

Saint Louis University School of Law
Scholarship Commons

All Faculty Scholarship

2021

Vaccine Clinical Trials and Data Infrastructure

Ana Santos Rutschman

Follow this and additional works at: <https://scholarship.law.slu.edu/faculty>



Part of the [Clinical Epidemiology Commons](#), [Databases and Information Systems Commons](#), [Data Science Commons](#), [Health Law and Policy Commons](#), [Infectious Disease Commons](#), [Influenza Virus Vaccines Commons](#), and the [Translational Medical Research Commons](#)



SAINT LOUIS UNIVERSITY SCHOOL OF LAW
Legal Studies Research Paper Series

No. 2021-01

Vaccine Clinical Trials and Data Infrastructure

Ana Santos Rutschman
Saint Louis University - School of Law

Utah Law Review, Forthcoming (2021)

VACCINE CLINICAL TRIALS AND DATA INFRASTRUCTURE

Ana Santos Rutschman*

Introduction.....	1
I. Vaccine Clinical Trials and Data Infrastructure: A Historical Perspective	3
A. The Polio Vaccine and the Origins of Modern Clinical Trials.....	3
B. From Polio to COVID-19 and the Emergence of New Vaccine Technology	8
II. Vaccine Clinical Trial Data as Building Blocks.....	15
A. Data Collection: Limitations of the Current Vaccine Clinical Trial Data Infrastructure..	15
B. Data Sharing: Enabling Scrutiny and Follow-on Innovation	24
III. Towards a Richer Vaccine Clinical Trial Data Infrastructure.....	30

INTRODUCTION

We find ourselves at a momentous turn in the history of vaccines. The COVID-19 pandemic triggered a quasi-global vaccine race that not only compressed vaccine research and development (R&D) timelines, but also paved the way for the administration of a new type of vaccine technology – mRNA vaccines, which work in substantially different ways from the vaccines in use before the pandemic.¹

While the process of bringing emerging COVID-19 vaccines to market has taken place in an unusually short timeframe,² it was largely predicated on the same scientific and regulatory processes that govern the development, approval and deployment of new vaccines. For decades, these processes have encompassed several phases of vaccine testing – first without and

* Assistant Professor, Saint Louis University School of Law, Center for Health Law Studies. S.J.D., Duke Law School. I thank the organizers of the 2020 Lee E. Teitelbaum Utah Law Review Symposium on the law and ethics of medical for the invitation to participate and develop this writing project, as well as participants in the panel on clinical trials and legal and ethical issues in the age of COVID-19. I also thank Jesse Goldner for comments on early versions of the essay, and Kaena Kao and Hannah Schweissguth for research assistance.

¹ See e.g. CTRS. DISEASE CONTROL & PREVENTION, *Understanding and Explaining mRNA COVID-19 Vaccines*, <https://www.cdc.gov/vaccines/covid-19/hcp/mrna-vaccine-basics.html> (describing the new type of vaccine technology that emerged during the COVID-19 pandemic).

² See e.g. Will Brothers, *A Timeline of COVID-19 Vaccine Development*, BIOSPACE (Dec. 3, 2020), <https://www.biospace.com/article/a-timeline-of-covid-19-vaccine-development/> (providing an overview of the compressed timeline for the development of COVID-19 vaccine candidates).

subsequently with the involvement of human subjects³ – followed by an analysis of the emerging data.⁴

This Essay reflects on the evolution and status quo of the ways in which these data are gathered and disseminated within the context of the development of new vaccines. It treats information stemming from clinical trials as the initial building blocks of our vaccine data infrastructure, and surveys problems related to data collection and disclosure that have long been pervasive in the vaccine R&D ecosystem.

Part I of the Essay situates the discussion of vaccine clinical trial data within historical boundaries. Part I.A travels back in time to the polio vaccine trials of the 1950s in the United States, which were one of the main catalysts of the adoption of the clinical trial structure now in place throughout the world. Part I.B then charts the formalization of the modern vaccine clinical trial model through legislation adopted between the polio and the COVID-19 vaccine races.

Even though this formalization has resulted in a seemingly robust legal framework, there remain multiple problems that affect both the ways in which vaccine clinical trial data is actually generated and then utilized. Using examples from both past vaccine clinical trials and the COVID-19 vaccine race, Part II.A focuses on data collection issues, with an emphasis on the underrepresentation of minority populations in vaccine clinical trials. Part II.B then considers how imperfectly generated data meet further roadblocks in the form of delayed reporting or lack of reporting of clinical trial results, as well as restrictions to data sharing often attributable to agency interpretations of trade secrecy provisions that have long been disputed by several legal scholars.⁵

These problems affect both the transparency and accountability of vaccine innovation processes, and pose significant hurdles to follow-on R&D. Moreover, and relatedly, they can impair public trust on vaccine innovation processes at a time in which vaccine misinformation is quickly eroding overall levels of trust in vaccination as a public health tool.⁶ Part III concludes the

³ See generally CARL H. COLEMAN ET AL., *THE ETHICS AND REGULATION OF RESEARCH WITH HUMAN SUBJECTS* (2005).

⁴ See e.g. HARRY M. MARKS, *THE PROGRESS OF EXPERIMENT: SCIENCE AND THERAPEUTIC REFORM IN THE UNITED STATES, 1900–1990* (2000) (providing a historical overview of clinical trials in the United States throughout the twentieth century).

⁵ See *infra*, notes 184-186 and accompanying text.

⁶ See Alexandre de Figueiredo et al., *Mapping Global Trends in Vaccine Confidence and Investigating Barriers to Vaccine Uptake: A Large-Scale Retrospective Temporal Modelling Study*, 396 *LANCET* 898 (2020), [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)31558-0/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31558-0/fulltext)

Essay by pointing towards emerging ways to enrich the existing vaccine clinical trial data infrastructure. Specifically, it provides a short case study on the COVID-19 data sharing policy implemented in the European Union by its counterpart to the U.S. Food and Drug Administration, the European Medicines Agency. This *ad hoc* policy quickly expanded the disclosure of information about emerging COVID-19 drugs and vaccines in response to mounting pressure for more transparency about the drug and vaccine approval process. As such, it may be used as a blueprint by regulators elsewhere, as well as by proponents of a more robust system for the disclosure and sharing of clinical trial data.

