherkow, Zettler & Greely, *supra* note 44, at 788–89 (discussing FDA's challenges).

46. Sherkow, Zettler & Greely, *supra* note 44, at 789.

47. Rachel E. Sachs & Carolyn A. Edelstein, *Ensuring the Safe and Effective FDA Regulation of Fecal Microbiota Transplantation*, 2 J.L. & BIOSCIENCES 396, 397 (2015).

48. *Id.* at 398.

49. Janet Woodcock & Peter Marks, *Drug Regulation in the Era of Individualized Therapies*, 381 NEW ENG. J. MED. 1678, 1679 (2019).

50. R. Alta Charo, *Speed Versus Safety in Drug Development*, *in* FDA IN THE TWENTY-FIRST CENTURY 251, 263 (Holly Fernandez Lynch & I. Glenn Cohen eds.) (2015).

firms "to ensure that the relevant markets function well."[51] "Well" in this instance refers to "identifying ways to support the adoption of technologies that facilitate compliance with regulatory requirements."[52] As established by the FCA, a regulatory sandbox is "a 'safe space' in which businesses can test innovative products, services, business models and delivery mechanisms without immediately incurring all the normal regulatory consequences of engaging in the activity in question."[53] This connection between sandboxes and safe spaces is intentional, and derives from the longstanding use of the term "sandboxes" in computer science: "a very restricted environment in which to run untrusted code."[54] That is, a limited, well-defined space to play with new and potentially dangerous technology without a broader risk of harm.

An immediate purpose of the FCA's proposal was to support the UK's rapidly developing FinTech sector.[55] Among various technologies, this included testing the feasibility of blockchain technology in recording secure financial transactions.[56] Given the nascency of blockchain technology (and overhyped demand for it) the purpose of a sandbox, as opposed to waivers or exemptions from regulation, was to make "pragmatic, information- and experience-based [decisions], directed toward ongoing problem-solving, and built around highly participatory and carefully structured dialogue."[57] This is, in some sense, an analogous structure to virtual sandboxes in computer science; an environment "for testing new solutions, in real life situations."[58]

Mechanically, the FCA's proposal centers around "giving [firms] certainty that the FCA will not take enforcement action at a later date in relation to testing activities, provided firms abide by the conditions agreed with the sandbox unit."[59] For firms authorized to participate in the sandbox, this includes a variety of regulatory staples, such as no enforcement action letters, individual guidances, and, as a last resort, waivers.[60] The FCA's sandbox approach also includes means "to allow testing by [unauthorized] firms who need to become authorised to trial their new products or services."[61] Playing in the sandbox requires firms to conduct testing and monitoring of their products, and to submit a final report for

51. *See About the FCA*, FIN. CONDUCT AUTH. (Apr. 21, 2016), https://www.fca.org.uk/about/the-fca [https://perma.cc/742J-ELE3].

52. FIN. CONDUCT AUTH., *supra* note 5, at 13.

53. *Id.* at 2.

54. Li Gong, Marianne Mueller, Hemma Prafullchandra & Roland Schemers, *Going Beyond the Sandbox: An Overview of the New Security Architecture in the Java Development Kit 1.2*, *in* USENIX SYMPOSIUM ON INTERNET TECHNOLOGIES AND SYSTEMS 103 (1997); *see also* Dirk A. Zetzsche, Ross P. Buckley, Janos N. Barberis & Douglas W. Arner, *Regulating a Revolution: From Regulatory Sandboxes to Smart Regulation*, 23 FORDHAM J. CORP. FIN. L. 31, 45 (2017) ("While a new term in financial services, the sandbox concept is by no means novel, with its origins in computer science and other applications beyond financial services.").

55. FIN. CONDUCT AUTH., *supra* note 5, at 5.

56. *Id.* at 10.

57. Allen, *supra* note 1, at 582 (quoting Cristie Ford, *New Governance in the Teeth of Human Frailty: Lessons from Financial Regulation*, 2010 WIS. L. REV. 441, 445).

58. FIN. CONDUCT AUTH., *supra* note 5, at 6.

59. *Id.* at 9.

60. *Id.*

61. *Id.* at 8.

review by the FCA.[62] The FCA then reviews the report and provides its opinion of whether and how the new technology can be introduced to the broader market.[63]

By some measures, this regulatory sandbox model can be viewed as a success. The FCA's proactive approach to creating a welcoming environment for FinTech entrepreneurs "has been credited with helping London become the foremost fintech hub in the world and other countries have hurriedly adopted their own versions in order to telegraph a welcome to fintech entrepreneurs."[64] This has included a parallel proposal by the U.S. Treasury Department,[65] as well as announcements or explorations of FinTech regulatory sandboxes from at least twenty-six other countries as of 2017.[66] And, as of September 2020, the European Commission announced an E.U.-wide regulatory sandbox for another variant of blockchain technology.[67] This is amazing for a legal device first proposed only several years earlier. Seen through the lens of adjusting regulatory policy in response to new technology, it is downright incredible. Dirk A. Zetzsche and colleagues have likened it to a "revolution."[68]

And yet, to date, regulatory sandboxes appear to be largely limited to the FinTech industry.[69] Despite the fact that many other industries face similar issues regarding the implementation of new technology, none of their respective agencies, it seems, have explicitly adopted regulatory sandboxes. Perhaps for this reason, there is a dearth of scholarship on the topic outside of the FinTech context. Of the over 200 articles that mention "regulatory sandboxes" in one popular repository for legal journals, almost none appear to be focused outside the financial industry.[70] Understanding regulatory sandboxes at a higher conceptual level—and outside the FinTech setting—seems important to assessing whether they could, in fact, work in other fields, or even already exist by other names.

62. *Id.* at 11.

63. *Id.*

64. Allen, *supra* note 1, at 580.

65. *Id.* at 584–85.

66. Zetzsche et al., *supra* note 1, at 64–68.

67. Ringe & Ruof, *supra* note 1.

68. Zetzsche et al., *supra* note 1.

69. There are some narrow exceptions, to be clear, including one related to energy service in the UK, safety testing driverless cars in Singapore, and legal technologies for Utah's court system. *See Innovation Sandbox Service Overview*, OFGEM (Feb. 27, 2020), https://www.ofgem.gov.uk/publications-and-updates/innovation-sandbox-service-overview [https://perma.cc/S6GD-37V4]; Si Ying Tan & Araz Taeihagh, *Adaptive and Experimental Governance in the Implementation of Autonomous Vehicles: The Case of Singapore*, 4TH INT'L CONF. ON PUB. POL'Y (June 26–28, 2019), https://www.ippapublicpolicy.org/file/paper/5cea683b9a45b.pdf [https://perma.cc/2VZB-JTCZ]; *see also* sources cited *supra* note 3 and accompanying text. But these are ad hoc regimes designed to test a single iteration of a technology and not well characterized. With that said, the European Commission's recent proposal to create a regulatory sandbox for artificial intelligence appears to be a significant move toward expanding the framework. *See* EC AI PROPOSAL, *supra* note 3, at 79–80.

70. That is HeinOnline, using a search for the term "regulatory sandbox" across all journals. *See* https://heinonline.org/HOL/LuceneSearch?terms=%22regulatory+sandbox%22&collection=journals&searchtype=advanced&typea=text&tabfrom=&other_cols=yes&submit=Go&sendit=; *see also* sources cited *supra* note 3 and accompanying text.

C. A Theory of Regulatory Sandboxes

A working theory of regulatory sandboxes is best served by first contrasting them to what they are not: other models of top-down regulation. Traditional, top-down regulation often begins with the premise that the governing agency's primary objective is public safety.[71] And given the uncertainties present in many new technologies, the risk–benefit calculus often merits caution if not outright skepticism or hostility.[72] The governing agency's objective, then, is to best use currently existing regulatory frameworks to guard against potential harms or, at an extreme, to employ creative interpretations of its authority preserve the status quo until further investigations can take place.[73] In this sense, regulation, like the Ten Commandments, is delivered from the agency up on high to its charges below, who must then conform their behavior accordingly. Change must come through demonstrating the technology's safety—often in a sterile testing setting—or by a direct plea to the agency or the legislature.[74] This all takes time, a factor contributing to the complaint that regulation "slows" technological development.[75]

Regulatory sandboxes, by contrast, are "principles-based regulation because firms participating in the sandbox will be given flexibility and discretion in adapting their innovation to comply with the enumerated goals of the sandbox regime."[76] They are also not impediments to experimental uses of a technology prior to its public release; the very purpose of the sandbox is to allow developers to deploy the technology in the wild to capture real-world user behavior.[77] Documenting this behavior is crucial to a sandbox regime, too, because regulatory sandboxes—as currently conceived—require developers to report data back to the agency so the agency can effectively monitor the technology.[78] These differences to the developer notwithstanding, authorization as part of a sandbox may not look much different from formal approval to end users. And that's the point.

At the same time, regulatory sandboxes—in comparison to approvals—are limited. Regulatory sandboxes may be limited in scope, e.g., that a technology

71. *See* Adler, *supra* note 28, at 195; Carp, *supra* note 39, at 83–84; Daniel Gervais, *The Regulation of Inchoate Technologies*, 47 HOUS. L. REV. 665, 693–99 (2010).

72. Adler, *supra* note 28, at 195–97; Carp, *supra* note 39, at 83–84; Gervais, *supra* note 71, at 693–99.

73. Carp, *supra* note 39, at 147; Charo, *supra* note 50, at 261–62; Ryan Hagemann, Jennifer Huddleston Skees & Adam Thierer, *Soft Law for Hard Problems: The Governance of Emerging Technologies in an Uncertain Future*, 17 COLO. TECH. L.J. 37, 122–23 (2018); Sachs & Edelstein, *supra* note 47, at 398.

74. *See, e.g.*, Carp, *supra* note 39, at 131–32 (discussing problems with testing autonomous vehicles with human drivers or on closed courses); Hagemann et al., *supra* note 73, at 122–123 ("Ideally, if regulation of an emerging technology is necessary, Congress ought to speak directly to the issue and clarify what, if any, new regulatory authority is needed for those technologies and to what extent existing laws or agency rules should (or should not) cover those technologies."); Sachs & Edelstein, *supra* note 47, at 398 (describing the complexities of traditional drug clinical trials for FMT).

75. *See supra* notes 26–31 and accompanying text.

76. Allen, *supra* note 1, at 582.

77. FIN. CONDUCT AUTH., *supra* note 5, at 6; Allen, *supra* note 1, at 592; Zetzsche et al., *supra* note 1, at 84–85.

78. FIN. CONDUCT AUTH., *supra* note 5, at 11; Zetzsche et al., *supra* note 1, at 94–95; DELOITTE, *supra* note 7, at 6.

may only be deployed for particular uses or for a particular segment of consumers or the population.[79] Regulatory sandboxes may also be limited by time, such as for a fixed duration or until the identification of some intervening event.[80] Regulatory sandboxes may also limit the quantity of a given piece of technology authorized under its purview.[81] Or they may limit the particular developers allowed to make use of the sandbox model, such as a "trusted players only" regime.[82]

Taken broadly, regulatory sandboxes can be thought of as consisting of several elements:

- the collection of experimental data;
- structure based on industry or regulated entity input;
- flexibility for different iterations of a broader technology;
- deployment in real-world settings; and
- limits on use, scope, and duration.

Lastly, the idea of regulatory sandboxes isn't to *supplant* regulation. To the contrary, regulatory sandboxes—at least ideally—are meant to *improve* regulation by allowing developers to generate real-world information about new technologies that may otherwise be missing from controlled laboratory experiments in sterile settings.[83] This benefits developers, agencies, and consumers alike—or so one hopes.

D. Risks and Criticisms of Regulatory Sandboxes

There are, of course, potential downsides to implementing regulatory sandboxes. First and foremost, there is the significant potential for consumer harm. The aim of many formal regulatory programs is to guard against consumer harm *before* the introduction of a potentially unsafe technology.[84] In the FinTech context, some of the technologies considered under the FCA's regulatory sandbox approach "may ultimately subject consumers to harm, including discrimination and privacy violations."[85] These potential harms can easily become actual if such technologies are, indeed, made available to consumers, even if experimentally. To take another example, the very purpose of FDA's preapproval is to make sure unsafe or ineffective therapies do not reach the market in the first instance.[86] A sandbox model—by design—allows developers to shoot first and ask questions later.

79. FIN. CONDUCT AUTH., *supra* note 5, at 17–18; Allen, *supra* note 1, at 597; Zetzsche et al., *supra* note 1, at 69–75; DELOITTE, *supra* note 7, at 16; Ringe & Ruof, *supra* note 1.

80. Allen, *supra* note 1, at 638–39; Zetzsche et al., *supra* note 1, at 76; DELOITTE, *supra* note 7, at 18; Ringe & Ruof, *supra* note 1.

81. Allen, *supra* note 1, at 599; Zetzsche et al., *supra* note 1, at 76; DELOITTE, *supra* note 7, at 27.

82. *See* FIN. CONDUCT AUTH., *supra* note 5, at 8; Allen, *supra* note 1, at 596–97; Zetzsche et al., *supra* note 1, at 71–73; Ringe & Ruof, *supra* note 1.

83. Allen, *supra* note 1, at 640; DELOITTE, *supra* note 7, at 6.

84. Adler, *supra* note 28, at 195–97; Carp, *supra* note 39, at 83–84; Gervais, *supra* note 71, at 693–99.

85. Allen, *supra* note 1, at 610.

86. *See* Margaret A. Hamburg & Joshua M. Sharfstein, *The FDA as a Public Health Agency*, 360 NEW ENGL. J. MED. 2493, 2493–94 (2009) ("[T]he agency's 'overriding purpose,' in the words of the Supreme Court [is] protecting the public health.") (quoting United States v. Bacto-Unidisk, 394 U.S. 784, 798 (1969)).

Second, and relatedly, a widespread deployment of less-than-safe-or-functional new technologies may diminish greater public trust in the regulatory sandbox's field. A regulatory sandbox for avionics—the instrumentation that controls airplanes' flight—that produces unsafe planes is almost certain to dissuade people from flying.[87] Similarly, a suite of FinTech products that fail to operate—or harm consumers—are likely to diminish public confidence in FinTech, generally. Australia's FinTech regulatory sandbox, for example, explicitly "notes that its commitment to promoting innovation needs to be balanced with efforts to ensure that 'new products and services are regulated in an appropriate way that promotes investor and financial consumer trust and confidence.'"[88] There is also the potential that consumers will reject products available through a regulatory sandbox because they have not received the overseeing agency's official stamp of approval, i.e., that they are not "fully regulated."[89] Regulatory sandboxes that allow consumers to interface with dangerous or poorly designed products are likely to cause the public to second-guess all products in the field, whether available through a regulatory sandbox or formal approval.

Third, regulatory sandboxes may have the unwanted effect of diminishing public trust in the overseeing agency. To the degree the public trust in an agency's deliberations hinges on traditional models' mode of slow and careful deliberation, the deployment of regulatory sandboxes for new technologies—quicker, less careful—may cause the public to question whether the agency is, in fact, adequately protecting it. This reputational reserve, built-up from an attention to procedure, a low risk-tolerance, and careful public communication, is crucial for some agencies, like FDA, whose decisions will not have their intended, beneficial effects without public buy-in.[90] For others, regulatory sandboxes' potential for opacity may breed mistrust in the agency. Firms participating in regulatory sandboxes may wish to ensure that "regulators are not concealing a race-to-the-bottom within the sandbox."[91] Similarly, regulatory sandboxes augment agencies' discretionary power to move, and move quickly, creating an environment prone to mistrust and political polarization.[92]

Fourth, regulatory sandboxes can put strain on the pertinent agency. A regulatory sandbox that invests much discretion in the agency has the potential of

87. *See* U.S. SENATE COMM. ON COMMERCE, SCI., & TRANSP., COMMITTEE INVESTIGATION REPORT: AVIATION SAFETY OVERSIGHT 6 (Dec. 2020), https://www.commerce.senate.gov/services/files/FFDA35FA-0442-465D-AC63-5634D9D3CEF6 [https://perma.cc/AS7J-DKR2] (detailing regulatory lapses, including loose testing standards, that contributed to avionics related fatal crashes of Boeing's 737 MAX aircraft); Thomas Pallini, *The Boeing 737 Max Returns to US Skies Next Week with American Airlines—Here's How To Tell If You're Flying On One*, BUS. INSIDER (Dec. 29, 2020, 1:50 PM), https://www.businessinsider.com/how-to-tell-if-flying-on-boeing-737-max-flight-2020-12 [https://perma.cc/E8W6-FJCD] ("All airlines flying the Max are touting its safety features, but after two fatal crashes and a scathing report from the US Senate criticizing Boeing and the Federal Aviation Administration's handling of the aircraft's return to service, some passengers are understandably skeptical of stepping back aboard.").

88. Allen, *supra* note 1, at 616.

89. Zetzsche et al., *supra* note 1, at 79.

90. *See* CARPENTER, *supra* note 24, at 10–13 (characterizing the puzzle of public trust in FDA as stemming partially from its good reputation).

91. Zetzsche et al., *supra* note 1, at 80.

92. Baxter, *supra* note 1, at 595.

being more resource intensive than traditional modes of regulation. As with one proposed implementation of the FCA's regulatory sandbox, the FCA noted that it would be "resource-intensive, complex to issue, and require disclaimers."[93] Where the technology is especially pathbreaking, the pertinent agency may also have difficulty staffing experts to oversee it as efficiently as it would under its traditional approval process.[94] And, at an extreme, the discretion inherent in regulatory sandboxes "fails to capture both the standardization and cost reduction functions of law."[95] This would make regulatory sandboxes *worse* than traditional modes of regulation in encouraging the adoption of new technologies.

Lastly, there is the fear that having parallel tracks of regulation—one, slow, deliberate, and punitive when errors occur; another, quick, liberal, and forgiving—will lead to a slippery slope toward the less restrictive model. As noted by the FCA in regard to yet another proposed implementation of its sandbox, "There is a risk that some firms would seek to take advantage of this option when conducting unauthorised business."[96] Why go through a formal approval process if you don't have to?

Whether these risks have come to pass for FinTech regulatory sandboxes remain to be fully seen. Much of the scholarly account of regulatory sandboxes are idealized in nature—and some recent evidence suggests that they often fail to live up to their own promises.[97] Nonetheless, the sandbox revolution is still new and, perhaps like sand itself, constantly shifting. Assessing whether these downsides are real risks or mere hypotheticals in other contexts requires some investigation.

III. EUAs AS A FORM OF REGULATORY SANDBOXES

FDA approval for drugs, medical devices, and vaccines is typically lengthy, costly, and uncertain, and centered on empirically proving products' safety and efficacy under laboratory-like conditions.[98] EUAs, by contrast, are substantially different: they're authorized on a risk-benefit basis derived from the "totality of the scientific evidence"—an amorphous standard—even while they're limited in a variety of ways and easily revocable by FDA.[99] This part walks through FDA's

93. FIN. CONDUCT AUTH., *supra* note 5, at 17.

94. *See* Allen, *supra* note 1, at 637 (describing the need for agencies to hire new employees to oversee regulatory sandboxes); Christopher Woolard, *Innovate Finance Global Summit*, FIN. CONDUCT AUTH. (Sept. 5, 2016), https://www.fca.org.uk/news/speeches/innovate-finance-global-summit [https://perma.cc/6W82-CQMV] ("The sandbox is a world-first for financial services regulators. . . . I expect a high degree of bespoke engagement from our staff, so we will only be able to work with a small number of firms at a time.").

95. Zetzsche et al., *supra* note 1, at 79–80.

96. FIN. CONDUCT AUTH., *supra* note 5, at 20.

97. *See, e.g.*, Hilary J. Allen, *Experimental Strategies for Regulating FinTech*, 3 J.L. & INNOVATION 1, 26–29 (2020) (noting that much sandbox experimentation "has thus far sought to streamline *existing* regulatory functions").

98. Charo, *supra* note 50, at 255–56; Joseph A. DiMasi et al., *Development Times and Approval Success Rates for Drugs to Treat Infectious Diseases*, 107 CLINICAL PHARMACOLOGY & THERAPEUTICS 324, 327 (2020); Ariel Dora Stern, *Innovation Under Regulatory Uncertainty: Evidence from Medical Technology*, 145 J. PUB. ECON. 181, 186 (2017).

99. 21 U.S.C.A. § 360bbb-3(c)(2) (West 2020); *id.* § 360bbb-3(g)(2).

typical approval process for drugs, devices, and vaccines, and compares it to FDA's EUA program before analyzing EUAs as a form of regulatory sandbox.

A. FDA Approval and Authorization

1. The Typical Process

The FDA has some fairly expansive jurisdiction: it regulates some aspect of almost all food and drink consumed in the United States; therapeutics, like drugs, biologics, vaccines, and medical devices; cosmetics; tobacco; and many aspects of labeling, packaging, and manufacturing quality for all of the above.[100] For therapeutics and medical devices, in particular, FDA has particularly stringent regulations concerning what can and cannot be marketed in interstate commerce.[101] While drug and device regulation is an inordinately complex (and leviathan) field unto itself, the general rule is that drugs and medical devices cannot be marketed in interstate commerce without *prior* approval from the Agency.[102]

Depending upon the novelty of the drug or device, approval or clearance can be lengthy, expensive, and difficult.[103] Generally, for truly new drugs or devices, an applicant must demonstrate that its product is both *safe* and *effective* (although a variety of different statutes govern each class of therapeutic and each uses its own related, but distinct, terminology).[104] The primary vehicle for demonstrating safety and efficacy are clinical trials—experiments conducted on human subjects under close supervision of the Agency.[105] These trials proceed in phases, often with increasing sizes of subjects, and various testing "arms" to ensure all testing variables have been accounted for.[106] Once the last of such trials is completed, the matter may then be referred to an advisory committee, which scrutinizes, in microgranular detail, the trials' data.[107] Assuming the trials were a success—actually, a fairly *infrequent* occurrence—the advisory

100. *See generally* PETER BARTON HUTT, RICHARD A. MERRILL & LEWIS A. GROSSMAN, FOOD AND DRUG LAW: CASES AND MATERIALS 77–162 (4th ed.) (2013).

101. *See id.* at 89–101.

102. *See id.*

103. Stern, *supra* note 98, at 187.

104. *Compare* 21 U.S.C.A. § 355(b)(1) (West 2020) (using the terms "safe" and "effective" for drugs), *with id.* § 360c ("safe" and "effectiveness" for devices), *and* 42 U.S.C.A. § 262(a)(2)(C)(i)(I) (West 2020) ("safe, pure, and potent" for biologics).

105. *See, e.g.*, 21 U.S.C.A. § 355(d) (requiring "adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved").

106. 21 C.F.R. § 312.21 (2020); STEPHEN B. HULLEY, STEVEN R. CUMMINGS, WARREN S. BROWNER, DEBORAH G. GRADY & THOMAS B. NEWMAN, DESIGNING CLINICAL RESEARCH 237 (Nancy Winter eds., 3d ed. 2007) ("In randomized clinical trials, the intervention arms must be in equipoise . . . .").

107. 21 U.S.C.A. § 355(n)(1) (authorizing the Secretary to establish "panels of experts"); FDA, GUIDANCE FOR INDUSTRY: ADVISORY COMMITTEES*: IMPLEMENTING SECTION 120 OF THE FOOD AND DRUG ADMINISTRATION MODERNIZATION ACT OF 1997*, 1 (Oct. 1998) [hereinafter "FDA Advisory Committee Guidance"], https://www.fda.gov/media/72297/download [https://perma.cc/DU4C-BXCX] ("FDA understands the term panels of experts to mean advisory committees.").

committee then recommends that FDA formally "approve" the therapeutic product, which it may or may not do.[108]

This process, from start to finish, can take years—in some famous instances, almost two decades—and cost, at a high point, hundreds of millions of dollars.[109] Like all true experiments, it is far from guaranteed any of this will work—many, if not most, therapeutic candidates fail in experiments.[110] Every year, commercial firms pump billions of dollars into experiments that ultimately fail.[111]

And yet, this vicious system is designed precisely so that only safe and effective drugs reach the public market.[112] Health care providers and consumers need not necessarily second-guess whether medicaments taken or prescribed are effective and safe for treatment.[113] Physicians can be reasonably assured that the therapies they prescribe work for their intended uses.[114] There are instances, to be sure, where the process has failed, and spectacularly so; Prempro, Vioxx, and Xigris live in FDA infamy.[115] But these are noteworthy precisely because they're exceptions to the general rule that FDA does its job quite well.[116] In addition, the trial process is much more abbreviated for most medical devices sold in the U.S.[117] But that system—known as the 510(k) pathway, after the relevant provision in the Food, Drug & Cosmetics Act—is predicated on new devices being

108. FDA Advisory Committee Guidance, *supra* note 107, at 1; Chi Heem Wong, Kien Wei Siah & Andrew W. Lo, *Estimation of Clinical Trial Success Rates and Related Parameters*, 20 BIOSTATISTICS 273, 277 (2019) (estimating overall success rates to be 13.8%). To be clear, this estimate is derived from the number of drug development programs leading to the filing of an Investigational New Drug application, one of the first steps in the regulatory approval pathway For those applications that make it all the way to an advisory committee, the advisory committee recommends approval roughly 72% of the time. Audrey D. Zhang, Jason L. Schwartz & Joseph S. Ross, *Association Between Food and Drug Administration Advisory Committee Recommendations and Agency Actions, 2008–2015*, 97 MILBANK Q. 796, 804–05 (2019). The agency *disagrees* with these favorable recommendations 23% of the time. *Id.* at 804.

109. Stern, *supra* note 98, at 189; Thomas J. Moore, Hanzhe Zhang, Gerard Anderson & G. Caleb Alexander, *Estimated Costs of Pivotal Trials for Novel Therapeutic Agents Approved by the US Food and Drug Administration, 2015-2016*, 178 JAMA INTERNAL MED. 1451, 1454 (2018) (estimating the most expensive clinical trial to date, the sacubitril-valsartan noninferiority trial, to have cost $346.8 million).

110. Wong, Siah & Lo, *supra* note 108, at 277.

111. Moore et al., *supra* note 109, at 1455.

112. *See* Hamburg & Sharfstein, *supra* note 86, at 2494 ("A public health approach recognizes that the potential good of a new medical product or policy must be balanced against the potential harm.").

113. Lindsey R. Baden, Caren G. Solomon, Michael F. Greene, Ralph B. D'Agostino & David Harrington, *The FDA and the Importance of Trust*, NEW ENGL. J. MED. (2020), https://www.nejm.org/doi/pdf/10.1056/NEJMe2030687?articleTools=true [https://perma.cc/NKE8-XT52].

114. *Id.*

115. Writing Grp. for the Women's Health Initiative Investigators, *Risks and Benefits of Estrogen Plus Progestin in Healthy Postmenopausal Women: Principal Results from the Women's Health Initiative Randomized Controlled Trial*, 288 JAMA 321 (2002) (hormone replacement therapy); Paul A. Dieppe, Shah Ebrahim & Peter Juni, *Lessons from the Withdrawal of Rofecoxib*, 329 BMJ 867 (2004) (Vioxx); Mike Mitka, *Drug for Severe Sepsis Is Withdrawn From Market, Fails to Reduce Mortality*, 306 JAMA 2439 (2011) (Xigris).

116. *See* Charo, *supra* note 50, at 252 (noting that, historically, "FDA was lauded as a 'gold standard' for drug regulatory agencies, and its cautious approach was applauded as the best balance between patient safety and patient needs"). This perception has "withered" over time. CARPENTER, *supra* note 24, at 748–49.

117. Vinay K. Rathi & Joseph S. Ross, *Modernizing the FDA's 510(k) Pathway*, 381 NEW ENGL. J. MED. 1891, 1892 (2019) ("[M]ore than 90% of FDA-reviewed devices enter the market by means of the 510(k) pathway.").

safe from prior experience of older, similar devices.[118] In addition, medical device approval policy has typically been more open about weighing consumer choice with a reasonable assurance of a product's safety.[119] Besides, it is still true that the riskiest medical devices—such as heart valve replacements—are subject to rigorous clinical trials.[120] For all these reasons, FDA approval remains—for now, at least—the "gold standard" of agency approval worldwide.[121]

2. Emergency Use Authorizations

But cumbersome clinical trials and formal approval processes are not the only way to widely introduce a drug or device onto the market. FDA also has the power to "authorize"—note the subtle shift in nomenclature; not "approve"—drugs and devices in emergency situations.[122] This is FDA's power to issue Emergency Use Authorizations ("EUAs").[123] Indeed, EUAs are the vehicle used by FDA to rapidly introduce drugs and devices during public health emergencies—say, for example, a global, lethal, viral pandemic.[124]

Section 564 of the Food, Drug & Cosmetics Act governs EUAs.[125] Authorization under an EUA begins with a national declaration of an emergency or a "material threat . . . sufficient to affect national security."[126] This allows the Secretary of Health and Human Services, otherwise formally responsible for *approving* new drugs and devices by way of FDA, to *authorize* them under limited circumstances.[127] First, there must be a "reasonable belief" that the product "may be effective in diagnosing, treating, or preventing" the agent of the emergency.[128] This assessment is based on a "lower level of evidence than the 'effectiveness'

118. As codified at 21 U.S.C. § 360(k). FDA, FD&C Act Chapter V: Drugs and Devices (Mar. 28, 2018), https://www.fda.gov/regulatory-information/federal-food-drug-and-cosmetic-act-fdc-act/fdc-act-chapter-v-drugs-and-devices [https://perma.cc/VFM6-5ELP]. *See also* Mateo Aboy & Jacob S. Sherkow, The FDA De Novo Medical Device Pathway, Patents, and Anticompetition (unpublished manuscript on file with author) (briefly reviewing the mechanics of the 510(k) pathway).

119. *See* Owen Faris & Jeffrey Shuren, *An FDA Viewpoint on Unique Considerations for Medical-Device Clinical Trials*, 376 NEW ENGL. J. MED. 1350, 1351 (2017) ("The FDA has in many cases accepted a somewhat greater degree of uncertainty regarding those benefits and risks early in the life cycle of a device, while allowing patients access to potentially important technologies and supporting the iterative refinement of the technologies."); *see also* Lewis A. Grossman, *FDA and the Rise of the Empowered Consumer*, 66 ADMIN. L. REV. 627, 664 (2013) (noting that the availability of over-the-counter medical devices "reflects FDA's embrace of a modern vision of consumers as autonomous, capable guardians of their own health").

120. *See, e.g.*, Premarket Approval, FDA, https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P140031 [https://perma.cc/DNK5-FSHU] (noting clinical trials conducted for a transcatheter heart valve).

121. CARPENTER, *supra* note 24, at 301; Charo, *supra* note 50, at 252.

122. 21 U.S.C.A. § 360bbb-3 (West 2020).

123. *Id.*; FDA EUA Guidance, *supra* note 17.

124. FDA EUA Guidance, *supra* note 17, at 11.

125. As codified at 21 U.S.C. § 360bbb-3. FDA, FD&C Act Chapter V: Drugs and Devices (Mar. 28, 2018), https://www.fda.gov/regulatory-information/federal-food-drug-and-cosmetic-act-fdc-act/fdc-act-chapter-v-drugs-and-devices [https://perma.cc/VFM6-5ELP].

126. 21 U.S.C.A. § 360bbb-3(b)(1)(D) (West 2020).

127. *Id.* § 360bbb-3(a)(1).

128. *Id.* § 360bbb-3(c)(2)(A).

standard that FDA uses for product approvals"[129] and is made on "a case-by-case basis" for each EUA-sought product.[130] The "reasonable belief" contemplated by the statute need not be grounded in data from clinical trials—although the statute specifically welcomes them—but may be predicated on "the totality of scientific evidence" available at the time.[131] This "may include (but is not limited to): results of domestic and foreign clinical trials, *in vivo* efficacy data from animal models, and *in vitro* data, available for FDA consideration."[132]

Second, the Secretary must make an assessment that the "known and potential benefits of the product" outweigh its potential risks.[133] This risk-benefit analysis is FDA's bread and butter; it's what it does for approving new drugs or clearing medical devices.[134] For EUAs, however, FDA again looks at the "totality" of scientific evidence—not just that from well-controlled clinical trials—and also "must take into consideration the material threat" posed by the emergency.[135] The more extreme the emergency, the more likely a risk-benefit analysis favors authorization, all else being equal.[136]

Third, any product sought to be authorized under an EUA cannot otherwise be approved for the same indication by FDA.[137] This makes sense insofar as it would be unnecessary: if a product is fully approved by the Agency, why would it also need to be authorized? But this negative requirement is also one of administrative comity: Authorization under an EUA brings with it several challenges and exceptions likely to be inappropriate for, or conflicting with the requirements for, a fully authorized product. Exceptions include different rules regarding manufacturing, distribution and advertising,[138] limitations on prescribing,[139] and developers' coverage under the PREP Act, a statute that "provide[s] for immunity from tort liability related to activities authorized" under an EUA.[140] In addition, because products "authorized" under an EUA are not "approved" as a legal matter—again, this salient difference between the two terms—there are likely to be "conflicts between federal and state law . . . if states have existing requirements governing . . . unapproved medical products or approved medical products for

129. FDA EUA Guidance, *supra* note 17, at 8.

130. *Id.*

131. 21 U.S.C.A. § 360bbb-3(c)(2).

132. FDA EUA Guidance, *supra* note 17, at 8.

133. 21 U.S.C.A. § 360bbb-3(c)(2)(B).

134. Hamburg & Sharfstein, *supra* note 86, at 2494.

135. FDA EUA Guidance, *supra* note 17, at 8.

136. This is certainly how things have played out for COVID-19, given the lethality of the disease and its widespread transmission. *See* discussion *infra* Section III.B.2 (detailing the COVID-19 EUAs). Whether this functionally operates as a sliding scale, as described, would need further investigation—such as a few more pandemics. One hopes to never find out. For criticisms of this sliding scale approach, see 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 [https://perma.cc/37ED-YZU2].

137. 21 U.S.C.A. § 360bbb-3(a)(2)(A) (West 2020).

138. FDA EUA Guidance, *supra* note 17, at 26–27.

139. *Id.* at 27–28.

140. *Id.* at 41–42.

unapproved uses."[141] Having a product be both approved *and* authorized, especially for different indications, only complicates this picture.

Fourth, there can be "no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating such disease or condition."[142] If a patient can receive similar treatment from an approved product, the complications presented by an EUA—not to mention its risk to the public health—are likely not worth the gamble. With this said, FDA's interpretation of "unavailable" and "inadequate" is not overly formalistic and errs on the side of authorization. For example, "A potential alternative product may be considered 'unavailable' if there are insufficient supplies of the approved alternative to fully meet the emergency need."[143] Similarly, a product may be deemed "inadequate" if there are "contraindicating data for special circumstances or populations" potentially at risk from the emergency.[144]

Besides these specific requirements, the Secretary has the power under a catch-all provision of the statute to authorize (or reject) products under an EUA for any *additional* conditions or "such other criteria as the Secretary may by regulation prescribe."[145] Furthermore, the EUA statute contains built-in shortcuts concerning manufacturing inspections—waivable by the Secretary—that have recently plagued manufacturers of complex biologic therapeutics.[146] In addition, if unrestricted distribution of the product itself poses a risk to the public health—think opioids—the Secretary may waive the Agency's typical requirements governing their distribution, often referred to as Risk Evaluation and Mitigation Strategy ("REMS") requirements, for an EUA.[147]

These requirements, though, are only the first hurdle. Marketers of EUA-authorized products have continuing obligations to FDA to report information back to the Agency concerning the deployment of their products in the real world. Marketers must inform, and continually update, health care professionals and patients about the limited nature of a product's authorization, including "the extent to which [the product's] benefits and risks are unknown."[148] This doesn't merely require the prompt reporting of information about adverse events back to the Agency, but "enabl[ing] the collection and analysis of information on the safety and effectiveness of the EUA product during the period when the authorization is in effect and for a reasonable time following such period."[149] Making

141. *Id.* at 39.

142. 21 U.S.C.A. § 360bbb-3(c)(3) (West 2020).

143. FDA EUA Guidance, *supra* note 17, at 8.

144. *Id.*

145. 21 U.S.C.A. § 360bbb-3(c)(5).

146. *Id.* § 360bbb-3(e)(3); *see also* Jonathan Gardner, *FDA Gene Therapy Holdups Suggest Closer Scrutiny by Agency*, BIOPHARMA DIVE (Nov. 5, 2020), https://www.biopharmadive.com/news/fda-gene-therapy-manufacturing-delays-scrutiny/588382/ [https://perma.cc/R77D-KK77]; Ed Silverman, *Emergent Was Aware of Vaccine Manufacturing Issues Even as It Collected $27 Million a Month From U.S.*, STAT NEWS (May 19, 2021), https://www.statnews.com/pharmalot/2021/05/19/emergent-jnj-covid19-coronavirus-vaccine-congress/ [https://perma.cc/W5XK-65HF].

147. FDA EUA Guidance, *supra* note 17, at 28 (describing REMS controls).

148. *Id.* at 22.