I. VACCINE CLINICAL TRIALS AND DATA INFRASTRUCTURE: A HISTORICAL PERSPECTIVE

A. THE POLIO VACCINE AND THE ORIGINS OF MODERN CLINICAL TRIALS

April 26, 1954. Franklin Sherman Elementary School in McLean, Virginia.

This date and place marked the beginning of the field trials⁷ for the polio vaccine candidate developed by Jonas Salk.⁸ This was a momentous occasion in the history of vaccinology. Called the largest experiment in public health to date, these trials encapsulated the evolution of vaccine research, development and testing.⁹

Poliomyelitis – a compound word bringing together the Greek for gray (*polios*) and marrow (*myelos*) with the Latin suffix used to denote inflammation (*itis*)¹⁰ – is a highly contagious infectious disease transmitted by the poliovirus.¹¹ While 90% of people who contract the disease experience mild symptoms like fatigue or fever, or no symptoms at all, the virus causes paralysis

⁷ Vaccine field trials are tests typically conducted in multiple sites across one or several countries in order to assess the performance of an experimental pharmaceutical or biopharmaceutical product. See W. Charles Cockburn, *Field Trials in the Evaluation of Vaccines*, 47 AM. J. PUB. HEALTH (1957).

⁸ See generally DAVID M. OSHINSKY, *POLIO: AN AMERICAN STORY* (2006).

⁹ Paul Meier, *The Biggest Public Health Experiment Ever: The 1954 Field Trial of the Salk Poliomyelitis Vaccine*, in STATISTICS: A GUIDE TO THE UNKNOWN (JUDITH M. TANUR ET AL., EDS) (1972), https://www.medicine.mcgill.ca/epidemiology/hanley/c622/salk_trial.pdf

¹⁰ Oshinsky, *supra* note 8, at 9.

¹¹ See WORLD HEALTH ORG., *Poliomyelitis (Polio): Overview*, https://www.who.int/health-topics/poliomyelitis#tab=tab_1.

in the remaining 10% of the patient population.¹² Affecting most commonly the legs,¹³ paralysis is permanent in most cases, and 5% to 10% of paralyzed patients die.¹⁴ The disease affects primarily children under the age of five,¹⁵ and before a vaccine was developed – and the disease incidence reduced by 99%¹⁶ – polio outbreaks struck fear, especially among parents of young children.¹⁷

The 1950s brought about a series of scientific breakthroughs that eventually resulted in two foundational vaccines becoming available in the United States and then abroad.¹⁸ Building on recent work on the poliovirus,¹⁹ the research teams of Hilary Koprowski, Jonas Salk and Albert Sabin developed different types of polio vaccine candidates.²⁰ Salk’s vaccine using a killed virus was the first one to be licensed,²¹ following the largest human trials for any medical product up to that point in history.²²

¹² See WORLD HEALTH ORG., *Poliomyelitis (Polio): Symptoms*, https://www.who.int/health-topics/poliomyelitis#tab=tab_2

¹³ See e.g. Amy Berish, *FDR and Polio*, Franklin D. Roosevelt Presidential Library & Museum, <https://www.fdrlibrary.org/polio> <https://www.fdrlibrary.org/polio> (describing President Roosevelt’s lower limb paralysis after contracting polio at the relative late age of 39).

¹⁴ WORLD HEALTH ORG., *Poliomyelitis (Polio): Symptoms*, *supra* note 12.

¹⁵ WORLD HEALTH ORG., *Poliomyelitis: Key Facts* (2019), <https://www.who.int/news-room/factsheets/detail/poliomyelitis>

¹⁶ See WORLD HEALTH ORG., *Does Polio Still Exist? Is It Curable?* (2020), <https://www.who.int/news-room/q-a-detail/does-polio-still-exist-is-it-curable>; THOMAS ABRAHAM, *POLIO: THE ODYSSEY OF ERADICATION* (2018); Anna N. Chard et al., *Progress Toward Polio Eradication — Worldwide, January 2018–March 2020*, MORBIDITY & MORTALITY WEEKLY REPORT (Jun. 26, 2020), <https://www.cdc.gov/mmwr/volumes/69/wr/mm6925a4.htm>; CTRS. DISEASE CONTROL & PREVENTION, *Polio Elimination in the United States* (2019), <https://www.cdc.gov/polio/what-is-polio/polio-us.html>

¹⁷ See Volker Janssen, *When Polio Triggered Fear and Panic Among Parents in the 1950s*, History (Mar. 27, 2020), <https://www.history.com/news/polio-fear-post-wwii-era>. See also PHILP ROTH, *NEMESIS* (2010) (portraying widespread parental fear during polio outbreaks in summertime).

¹⁸ See generally Oshinsky, *supra* note 8 (describing the polio vaccine race).

¹⁹ See Hans J. Eggers, *Milestones in Early Poliomyelitis Research (1840 to 1949)*, 73 J. VIROL. 4533 (1999), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC112492/> (providing an overview of the research that enabled the development of polio vaccines in the 1950s); John F. Enders et al., *Cultivation of the Lansing Strain of Poliomyelitis Virus in Cultures of Various Human Embryonic Tissues*, 109 SCIENCE 85 (1949), <https://science.sciencemag.org/content/109/2822/85> (reporting the successful in vitro propagation of the poliovirus).

²⁰ Oshinsky, *supra* note 8.

²¹ See U.S. FOOD & DRUG ADMIN., *Science and the Regulation of Biological Products* (2018), <https://www.fda.gov/about-fda/histories-product-regulation/science-and-regulation-biological-products>

²² See Meier, *supra* note 9. See also Marcia Meldrum, “A Calculated Risk”: *The Salk Polio Vaccine Field Trials of 1954*, 317 BRIT. MED. J. 1233 (1998), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1114166/>

The 1954-55 trials of the Salk vaccine were sponsored by the National Foundation for Infantile Paralysis,²³ now known as March of Dimes,²⁴ and are generally regarded as marking the beginning of modern clinical trials.²⁵ The trials focused on young children (first through third grade),²⁶ and used a dual protocol, with both placebo and observed controls in place.²⁷ Placebos are inert substances that do not produce a therapeutic effect.²⁸ During the polio vaccine trials, 623,972 children participated in the placebo-controlled trial, in which some received the vaccine candidate while others received a placebo.²⁹ At the same time placebo-controlled trials were taking place, an even larger trial unfolded, in which over a million other children received the vaccine and no placebo was administered.³⁰

The results of these combined trials were announced in 1955, showing that the Salk vaccine was 80% to 90% effective in generating protective immunity to polio.³¹ Broad administration of the Salk vaccine—and later on of other types of polio vaccines³²—led to a drastic reduction in the number of polio cases in the United States and around the world.³³ In 1979, polio was officially eliminated in the United States.³⁴ No cases have originated domestically since then, and the

²³ Meldrum, *ib.*

²⁴ MARCH OF DIMES, *About Us*, <https://www.marchofdimes.org/#>

²⁵ See e.g. Arnold S. Monto, *Francis Field Trial of Inactivated Poliomyelitis Vaccine: Background and Lessons for Today*, 21 EPIDEMIOLOGICAL REVS. 7, 7 (1999) (listing the characteristics of the 1954-55 polio vaccine trials that place them “squarely at the start of the modern era” of clinical trials).

²⁶ Meldrum, *supra* note 22.

²⁷ *Id.*, *ib.*

²⁸ See Usha Gupta & Menka Verma, *Placebo in Clinical Trials*, 4 PERSPECT. CLIN. RES. 49 (2013), (describing the use of placebo in clinical trials in general); Annette Rid et al., *Placebo Use in Vaccine Trials: Recommendations of a WHO Expert Panel*, 32 VACCINE 4708 (2014), <https://pubmed.ncbi.nlm.nih.gov/24768580/> (addressing the specificities associated with the use of placebo in vaccine clinical trials).

²⁹ Meldrum, *supra* note 22, at 1233.

³⁰ *Id.*, *ib.*

³¹ *Id.*, *ib.*

³² See generally Lee Hampton, *Albert Sabin and the Coalition to Eliminate Polio from the Americas*, 99 AM. J. PUB. HEALTH 34 (2009), <https://pubmed.ncbi.nlm.nih.gov/19008524/>; Anda Baicus, *History of Polio Vaccination*, 1 WORLD J. VIROL. 108 (2012), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3782271/>

³³ See *supra* note 16 and accompanying text. See also Philip D. Minor, *Polio Vaccines and the Cessation of Vaccination*, 2 EXPERT REV. VACCINES 99 (2003), <https://pubmed.ncbi.nlm.nih.gov/12901601/>; Ananda S. Bandyopadhyay et al., *Polio Vaccination: Past, Present and Future*, 10 FUTURE MICROBIOL. 791 (2015), <https://pubmed.ncbi.nlm.nih.gov/25824845/>

³⁴ U.S. CTRS. DISEASE CONTROL & PREVENTION, *Polio Elimination in the United States* (2019), <https://www.cdc.gov/polio/what-is-polio/polio-us.html>

instances in which travelers have brought the virus to the United States have been few and far between, the last one occurring in 1993.³⁵

In addition to generating the data necessary to support the licensure of the vaccine,³⁶ the 1954-55 polio vaccine trials also established the standard now in place for clinical trials involving both vaccines and other types of pharmaceutical products: randomized controlled trials.³⁷ But while the polio trials in the United States provided the blueprint for what would become the global clinical trial standard, it took a major public health incident in the early 1960s for clinical trials to become mandatory for new drugs and vaccines entering the market.³⁸

The hypnotic drug thalidomide, which was administered in several countries outside the United States in the late 1950s to pregnant women for several conditions, caused extensive birth defects in children.³⁹ Working as a medical officer at the FDA, Dr. Frances Kelsey reviewed and rejected the application to market thalidomide in the United States due to insufficiencies in the information provided by the sponsor.⁴⁰ While Dr. Kelsey's intervention averted what would otherwise have almost certainly been an enormous public health crisis, the problems associated with review of thalidomide by regulatory agencies across the world called attention to the lacking legal framework governing the approval of new drugs and vaccines.⁴¹

Prior to the 1938 Federal Food, Drug and Cosmetic Act (FDCA), there were no statutory requirements that drug sponsors submit data demonstrating the safety and efficacy of the products

³⁵ *Id.*, *ib.*

³⁶ See Rebekah H. Griesenauer & Michael S. Kinch, *An Overview of FDA-Approved Vaccines & Their Innovators*, 16 EXPERT REV VACCINES 1253 (2017), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6112117/>. See also *Science and the Regulation of Biological Products*, *supra* note 21.

³⁷ Monto, *supra* note 25. See also Coleman et al., *supra* note 3; ROBERT J. LEVINE, *ETHICS AND REGULATION OF CLINICAL RESEARCH* (1988) (collectively providing an overview of the regulation of clinical research leading to, and including, clinical trials).

³⁸ See e.g. Lewis A. Grossman, *AIDS Activists, FDA Regulation, and the Amendment of America's Drug Constitution*, 42 AM. J. L. & MED. 687 (2016); Joshua M. Sharfstein, *Crises and Population Health*, 96 *Milbank Quarterly* 223 (2018); Sharon B. Jacobs, *Crises, Congress, and Cognitive Biases: A Critical Examination of Food and Drug Legislation in the United States*, 64 *Food & Drug L. J.* 599 (2009) (collectively describing how the 1961 thalidomide crisis directly led to the passage of the 1962 Drug Amendments in the United States).