149. *Id.* at 26.

this a reality is an effort in real-time data-sharing between applicant and agency, requiring "FDA [to] work with product sponsors in some circumstances to develop proposals for more active data collection and follow-up mechanisms" both before and after the EUA application has been submitted.[150] This extends to manufacturers with whom "FDA must establish conditions for a manufacturer of an unapproved product to maintain records and to grant FDA access to records concerning the EUA product."[151] This is different from the typical approval process which largely requires such information *prior* to agency approval and imposes few obligations to gather such information in a continuous manner afterwards.[152]

As one can imagine, EUAs are not meant to last forever. They can—and, in some ways are *designed* to—be revoked when no longer necessary. An EUA ends, first and foremost, when the declared emergency itself ends.[153] Without the emergency in place, the need for EUAs—and their risk to the public health—no longer seems warranted. In addition, the Secretary, may revoke a given EUA if the criteria for its authorization no longer exist.[154] Namely, that the product itself is formally approved by FDA;[155] if during the course of the product's administration evidence arises to suggest that the product is ineffective;[156] or, similarly, if data suggests that the product's risks begin to outweigh its benefits, including the availability of alternatives.[157]

Prior to COVID-19, EUAs were routinely used by FDA in response to major public health emergencies, such as the 2014 Ebola outbreak,[158] the 2016 Zika epidemic,[159] ongoing concerns related to anthrax,[160] and even nerve gas terrorism.[161] But EUAs for these emergencies were only for a small number of

150. *Id.*

151. *Id.*

152. *See* 21 C.F.R. § 312.62 (2020) (requiring maintenance of these records to be established as part of an IND application, i.e., *before* approval, if any). Granted, FDA routinely requires postmarketing studies for many approved products. Joshua D. Wallach, Anita T. Luxkaranayagam, Sanket S. Dhruva, Jennifer E. Miller, & Joseph S. Ross, *Postmarketing Commitments for Novel Drugs and Biologics Approved by the US Food and Drug Administration: A Cross-Sectional Analysis*, 17 BMC MED. 117, 124 (2019), https://bmcmedicine.biomedcentral.com/track/pdf/10.1186/s12916-019-1344-3.pdf [https://perma.cc/XK42-9URT]. But FDA's postmarketing surveillance system has long been criticized, including, in a famous *New England Journal of Medicine* editorial, as "timid and toothless." Susan Okie, *What Ails the FDA?*, 352 NEW ENG. J. MED. 1063, 1063 (2005); *see also* U.S. GOV'T ACCOUNTABILITY OFF., GAO-06-402, IMPROVEMENT NEEDED IN FDA'S POSTMARKET DECISION-MAKING AND OVERSIGHT PROCESS 5 (2006), https://www.gao.gov/assets/250/249535.pdf [https://perma.cc/69SE-FJQK] ("FDA lacks a clear and effective process for making decisions about, and providing management oversight of, postmarket drug safety issues.").

153. 21 U.S.C.A. § 360bbb-3(f)(1) (West 2020).

154. *Id.* § 360bbb-3(g)(2)(A).

155. *Id.* § 360bbb-3(a)(2)(A).

156. *Id.* § 360bbb-3(b)(2)(B).

157. *Id.* § 360bbb-3(c)(2)(B).

158. Declaration Regarding Emergency Use of In Vitro Diagnostics for Detection of Ebola Virus, 79 Fed. Reg. 47141, 47141 (Aug. 12, 2014).

159. Authorization of Emergency Use of an In Vitro Diagnostic Device for Detection of Zika Virus; Availability, 81 Fed. Reg. 61690, 61691 (Sept. 7, 2016).

160. Determination and Declaration Regarding Emergency Use of Anthrax Vaccine Adsorbed for Prevention of Inhalation Anthrax, 70 Fed. Reg. 5450, 5451 (Feb. 2, 2005).

161. Authorization of Emergency Use of an Injectable Treatment for Nerve Agent or Certain Insecticide (Organophosphorus and/or Carbamate) Poisoning; Availability, 82 Fed. Reg. 29867, 29868 (June 30, 2017).

products and limited in scope. Furthermore, some, such as diagnostics for Zika infection, were eventually formally approved by FDA.[162] EUAs for COVID-19, however, present different challenges.

B. COVID-19 EUAs

1. FDA and the COVID-19 Pandemic

Without qualification, COVID-19 has been the most significant public health emergency in modern FDA history.[163] As of this writing, it has killed 5 million globally and sickened another 242 million—45 million in the United States, alone.[164] These numbers will be woefully out of date by the time you read this. Every day the world spends waiting for treatments, 7,000 more people die from COVID-19—a number that has remained roughly consistent throughout continuous waves of viral variants.[165]

The path forward to containing the virus is now fairly clear.[166] We need widespread and globally scaled distribution of effective vaccines.[167] We need a massive screening and tracing program to identify the currently infectious and recognize potentially troublesome variants of the virus.[168] We also need to support the infected and ill who are quarantined.[169] And we need therapeutic interventions to treat those who are ill to either prevent them from becoming hospitalized—and overwhelming health care systems—or to ensure that those who do become hospitalized don't die.[170]

These solutions largely depend on three types of medicaments—vaccines, diagnostics, and therapeutics—all of which are regulated by FDA.[171] Vaccines are "immunogen[s], the administration of which is intended to stimulate the immune system to result in the prevention, amelioration or therapy of any disease or infection."[172] Diagnostics are "reagents, instruments, and systems intended for

162. *See* Letter from Uwe Scherf, Director, Div. of Microbiology Devices, FDA, to Estela Raychaudhuri, President, InBios Int'l, Inc. (May 23, 2019), https://www.accessdata.fda.gov/cdrh_docs/pdf18/DEN180069.pdf [https://perma.cc/P76X-6B3B] (clearing a Zika diagnostic).

163. *See generally* CARPENTER, *supra* note 24.

164. *The Covid-19 Tracker*, STAT NEWS, https://www.statnews.com/feature/coronavirus/covid-19-tracker/ (last visited Nov. 23, 2021) [https://perma.cc/38DT-M6EU].

165. *Id.*

166. Ruchir Agarwal & Gita Gopinath, *A Proposal to End the COVID-19 Pandemic*, IMF STAFF DISCUSSION NOTE (Int'l Monetary Fund), 1, at 10–11 (May 2021), https://www.imf.org/-/media/Files/Publications/SDN/2021/English/SDNEA2021004.ashx [https://perma.cc/S367-TQWE].

167. *See* Danielle Allen, et al., *Roadmap to Pandemic Resilience: Massive Scale Testing Tracing, and Supported Isolation (TTSI) as a Path for Pandemic Resilience for a Free Society*, (Harvard Univ./Edmund J. Safra Ctr. For Ethics), Apr. 20, 2020, at 14, https://ethics.harvard.edu/files/center-for-ethics/files/roadmaptopandemicresilience_updated_4.20.20_1.pdf [https://perma.cc/H6K6-WNF8].

168. *Id.* at 7.

169. *Id.*

170. *Id.* at 20.

171. *See supra* note 104 and accompanying text.

172. FDA, GUIDANCE FOR INDUSTRY: CONTENT AND FORMAT OF CHEMISTRY, MANUFACTURING AND CONTROLS INFORMATION AND ESTABLISHMENT DESCRIPTION INFORMATION FOR A VACCINE OR RELATED PRODUCT (Jan. 1999), at 1, https://www.fda.gov/media/73614/download [https://perma.cc/W36V-CXR3].

use in the diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease."[173] COVID "tests" for assessing whether someone is infected or has been infected in the past are diagnostics.[174] And therapeutics are products intended to "cure, mitigate, treat, or prevent disease, or affect the structure or any function of the body."[175] Drugs to treat those suffering from COVID-19 are consequently therapeutics.

In typical circumstances, the approval processes for each could be long and complex. Vaccine clinical trials, for example, take an average of 65.4 months—about five-and-a-half years—to complete, not including the years of research required to develop a vaccine model or the years of follow-up studies post-approval.[176] Therapeutics, such as drugs and biologics, take, on average, 85.3 and 58.8 months, respectively.[177] And while the pathway for some diagnostics tends to be shorter given complications regarding FDA's jurisdiction to police them, many nonetheless take years to develop.[178] None of these timelines befit a lethal and rapidly spreading pandemic. For COVID-19, for example, waiting for the full completion of an "average" vaccine clinical trial would have resulted, at current case fatality rates, in the deaths of a staggering 13.7 million people.[179]

2. EUAs for COVID-19

FDA's EUA program for COVID-19 began on January 31, 2020, with the Secretary's first declaration of an emergency regarding COVID-19.[180] In the same declaration, the Secretary granted FDA authority to provide EUAs for "in vitro diagnostics for detection and/or diagnosis of this novel coronavirus."[181] As the pandemic spread, additional declarations were made to include EUAs for personal protective equipment, medical devices, and therapeutics.[182] To encourage industry to develop products diagnosing or treating the disease, FDA issued a Guidance walking through its standards for authorization under an EUA on February 29, 2020; this was subsequently updated on March 16, 2020 and again

173. 21 C.F.R. § 809.3(a) (2020).

174. Umbrella EUA, *supra* note 19, at 1.

175. 21 C.F.R. § 3.2(k) (2019).

176. DiMasi et al., *supra* note 98, at 327.

177. *Id.*

178. *See, e.g.*, Anna K. Füzéry, Joshua Levin, Maria M. Chan & Daniel W. Chan, *Translation of Proteomic Biomarkers into FDA Approved Cancer Diagnostics: Issues and Challenges*, 10 CLINICAL PROTEOMICS 1, 5 (2013) (discussing the length of time to develop cancer biomarker diagnostics).

179. *See The Covid-19 Tracker*, *supra* note 164 (assuming a constant fatality rate of 7,000 deaths per day and 30 days in a month).

180. *Determination that a Public Health Emergency Exists*, U.S. DEP'T OF HEALTH & HUM. SERVS. (Jan. 31, 2020), https://www.phe.gov/emergency/news/healthactions/phe/Pages/2019-nCoV.aspx [https://perma.cc/MUW9-ZA9N]; Determination of Public Health Emergency, 85 Fed. Reg. 7316, 7316 (Feb. 7, 2020).

181. *Determination that a Public Health Emergency Exists*, *supra* note 180, at 7316.

182. Emergency Use Authorization Declaration, 85 Fed. Reg. 17335, 17336 (Mar. 27, 2020); Letter from Denise M. Hinton, Chief Scientist, FDA, to Mfrs. of Face Masks; Health Care Pers.; Hosp. Purchasing Dep'ts and Distribs.; and Any Other Stakeholders (Apr. 24, 2020) (granting EUA for PPE); *see also* Jason Gallagher, *Emergency Use Authorization for COVID-19 Therapeutics: The Good, the Bad, and the Data-Deficient*, 5 CONTAGIONLIVE 1, 7 (2020) (critiquing the effectiveness of therapeutic EUAS for COVID-19).

on May 4, 2020.[183] During this time, FDA even offered document templates to assist developers in speeding up their paperwork to be delivered to the Agency.[184]

Balancing the dire need for quick solutions to these problems with COVID-19's astronomical public health burden, FDA has been generous with authorizing diagnostics and treatments through these EUAs rather than its formal approval processes. This has made FDA's COVID-19 EUA program the most expansive in its history: more EUAs have been issued for COVID-19 than all of its previous EUAs combined.[185] Currently, the Agency has issued EUAs for a wide variety of diagnostics and, as of this writing, three vaccines, one of which has since been fully approved.[186] By mid-June 2021, there were 350 EUAs for in vitro diagnostic devices; 126 for non-IVD devices; and 10 for therapeutics.[187] This did not include EUAs authorized "by reference" under a larger "umbrella" EUA—that is, by creating a diagnostic or therapy using umbrella EUAs with prespecified lists of components or reagents.[188] Nor did this include diagnostic tests offered under the rubric of "bridging studies," tests comparing their validity to already authorized tests.[189] The latter of these include the University of Illinois' campus-wide testing program, which, during much of the pandemic, routinely tested over 10,000 individuals a day—roughly 2% of *all* coronavirus tests administered in the U.S., daily.[190]

Authorization for each EUA is formalized by FDA sending the applicant a Letter of Approval, much in the same way it does for fully approved therapeutics and devices.[191] These letters—all publicly available—contain a "Scope of Authorization" section that includes specific details about the device or medicament, such as the type of controls used to ensure it is operating correctly;[192] the

183. FDA, POLICY FOR CORONAVIRUS DISEASE-2019 TESTS DURING THE PUBLIC HEALTH EMERGENCY (REVISED) IMMEDIATELY IN EFFECT: GUIDANCE FOR CLINICAL LABORATORIES, COMMERCIAL MANUFACTURERS, AND FOOD AND DRUG ADMINISTRATION STAFF (May 11, 2020) [hereinafter Revised Test Guidance], https://www.fda.gov/media/135659/download [https://perma.cc/W8MZ-WY7S].

184. *In Vitro Diagnostic EUAs*, FDA, https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas (last visited Nov. 28, 2021) [https://perma.cc/7GTM-W5VZ].

185. *Emergency Use Authorization*, FDA https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization (last visited Nov. 18, 2021) [https://perma.cc/2VMV-83UZ].

186. *In Vitro Diagnostic EUAs*, *supra* note 184; J&J EUA, *supra* note 16; Moderna EUA, *supra* note 16; Pfizer EUA, *supra* note 16.

187. *Emergency Use Authorization*, supra note 185.

188. Umbrella EUA, *supra* note 19.

189. Revised Test Guidance, supra note 183, at 10.

190. Liz Ahlberg Touchstone, *Illinois Validates Saliva-Based Test for COVID-19*, ILL. NEWS BUREAU (Aug. 19, 2020), https://news.illinois.edu/view/6367/1795135071 [https://perma.cc/557Z-LD43]; Meredith Deliso & Jay Bhatt, *Inside University of Illinois' Massive COVID-19 Testing Operation*, ABC NEWS (Sept. 10, 2020), https://abcnews.go.com/US/inside-university-illinois-massive-covid-19-testing-operation/story?id=72686799 [https://perma.cc/S4SH-6FLZ].

191. *E.g.*, Letter from Denise M. Hinton, Chief Scientist, FDA to Christine Phillips, Advisor Glob. Regul. Affs. - US, Eli Lilly & Co. (Nov. 10, 2020) [hereinafter Bamlanivimab EUA], https://www.fda.gov/media/143602/download [https://perma.cc/3WP4-XXCL].

192. *E.g.*, *id.* at 2–3.

reagents used in making the therapeutic;[193] who manufactures them;[194] and any methods used to analyze the output of any device or diagnostic.[195] The letters also specify "Conditions of Authorization," many of which focus on information collection and communication to and from the FDA.[196] For in vitro diagnostics, for example, these conditions include keeping records of false positive and false negative rates, updating any labeling to reflect new information as it comes to the attention of the developer, and to make any other information available to FDA upon request.[197] In addition, FDA has recently begun to push to require developers to make this information publicly available, not simply as a matter of transparency, but in an effort to allow other developers to assess what works and what doesn't.[198] Apart from this, applicants must also work with FDA to develop "Fact Sheets" to be distributed to health care providers and patients, including sets of instructions, for the EUA-sought product, informing recipients of its experimental nature.[199]

Experimental or not, virtually all of the products authorized under an EUA are available to COVID-19 patients in the wild, not controlled laboratory settings; that is, indeed, the purpose of an EUA.[200] Despite the novelty of taking a coronavirus test—at least back in 2020—there has been no difference to patients in taking one authorized under an EUA than one fully approved or cleared by FDA.[201] Most therapeutics, similarly, are administered in a like manner, through in-hospital services, by a patient's physician, or in another clinic setting.[202] Even payment—at least on the patient end—feels largely the same, with diagnostics

193. *E.g.*, Moderna EUA, *supra* note 16.

194. *E.g.*, *id.*

195. *E.g.*, Letter from Denise M. Hinton, Chief Scientist, FDA to Tara Viviani, Director Regul. & Clinical Affs., Applied BioCode, Inc. (Dec. 7, 2020), at 3–4 https://www.fda.gov/media/139046/download [https://perma.cc/3D79-UVCH].

196. *E.g.*, *id.* at 5–9.

197. *E.g.*, *id.* at 6.

198. Press Release, Stephen M. Hahn, Comm'r, FDA, COVID-19 Update: FDA's Ongoing Commitment to Transparency for COVID-19 EUAs (Nov. 17, 2020), https://www.fda.gov/news-events/press-announcements/covid-19-update-fdas-ongoing-commitment-transparency-covid-19-euas [https://perma.cc/646Z-NC35]. This parallels a broader push for an "open science" in developing COVID-19 treatments. *See, e.g.*, E. Richard Gold, *The Coronavirus Pandemic Has Shattered the Status Quo on Drug Development. We Should Build on That*, FORTUNE (Mar. 26, 2020), https://fortune.com/2020/03/26/coronavirus-vaccine-drug-development-open-science-covid-19-treatment/ [https://perma.cc/8ZNF-27RQ].

199. Press Release, Stephen M. Hahn, *supra* note 198.

200. *See Emergency Use Authorization*, *supra* note 185 ("The Emergency Use Authorization (EUA) authority allows FDA to help strengthen the nation's public health protections against chemical, biological, radiological, and nuclear (CBRN) threats including infectious diseases, by facilitating the availability and use of medical countermeasures (MCMs) needed during public health emergencies.").

201. Alexandra E. Petri, *The Experience of Getting Tested for Coronavirus*, N.Y. TIMES (June 25, 2020), https://www.nytimes.com/article/test-for-coronavirus.html [https://perma.cc/V984-H3JD]. In addition, the author can attest to these similarities based on personal experience; as of this writing, and as part of the University of Illinois SHIELD testing program, I've been tested for COVID–19 eighty times—and counting.

202. *See, e.g.*, FDA, FDA COMBATING COVID-19 WITH THERAPEUTICS 1 (2020), https://www.fda.gov/media/136832/download [https://perma.cc/ZB99-7WDN] (noting Veklury's administration in a hospital setting).

or treatments being covered by patients' health insurance.[203] And though the EUA program presents technical challenges to public payers, some, like the Centers for Medicare & Medicaid Services ("CMS"), have otherwise expanded their reimbursement decisions to cover COVID-19 products authorized under EUAs.[204]

Not all of these developments have been successes, however, and EUAs for some therapeutics have generated significant controversy, as discussed more below.[205] In addition, many early in vitro diagnostic tests were found to be highly inaccurate despite being widely used.[206] This, combined with a lack of available diagnostics during the early days of the pandemic, ultimately led then Department of Health and Human Services Secretary Alex Azar to essentially rescind FDA's authority to police laboratory developed tests.[207] This is the flipside of experiments; sometimes experiments fail. Nonetheless, FDA's solution to the COVID-19 pandemic, through its oversight of therapeutics and vaccines, largely runs and will likely continue to run, through EUAs until the pandemic's end. Much of the COVID-19 pandemic is likely to come and go with little, if any, interaction of FDA's more typical approval processes.