³⁹ See e.g. Jack Botting, *The History of Thalidomide*, 15 *DRUG NEW PERSPECT.* 604 (2002), <https://pubmed.ncbi.nlm.nih.gov/12677202/>

⁴⁰ U.S. FOOD & DRUG ADMIN., *Frances Oldham Kelsey: Medical Reviewer Famous for Averting a Public Health Tragedy*, <https://www.fda.gov/about-fda/virtual-exhibits-fda-history/frances-oldham-kelsey-medical-reviewer-famous-averting-public-health-tragedy>

⁴¹ *Supra* note 38.

they intended to bring to market.⁴² The 1938 Act established the principle that safety data must be submitted to the FDA before a new drug or vaccine comes to market by requiring that sponsors conduct “adequate tests by all methods reasonably applicable to show whether or not the drug is safe.”⁴³ In 1962, in direct response to the thalidomide crisis, Congress passed the Kefauver-Harris Amendments to the FDCA, which introduced the requirement that sponsors of new drugs and vaccines demonstrate that their product is “efficacious” before becoming to market.⁴⁴ Sponsors were thus require to produce “substantial evidence” of the effectiveness of a drug or vaccine by presenting data generated through “adequate and well-controlled studies.”⁴⁵

While the new law made clinical trials a pre-requisite of market entrance, it did not define the concepts of “adequate” or “well-controlled” studies, nor did FDA guidance provide much more information to sponsors immediately after the Kefauver-Harris Amendments were enacted.⁴⁶ The legal framework that would make clinical trials the *sine qua non* of drug and vaccine approval was nonetheless in place, and it was incrementally strengthened through legislative and regulatory interventions in the following decades.⁴⁷

The clinical trial paradigm applied on a large scale during the 1954-55 polio vaccine trials and codified in 1962 in the United States quickly became part of the regulatory frameworks in other countries.⁴⁸ Randomized controlled trials became known as the “gold standard” in drug and

⁴² See e.g. Suzanne White Junod, *FDA and Clinical Drug Trials: A Short History*, at 5, <https://www.fda.gov/media/110437/download>

⁴³ Junod, *id.*, *ib.*

⁴⁴ *Id.*, at 8-12 (also noting other measures introduced to strengthen the role of the FDA in drug review). See also U.S. FOOD & DRUG ADMIN., *Kefauver-Harris Amendments Revolutionized Drug Development*, (2012), <https://www.fda.gov/consumers/consumer-updates/kefuver-harris-amendments-revolutionized-drug-development>.

⁴⁵ See Junod, *id.*, at 11-12.

⁴⁶ Junod at 12.

⁴⁷ *Id.*, *ib.* See also e.g. Clinical Trial Regulations of 1970; Food and Drug Administration Modernization Act of 1997, *infra* note 74 and accompanying text; Food and Drug Administration Amendments Act of 2007, *infra* note 76 and accompanying text; U.S. FOOD & DRUG ADMIN., *Clinical Trials Guidance Documents* (2020), <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/clinical-trials-guidance-documents>

⁴⁸ See e.g. Gail A. Van Norman, *Drugs and Devices: Comparison of European and U.S. Approval Processes*, 1 *JACC: BASIC TO TRANSLATIONAL SCI.* 399 (2016), <https://www.sciencedirect.com/science/article/pii/S2452302X16300638> (noting similar substantive drug review procedures and standards in the United States and countries in the European Union in spite of organizational differences between the FDA and the European Medicines Agency).

vaccine effectiveness research and have remained a core component of the scientific and drug review processes ever since.⁴⁹

B. FROM POLIO TO COVID-19 AND THE EMERGENCE OF NEW VACCINE TECHNOLOGY

March 16, 2020. Kaiser Permanente Washington Research Institute in Seattle.

This date and place marked the beginning of the clinical trials for the first COVID-19 vaccine candidate. Less than nine months later, the FDA authorized the emergency use of the first COVID-19 vaccines ever developed.⁵⁰

Several parallels have been drawn between the COVID-19 and the polio vaccine races, even though more than six decades separate these events.⁵¹ In both cases, an infectious pathogen not fully understood by the scientific community triggered a major public health crisis, spread fear among the populations most vulnerable to the disease and their families, and prompted a vaccine race amidst multiple competitors in different countries, resulting in the development, manufacturing and distribution of groundbreaking vaccines within extremely compressed timelines.⁵²

By the time the COVID-19 trials began, however, the legal framework regulating clinical trials had evolved considerably, both to reflect evolving scientific notions and to strengthen the protection of clinical trial volunteers.

⁴⁹ *Supra* note 37 and accompanying text. See also e.g. Elliott M. Antman & Barbara E. Bierer, *Standards for Clinical Research: Keeping Pace with the Technology of the Future*, 133 CIRCULATION 823 (2016), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4778966/>

⁵⁰ See 21 U.S.C. § 360bbb-3; U.S. FOOD & DRUG ADMIN., *Emergency Use Authorization of Medical Products and Related Authorities—Guidance for Industry and Other Stakeholders* (2017), <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-medical-products-and-related-authorities>

⁵¹ See e.g. David Oshinsky, *What the Polio Vaccine Can Teach Us About the Covid-19 Vaccine*, CNN (Nov. 17, 2020), <https://www.cnn.com/2020/11/17/opinions/covid-polio-vaccine-parallels-oshinsky/index.html>; Arthur Allen, *Trust, Fear and Solidarity Will Determine the Success of a COVID Vaccine*, KAISER HEALTH NEWS (Aug. 17, 2020), <https://khn.org/news/trust-fear-and-solidarity-will-determine-the-success-of-a-covid-vaccine/>

⁵² See e.g. Ewen Callaway, *The Race for Coronavirus Vaccines: A Graphical Guide*, NATURE (Apr. 28, 2020), <https://www.nature.com/articles/d41586-020-01221-y> (chronicling the early stages of the COVID-19 vaccine race); Gilbert King, *Salk, Sabin and the Race Against Polio*, SMITHSONIAN MAG. (Apr. 3, 2012), <https://www.smithsonianmag.com/history/salk-sabin-and-the-race-against-polio-169813703/> (chronicling the polio vaccine race).

While the polio vaccine trials are still hailed by many commentators as a great achievement in medical research,⁵³ they were also conducted partly in ways that would constitute a violation of modern ethical principles governing biomedical research, such as the testing of the vaccine on institutionalized physically and intellectually disabled children during the early stages of research.⁵⁴

There were cases of even more extensive ethical violations in medical research even as clinical trials became progressively more regulated, both in the context of vaccine research and in other areas. The most well-known example is the Tuskegee Study, a forty-year federally funded medical research program (1932-1972) conducted with the purpose of observing the evolution of untreated syphilis in black male populations, during the course of which several egregious ethical violations were repeatedly committed.⁵⁵ These violations included deceptive statements about the purpose of the study made by researchers to economically disadvantaged volunteers,⁵⁶ as well as the intentional deprivation of available treatments to syphilis patients, which produced detrimental effects to both the health of the individuals involved in the study and that of their families and communities.⁵⁷ The repercussions of the Tuskegee Study are felt to this day, with lower levels of trust in medical research registered among minority communities being partially connected to the memory and impact of Tuskegee.⁵⁸ A study published in 2018 – forty-six years after the end of Tuskegee – found that, in addition to giving rise to medical mistrust issues, the Tuskegee Study

⁵³ See *supra* note 9 and accompanying text.

⁵⁴ History of Vaccines, *Polio Brochure 1* (1952), <https://www.historyofvaccines.org/content/salk-begins-early-polio-vaccine-tests-0>. For further discussion of ethical aspects of the Salk vaccine development and testing, see also Allan M. Brandt, *Polio, Politics, Publicity, and Duplicity: Ethical Aspects in the Development of the Salk Vaccine*, 8 INT'L J. HEALTH SERVICES 257 (1979), <https://repository.library.georgetown.edu/handle/10822/717614>

⁵⁵ See Ruqaiijah Yearby, *Exploitation in Medical Research: The Enduring Legacy of the Tuskegee Syphilis Study*, 67 CASE W. RES. L. REV. 1171 (2017).

⁵⁶ *Id.* at 1172.

⁵⁷ *Id.* at 1172-73.

⁵⁸ *Id.* See also Allan M. Brandt, *Racism and Research: The Case of the Tuskegee Syphilis Study*, 8 HASTINGS CTR. REP. 21 (1978); et al., *Knowledge of the Tuskegee Study and Its Impact on the Willingness to Participate in Medical Research Studies*, 92 J. NAT'L MED. ASS'N. 563 (2000). See also generally HARRIET A. WASHINGTON, *MEDICAL APARTHEID: THE DARK HISTORY OF MEDICAL EXPERIMENTATION ON BLACK AMERICANS FROM COLONIAL TIMES TO THE PRESENT* (2006) (detailing the history of the exploitation of Black American populations in medical research before and after Tuskegee).

“correlated with increases in (...) mortality and decreases in both outpatient and inpatient physician interactions for older black men.”⁵⁹

In the case of vaccine-related research, one of the most prominent examples is the so-called “experiment” at Willowbrook State School in Staten Island.⁶⁰ Researchers interested in understanding more about hepatitis C with the eventual goal of developing a vaccine conducted a non-therapeutic study for roughly fifteen years (1955/56–1971)⁶¹ on developmentally disabled children by deliberately infecting them with the virus and monitoring their progress.⁶²

A *Forbes* journalist interviewed the mother of one of these children over fifty years after the Willowbrook study began, and aptly characterized some of the ways in which parental consent was obtained as a “Faustian bargain.”

In order to get [her severely autistic daughter] a spot at the overcrowded facility, however, she had to make a Faustian bargain—consenting to allow her daughter to be part of a quest to find a vaccine for hepatitis. “I had no choice,” McCourt says, “I had tried so many different places and so many arrangements, and they didn't work out, so I went along with it.”⁶³

⁵⁹ Marcella Alsan & Marianne Wanamaker, *Tuskegee and the Health of Black Men*, 133 Q. J. ECON 407 (2018), <https://pubmed.ncbi.nlm.nih.gov/30505005/>

⁶⁰ See Stephen Goldby, *Experiments at the Willowbrook State School*, 297 LANCET 749 (1971), [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(71\)92009-5/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(71)92009-5/fulltext). But see Saul Krugman, *The Willowbrook Hepatitis Studies Revisited: Ethical Aspects*, 8 REV. INFECTIOUS DIS. 157 (1986), <https://academic.oup.com/cid/article-abstract/8/1/157/350487?redirectedFrom=fulltext> (offering a defense of the study design by the lead researcher in the Willowbrook study).

⁶¹ There are disparities in the reporting of the starting date for the Willowbrook study. See e.g. *Willowbrook Hepatitis Experiments* in NAT'L INST. HEALTH, EXPLORING BIOETHICS, (2009), https://science.education.nih.gov/supplements/webversions/bioethics/guide/pdf/master_5-4.pdf (providing a 1955 starting date); James M. DuBois, *Hepatitis Studies at the Willowbrook State School for Children with Mental Retardation*, ETHICS IN MENTAL HEALTH RESEARCH, <https://sites.google.com/a/narrativebioethics.com/emhr/contact/hepatitis-studies-at-the-willowbrook-state-school-for-children-with-mental-retardation> (providing a 1956 starting date).