3. Specific Issues Regarding COVID-19 EUAs

FDA's approach to EUAs during the pandemic nonetheless raises several issues regarding regulatory governance that are likely specific to FDA or the COVID-19 pandemic more generally. First, FDA's authority to regulate some in vitro diagnostics is controversial and has recently come under fire.[208] Because FDA's jurisdiction covers "devices"—rather than the medical practice of using them or the services employed surrounding them—it has long been unclear whether FDA has authority to oversee laboratory developed tests ("LDTs"), "in vitro diagnostic test[s] that [are] designed, manufactured and used within a single laboratory."[209] Historically, FDA has selectively (and rarely) enforced its

203. *Health Insurance Providers Respond to Coronavirus (COVID-19)*, AHIP, https://www.ahip.org/health-insurance-providers-respond-to-coronavirus-covid-19/ (last visited Nov. 18, 2021) [https://perma.cc/2B2T-SX5G].

204. *E.g.*, CMS, Medicare Monoclonal Antibody COVID-19 Infusion Program Instruction, https://www.cms.gov/files/document/covid-medicare-monoclonal-antibody-infusion-program-instruction.pdf (last visited Nov. 18, 2021) [https://perma.cc/7M9Z-UHDL].

205. *See infra* notes 298–301 and accompanying text; *see also* Tracey & Brennan, *supra* note 136.

206. Removal Lists of Tests that Should No Longer Be Used and/or Distributed for COVID-19: FAQs on Testing for SARS-CoV-2, FDA, https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/removal-lists-tests-should-no-longer-be-used-andor-distributed-covid-19-faqs-testing-sars-cov-2 (last visited Nov. 23, 2021) [https://perma.cc/6F88-GFLW].

207. *Rescission of Guidances and Other Informal Issuances Concerning Premarket Review of Laboratory Developed Tests*, HHS (Sept. 1, 2020) [hereinafter *HHS LDT Rescission*], https://www.hhs.gov/coronavirus/testing/recission-guidances-informal-issuances-premarket-review-lab-tests/index.html [https://perma.cc/H484-JK6Y].

208. Jeffrey K. Shapiro, *In Support of the New HHS Policy Barring FDA from Premarket Review of LDTs*, FDA L. BLOG (Aug. 31, 2020), https://www.fdalawblog.net/2020/08/in-support-of-the-new-hhs-policy-barring-fda-from-premarket-review-of-ldts/ [https://perma.cc/Y29M-MG7F].

209. Laboratory Developed Tests, FDA, https://www.fda.gov/medical-devices/vitro-diagnostics/laboratory-developed-tests (last visited Nov. 23, 2021) [https://perma.cc/GXY9-HHMW].

authority to regulate LDTs.[210] But its choice to do so for COVID-19 diagnostics—even under an EUA regime—prompted significant backlash, and was blamed for delays in the availability of testing early in the pandemic.[211] At the end of August 2020, this resulted in the Secretary announcing a policy effectively stripping whatever jurisdiction FDA had over LDTs, "determin[ing] that the Food and Drug Administration . . . will not require premarket review of laboratory developed tests . . . absent notice-and-comment rulemaking, as opposed to through guidance documents, compliance manuals, website statements, or other informal issuances."[212] This likely means that future LDT COVID-19 diagnostics will not go through FDA's EUA regime.[213]

Second, regarding therapeutics, it has been persistently difficult to generate controlled, real-world evidence to determine whether they are effective, let alone safe.[214] Some of this difficulty stems from political and popular enthusiasm for certain treatments—some of which are comically ineffective—making placing patients in a control group impractical.[215] The Agency has nonetheless issued EUAs for several therapies, including hydroxychloroquine, remdesivir, and convalescent plasma, even where evidence of efficacy has been poor.[216] For hydroxychloroquine, in particular, an absence of good control data revealed—three months after FDA issued its EUA for the drug—that not only was it *not* efficacious, but was affirmatively harmful for some patients.[217] (This led FDA to revoke the EUA covering hydroxychloroquine in June 2020.[218]) Relatedly—and like the difficulty in placing subjects in a control group to test popular therapeutics—the presence of authorized therapeutics has had a dampening effect,

210. Jeffrey K. Shapiro, *Regulation of Laboratory Developed Tests by FDA: Time for the Agency to Cease and Desist Until Congress Enacts Legislation*, FDA L. BLOG (Oct. 21, 2019), https://www.fdalawblog.net/2019/10/regulation-of-laboratory-developed-tests-by-fda-time-for-the-agency-to-cease-and-desist-until-congress-enacts-legislation/ [https://perma.cc/5TZU-BCNC].

211. Barbara J. Evans & Ellen Wright Clayton, *Deadly Delay: The FDA's Role in America's COVID-Testing Debacle*, 130 YALE L.J. FORUM 78, 78–100 (2020); Gail H. Javitt, Jeffrey N. Gibbs, Richard A. Lewis & McKenzie E. Cato, *FDA, Testing, and COVID-19: A "Mid-Mortem,"* FDA L. BLOG (Aug. 25, 2020), https://www.fdalawblog.net/2020/08/fda-testing-and-covid-19-a-mid-mortem/ [https://perma.cc/8MH2-7A27].

212. HHS LDT Rescission, *supra* note 207.

213. *Id.*; Amanda K. Sarata, *HHS Announcement on FDA Premarket Review of Laboratory-Developed Tests (LDTs)*, CONG. RSCH. SERV. (Dec. 3, 2020), https://crsreports.congress.gov/product/pdf/IN/IN11548 [https://perma.cc/83E2-HN4T].

214. Andre C. Kalil, *Treating COVID-19—Off-Label Drug Use, Compassionate Use, and Randomized Clinical Trials During Pandemics*, 323 JAMA 1897, 1897–98 (2020).

215. *See* Rachel Sachs, Jacob S. Sherkow, Lisa Larrimore Ouellette & Nicholson Price, *Remdesivir Part I: Incentivizing Antiviral Innovation*, WRITTEN DESCRIPTION (May 12, 2020), https://writtendescription.blogspot.com/2020/05/remdesivir-part-i-incentivizing.html [https://perma.cc/87XJ-N99N] (discussing this in the context of remdesivir); *see also Why You Should Not Use Ivermectin to Treat or Prevent COVID-19*, FDA, https://www.fda.gov/consumers/consumer-updates/why-you-should-not-use-ivermectin-treat-or-prevent-covid-19 (last visited Nov. 23, 2021) [https://perma.cc/DH8H-WW7K]

216. *See* Tracey & Brennan, *supra* note 136 (discussing the lack of controlled efficacy data for these treatments).

217. The RECOVERY Collaborative Group, *Effect of Hydroxychloroquine in Hospitalized Patients with Covid-19*, 383 NEW ENGL. J. MED. 2030, 2034–36 (2020).

218. Letter from Denise M. Hinton, Chief Scientist, FDA, to Gary L. Disbrow, Deputy Assistant Secretary, BARDA (June 15, 2020)] [hereinafter HCQ Revocation], https://www.fda.gov/media/138945/download [https://perma.cc/58EX-DHXQ].

crowding out the ability of other developers to enroll patients in clinical trials to test other therapies.[219] Given the virus's lethality, hospitalized patients are wary of gambling their health to test new treatments—even while "old" treatments, under an EUA, are themselves a test. In addition, it has been challenging recruiting patients in racial minorities, such as Black and Latino patients, for controlled trials given the significant and historical distrust over such programs.[220] This is true despite the fact that Black and Latino patients fare far worse from COVID-19 than other groups, and treatments for them should be prioritized.[221]

Third, vaccines presented significant challenges to FDA regarding the timing of their authorizations. At the beginning of the vaccines' development timeline, public health experts widely recognized that the agency could not sensibly have required vaccine developers to wait until the completion of multi-year clinical trials before allowing a vaccine on the market.[222] Indeed, the Agency introduced three vaccines via its EUA program even while it required rapid clinical trials.[223] But this has created some difficulties regarding issuing standards for efficacy and the length of follow-up studies to determine how protective a vaccine candidate should be.[224] Given the ways the trials were structured, any long-term effects of a vaccine were not known at the time of authorization, let alone whether candidate vaccines slowed transmission of the virus or simply conferred protective immunity to their recipients.[225] At the same time, shortened standards and the massive appetite for vaccines led many developers to enter the race for vaccines through a variety of molecular mechanisms, such as mRNA, protein subunits, and an inactivated form of the COVID-19 virus itself.[226] This is responsible, in part, for widespread vaccine skepticism, the public being cautious about taking a vaccine not fully approved by FDA even where the "totality of scientific

219. *See* Kalil, *supra* note 214, at 1897.

220. Jocelyn Ashford, *Clinical Trials Need to Include More Black and Other Minority Participants. Here's How*, STAT NEWS (July 22, 2020), https://www.statnews.com/2020/07/22/clinical-trials-include-more-black-and-other-minority-participants/ [https://perma.cc/93V9-S7ZD].

221. Don Bambino, Geno Tai, Aditya Shah, Chyke A. Doubeni, Irene G. Sia, & Mark L. Wieland, *The Disproportionate Impact of COVID-19 on Racial and Ethnic Minorities in the United States*, CLINICAL INFECTIOUS DISEASES (2020), https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa815/5860249?login=true [https://perma.cc/WL2F-78CH]; Clyde W. Yancy, *COVID-19 and African Americans*, 323 JAMA 1891 (2020).

222. Jerry Avorn & Aaron Kesselheim, *Regulatory Decision-Making on COVID-19 Vaccines During a Public Health Emergency*, 324 JAMA 1284 (2020).

223. J&J EUA, *supra* note 16; Pfizer EUA, *supra* note 16; Moderna EUA, *supra* note 16.

224. *See* Susanne H. Hodgson et al., *What Defines an Efficacious COVID-19 Vaccine? A Review of the Challenges Assessing the Clinical Efficacy of Vaccines Against SARS-CoV-2*, 21 LANCET INFECTIOUS DISEASES e26, e30 (2021) ("The US FDA recommends that follow-up of study participants should continue for as long as is feasible . . . . [I]t will be important that robust, ongoing pharmacovigilance is in place post licensure to identify safety signals that large-scale RCTs might not capture."); Jacob S. Sherkow, Lisa Larrimore Ouellette, Nicholson Price & Rachel Sachs, *What's the Difference Between Vaccine Approval (BLA) and Authorization (EUA)?*, WRITTEN DESCRIPTION (June 3, 2021), https://writtendescription.blogspot.com/2021/06/whats-difference-between-vaccine.html [https://perma.cc/L562-Q7FT] (identifying the difference in standards).

225. Hodgson et al., *supra* note 224, at e31.

226. Damien Garde, *STAT Covid-19 Drugs & Vaccines Tracker*, STAT NEWS, https://www.statnews.com/2020/04/27/drugs-vaccines-tracker/#vaccines (last visited Nov. 23, 2021) [https://perma.cc/9RH6-AZ4C].

evidence" strongly suggest the benefits outweigh the risks.[227] Nonetheless, FDA designed its vaccine EUAs in a way that largely mimicked its formal approval process, namely, by requiring large-scale, randomized, controlled trials and by asking developers to submit data from such trials to an advisory committee for review.[228] Whether this defeated the purpose of EUAs or was a necessary particular for vaccines in the pandemic is worth future exploration.

C. The EUA Program as a Form of Regulatory Sandbox

While issues like those described above for COVID-19 EUAs should raise significant concerns under the strictures of FDA's formal approval mechanisms, they may be less concerning if viewed through a different lens: as a form of regulatory sandboxes. That is, FDA's EUA program may, at a high level, be like the FCA's and others' regulatory sandbox programs for FinTech—not a dumbing down of standards or an abdication of authority, but an attempt to allow more industry experimentation to improve the regulatory process for new technologies.[229] To be clear, it does not appear that FDA considers its EUA program to be a regulatory sandbox; it's not even clear that FDA, as an institution, is aware of regulatory sandboxes in general.[230] And while there have been some efforts by others to explicitly develop regulatory sandboxes for devices and therapeutics, it does not appear that these have gained traction at the Agency.[231] Nonetheless, if FDA's EUA program fits the model of regulatory sandboxes, FDA may, in fact, have one in hand.

1. Experimentation and Data Sharing

And indeed, it seems like EUAs fit well within the framework of regulatory sandboxes.[232] Most significantly, EUAs—like the core of regulatory sandboxes,

227. COMM. EQUITABLE ALLOCATION OF VACCINE FOR THE NOVEL CORONAVIRUS, *supra* note 25, at 188–91.

228. *See* FDA Briefing Document: Pfizer-BioNTech COVID-19 Vaccine, Vaccines and Related Biological Products Advisory Committee Meeting (Dec. 10, 2020) [hereinafter Pfizer VRBPAC Briefing Document]; FDA Briefing Document: Moderna COVID-19 Vaccine, Vaccines and Related Biological Products Advisory Committee Meeting, FDA (Dec. 17, 2020), [hereinafter Moderna VRBPAC Briefing Document], https://www.fda.gov/media/144434/download [https://perma.cc/M4P8-D3G9]; FDA Briefing Document: Janssen Ad26.COV2.S Vaccine for the Prevention of COVID-19, Vaccines and Related Biological Products Advisory Committee Meeting, FDA (Feb. 26, 2021) [hereinafter J&J VRBPAC Briefing Document], https://www.fda.gov/media/146217/download [https://perma.cc/4684-42XQ].

229. *See* Zetzsche et al., *supra* note 1, at 45 ("In finance, a regulatory sandbox refers to a regulatory 'safe space' for experimentation with new approaches involving the application of technology to finance.").

230. From parsing FDA's website, the Federal Register, and issued guidances, it does not appear—with one exception—that as of this writing, any FDA program refers to any of its programs explicitly as a "sandbox." The one exception is a single slide on a single webpage of FDA's PrecisionFDA initiative that states, "PrecisionFDA is a research sandbox." *Community Guidelines*, FDA, https://precision.fda.gov/guidelines (last visited Nov. 23, 2021) [https://perma.cc/WW58-9CFD]. It's not clear what this means.

231. *E.g.*, Kim Roth, *Improving Medical Devices: Collaboration by Design*, UNIV. MICH. DEP'T BIOMED. ENG'R, https://bme.umich.edu/tag/medical-device-sandbox/ (last visited Nov. 23, 2021) [https://perma.cc/55KP-SGXG].

232. *See supra* Section II.C.

in general—are designed around developer experimentation and the collection of any resulting data.[233] This is baked into EUAs' standard for authorization, the "totality of scientific evidence," which implies an ongoing process of data collection and review.[234] But it also shows up in a variety of more concrete ways, from FDA's focus on information collection in EUAs' Conditions of Authorization, to developers' unprecedented publication of their testing protocols, to the Agency's recent push for greater data transparency.[235] The latter of these, in particular, allows developers and FDA to assess and modify authorized products as new data walks into the Agency's door.[236] Products approved by FDA's more command-and-control regulatory models are not continually assessed in the same manner, nor are they considered, in word or deed, to be experimental.[237] Instead, the goal of these measures, as it is with other regulatory sandboxes, is to create "an experimental environment where the regulator may tweak regulations, assess impact of regulatory changes and then use this data for final policy making."[238]

2. Developer Input

The COVID-19 EUAs, for example, are individually structured based on input from developers as they make their way through the application cycle. For vaccines, in particular, there has been substantial give-and-take between FDA and developers throughout the EUA application process to develop the scientific evidence needed to assess whether the proposed product's benefits outweigh its risks, how to continually report such information back to FDA, and what's technically feasible in the field given the spread of the pandemic.[239] For other products, EUAs' requirements for information sharing and guided development are

233. *See* FIN. CONDUCT AUTH., *supra* note 5, at 11; Zetzsche et al., *supra* note 1, at 94–95; DELOITTE, *supra* note 7, at 6.

234. *See supra* notes 125–132 and accompanying text.

235. *See supra* notes 148–152 and accompanying text; PFIZER, INC., A PHASE 1/2/3, PLACEBO-CONTROLLED, RANDOMIZED, OBSERVER-BLIND, DOSE-FINDING STUDY TO EVALUATE THE SAFETY, TOLERABILITY, IMMUNOGENICITY, AND EFFICACY OF SARS-COV-2 RNA VACCINE CANDIDATES AGAINST COVID-19 IN HEALTHY INDIVIDUALS, PFIZER, INC., https://pfe-pfizercom-d8-prod.s3.amazonaws.com/2020-09/C4591001_
Clinical_Protocol.pdf (last visited Nov. 23, 2021) [https://perma.cc/8WGH-UUQB]; A PHASE 3, RANDOMIZED, STRATIFIED, OBSERVER-BLIND, PLACEBO-CONTROLLED STUDY TO EVALUATE THE EFFICACY, SAFETY, AND IMMUNOGENICITY OF MRNA-1273 SARS-COV-2 VACCINE IN ADULTS AGED 18 YEARS AND OLDER, MODERNA, https://www.modernatx.com/sites/default/files/mRNA-1273-P301-Protocol.pdf (last visited Nov. 23, 2021) [https://perma.cc/8CQE-AF2U]; Press Release, Stephen M. Hahn, *supra* note 198.

236. Press Release, Stephen M. Hahn, *supra* note 198 ("If the available scientific evidence changes or if new information becomes available, we can pivot and potentially adapt the EUA, including revising the authorized use or revoking the EUA. These are both steps that we have taken during the COVID-19 pandemic.").

237. *See* U.S. GOV'T ACCOUNTABILITY OFF., *supra* note 152, at 10-11 (describing the limits of FDA authority post-approval).