⁶² Trials in which healthy participants are infected with a pathogen are also known as challenge studies. See e.g. Annette Rid & Meta Roestenberg, *Judging the Social Value of Controlled Human Infection Studies*, 34 BIOETHICS 749 (2020). The topic of challenge studies has also been discussed in the context of the COVID-19 vaccine race. See e.g. Jeffrey P. Kahn et al., *For Now, It's Unethical to Use Human Challenge Studies for Sars-Cov-2 Vaccine Development*, 117 PNAS 28538 (Nov. 17, 2020), <https://www.pnas.org/content/117/46/28538> (arguing against the use of challenge studies in the COVID-19 vaccine race); Seán O'Neill McPartlin et al., *Covid-19 Vaccines: Should We Allow Human Challenge Studies to Infect Healthy Volunteers With Sars-Cov-2?* 371 BRIT. MED. J. m4258 (2020) (exploring arguments both in favor and against challenge studies for COVID-19 vaccines).

⁶³ Leah Rosenbaum, *The Hideous Truths of Testing Vaccines on Humans*, FORBES (Jun. 12, 2020), <https://www.forbes.com/sites/leahrosenbaum/2020/06/12/willowbrook-scandal-hepatitis-experiments-hideous-truths-of-testing-vaccines-on-humans/?sh=10e391a4279c>. See also Coleman et al., *supra* note 3, at 40 (further describing the Willowbrook study).

In response to systemic ethical failures long observed in medical research, and in particular as a direct response to the publicization of the Tuskegee Study, a code of conduct known as the Belmont Report was published in the United States in 1979, providing a set of ethical principles and guidelines designed to protect participants in clinical research.⁶⁴

The subsequent decades brought about significant changes in the legal protections offered to participants in biomedical research. Some of these changes were directly aimed at protecting volunteers participating in clinical trials, as is the case of laws regulating informed consent, while others protected volunteers indirectly by focusing on the collection of data during trials and ensuing permissible uses.

In 1981, the principles enshrined in the Belmont Report became the foundation of the legal framework governing federal protection of human subjects involved in clinical research, primarily through the regulation of informed consent.⁶⁵ In 1991, they were codified in the Common Rule,⁶⁶ which was revised in 2018.⁶⁷

In an attempt to correct asymmetries in data collection, particularly with regard to the representation of women and racial and ethnic minorities, the NIH Revitalization Act of 1993 was introduced to mandate appropriate inclusion of minority volunteers in research funded by the National Institutes of Health.⁶⁸ As noted in Part II in the context of COVID-19 vaccine trials,

⁶⁴ Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research, Report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 44 Fed. Reg. 23,192, 23,194 (Apr. 18, 1979) (establishing the ethical principles of respect for persons, beneficence and justice, and requiring three elements in connection with informed consent: information, comprehension and voluntariness). See also Eli Y Adashi et al., *The Belmont Report at 40: Reckoning with Time*, 108 AM. J. PUB. HEALTH 1345 (2018), <https://pubmed.ncbi.nlm.nih.gov/30138058/> (surveying the application of the Belmont report and emerging issues not contemplated by the drafters of the Report).

⁶⁵ General Requirements for Informed Consent, 45 C.F.R. § 46.116 (2005).

⁶⁶ See 45 C.F.R. § 46 and 21 C.F.R. § 50 (collectively laying out the regulatory regime for the protection of human subjects in clinical trials, the former in the context of federally funded research, and the latter in the context of clinical trials overseen by the FDA).

⁶⁷ DPT. HEALTH & HUM. SERVICES, *Revised Common Rule*, <https://www.hhs.gov/ohrp/regulations-and-policy/regulations/finalized-revisions-common-rule/index.html>. See also Jerry Menikoff et al., *The Common Rule, Updated*, 376 N. ENGL. J. MED. 613 (2017), <https://pubmed.ncbi.nlm.nih.gov/28103146/>; Valerie Gutmann Koch & Kelly Todd, *Research Revolution or Status Quo?: The New Common Rule and Research Arising From Direct-to-Consumer Genetic Testing*, 56 HOUS. L. REV. 81 (2018).

⁶⁸ NIH Revitalization Act of 1993, Public Law 103-43. But see Stacie E. Geller et al., *The More Things Change, the More They Stay the Same: A Study to Evaluate Compliance with Inclusion and Assessment of Women and Minorities in Randomized Controlled Trials*, 93 ACAD. MED. 630 (2018), <https://pubmed.ncbi.nlm.nih.gov/29053489/> (finding that “NIH policies have not resulted in significant increases in reporting results by sex, race, or ethnicity”).

problems of under-representation of racial and ethnic minorities persist in spite of these legislative efforts.

As also described in the following section, another strand of long-standing problems affects the collection and dissemination of clinical trial data. On the one hand, not all clinical trials are registered, a phenomenon that poses significant hurdles to research transparency and accountability, as well as to access to existing data for purposes of follow-on innovation.⁶⁹ On the other hand, even in the case of registered trials with published results, current industry practices result in the availability of severely incomplete data, which similarly impairs transparency, accountability and follow-on research.⁷⁰

The Declaration of Helsinki, originally adopted in 1964 and last amended in 2013, established that clinical trials must be registered in publicly available databases,⁷¹ and imposed a duty of dissemination of clinical trial results on medical researchers.⁷² The United States codified clinical trial reporting requirements consistent with the Declaration of Helsinki,⁷³ and in 1997 the Food and Drug Administration Modernization Act (FDAMA) required the registration of clinical trials for serious or life-threatening diseases and conditions.⁷⁴ Three years later, the National Institutes of Health launched a national registry of clinical trials hosted by the U.S. National Library of Medicine, Clinicaltrials.gov.⁷⁵ Registration requirements for clinical trials were scaled up in 2007 by the Food and Drug Administration Amendments Act (FDAAA),⁷⁶ which required the government to expand the federal clinical trial data bank.⁷⁷ However, as further detailed in Part

⁶⁹ *Infra*, Part II.B.

⁷⁰ *Ib.*

⁷¹ World Med. Ass'n Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects [hereinafter Declaration of Helsinki] 35, <https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/>

⁷² *Id.*, 36.

⁷³ See Final Rule for Clinical Trials Registration and Results Information Submission (42 CFR § 11); Food and Drug Administration Amendments Act of 2007 (FDAAA 801) § 801.

⁷⁴ Food and Drug Administration Modernization Act of 1997, Pub. L. No. 105-115, 111 Stat. 2296 (1997). See also U.S. FOOD & DRUG ADMIN., *Regulations: Good Clinical Practice and Clinical Trials* (2020), <https://www.fda.gov/science-research/clinical-trials-and-human-subject-protection/regulations-good-clinical-practice-and-clinical-trials>

⁷⁵ CLINICALTRIALS.GOV, <https://clinicaltrials.gov>

⁷⁶ Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, 121 Stat. 823.

⁷⁷ 42 U.S.C. § 282(j)(2)(A)(i).

II, registration of clinical trials remains far from uniform,⁷⁸ and there has been very little institutional support within the Department of Health and Human Services (HHS) for the enforcement of the trial registration requirements set by FDAMA and FDAAA. In 2016, six years after the statutory deadline,⁷⁹ the Department of Health and Human Services issued a final rule implementing the reporting requirements set forth in FDAAA.⁸⁰ The rule, which entered into force in January of the following year, exempted clinical trials completed⁸¹ before January 18, 2017 from data reporting requirements in cases in which the sponsored product had not been approved by the FDA at the date of completion of the trial.⁸² In 2020, the District Court for the Southern District of New York found that the FDAAA unambiguously required sponsors to submit data and HHS to include it in ClinicalTrials.gov irrespective of trial completion date or product approval, thus striking down the reporting exemption.⁸³

Contemporary vaccine clinical trials thus take place against a legal and normative background that is vastly different from the ones in which the polio vaccine trials were conducted – albeit one in which profound shortcomings persist at the representativity, registration, data reporting and data sharing levels, as illustrated by the vaccine-specific examples provided in the following section.⁸⁴

Recently, the introduction of new and disruptive vaccine technology has ratcheted up the challenges posed to the clinical trial ecosystem and the data infrastructure it generates. After over a decade of study, the COVID-19 vaccine race provided the final catalyst for late-stage development of a novel type of vaccine: mRNA vaccines.⁸⁵ Messenger RNA is a type of genetic

⁷⁸ *Infra*, Part II.B.

⁷⁹ See 42 U.S.C. § 282(j)(3)(D)(i). See also Complaint, *Seife v. US Department of Health & Human Services*, 18-cv-11462 (2018), at 11, https://law.yale.edu/sites/default/files/area/center/crit/document/01_complaint.pdf

⁸⁰ 81 Fed. Reg. 64,981 (Sept. 21, 2016), Clinical Trials Registration and Results Information Submission, codified at 42 C.F.R. § 11.

⁸¹ The rule applies to “primary completion” of clinical trials. See 42 C.F.R. § 11.42(b), which is interpreted as meaning the date of completion, defined as “date that the final subject was examined or received an intervention for the purposes of final collection of data for the primary outcome, whether the clinical trial concluded according to the pre-specified protocol or was terminated.” See 42 C.F.R. § 11.10 (a).

⁸² 42 C.F.R. § 11.42(b) (exempting trials completed before January 18, 2017).

⁸³ *Seife v. US Department of Health & Human Services*, WL 883478 (S.D.N.Y. Feb. 24, 2020).

⁸⁴ See *infra* Part II.A (surveying representativity issues) and Part II.B. (surveying registration, data reporting and data sharing issues).

⁸⁵ See e.g. CTRS. DISEASE CONTROL & PREVENTION, *supra* note 1.

material that contains instructions for the human body to create certain types of proteins.⁸⁶ In the case of mRNA vaccines, scientists use a synthetic version of mRNA to direct the human body to produce some of the same proteins that the virus normally produces, without actually ever introducing viral matter into the body.⁸⁷ In response to the presence of these proteins, the immune system triggers a protective response.⁸⁸ By contrast, vaccines available before the pandemic had to rely on small amounts of viral matter as a way to trigger the same type of response.⁸⁹

The COVID-19 mRNA vaccine candidates were developed in a matter of months – faster than COVID-19 vaccines based on older technology – followed by a short period of clinical trials thus testing a medical technology never before used in humans.⁹⁰ Regulators across the world were called to evaluate data generated under these extreme circumstances and decide whether to authorize the emergency use of vaccines before enough data was gathered for sponsors to request a full approval of their vaccine candidates.⁹¹ As a trade-off for making critical public health tools available to large segments of the population, these regulators – including the FDA – eventually granted emergency use authorizations to the leading COVID-19 vaccine candidates by relying on data inherently far more limited than the data normally supplied in support of applications to market new vaccines.⁹²

⁸⁶ U.S. NAT'L HUM. GENOME RESEARCH INST., *Messenger RNA (mRNA)*, <https://www.genome.gov/genetics-glossary/messenger-rna>

⁸⁷ See generally Jennifer Abbasi, *COVID-19 and mRNA Vaccines—First Large Test for a New Approach*, 324 J. AM. MED. ASS'N. 1125 (2020), <https://jamanetwork.com/journals/jama/fullarticle/2770485>. Carlo Iavarone et al., *Mechanism of Action of mRNA-based Vaccines*, 16 EXPERT REV. VACCINES 871 (2017), <https://pubmed.ncbi.nlm.nih.gov/28701102/>. See also MODERNA, *The Science and Fundamentals of mRNA Technology*, <https://www.modernatx.com/mrna-technology/science-and-fundamentals-mrna-technology> (including a description of mRNA vaccine technology provided by one of the sponsors mRNA COVID-19 vaccines authorized in the United States in late 2020).

⁸⁸ See *Understanding and Explaining mRNA COVID-19 Vaccines*, *supra* note 85.

⁸⁹ *Id.*, *ib.*

⁹⁰ See *A Timeline of COVID-19 Vaccine Development*, *supra* note 2.