238. Allen, *supra* note 1, at 640 n.345.

239. *COVID-19 Vaccines*, FDA, https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-vaccines (last visited Nov. 18, 2021) [https://perma.cc/VMW8-SG9D]; Pfizer VRBPAC Briefing Document, *supra* note 228; Moderna VRBPAC Briefing Document, *supra* note 228; J&J VRBPAC Briefing Document, *supra* note 228.

subject to revision, both during the application process and post-authorization.[240] In this way, EUAs, like regulatory sandboxes elsewhere, are "pragmatic, information- and experience-based, directed toward ongoing problem-solving, and built around highly participatory and carefully structured dialogue."[241] Or, in the words of former FDA Commissioner Stephen M. Hahn, "We work with sponsors so that additional data about the product's safety and effectiveness continue to be collected and reviewed. If the available scientific evidence changes, or if new information becomes available, we can pivot and potentially adapt the EUA, including revising the authorized use or revoking the EUA."[242]

This also makes EUAs different from applications submitted through FDA's more formal approval processes. By and large, those tend to be set by regulations and guidances that cover entire classes of products, not tailored for each individual application.[243] Nor are these formal approval mechanisms typically "directed toward ongoing problem-solving" in the same manner as EUAs; FDA's role in overseeing full approvals is as a gatekeeper not an usher.[244] As stated by Daniel P. Carpenter in his magisterial volume about the Agency, what FDA traditionally does is "separate[ ] would-be entrants from the space they wish to inhabit,"[245] not, as with EUAs, "work[ ] with industry to make treatment options available to patients and providers."[246] And while it is true that developers do engage (and engage substantially) with the Agency in developing FDA guidances, the guidances are not—as EUAs are—individually negotiated for each application.[247] Products are routinely denied approval based on guidance standards developers have themselves advocated for.[248]

3. Technological Flexibility

Relatedly, EUAs, like other forms of regulatory sandboxes, are flexible enough to apply to different iterations of a broader technology.[249] While each EUA is specific to a particular product, some allow for significant variation

240. Press Release, Stephen M. Hahn, *supra* note 198.

241. Allen, *supra* note 1, at 582.

242. Press Release, Stephen M. Hahn, *supra* note 198.

243. K.M. Lewis, *Informal Guidance and the FDA*, 66 FOOD & DRUG L.J. 507, 521–523 (2011); *see also* Cortez, *supra* note 36, at 209–13 (discussing FDA guidances for "disruptive" technologies); Stern, *supra* note 98, at 183 (discussing FDA guidances for medical devices).

244. Allen, *supra* note 1, at 582; CARPENTER, *supra* note 24, at 7.

245. CARPENTER, *supra* note 24, at 7.

246. FDA Combating COVID-19 With Therapeutics, *supra* note 202.

247. Cortez, *supra* note 36, at 209–13; Lewis, *supra* note 243, at 521–23; Stern, *supra* note 98, at 183.

248. *Compare, e.g.*, George Vradenburg & Howard Fillit, *The FDA Can Declare War on Alzheimer's*, WALL ST. J. (Apr. 4, 2017), https://www.wsj.com/articles/the-fda-can-declare-war-on-alzheimers-1491347437 [https://perma.cc/Q5QU-XGFQ](advocating for a modernization to FDA's Alzheimer's test guidance), *with* FDA, EARLY ALZHEIMER'S DISEASE: DEVELOPING DRUGS FOR TREATMENT GUIDANCE FOR INDUSTRY 3–4 (2018), https://www.fda.gov/media/110903/download [https://perma.cc/6C3R-E7AZ] (permitting a biomarker approach for Alzheimer's clinical trials), *and* Amirah Al Idrus, *FDA panel slams Biogen's controversial Alzheimer's Med*, FIERCE BIOTECH (Nov. 6, 2020), https://www.fiercebiotech.com/biotech/fda-panel-slams-biogen-s-controversial-alzheimer-s-med [https://perma.cc/8RD2-C5UP] (reporting the rejection of an Alzheimer's drug candidate based, in part, on inconclusive biomarker data).

249. *See, e.g.*, Umbrella EUA, *supra* note 19.

among developers.[250] This notably occurs for diagnostics, including the FDA's umbrella EUAs that allow developers to build their own authorized products using what appears to be a reference list of suitable components and the Agency's flexibility for allowing some tests, tweaked from another's EUA, to be marketed under a bridging study.[251] This moves EUAs from hard rules or even softer standards, as seen in the context of formal approvals, to a broader "form of principles-based regulation [where] firms participating in the sandbox will be given flexibility and discretion in adapting their innovation to comply with the enumerated goals of the sandbox regime."[252] True: the principles undergirding EUAs, namely risk-benefit analyses, parallel those from many other of FDA's areas of oversight.[253] And some forms of clearances for medical devices are similarly technologically flexible.[254] But these similarities belie the fact that changing core technology in an already approved or cleared product still typically requires pre-approval from FDA—a stark contrast to EUAs with built in flexibilities for experimentation.[255] And, like regulatory sandboxes writ large, such flexibilities are encouraged precisely to effectuate the regulator's larger goals, here, "strengthen[ing] the nation's public health . . . by facilitating the availability and use of [medical countermeasures] needed during public health emergencies."[256]

4. Real-World Deployment

Products authorized via EUA are also deployed in real-world settings, much like those for FinTech regulatory sandboxes. In the FinTech context, "firms permitted to take advantage of a regulatory sandbox will be able to test their products with real customers in an environment that is not subject to the full panoply of rules."[257] The same goes for products authorized via EUA, which—despite not being fully approved—are nonetheless available in the ordinary course of treating patients affected by the underlying emergency.[258] For COVID-19 EUAs, this means everybody. This leniency with respect to who is entitled to participate in developers' experiments stands in contrast to even "experimental" treatments labeled as such by FDA. The Agency's Expanded Access ("EA") program or its regulation over clinical trial extensions control the distribution of the experimental product so tightly as to often require investigators to submit applications on behalf of identified, individual patients.[259] In addition, FDA

250. *Id.*

251. *Id.*

252. Allen, *supra* note 1, at 582.

253. Hamburg & Sharfstein, *supra* note 86, at 2494.

254. Jacob S. Sherkow & Mateo Aboy, *The FDA De Novo Medical Device Pathway, Patents, and Anticompetition*, 38 NATURE BIOTECHNOLOGY 1028, 1028 (2020) (describing this flexibility for the De Novo pathway); Aboy & Sherkow, *supra* note 118 (describing this flexibility with respect to 510(k) applications).

255. *See* Aboy & Sherkow, *supra* note 118.

256. *See Emergency Use Authorization*, *supra* note 185.

257. Allen, *supra* note 1, at 592.

258. *See supra* notes 200–204 and accompanying text.

259. 21 C.F.R. § 312.305(b)(2)(iii) (2021) (requiring, for an expanded access submission, "for an individual patient, a description of the patient's disease or condition, including recent medical history and previous

stringently limits whether and how much developers can charge for therapies under an Expanded Access protocol.[260] This is not, as regulatory sandboxes are, "a 'safe space' in which businesses can test innovative products, services, business models and delivery mechanisms without immediately incurring all the normal regulatory consequences of engaging in the activity in question."[261] But EUAs allow developers to do precisely that: to not just test but sell their products in the marketplace under real-world conditions.[262]

5. Limits on Scope, Duration, Identity, and Participant

Lastly, like other regulatory sandboxes, EUAs can also be limited in a variety of ways, such as scope, duration, identity, and even by developer. Regarding scope of use, EUAs are authorized much in the same way drugs are formally approved—by a particular indication.[263] EUAs are specific to a particular use, as hashed out between the developer and FDA.[264] This is even more limited than full-blown approvals because physicians are seemingly not free to prescribe EUA-authorized therapies "off-label."[265] EUAs are also limited in time—that is, of course, for the duration of the emergency or, as by statute, until an approved alternative comes along or the EUA-authorized product itself is otherwise formally approved by the Agency.[266] Now with three COVID-19 vaccines available to the public under respective EUAs, FDA has begun to raise the bar for future developers of COVID-19 vaccines.[267] EUAs may also be limited by identity of the developer, akin to FinTech regulatory sandboxes' trusted player model, in that developers utilizing unauthorized manufacturing plants must seek a specific waiver from the Secretary to do so.[268] To date, though, FDA has *not* adopted a "trusted player" model for its COVID-19 EUAs; the liberal availability of EUAs has spurred a host of first-time developers to the COVID-19 therapeutic

treatments of the disease or condition"). Notably, and somewhat ironically, the Expanded Access program arose during another pandemic—the AIDS crisis of the 1980s. Political pressure on the Agency during the AIDS crisis led to the establishment of a "treatment IND" protocol that allowed some experimental AIDS drugs to be administered to a great many AIDS sufferers—a much broader class of participants than that allowed under modern Experimental Access protocols. *See* Grossman, *supra* note 12, at 700–04.

260. 21 C.F.R. § 312.8(c) (2021).

261. FIN. CONDUCT AUTH., *supra* note 5, at 2.

262. *See supra* notes 200–204 and accompanying text.

263. FDA EUA Guidance, *supra* note 17, at 23 ("For unapproved drug products, which do not have FDA-approved labeling for any indication, FDA recommends that, in addition to the brief summary information found in a Fact Sheet, the sponsor also develop more detailed information similar to what health care professionals are accustomed to finding in FDA-approved package inserts.").

264. FDA EUA Guidance, *supra* note 17, at 22–29.

265. 21 U.S.C.A. § 360bbb-3(e)(1)(B)(ii) (West 2020) (allowing EUAs to set "[a]ppropriate conditions on who may administer the product . . . . and on the categories of individuals to whom, and the circumstances under which, the product may be administered with respect to such use.").

266. *See supra* notes 153–157 and accompanying text.

267. EMERGENCY USE AUTHORIZATION FOR VACCINES TO PREVENT COVID-19: GUIDANCE FOR INDUSTRY, FDA (May 25, 2021) [hereinafter May 2021 Vaccine Guidance], https://www.fda.gov/media/142749/download [https://perma.cc/7DDU-WWJ2].

268. *See supra* notes 145–147 and accompanying text.

market.[269] Perhaps relatedly, FDA has not been shy about pulling authorizations for less reputable products—often from less reputable developers—as it did, en masse, for antibody tests in July 2020.[270]

Taken as a whole, these limits on EUAs are of a different character than products approved in the ordinary course. Whereas EUA-authorized products may be limited in scope by indication, as their typically approved counterparts, they tend to be broad—broad enough to cover most forms of treatment under the given emergency—rather than honed, hair-fine, as are some formally approved products.[271] The authorization for EUA products is also time-limited, whereas fully approved products are approved, essentially, indefinitely until the Agency says otherwise;[272] some drugs have continuously marketed for almost 200 years, before and throughout the existence of FDA.[273] FDA's rules on manufacturing, too, are much more strict—and very rarely waivable—for formally approved products, a testament to formal approval's supposed favoritism for legacy players. This stands quite in contrast to diagnostic EUAs' dogpile of new entrants.[274] EUAs' strictures—short and narrow, but available to many—are quite different from the same for formal approval mechanisms.

D. Contrasting EUAs with Other FDA Programs

Besides these differences among the FDA's formal approval mechanisms and EUAs, it may be helpful, too, to distinguish regulatory sandboxes from other programs at the FDA that govern experimental products. First, regulatory sandboxes should be distinguished from controlled experimental testing such as clinical trials. Clinical trials, while experimental, are not partnerships with the Agency, nor are they, in any appreciable sense, deployed in the wild to capture real user behavior.[275] The goal of clinical trials is to establish the statistical significance of the proposed treatment relative to some control, not to see, in real-time, how users will respond an experimental product on the ground—control or

269. *See* FDA Virtual Town Hall Series—Immediately in Effect Guidance on Coronavirus (COVID-19) Diagnostic Tests, FDA (Sept. 9, 2020), https://www.fda.gov/media/142352/download [https://perma.cc/Y6LP-KMNX] (noting that developing diagnostics can be "challenging for some new developers who don't have connections in the community").

270. Letter from Denise M. Hinton, Chief Scientist, FDA, to Manufacturers and Other Stakeholders (July 21, 2020) [hereinafter Serology EUA Revocation], https://www.fda.gov/media/140351/download [https://perma.cc/47P6-P54A].

271. *E.g.*, Highlights of Prescribing Information: Korlym, https://www.accessdata.fda.gov/drugsatfda_docs/label/2012/202107s000lbl.pdf [https://perma.cc/ZD8U-78E7] (indicating Korlym to "control hyperglycemia secondary to hypercortisolism in adult patients with endogenous Cushing's syndrome who have type 2 diabetes mellitus or glucose intolerance and have failed surgery or are not candidates for surgery").

272. U.S. GOV'T ACCOUNTABILITY OFF., *supra* note 152, at 4–6.

273. Michael S. Kinch, Austin Haynesworth, Sarah L. Kinch & Denton Hoyer, *An Overview of FDA-Approved New Molecular Entities: 1827-2013*, 19 DRUG DISCOVERY TODAY 1033, 1034 (2014) ("Specifically, the earliest compound identified in our assessment [of new molecular entities] was morphine, which was first introduced into the USA after Merck initiated commercial sales in Germany in 1827.").

274. *See In Vitro Diagnostic EUAs*, *supra* note 184.

275. Grossman, *supra* note 12, at 694.

otherwise.[276] In addition, the regulations concerning enrollment and testing are far, far too fine-grained for the "flexibility and discretion" characteristic of EUAs, or, for that matter, regulatory sandboxes.[277]

Second, EUAs substantially differ from other FDA mechanisms that provide access to experimental treatments, such as the Agency's EA program or right-to-try protocols. Under the EA program, putative but unapproved treatments are narrowly limited to individual or small groups of patients who cannot obtain satisfactory treatment from an approved product.[278] Furthermore, the EA sponsor—often the clinician administering the treatment—must apply for dispensation to use the treatment, limit the treatment to a single course of therapy, provide monitoring reports, and—even after all that—sometimes file a formal application with FDA, an Investigational New Drug Application or IND.[279] Right-to-try access is even narrower, restricting prospective patients to those who have a life-threatening disease or condition and are unable to participate in a clinical trial.[280] These stand in contrast to products available via EUAs which, once authorized, require no further approval from FDA and are available to anyone so indicated for treatment.

Third, EUAs are not merely a more robust procedure to assess "real world evidence"—RWE in FDA parlance—something the Agency has recently been commanded to consider in even formal approvals.[281] That requirement, as first specified in 2016 in the 21st Century Cures Act, focuses on "information on health care that is derived from multiple sources outside typical clinical research settings, including electronic health records (EHRs), claims and billing data, product and disease registries, and data gathered through personal devices and health applications."[282] It is *not* the evidence generated by user-behavior from products that have yet to otherwise receive approval—as EUAs essentially are.

Fourth, the patient experience of EUAs, in contrast, to other programs that make experimental drugs available to patients, are not noticeably different from the same therapies marketed under traditional approval. Rollout and priority phasing issues notwithstanding, the COVID-19 vaccines have largely been deployed in a manner parallel to those for influenza inoculations: out-of-pocket cost-free shots, delivered in vaccine clinics, pharmacies, and employers'

276. *See* Jonathan J. Darrow, *Pharmaceutical Efficacy: The Illusory Legal Standard*, 70 WASH. & LEE L. REV. 2073, 2111–21 (2013) (describing a narrow-minded focus on statistical significance); Grossman, *supra* note 12, at 694.

277. *Clinical Trials Guidance Documents*, FDA, https://www.fda.gov/regulatory-information/search-fda-guidance-documents/clinical-trials-guidance-documents [https://perma.cc/29QX-XT47] (last visited Nov. 18, 2021) [https://perma.cc/29QX-XT47] (listing 128 separate, entire guidance documents governing clinical trials).

278. 21 C.F.R. § 312.310.

279. *Id.* § 312.305(c).

280. Trickett Wendler, Frank Mongiello, Jordan McLinn, & Matthew Bellina Right to Try Act of 2017, PUB. L. NO. 115–76, § 561B, 132 Stat. 1372, 1372 (2018).

281. 21st Century Cures Act, PUB. L. NO. 114–255, § 505F, 130 Stat. 1033, 1098–97 (2016) (requiring FDA to consider "real world evidence").

282. Rachel E. Sherman et al., *Real-World Evidence—What Is It and What Can It Tell Us?*, 375 NEW ENGL. J. MED. 2293, 2293 (2016).

offices.[283] For consumers being administered COVID-19 experimental products, like remdesivir, they and their treating physicians will notice little difference between administering the EUA authorized drug from the formally approved one: patients unfortunately admitted to the hospital suffering from COVID-19 will be prescribed the drug (and similarly billed) by their physicians.[284] Delivery of the drug itself may similarly be through specialty pharmacies, if needed, or directly from the developer—as in the case of other complex biologics.[285] And while it is true that there may be some significant differences with respect to reimbursement for EUA-authorized, as opposed to approved, drugs, it seems unlikely to affect consumer behavior in any measurable way. Those hospitalized with severe cases of COVID-19, for example, tend not to ask about copays before being admitted.[286]

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For public health scholars and FDA stalwarts concerned that EUAs' massive and rapid expansion during the COVID-19 crisis represent a decline in the Agency's commitment to safeguarding the public health, perhaps this framing provides some comfort. EUAs, ultimately, are not designed to supplant regulation but to improve it, especially in light of the urgent nature of public health disasters. They allow broader experimentation, under real-world settings, to ideally improve regulatory assessments of follow-on products; to generate more evidence on products' risks and benefits where there would otherwise be none and where countless of people may die waiting for more statistically robust data. If not better, the results are, at least, faster and cheaper, with costs borne by industry, and with many minds dedicated to solving the same crisis in myriad ways. In addition, products' recognition via an EUA does not take place of an actual approval— which could end at a moment's notice with no opportunity for appeal. And, for those with a private regulatory bent, products approved via an EUA are not usually subject to the PREP Act—making them a rat's nest of tort liability if something goes wrong. Manufacturers are well incentivized to get things right—that is, while they experiment in EUAs' sandbox to get them to work.

IV. LESSONS LEARNED?

If EUAs are regulatory sandboxes, what does this tell scholars and regulators about regulatory sandboxes more generally? If the COVID-19 EUAs are instructive, a few things: the effect of regulatory sandboxes on public trust of the technology and the agency; the susceptibility of regulatory sandboxes to political

283. *How Do I Find a COVID-19 Vaccine?*, CDC (May 12, 2021), https://www.cdc.gov/coronavirus/2019-ncov/vaccines/How-Do-I-Get-a-COVID-19-Vaccine.html [https://perma.cc/9C7Z-XJ9G].

284. *See* Jessica Wapner, *Covid-19: Medical Expenses Leave Many Americans Deep in Debt*, 370 BMJ m3097, 2 (2020) ("[P]atients with covid-19 are susceptible to the same issues always presented by health insurance").

285. *See* G. Caleb Alexander & Dima M. Qato, *Ensuring Access to Medications in the US During the COVID-19 Pandemic*, 324 JAMA 31, 31–32 (2020) (discussing similarities in pharmaceutical supply chain for COVID-19 and non-COVID-19 therapies).

286. *See* Wapner, *supra* note 284, at 2 (discussing surprise billing).

interference; risks that sandboxes will cause an erosion of regulatory standards; and the connection between lowering regulatory standards and the speed of innovation. But perhaps the COVID-19 EUAs are not instructive. They're focused on public health and work through FDA, a domain and an agency long-thought exceptional in administrative law. And even besides that, the COVID-19 EUAs arose during the COVID-19 pandemic—a once-in-a-century global catastrophe that has no comparator during the modern regulatory area. This part explores some of the broader potential lessons—and limits—on using the COVID-19 EUAs for prescriptions of regulatory sandboxes generally.

A. Public Trust

Regulatory sandboxes are essentially procedures—however well-intentioned—for circumventing regulatory agencies' usual procedures for approval. EUAs, for example, are mutually exclusive with other forms of FDA approval or clearance.[287] Whether the public will respect this difference in form going forward—abbreviated and outside the norm—is unclear. But especially for agencies with high levels of public trust, regulatory sandboxes run the risk of threatening that trust. This may undermine the regulatory sandbox itself—developers can't test products in real-world settings if the world refuses to participate—but may also undercut other work being conducted by the agency.

This decay in public trust in the regulatory agency has been put on parade by the COVID-19 EUAs. Unfortunately, there is *a lot* of skepticism over the COVID-19 EUAs, and specifically with respect to vaccines. Adding to an epidemic of broader vaccine skepticism, many have expressed concerns that rapid authorizations of COVID-19 vaccines will do little to either protect themselves against the disease or guarantee their safety.[288] A slightly more nuanced variation of this complaint is that the EUA process itself, due to its rapid nature, cannot assess any long-term effects from the vaccines being authorized.[289] Yet others have expressed hostility to the experimental design underpinning the vaccine authorizations, which measured protection against severe forms of COVID-19 not necessarily viral transmission.[290] Assuming such complaints are genuine—perhaps an overly generous assumption—many, if not all, of these concerns could and likely would have been addressed had these vaccines been subject to FDA's formal approval mechanisms.[291]

In the U.S. at least, this distrust in the vaccine authorization process has boded poorly for deploying COVID-19 vaccines as widely as possible. Even before mass vaccination was underway, an October 2020 survey from *STAT News* and The Harris Poll found that only "58% of the U.S. public said they would get vaccinated as soon as a vaccine was available when asked earlier this month,

287. 21 U.S.C.A. § 360bbb-3(a)(2) (2020).

288. COMM. EQUITABLE ALLOCATION OF VACCINE FOR THE NOVEL CORONAVIRUS, *supra* note 25, at 188–91.

289. U.S. GOV'T ACCOUNTABILITY OFF., *supra* note 15, at 30.

290. *E.g.*, Hodgson et al., *supra* note 224, at 2–3.

291. *See id.* at 1–4.

down considerably from 69% who said the same thing in mid-August."[292] Even more problematic was a racial disparity in this diminishment of public trust. While "59% of white Americans indicated they would get vaccinated as soon as a vaccine is ready . . . . [o]nly 43% of Black individuals said they would pursue a vaccine as soon as it was available."[293] Some of this is to be expected given longstanding racial disparities in trust in FDA and vaccines, more generally.[294] But it's particularly tragic in the context of COVID-19, a disease that has disproportionately harmed Black Americans at a startling rate.[295] Now, post-authorization and after a long campaign of mass vaccinations, many vaccine skeptics still reference the vaccine—now distributed to hundreds of millions worldwide, with a remarkable safety profile—in terms of "risk."[296] In tension with the purpose of FDA's EUA program, such distrust may ultimately diminish vaccines' real-world efficacy. "Vaccines work only if people agree to get them. Acceptance of [COVID-19] vaccines requires the public to trust the assurances of scientists, physicians, and governments that they are safe."[297]

This same logic extends to therapeutics. FDA's rapid authorization—and subsequent withdrawal—of hydroxychloroquine caused a number of prominent physicians to cast aspersions on the Agency. Vinay Prasad, a professor at UCSF's Department of Epidemiology & Biostatistics, called FDA's authorization of hydroxychloroquine and other therapies "awful . . . not un-authorized (they are legally permissible), but they are not wise . . . . They undermine the credibility of the Agency."[298] Prasad's comments came shortly after FDA published a report showing that not only was hydroxychloroquine not efficacious in treating patients hospitalized with COVID-19, but that, in some cases, it was affirmatively *harmful*.[299] This included documented cases of "serious heart rhythm problems and other safety issues, including blood and lymph system disorders,

292. Ed Silverman, *STAT-Harris Poll: The Share of Americans Interested in Getting Covid-19 Vaccine as Soon as Possible Is Dropping*, STAT NEWS (Oct. 19, 2020), https://www.statnews.com/pharmalot/2020/10/19/covid19-coronavirus-pandemic-vaccine-racial-disparities/ [https://perma.cc/6ULF-C339].

293. *Id.*

294. *Id.*

295. Bambino et al., *supra* note 221, at 1; Yancy, *supra* note 221, at 1891.

296. Derek Thompson, *Millions Are Saying No to the Vaccines. What Are They Thinking?*, THE ATLANTIC (May 3, 2021), https://www.theatlantic.com/ideas/archive/2021/05/the-people-who-wont-get-the-vaccine/618765/ [https://perma.cc/Q5HS-5SPE].

297. Diane E. Meier, R. Sean Morrison & Chris Barker, *Covid-19 Vaccine Safety and the Public Trust: Lessons from Paul Meier and Polio*, STAT News (Dec. 7, 2020), https://www.statnews.com/2020/12/07/covid-19-vaccine-safety-lessons-paul-meier-polio/ [https://perma.cc/A979-ZZKF].

298. Vinay Prasad (@VPrasadMDMPH) TWITTER (Aug. 30, 2020, 4:25 PM) https://mobile.twitter.com/VPrasadMDMPH/status/1300182877296979969 [https://perma.cc/6WCN-5DNQ].

299. *FDA Cautions Against Use of Hydroxychloroquine or Chloroquine for COVID-19 Outside of the Hospital Setting or a Clinical Trial Due to Risk of Heart Rhythm Problems*, FDA [hereinafter FDA HCQ Caution], https://www.fda.gov/drugs/drug-safety-and-availability/fda-cautions-against-use-hydroxychloroquine-or-chloroquine-covid-19-outside-hospital-setting-or (last visited Nov. 23, 2021) [https://perma.cc/LFY6-GGP5]; Memorandum from Dep't of Health & Hum. Servs., Pub. Health Serv., FDR, Ctr. For Drug Evaluation & Rsch., Off. Of Surveillance & Epidemiology on Pharmacovigilance (May 19, 2020), https://www.accessdata.fda.gov/drugsatfda_docs/nda/2020/OSE%20Review_Hydroxychloroquine-Cholorquine%20-%2019May2020_Redacted.pdf [https://perma.cc/GV6N-FU64].

kidney injuries, and liver problems and failure."[300] Evidence for the efficacy of other authorized therapies, even under EUAs "totality of the scientific evidence" standard has similarly been poor and physicians have held the FDA to account.[301]

Relatedly, it seems that the interested public has also experienced a diminished view of the agency itself, at least partially stemming from the EUA process. A September 2020 Axios-Ipsos poll found that 42% of Americans "said they had either not very much trust in the FDA or none at all."[302] This led to seven former Commissioners of FDA to write an opinion piece for *The Washington Post* calling this dip in the Agency's approval "a striking departure from previous levels of trust."[303] The U.S. Government Accountability Office accordingly noted:

> The evidence to support FDA's COVID-19 therapeutic authorization decisions has not always been transparent, in part because FDA does not uniformly disclose its scientific review of safety and effectiveness data for EUAs, as it does for approvals for new drugs and biologics. Given the gravity of the pandemic, it is important that FDA identify ways to uniformly disclose this information to the public. By doing so, FDA could help improve the transparency of, and ensure public trust in, its EUA decisions.[304]

Less charitably, FDA has also recently been the subject of wild conspiracy theories regarding conflicts of interest over its EUA program.[305] In an interview on NBC, Francis S. Collins, Director of the National Institutes of Health, appealed to people to "hit the reset button . . . . put the noise aside and disregard all those terrible conspiracy theories" about FDA.[306]

Sadly, much of this commentary does not compare the difference between EUAs and FDA's typical approval programs. Having different sets of standards makes sense given the differences in aims, criteria, and scope of the two regulatory regimes, not to mention EUAs' emergency nature. Failures of efficacy and safety *should* be expected at a higher rate than FDA's formal approval programs; were it otherwise, it would be fair to say that FDA acts too cautiously in its typical approval programs. And while the public may be concerned that the long-term effects of any EUA-authorized therapeutic or vaccine are unknown, the

300. FDA HCQ Caution, *supra* note 299.

301. *E.g.*, Tracey & Brennan, *supra* note 136.

302. Margaret Talev, *Axios-Ipsos Poll: Distrusting Big Pharma and the FDA*, AXIOS (Sept. 15, 2020), https://www.axios.com/axios-ipsos-poll-distrusting-pharma-fda-coronavirus-index-7605a67b-606d-4e0a-b85f-1887147aa8f8.html [https://perma.cc/8RNC-CXEV].

303. Robert Califf et al., *7 Former FDA Commissioners: The Trump Administration is Undermining the Credibility of the FDA*, WASH. POST (Sept. 29, 2020), https://www.washingtonpost.com/opinions/2020/09/29/former-fda-commissioners-coronavirus-vaccine-trump/ [https://perma.cc/29UA-FSEJ]

304. U.S. GOV'T ACCOUNTABILITY OFF, *supra* note 15, at Executive Summary.

305. *E.g.*, Howard Bauchner, Preet N. Malani & Joshua Sharfstein, *Reassuring the Public and Clinical Community About the Scientific Review and Approval of a COVID-19 Vaccine*, 324 JAMA 1296, 1296 (2020) ("[C]onspiracy theories about a vaccine abound . . . ."); H. Holden Thorp, *We're On Our Own*, 12 SCI. TRANSLATIONAL MED. (EDITORIAL) 1 (2020) ("Trump has already denigrated FDA scientists as part of a 'deep state' conspiracy to harm him politically . . . .").

306. Ben Kamisar, *NIH Director Asks Americans to Leave "Conspiracy Theories" Behind on Vaccines and "Look at the Facts"*, NBC NEWS (Dec. 13, 2020, 9:10 AM), https://www.nbcnews.com/politics/meet-the-press/nih-director-asks-americans-leave-conspiracy-theories-vaccines-behind-look-n1251036?cid=sm_npd_nn_tw_np [https://perma.cc/P65X-FAPH].

truth is they *cannot* be known without concomitantly suffering a significant loss of human life.[307] Perhaps ironically, these criticisms of FDA—that it is moving too quickly for the public health—stand in opposition to another pandemic the Agency once faced: AIDS. During the height of the AIDS crisis, the Agency was excoriated for moving too slowly to approve or authorize experimental treatments.[308] In a famous incident, protesters and activists surrounded an FDA building demanding, "Release the drugs now!"[309] "Ultimately the FDA is simply a reflection of our societal values."[310] But FDA cannot be all things to all people.

If FDAs experience with EUAs are instructive, there are some potential lessons to be learned concerning regulatory sandboxes and the public trust. First, agencies interested in regulatory sandboxes should tread with caution—perhaps more caution than they would suppose—to cut their own red tape. Even FDA, an agency built on reputation and power, can easily squander its goodwill.[311] Failures can be serious. The public remembers; it may not trust the regulator the next time. Second, none of this is a reason to abandon regulatory sandboxes entirely. Indeed, it seems the solution, analogous to those advocated by GAO and others, is to be more transparent—that is, to be up-front and explicit that regulatory sandboxes are by their nature risky and experimental. This may very well mean being explicit that some regulatory activities are "sandboxes"—indeed, using the phrase to connote an area where mistakes are likely to occur and where the rules are designed to be different. Agencies could do this by providing more information, side-by-side, about how such sandboxes differ from the ordinary course of regulatory activity—something FDA has made opaque with respect to vaccines.[312] And, where possible, to establish and continue separate programs for compensation where consumers are harmed by activities otherwise governed by sandboxes. The U.S. already has such a program in place for the COVID-19 vaccines, specifically;[313] policymakers should consider extending these to products governed by regulatory sandboxes, broadly. Such work would demonstrate, if not advertise, that the agency is doing things differently for a limited subset of products, hopefully shielding its reserve of trust if such products go awry. Furthermore, engaging more frequently with regulatory sandboxes is likely to have the added benefit of improving them; agencies may get better results for no other reason than practice and experience.

B. Political Interference

Simplistically, regulatory sandboxes are a recognition that two pathways for regulatory compliance exist: a limited, fast, experimental way; and the slow, traditional, formal way. Faced with a rapidly evolving crisis or an overhyped

307. *See* Sherkow et al., *supra* note 224.
308. Grossman, *supra* note 12, at 688–89.
309. *Id.* at 689.
310. *See* Prasad, *supra* note 298.
311. CARPENTER, *supra* note 24, at 748–49.
312. *See* Sherkow et al., *supra* note 224 (unpacking the differences).
313. Nachlis, *supra* note 20.

technology, the existence of the regulatory sandbox opens up an agency to the possibility of political interference. In the U.S., for example, the Agency may need to contend with a President or a cabinet secretary who will push for expansion or use of the program for political ends. This includes pressuring the Agency to authorize technologies that are unsafe or ineffective but politically popular. Or, more broadly, that regulatory sandboxes, once in place, will be used as instrument of political pressure over and above traditional approval processes.

At least four COVID-19 products—all the subject of EUAs—were the subject of intense political pressure from the White House directed at FDA: hydroxychloroquine, convalescent plasma, neutralizing antibody therapy, and vaccines. Early in 2020, hydroxychloroquine, a malaria drug with the potential for serious side-effects, was reported as possibly efficacious in treating COVID-19 following a small non-randomized study and a smaller observational one.[314] The drug was then praised by President Trump in March 2020 as a "game changer."[315] Nine days later, FDA issued an EUA authorizing its use for COVID-19.[316] In reality, the underlying study latched onto by the White House was likely fraudulent—retracted by the two journals that published it with some of its own authors claiming they could "no longer vouch for the veracity of the primary data sources."[317] In August 2020, President Trump hosted a press conference with FDA Commissioner Hahn in tow, claiming that convalescent plasma—literally, spun down blood from previously infected patients—was "proven to reduce mortality by 35%."[318] Again, these statements were later proven to be incorrect, both as a matter of math—the underlying reduction was a relative difference not absolute mortality—and science, in that convalescent plasma has since failed to be proven substantially effective in treating COVID-19 patients.[319] Then later, in November, after the President himself contracted COVID-19, he touted a neutralizing antibody therapy developed by Regeneron—falsely—as a "cure."[320] FDA subsequently authorized it.[321] And most recently, President Trump had

314. Neil W. Schluger, *The Saga of Hydroxychloroquine and COVID-19: A Cautionary Tale*, 173 ANNALS INTERNAL MED. 662, 662 (2020).

315. 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/ [https://perma.cc/J9KF-ZJXA].

316. *See* HCQ Revocation, *supra* note 218, at 1 (mentioning the original authorization).

317. Elisabeth Mahase, *Hydroxychloroquine for Covid-19: The End of the Line?*, 369 BMJ m2378, *1 (2020).

318. Kai Kupferschmidt & Jon Cohen, *In Plasma OK, Critics See Politics, not Science*, 369 SCIENCE 1038, 1038 (2020); Nicholas Florko, *FDA, Under Pressure from Trump, Authorizes Blood Plasma as Covid-19 Treatment*, STAT NEWS (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/AF43-LKA4].

319. Kupferschmidt & Cohen, *supra* note 318, at 1038; Elizabeth B. Pathak, *Convalescent Plasma Is Ineffective for Covid-19*, 371 BMJ m4072 (2020).

320. Berkeley Lovelace, Jr., *FDA Authorizes Regeneron's Covid Treatment, Taken by Trump, for Emergency Use*, CNBC (Nov. 21, 2020), https://www.cnbc.com/2020/11/21/covid-treatment-fda-authorizes-regeneron-drug-used-by-trump.html [https://perma.cc/E2KT-VJ3Q].

321. Letter from Denise M. Hinton, Chief Scientist, FDA, to Yunji Kim, Director, Regulatory Affairs, Regeneron (Nov. 21, 2020), https://www.fda.gov/media/143891/download [https://perma.cc/P4U9-2AFJ].

attempted to put pressure on FDA to authorize a vaccine by 2020's election day,[322] and—once his demand fell flat—then to demand that FDA authorize the vaccine the day after the Vaccine and Related Biological Products Advisory Committee (VRBPAC) voted in favor of it, on penalty of the FDA Commissioner's firing.[323] Political interference of this magnitude in regulatory science, even if consistently wrong, was previously unheard of in the United States.[324] But the reasons for it are obvious: taming the virus is good politics and FDA holds the whip.

It would be easy, then, to chalk up these instances of political interference to the particulars of the Trump administration and the pandemic, and to suggest that such things are unlikely to occur again in tandem. But agencies that serve as gatekeepers to new technologies routinely face some form of political pressure to approve new technologies that could be viewed as political wins by those in office. The National Aeronautics and Space Administration, of course, is routinely compelled to adopt new technologies in favor of the Executive Branch.[325] Spectrum auctions for things like satellite radio and WiFi, as overseen by the Federal Communications Commission, have been political footballs for years.[326] And in 2004, the EPA succumbed to political pressure to allow hydrofracking, a technology for more efficiently drilling for natural gas, with only minimal regulation.[327] Regulatory sandboxes make these sorts of activities more troublesome, perhaps, because they can more easily be used as an end-around by politicians when traditional processes prove too strict. The EUA statute invests a significant amount of discretionary power in the Secretary of Health and Human Services—a political appointee—in ways far greater than ordinary FDA approvals.[328]

322. Philip Rucker, Josh Dawsey & Yasmeen Abutaleb, *Trump Fixates on The Promise of A Vaccine—Real Or Not—As Key To Reelection Bid*, WASH. POST (Sept. 5, 2020), https://www.washingtonpost.com/politics/trump-vaccine-election/2020/09/05/c0da86d6-edf5-11ea-99a1-71343d03bc29_story.html [https://perma.cc/7PXN-UYYH].

323. Laurie McGinley, Carolyn Y. Johnson & Josh Dawsey, *FDA Authorizes the First Coronavirus Vaccine, a Rare Moment of Hope in the Deadly Pandemic*, WASH. POST (Dec. 12, 2020), https://www.washingtonpost.com/health/2020/12/11/trump-stephen-hahn-fda-covid-vaccine/ [https://perma.cc/F9YH-FGPJ].

324. *See* Lev Facher, *Trump Has Launched an All-Out Attack on the FDA. Will Its Scientific Integrity Survive?*, STAT NEWS (Aug. 27, 2020), https://www.statnews.com/2020/08/27/trump-has-launched-an-all-out-attack-on-the-fda-will-its-scientific-integrity-survive/ [https://perma.cc/TUQ7-8CQ8] ("[President Trump's] actions represent an extraordinary new frontier for presidential attacks on the scientific agency.").

325. *See, e.g.*, Marcia Smith, *Political Pressure Grows on NASA's Lunar Program*, SPACEPOLICYONLINE (Mar. 24, 2019), https://spacepolicyonline.com/news/political-pressure-grows-on-nasas-lunar-program/ [https://perma.cc/H7E3-UR9X].

326. *See, e.g.*, John Friedman, *Fostering Development of Advanced Telecommunications Technologies: The F.C.C., the Pioneer's Preference & Personal Communications Services*, 12 CARDOZO ARTS & ENT. L.J. 545, 563 (1994); Colleen A. Mallick, *Spectrum Sharing in the Context of Vehicle-to-Vehicle Technology: Bureaucratic Hoops, Fierce Competition, Political Maneuverings, and the Larger Policy Issue*, 16 U. PITT. J. TECH. L. & POL'Y 116, 127 (2015).

327. Ian Urbina, *Pressure Limits Efforts to Police Drilling for Gas*, N.Y. TIMES (Mar. 3, 2011), https://www.nytimes.com/2011/03/04/us/04gas.html?pagewanted=all [https://perma.cc/6NMY-8BSD].

328. *Compare, e.g.*, 21 U.S.C.A. § 360bbb-3 (West 2020) (allowing the Secretary to declare an emergency, authorize and revoke treatments, and waive manufacturing inspections, among other powers), *with id.* § 355 (requiring the Secretary to adhere to certain guidelines and application requirements for applications on new drugs).

Regulatory sandboxes outside of the EUA context are likely to have similar structures.

This recognition presents several opportunities to better insulate independent agencies from political actors treading on their own turf. First, agencies should formalize authorization procedures under regulatory sandboxes as much as possible, including establishing review standards early on and outside of the context of political emergencies.[329] These should include not only the specific level of evidence required for authorization, ongoing criteria for authorization, and the specifics of withdrawal, but the mechanical procedures for review: who in the agency is responsible, how decisions are to be made, and when they can (and cannot) be made by. FDA adopted these procedures, with at least partial success, in its EUAs for COVID-19 vaccines by moving their review to a VRBPAC, a previously constituted committee within FDA.[330] Doing so allowed Agency heads to largely disclaim responsibility for the determination of the Agency, shielding themselves from political reprisals.[331] Second, agencies should view data transparency as a bulwark against political interference. Data transparency in the review of sandboxed products makes it difficult to allow agencies to succumb to the whims of a political actor; if a product is unsafe, the Agency's scientists and the public will know. This has been one of the principal advantages of FDA's advocation for data sharing for the COVID-19 vaccines—an alibi for the accusation that ineffective vaccines are being hurried through the authorization process as a political stunt. Data transparency ideally makes individual instances of political interference transparent, and allows the public to know whether the agency is basing its decisions on politics or science.

C. Standard Decay

In the FinTech context, some have expressed concern that regulatory sandboxes are "a race-to-the-bottom style competition,"[332] with sandbox entrants ever pushing the boundaries of regulation to their minima. Firms, upon seeing the success or failures of their competitors, will test regulations with increasingly sloppier and cheaper technology to gain authorization, using the sandbox less to experiment with cutting edge products as a way to get on the market while cutting costs.[333] Where there are multiple avenues for regulation—different sandboxes, perhaps—a regulator may be indifferent to this diminishment of standards

329. *Cf.* Nathan Cortez & Jacob S. Sherkow, *Presidential Administration and FDA Guidance: A New Hope*, 2021 UNIV. ILL. L. REV. ONLINE 179, 181–82 (advocating for similar practice with respect to FDA guidance).

330. *Charter of the Vaccines and Related Biological Products Advisory Committee*, FDA, (Jan. 12, 2020) https://www.fda.gov/advisory-committees/vaccines-and-related-biological-products-advisory-committee/charter-vaccines-and-related-biological-products-advisory-committee [https://perma.cc/ZZY2-U7M9].

331. Helen Branswell, *Why This Week's Meeting of an FDA Advisory Panel on Covid-19 Vaccines Matters*, STAT NEWS (Oct. 20, 2020), https://www.statnews.com/2020/10/20/dry-technical-but-important-why-an-fda-advisory-panels-meeting-on-covid-19-vaccines-matters/ [https://perma.cc/M6WN-2Z4A].

332. Zetzsche et al., *supra* note 1, at 78.

333. *See* Allen, *supra* note 1, at 608 (summarizing concerns that regulatory sandboxes will encourage "financial institutions [to] have often made their innovations unnecessarily complicated in order to inhibit competitors seeking to provide cheaper, commoditized versions of the innovations").

because it nonetheless retains the agency's jurisdictional ambit. There, the "race to the bottom" entails "startups consistently approaching the most lenient regulator to seek an enforceable compliance agreement, and regulators competing to be the most lenient so as to increase their regulatory turf."[334]

This has been a mixed concern for the COVID-19 EUAs. FDA's early authorization of serology diagnostics—tests to see whether a patient harbors antibodies against the virus to determine whether they were previously infected—spawned a horde of cheap, unreliable imitators eager to make a few bucks preying on the worried well.[335] As mentioned earlier, FDA revoked these authorizations en masse after fielding numerous complaints.[336] At the same time, the scientific community's hawk-eyed surveillance over many of the authorized technologies seems to have inculcated some sense of pride and shame for many other developers; many of the authorized technologies are developed by leaders in the field who have diligently worked to ensure their products are safe and effective and have put their preliminary data up for robust review.[337] If there's a race among these technologies, it certainly isn't to the bottom.

Nor does it appear that FDA—on the whole—has condoned a diminishment in product quality even as its operates under a statutorily lax standard and extreme political pressure.[338] While proving this would require some evidence of EUAs FDA refused to authorize—evidence the Agency has not yet made public—there are numerous technologies publicly trumpeted as being effective against COVID-19, but for which, curiously, there has been no EUA.[339] These suggest that they either failed to work as advertised, FDA rejected an EUA for them, or both. In addition, it appears that FDA has been, for all practical

334. *Id.* at 622.

335. *See* Serology EUA Revocation, *supra* note 270; *FBI Warns of Potential Fraud in Antibody Testing for COVID-19*, FBA (June 26, 2020), https://www.fbi.gov/news/pressrel/press-releases/fbi-warns-of-potential-fraud-in-antibody-testing-for-covid-19 [https://perma.cc/K7CM-6UYJ].

336. Serology EUA Revocation, *supra* note 270.

337. *See, e.g.*, Fatima Amanat et al., *A Serological Assay to Detect SARS-CoV-2 Seroconversion in Humans*, MEDRXIV (Apr. 16, 2020), https://www.medrxiv.org/content/10.1101/2020.03.17.20037713v2 [https://perma.cc/WG32-V6MR] (putting up data about an antibody test, since verified, on a preprint server).

338. *See, e.g.*, Philip R. Krause & Marion F. Gruber, *Emergency Use Authorization of Covid Vaccines—Safety and Efficacy Follow-Up Considerations*, 383 NEW ENGL. J. MED. e107 (2020); Neeraja Ravi, Dana L. Cortade, Elaine Ng & Shan X. Wang, *Diagnostics for SARS-CoV-2 Detection: A Comprehensive Review of the FDA-EUA COVID-19 Testing Landscape*, 165 BIOSENSORS & BIOELECTRONICS 112454 (2020).

339. For example, a company called Bambu Global, claimed to have developed a rapid COVID-19 testing kit in March 2020 based on "rapid color-change chemistry." *Instant Color Chemistry Expert, Bambu Vault, Is Developing Rapid Covid-19 Test Kit in Response to President Trump's Call to Action*, BAMBUVAULT (Mar. 12, 2020) https://www.globenewswire.com/news-release/2020/03/12/1999589/0/en/INSTANT-COLOR-CHEMISTRY-EXPERT-BAMBU-VAULT-IS-DEVELOPING-RAPID-COVID-19-TEST-KIT-IN-RESPONSE-TO-PRESIDENT-TRUMP-S-CALL-TO-ACTION.html [https://perma.cc/QA9V-3RKV]. No technical papers on the technology were published in scientific journals or on preprint servers; no technical information about the test was made available on the company's website; the author's inquiries to a person purporting to be a scientist to the company were not satisfactorily answered; and no such EUA was authorized by FDA. *In Vitro Diagnostic EUAs*, *supra* note 184.

purposes, *raising* its EUA standards as the pandemic has progressed, not *lowering* them—the opposite of the agency following its charges to "the bottom."[340]

Beyond this, EUAs always come with the threat of revocation, a power FDA has robustly exercised during the pandemic.[341] In contrast to its formal approval mechanisms, for which orders of withdrawal are altogether rare, FDA has been active—and fairly quick—in revoking COVID-19 EUAs where later evidence has suggested a lack of safety or ineffectiveness.[342] This has included products apparently made by smaller, less-experienced developers—those perhaps more likely to be attracted by diminishing entry standards—as well as treatments from larger, more well-established players.[343] And, as with hydroxychloroquine, this even includes treatments FDA first authorized when facing the political guillotine.[344]

A related concern to the one surrounding decreasing standards is that EUAs are a slippery slope: once regulatory sandboxes begin to be used, developers will reengineer their regulatory strategies to attempt to use it exclusively.[345] This is analogous to FDA's one-time exception of LDTs from the Agency's oversight if they were labeled for "investigational use only"—a strategy that encouraged its "overwhelming use."[346] But at least with respect to COVID-19 EUAs, these concerns don't appear to hold water; almost all developers of EUA products still seem quite interested in eventually obtaining formal approval from FDA knowing that their own work may end the very emergency giving rise to the EUA program in the first instance.[347] The COVID-19 vaccines—about to undergo formal review by FDA—are sterling examples.[348] Nor does it appear that any developers are toying with moving therapies currently undergoing formal approval into the sandbox.[349] This comes, perhaps, from a widespread recognition that the COVID-19 EUAs are limited and may soon be over. And some, too, may stem

340. *See* May 2021 Vaccine Guidance, *supra* note 267 (raising EUA standards for vaccines); Nachlis, *supra* note 20 ("While the politics surrounding the plasma EUA and EUA-plus guidance are problematic, as matters of regulatory policy they each represent important and underappreciated improvements in the FDA's approach to expedited vaccine and therapeutic authorizations.").

341. *See, e.g.*, HCQ Revocation, *supra* note 218; Serology EUA Revocation, *supra* note 270.

342. Press Release, Stephen M. Hahn, *supra* note 198.

343. *See, e.g.*, HCQ Revocation, *supra* note 218 (applying to Sanofi and Pfizer, large pharmaceutical companies); Serology EUA Revocation, *supra* note 270 (applying to many smaller developers).

344. HCQ Revocation, *supra* note 218.

345. *Cf.* Hagemann et al., *supra* note 73, at 37 ("For a great many emerging technologies, as well as many existing ones, we are witnessing the twilight of the traditional regulatory system and its gradual replacement by an amorphous and constantly evolving set of informal "soft law" governance mechanisms.").

346. Kayte Spector-Bagdady & Elizabeth R. Pike, *Consuming Genomics: Regulating Direct-to- Consumer Genetic and Genomic Information*, 92 NEB. L. REV. 677, 702 (2014).

347. *See, e.g.*, *Comirnaty*, FDA, https://www.fda.gov/vaccines-blood-biologics/comirnaty [https://perma.cc/2X78-9VUC] (Oct. 5, 2021); *see also* Lucy Parsons, *Moderna CEO Says COVID-19 Vaccine Will Be Ready for FDA Submission in Late November*, PMLIVE (Oct. 5, 2020), http://www.pmlive.com/pharma_news/moderna_ceo_says_covid-19_vaccine_will_be_ready_for_fda_submission_in_late_november_1352493 [https://perma.cc/4K4Q-27TX] (discussing Moderna's plan to submit a traditional biologics license application for its COVID-19 vaccine).

348. Sherkow et al., *supra* note 224.

349. That is, there doesn't appear to be any cases of therapies or diagnostics currently in clinical trials for a formal approval regime that are being discontinued for submission under an EUA.

from a fear of revocation of an EUA *after* a competing therapy has been approved—a standard, as discussed earlier, baked into the EUA statute.[350] Furthermore, even during COVID-19, FDA's advisory committees have been routinely doing their job for non-COVID-19 related therapies, suggesting that the Agency will have little difficulty shifting back to business as usual once the pandemic has subsided.[351]

At the same time, the Agency's experience with EUAs may alter what its regulators consider to be "business as usual." The existence of sandboxes—and regulators' comfortability with them—may decay the Agency's standards not just for sandboxes but for its bread-and-butter approval mechanisms as well. In at least one case—FDA's recent approval of Aduhelm (aducanumab), an antibody therapy indicated to treat Alzheimer's disease—this seems to have happened.[352] Aduhelm was designed to clear certain protein accumulations in the brain—amyloid plaques—long-associated with Alzheimer's, even while doubts have persisted regarding whether such an approach was treating the disease rather than its symptoms.[353] Aduhelm's initial data, in fact, was considered to be such a rank failure that its study was halted before it was fully completed.[354] Nonetheless, Aduhelm's manufacturer, Biogen, then retested the compound not to measure its *clinical* effect on patients—whether it, in fact, treated Alzheimer's—but simply whether it was effective in clearing amyloid plaques, a "surrogate" endpoint rather than a clinical one.[355] Even after reviewing that data, the FDA Advisory Committee responsible for review the therapy overwhelmingly voted to reject approval.[356] But FDA nonetheless approved Aduhelm on the promise that—perhaps, like a regulatory sandbox—its approval would "spark continuous innovation in the years to come."[357] While the cause of this shift in

350. *See supra* notes 153–157 and accompanying text. Notably, though, no vaccine EUAs have been revoked even though Pfizer-BioNTech's vaccine, Comirnaty, has since been fully approved. *Comirnaty*, *supra* note 347.

351. *See e.g.*, Idrus, *supra* note 248 (describing the work of the Peripheral and Central Nervous System Drugs Advisory Committee).

352. *Aducanumab (Marketed as Aduhelm) Information*, FDA (July 8, 2021), https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/aducanumab-marketed-aduhelm-information [https://perma.cc/PF74-7UX6].

353. *Id.*; *see* Sharon Begley, *The Maddening Saga of How an Alzheimer's 'Cabal' Thwarted Progress Toward a Cure for Decades*, STAT NEWS (June 25, 2019), https://www.statnews.com/2019/06/25/alzheimers-cabal-thwarted-progress-toward-cure/ [https://perma.cc/G484-8MCB] (describing the controversy over the amyloid plaque theory).

354. Adam Feuerstein, *Biogen Halts Studies of Closely Watched Alzheimer's Drug, A Blow to Hopes for New Treatment*, STAT NEWS (Mar. 21, 2019), https://www.statnews.com/2019/03/21/biogen-eisai-alzheimer-trial-stopped/ [https://perma.cc/U9KG-DM2D].

355. *See* Nicholas Florko, *Ellis Unger, An Outspoken FDA Veteran, Retires*, STAT NEWS (Aug. 12, 2021), https://www.statnews.com/2021/08/12/ellis-unger-an-outspoken-fda-veteran-resigns/ [https://perma.cc/JD2Y-3ML4] (discussing controversy over surrogate endpoints).

356. Matthew Herper, Adam Feuerstein, & Damian Garde, *Expert Panel Votes Down Biogen's Alzheimer's Drug, and Rebukes the FDA in the Process*, STAT NEWS (Nov. 6, 2020), https://www.statnews.com/2020/11/06/expert-panel-votes-down-biogens-alzheimers-drug-and-rebukes-the-fda-in-the-process/ [https://perma.cc/84WR-NR43

357. Adam Feuerstein & Damian Garde, *FDA Grants Historic Approval to Alzheimer's Drug Designed to Slow Cognitive Decline*, STAT NEWS (June 7, 2021), https://www.statnews.com/2021/06/07/fda-grants-historic-approval-to-alzheimers-drug-designed-to-slow-cognitive-decline/ [https://perma.cc/BRM8-B7J4].

standards is likely complex, FDA law practitioners most credibly pinned it on FDA's experience with EUAs during the pandemic, namely, "the review staff . . . applying a new statutory standard: that which supports Emergency Use Authorization (EUA) of a product for COVID."[358] FDA according to Frank J. Sasinowski and James E. Valentine, easily slipped from "reliance on an unvalidated surrogate [endpoint] that is merely 'reasonably likely to predict' clinical benefit . . . . [and the] 'potential benefit' part of the EUA standard."[359] The approval—"one of the most controversial and disputed decisions on a drug application in recent years"[360]—led to the high profile resignation of several Advisory Committee members and, according to some, prompted "soul-searching" at FDA.[361]

If this is a race to the bottom, agencies interested in making use of regulatory sandboxes should take cues from FDA's experience. First, they should make clear to developers, by word and deed, that authorizations under sandboxes are temporary and revocable, and that formal approval processes still operate just the same. Revocations of authorizations for failed products are likely to dissuade developers from attempts to enter the market on shoddy goods. In addition, agencies should stick to their guns on standards of safety and effectiveness, even if those are lower in a sandbox regime than in the formal approval process, and even if the purpose of the regulatory sandbox is its flexibility. Lowering safety and effectiveness standards midway through authorization is liable to turn any regulatory sandbox into quicksand. And lowering them persistently is likely to affect other aspects of the agency's mission. Lastly, agencies should further commit to making their standards, and authorization decisions, as transparent as possible. This would allow developers to accurately assess the agency's standards for review without presuming that competitors' authorized failures set a low bar for entry.

D. Innovation Speed

In theory, regulatory sandboxes do not simply allow experimentation but speed up innovation itself, bringing safer, more effective, and perhaps even cheaper goods to market quicker than more stringent regulatory regimes would otherwise allow.[362] By lowering barriers to entry, regulatory sandboxes—even

358. Frank J. Sasinowski & James E. Valentine, *FDA's Accelerated Approval of Biogen's Aduhelm for Alzheimer's: A Sign of Applying the Emergency Use Standard Beyond COVID?*, FDA L. BLOG (June 8, 2021), https://www.thefdalawblog.com/2021/06/fdas-accelerated-approval-of-biogens-aduhelm-for-alzheimers-a-sign-of-applying-the-emergency-use-standard-beyond-covid/ [https://perma.cc/W9QY-RXK7].

359. *Id.*

360. Feuerstein & Garde, *supra* note 357.

361. Bill Chappell, *3 Experts Have Resigned From An FDA Committee Over Alzheimer's Drug Approval*, NPR (June 11, 2021), https://www.npr.org/2021/06/11/1005567149/3-experts-have-resigned-from-an-fda-committee-over-alzheimers-drug-approval [https://perma.cc/8BVM-VNK3]; Gregg Gonsalves, Christopher Morten, Reshma Ramachandran & Joseph S. Ross, *The FDA is in Desperate Need of Some Soul-Searching*, WASH. POST (June 17, 2021), https://www.washingtonpost.com/opinions/2021/06/17/fda-aducanumab-alzheimers-drug-approval-erodes-confidence/ [https://perma.cc/BR7R-JW78].

362. FIN. CONDUCT AUTH., *supra* note 5, at 5; Allen, *supra* note 1, at 598.

if limited and temporary—create an environment where new entrants can compete, where new innovations can thrive, and where new products can be tested and improved.[363] Or, if you have an evolutionary bent, regulatory sandbox speed up the evolutionary process of development through both greater diversity and more rapid selection.[364]

To a certain extent, the COVID-19 EUAs tell this story. Despite the several highly publicized failures discussed earlier, many of the EUA-authorized interventions are, indeed, wildly successful by any metric, including as compared to traditional approval standards. These principally include a now riot of cheaper and increasingly accurate diagnostic tests of active infections, a triumph of innovative diversity being marshalled to solve a pressing problem.[365] Some tests, too, cost fractions of the cost of similar, fully approved tests for other infectious diseases, and can be expansively scaled for delivery to tens of thousands of participants daily.[366] This includes the University of Illinois' SHIELD Illinois testing program, which, while not technically governed by an EUA but a bridging study under a different EUA, has been a triumph of pandemic-related public health engineering in the U.S.[367] In some circumstances, regulatory sandboxes can indeed make things better, faster, cheaper.

And yet, a closer examination at other EUA-authorized products tells a more complex story. Case in point: EUA-authorized vaccines. Despite knowing little about the virus early in the pandemic, a host of developers—some established players, others first-time entrants to the regulated market, let alone the vaccine market—almost immediately began to vie to develop an effective vaccine.[368] This included first-in-class technologies, such as the mRNA vaccines developed by Pfizer–BioNTech and Moderna Therapeutics, as well as vaccines created using more traditional methods.[369] But many of these vaccines were the subject of significant government funding, both ex ante and ex post.[370] Moderna, for example, had been engaged in a collaboration agreement with Biomedical Advanced Research and Development Authority (BARDA), an arm of the

363. FIN. CONDUCT AUTH., *supra* note 5, at 5; Allen, *supra* note 1, at 581.

364. *Cf.* GRAHAM BELL, SELECTION: THE MECHANISM OF EVOLUTION 152 (1st ed. 1997) ("[T]he response to selection will be greater when there are more distinct kinds of individual initially present."); *id.* at 192–193 (discussing the effect of "speeding up" selection through artificial mechanisms).

365. *See* Cormac Sheridan, *COVID-19 Spurs Wave of Innovative Diagnostics*, 38 NATURE BIOTECHNOLOGY 769 (2020).

366. *Id.* at 769 (describing low-cost, scalable CRISPR-based tests).

367. *See supra* note 190 and accompanying text. Perhaps ironically, the one of the greatest triumphs of public health engineering by US federal agencies was conducted *outside* the US—the PEPFAR program in Africa, which has saved millions of lives and has dwarfed anything remotely like it in the US. Anthony S. Fauci & Robert W. Eisinger, *PEPFAR—15 Years and Counting the Lives Saved*, 378 NEW ENGL. J. MED. 314 (2018).

368. Helen Branswell, *Here Come the Tortoises: In the Race For a Covid-19 Vaccine, Slow Starters Could Still Win Out*, STAT NEWS (Sept. 24, 2020), https://www.statnews.com/2020/09/24/here-come-the-tortoises-in-the-race-for-a-covid-19-vaccine-slow-starters-could-still-win-out/ [https://perma.cc/GDZ4-JMGA].

369. *Id.*

370. Jacob S. Sherkow, Lisa Larrimore Ouellette, Nicholson Price & Rachel Sachs, *Multi-Agency Funding for COVID-19 Vaccine Development*, WRITTEN DESCRIPTION (Aug. 19, 2020), https://writtendescription.blogspot.com/2020/08/multi-agency-funding-for-covid-19.html [https://perma.cc/8RS4-KBWQ].

Department of Health and Human Service, for years.[371] And at least three leading vaccine contenders were the subject of unprecedented advanced market commitments—guaranteed purchases—totaling billions of dollars, if proven successful.[372] This is not to suggest that such public investments weren't worth the price; they were by any measure of the virus's destruction.[373] Rather, it suggests that describing the innovative drive toward COVID-19 vaccines by untangling these incentives from their attendant decreased regulatory barriers is impractical.

In other contexts, at FDA specifically, the evidence is similarly mixed. Medical devices, for example, have a variety of tiers of regulatory standards, from those needing little more than a perfunctory notice of marketing to others demanding full-blown, multi-armed clinical trials.[374] These standards include the well-trod 510(k) pathway requiring developers to attest to the similarity of the new product to an older, approved or cleared one.[375] This low-regulation pathway is the means by which the vast majority of medical devices enter the U.S. market.[376] But it's not entirely clear that the popularity of the 510(k) program rests on firms principally responding to the lower regulatory barriers themselves or larger difficulties in cracking the market for truly innovative medical devices.[377] Christopher Buccafusco recounts a case study concerning the iterative development of wheelchairs—guided less by regulatory barriers and more by fear of products liability lawsuits.[378] Ariel Dora Stern provides a detailed empirical analysis of medical device approvals, concluding that neither technological novelty nor regulatory stringency drive market entry but, instead, regulatory *certainty*: literally, the publication of a pertinent guidance detailing the format and content of device applications.[379] Given the kaleidoscopic complexity of medical device approvals and their markets, myriad other factors are similarly at play, including ones pertaining to patents, anticompetition, and technical standards.[380] Given the enormous complexities—and size—of the market for COVID-19 treatments, the answer may be similarly mixed.

If there are lessons to be drawn from the speed of development of COVID-19 products and EUAs, then, they are probably these: Regulatory sandboxes are likely best used where there is a built-in market. This almost certainly explains much of the dramatic development surrounding COVID-19 vaccines; there are

371. *Id.*

372. Lisa Larrimore Ouellette, Nicholson Price, Rachel Sachs & Jacob S. Sherkow, *How Should Policymakers Use "Pull" Mechanisms to Improve COVID-19 Innovation Incentives?*, WRITTEN DESCRIPTION (July 30, 2020), https://writtendescription.blogspot.com/2020/07/how-should-policymakers-use-pull.html [https://perma.cc/4RWP-QSQD].

373. Daniel J. Hemel & Lisa Larrimore Ouellette, Valuing the Vaccine 16–17 (Sept. 9, 2020) (unpublished manuscript) (on file with the author).

374. *See* Aboy & Sherkow, *supra* note 118 (reviewing FDA's medical device classification mechanisms).

375. *Id.*

376. Rathi & Ross, *supra* note 117, at 1892.

377. *See* Stern, *supra* note 98, at 185 (demonstrating that medical innovation responds to regulatory *certainty* not necessarily higher standards).

378. Buccafusco, *supra* note 38, at 981–82.

379. Stern, *supra* note 98, at 185; *see also* Cortez & Sherkow, *supra* note 329, at 181–82 (advocating for such an approach).

380. Aboy & Sherkow, *supra* note 118.

few other products where the estimated market is literally everyone on Earth, as paid for on the government's tab. In this way, regulatory sandboxes are likely best paired with prizes as a means to encourage the rapid development, testing, and deployment of novel but technologically uncertain products.[381] In addition, regulatory sandboxes may be best employed where there has been prior funding for basic research and development, such that different developers can be at least somewhat confident in adopting a diversity of approaches. Regulatory sandboxes without such safeguards are likely—as in the case of early wheelchairs—to breed pure copycats, furthering neither new technological development nor its speed.[382]

E. Public Health Exceptionalism

And yet, EUAs—and those pertaining to COVID-19 even more specifically—may be an extreme case to draw generalized conclusions about the success of regulatory sandboxes and how to improve them. Regulatory strategies employed in a pandemic to save human lives from rapid infection may, perhaps, not be easily equated to similar strategies to regulate, say, Bitcoin. Not only has the COVID-19 crisis been truly exceptional, but its closest analogue, the 1918 Influenza Pandemic, occurred over a century ago, well before the modern administrative state existed in the United States.[383] Novel legal solutions to combatting COVID-19 may simply be unprecedented. In addition, there have been few times in modern American history where an emergency so challenged the country's basic instruments of regulatory law.[384] Using—or bending—legal procedures to contain COVID-19 may not be instructive about how regulatory agencies should encourage the experimentation of consumer technology in the ordinary course of business.

Furthermore, there may be something special about regulating the public health that's not readily applicable outside the field to other agencies—that is, FDA's EUA program is special because it operates under a banner of "health exceptionalism." Health exceptionalism posits that "health is among the most important conditions of human life and a critically significant constituent of human capabilities which we have reason to value."[385] Under Elizabeth S. Anderson's rubric, health is a, if not *the* primary quality that drives a human's capabilities, "the sets of functionings she can achieve, given the personal, material, and social resources available to her."[386] Without some measure of health, few can engage in democratic participation as equal citizens.[387] For these reasons, regulating health—as opposed to other market goods—may be sufficiently different

381. *See* Ouellette et al., *supra* note 372 (discussing "pull" incentives).

382. Buccafusco, *supra* note 38, at 981–82.

383. *See supra* note 25.

384. Hiba Hafiz, Shu-Yi Oei, Diane Ring & Natalya Shnitser, *Regulating in Pandemic: Evaluating Economic and Financial Policy Responses to the Coronavirus Crisis*, (B.C., L. Sch. Legal Stud., Working Paper No. 527, 2020), https://papers.ssrn.com/sol3/Papers.cfm?abstract_id=3555980 [https://perma.cc/39TN-Q7HD].

385. Amartya Sen, *Why Health Equity?*, 11 HEALTH ECON. 659, 660 (2002).

386. Elizabeth S. Anderson, *What is the Point of Equality?*, 109 ETHICS 287, 316 (1999).

387. *Id.* at 316–21.

in character to merit different legal and ethical treatment. And indeed, there are a variety of legal regimes that treat claims related to health much differently from other cases.[388] Regulatory sandboxes for the public health may therefore be quite unlike regulatory sandboxes elsewhere—and for good reason.

Relatedly, regulatory sandboxes coming from FDA specifically may also be exceptional and poorly analogous to regulatory sandboxes elsewhere. FDA has long been considered "somehow unique in the realm of administrative law."[389] Its jurisdiction is truly vast, famously encompassing "about 25 cents of every dollar spent by American consumers each year."[390] Although a regulatory agency under the Administrative Procedures Act ("APA"), the Agency engages in oversight in a variety of ways not specifically contemplated by the APA, such as its heavy reliance on industry guidances and its use of external advisory committees.[391] In addition, because FDA, more than most agencies, possesses "product veto authority . . . its mere suggestions and intimations induce compliance even where they are not backed by legal authority."[392] FDA has the power to "dash the hopes and the expected earnings of drug sponsors, to negate tens or hundreds of millions of dollars of investment, many thousands of hours of research, and entire careers spent in the development of a new therapy."[393] Regulatory sandboxes from FDA may be different because many view the Agency as a "uniquely protective institution."[394]

All of this may make broader lessons about EUAs as regulatory sandboxes not generally applicable. The consequences of experimental failures for EUA may be not merely suboptimal but fatal. The importance and speed of innovation under an EUA regime—by definition, an emergency—is all the more urgent. The political significance of a given EUA may be more intense, and more liable to interference. Standards for EUAs may be more malleable than standards for other sandboxes. All in all, the stakes are higher, the risks are higher, and the consequences more dire for EUAs than for other forms of regulatory oversight. At an extreme measure, losing public trust in FDA means losing lives. But losing trust in the FCC? The consequences are unclear.[395] It may simply be inaccurate to extrapolate from one to the other.

388. *See, e.g.*, Nicolas P. Terry, *Big Data Proxies and Health Privacy Exceptionalism*, 24 HEALTH MATRIX 65, 87–89 (2014) (exploring the "stickiness" of "health data exceptionalism").

389. CARPENTER, *supra* note 24, at 361.

390. *Executive Summary: Strategic Plan for Regulatory Science*, FDA, https://www.fda.gov/science-research/advancing-regulatory-science/executive-summary-strategic-plan-regulatory-science (last visited Nov. 18, 2021) [https://perma.cc/T9XG-3DKG]. The accuracy of this oft-repeated statement is unclear and is unlikely to remain static in any event. A quick look at 2019 consumer expenditure data from the Bureau of Labor Statistics suggests that consumers spend, roughly, 21.1% of total expenditures on "Food" and "Healthcare." *Consumer Expenditures—2019*, U.S. BUREAU OF LABOR STATISTICS (Sept. 9, 2020), https://www.bls.gov/news.release/cesan.nr0.htm [https://perma.cc/8868-CUX3]. Assuming—and it's an incorrect assumption—that FDA regulates *all* "Food" and "Healthcare," we're still four cents short of a quarter.

391. Cortez, *supra* note 36, at 188–90.

392. CARPENTER, *supra* note 24, at 360.

393. *Id.* at 360

394. *Id.* at 15.

395. Although, surely, there are numerous examples in between. Lost trust in the Federal Aviation Administration or the National Transit Safety Board could—possibly—also means lives lost.

Scholars interested in gleaning lessons from these experiences with EUAs during the pandemic should therefore pay attention to several things before making any bold conclusions. First, careful attention should be paid to the size effect of downsides from regulatory sandboxes. For the COVID-19 EUAs, they are substantially large, but they may not be so in other cases, and understanding the magnitude of success and failure in a particular context may very lead regulators to draw different conclusions about their usefulness. Second, the social and political context in which the agency sits may be poorly analogous to FDA and regulatory sandboxes' successes or failures may not be judged on the same metrics as EUAs. For the COVID-19 EUAs, government and the lay public are ultimately judges of whether FDA has satisfactorily saved lives and slowed the pandemic. In other contexts, industry or a professional community may instead act as judges for whether a sandbox has been successful, and with different criteria. Third, an agency's reputation—its "set of symbolic beliefs about the unique or separable capacities, roles, and obligations of an organization"[396]—may take on more or less significance in the context of regulatory sandboxes depending on a variety of factors, including the products ultimately sought to be regulated, the public need for them, the agency's expertise in doing so, the legal instruments otherwise at the agency's disposal, and whether other agencies have overlapping jurisdiction. Last, scholars interested in using these EUAs as case studies must contend with the extent to which public health exceptionalism is real. Even if all else holds true—that the downsides of failure are roughly equivalent, that the Agency's siting in government and society is roughly equivalent, and that agency reputation is similarly meaningful—there may nonetheless be something exceptional about doing it all in the context of public health. Money can be repaid; agency reputations can be rebuilt; regulatory standards can be rewritten. But death cannot be undone.

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And yet, despite all these potential differences, EUAs appear to show the importance of regulatory sandboxes, in general: that even where differences are so extreme between one putative sandbox and another, that they demonstrate the existence of a pathway, other than executive fiat, to foster experimentation outside usual regulatory processes. Perhaps, then, these examples are instructive because they articulate a broader principle that, where real-world experimentation is likely to prove beneficial, sandboxes *should* be a feature of regulatory design. If regulators are invested in encouraging innovation, they should be invested in encouraging innovation *about* innovation.[397] Regulatory sandboxes allow just that.

396. CARPENTER, *supra* note 24, at 45.

397. *Cf.* Lisa Larrimore Ouellette, *Patent Experimentalism*, 101 VA. L. REV. 65, 84–87 (2015) (exploring the benefits, for patent administrative policy, of encouraging "innovation about innovation").

V. CONCLUSION

Regulatory sandboxes are "a 'safe space' in which businesses can test innovative products, services, business models and delivery mechanisms without immediately incurring all the normal regulatory consequences of engaging in the activity in question."[398] Writ large, they center on several elements, namely, an agency's collection of experimental data, a structure based on industry input, flexibility for different iterations of a broader technology, and testing in real-world settings. And despite their apparently novel provenance—seemingly first established by the UK's Financial Conduct Authority in 2015 for various FinTech technologies—they appear to have been waiting to be discovered in FDA law in emergency use authorizations (EUAs). In contrast to FDA's formal approval processes, EUAs allow FDA to authorize—and rapidly withdraw, if needed—new products in emergency settings, using a "totality of the scientific evidence" standard. The COVID-19 EUAs, as presented here, fit neatly even if not perfectly in this framework of regulatory sandboxes. And more broadly, the COVID-19 EUAs are well described by regulatory sandboxes' larger principles—as a pragmatic, dialogic, and principles-based form of regulatory governance, limited in time and scope, and designed to improve, rather than supplant, typical regulatory pathways. At the same time, these EUAs have raised a host of issues about regulatory sandboxes more generally. These include a risk diminishing the public trust, the specter of undue political interference, a decay in typical standards for approval, and issues pertaining to the speed of innovation itself.

Nonetheless, the general applicability of lessons from the COVID-19 EUAs for regulatory sandboxes remains unclear. EUAs tend to traffic on concepts of health exceptionalism—and even regulatory exceptionalism for FDA—without immediate parallel to other agencies and other regulatory sandboxes. The COVID-19 EUAs, in particular, arose in the context of public health exceptionalism in a truly exceptional time in public health.

This leaves the opportunity for other scholars to explore both the existence of and the possibilities for success or failure in other regulatory areas that do not readily implicate the public health. These may include, for example, the Federal Communications Commission's (FCC's) regulation of the internet; the Federal Aviation Administration's (FAA's) oversight of drones and other autonomous flying vehicles; and, of course, the Office of the Comptroller of the Currency's jurisdiction over Bitcoin. In Europe, this framework can be used to assess the utility and impact of regulatory sandboxes for artificial intelligence, should they come to pass.[399] To test some of this paper's descriptive theses, it may be worth assessing whether regulatory sandboxes exist under the rubric identified here, what those sandboxes are, and which technologies they regulate. Furthermore, it would be useful to assess whether any of the lessons learned from FDA's EUAs, COVID–19 or otherwise, apply to those agencies, in particular, whether they similarly implicate the public trust, are subject to political interference, risk a

398. FIN. CONDUCT AUTH., *supra* note 5, at 2.

399. *See* EC AI PROPOSAL, *supra* note 3, at 69–70.

decay in approval standards, and modulate the speed of innovation. Work of this kind would be ideal to understanding whether FDA's EUA program's "characteristics are representative of those shared by a larger population of research objects" or whether EUAs' "narrative may be so distinctive as to gesture to broader dynamics by casting the difference of almost all other cases in such stark relief, thereby illuminating what is normal about them."[400] If nothing else, FDA's implementation of EUAs to combat the pandemic has taught us that some approaches to regulatory sandboxes will succeed and some will fail. But that's the point of regulatory sandboxes themselves: to find out what works in the real world.

400. CARPENTER, *supra* note 24, at 20.