⁹¹ See EUR. MED. AGENCY, *EMA Recommends First COVID-19 Vaccine for Authorisation in the EU* (Dec. 21, 2020), <https://www.ema.europa.eu/en/news/ema-recommends-first-covid-19-vaccine-authorisation-eu>; HEALTH CANADA, *Statement on the U.S. Authorization of the Moderna COVID-19 Vaccine* (Dec. 18, 2020), <https://www.canada.ca/en/health-canada/news/2020/12/statement-on-the-us-authorization-of-the-moderna-covid-19-vaccine.html>; U.S. FOOD & DRUG ADMIN., *FDA Takes Key Action in Fight Against COVID-19 by Issuing Emergency Use Authorization for First COVID-19 Vaccine* (Dec. 11, 2020), <https://www.fda.gov/news-events/press-announcements/fda-takes-key-action-fight-against-covid-19-issuing-emergency-use-authorization-first-covid-19>

⁹² See *FDA Takes Key Action in Fight Against COVID*, *ib.*

The Essay has so far provided contextual information on the emergence of the contemporary vaccine clinical trial model, noting longstanding issues in the ways vaccine-related knowledge is produced in clinical trials and resulting data are disclosed, now combined with challenges to regulatory review of new vaccines when vaccine data are generated in timelines severely compressed by public health crises. Part II now focuses on systemic issues affecting the production and disclosure of vaccine clinical trial data.

II. VACCINE CLINICAL TRIAL DATA AS BUILDING BLOCKS

A. DATA COLLECTION: LIMITATIONS OF THE CURRENT VACCINE CLINICAL TRIAL DATA INFRASTRUCTURE

Data generated during vaccine clinical trials is the bedrock of the scientific and regulatory processes that bring new vaccines to market.⁹³ Yet, the ways in which those data are produced have long resulted in a data infrastructure marked by gaps in foundational knowledge related to the development and testing of new vaccines.⁹⁴ This, in turn, has an impact on the intrinsic completeness, accuracy and transparency of vaccine data collection – and by extension on instrumental uses of those data, such as the use of clinical trial data to support the approval (or denial) of a new vaccine, – as well as on public perceptions of how vaccines are developed, tested and made available to populations at large.⁹⁵

One of the most salient holes in the vaccine data infrastructure stems from the under-representation of certain segments of the population in vaccine clinical trials – most notably, minority populations.⁹⁶ Even though legislation has been introduced to address representativity

⁹³ See e.g. Cynthia Ho, *Avoiding the TRIPS Trap: A Path to Domestic Disclosure of Clinical Drug Data Consistent with International Norms* __ CORNELL INT'L L. J. __ at 15-18 (forthcoming, 2021) (on file with author) (linking the availability of clinical trial data to transparency); Jerome H. Reichman, *Rethinking the Role of Clinical Trial Data in International Intellectual Property Law: The Case for a Public Goods Approach*, 13 MARQ. INTELL. PROP. L. REV. 1, 51, 54-58 (2009) (making the case that treating clinical trial data as a public good would result in long-term follow-on innovation).

⁹⁴ See *supra*, Part II.

⁹⁵ *Ib.*

⁹⁶ There are additional categories of populations under-represented in vaccine clinical trials. Consider the case of pediatric populations during the COVID-19: clinical trials for coronavirus vaccines did not enroll children until late 2020. See e.g. Jeffrey I. Campbell et al., *A Call for Pediatric COVID-19 Clinical Trials*, 146 PEDIATRICS e20201081 (2020), <https://pediatrics.aappublications.org/content/146/2/e20201081>; Denise Grady, *Moderna Plans to Begin*

problems in clinical trials,⁹⁷ minorities have long been underrepresented in clinical trials, both in the United States⁹⁸ and elsewhere.⁹⁹ The landscape in vaccine clinical trials reflects this systemic problem. For instance, an online registry made available early in the pandemic by the COVID-19 Prevention Network to enable individuals to express interest in participating in COVID-19 vaccine clinical trials had enlisted around 350,000 people by late August 2020, of which only around 10% were Black or Hispanic.¹⁰⁰

COVID-19 clinical trials further illustrated systemic problems affecting the participation of racial and ethnic minorities. Researchers have found both problems of minority underrepresentation in clinical trial design and a lack of uniformity across trial sites in the collection and reporting of data on race and ethnicity.¹⁰¹ Consider the cases of the Pfizer/BioNTech vaccine candidate, which in December 2020 became the first vaccine authorized by the FDA for emergency use,¹⁰² and of the Moderna vaccine candidate, which was the first to enter clinical trials.¹⁰³

Phase 3 of the clinical trial that produced the data used to support the emergency use authorization granted to Pfizer/BioNTech was initially designed with target of 30,000 patients and

Testing Its Coronavirus Vaccine in Children, N.Y. TIMES (Dec. 2, 2020), <https://www.nytimes.com/2020/12/02/health/Covid-Moderna-vaccine-children.html>

⁹⁷ See *supra* note 68 and accompanying text.

⁹⁸ See Paula A. Rochon et al., *The Inclusion of Minority Groups in Clinical Trials: Problems of Under Representation and Under Reporting of Data*, 11 ACCOUNT RES. 215 (2004); Barbara A. Noah, *The Participation of Underrepresented Minorities in Clinical Research*, 29 AM. J. L. & MED. 221 (2003); Jill A. Fisher & Corey A. Kalbaugh, *Challenging Assumptions About Minority Participation in US Clinical Research*, 101 AM. J. PUB. HEALTH 2217 (2011); Ali Salman et al., *A Review of Barriers to Minorities' Participation in Cancer Clinical Trials: Implications for Future Cancer Research*, 18 J. IMM. MINOR. HEALTH 447 (2016); Andrea L. Gilmore-Bykovskiy et al., *Recruitment and Retention of Underrepresented Populations in Alzheimer's Disease Research: A Systematic Review*, 5 ALZHEIMER'S & DEMENTIA: TRANSLATIONAL RESEARCH & CLINICAL INTERVENTIONS 751 (2019); Bassel Nazha et al., *Enrollment of Racial Minorities in Clinical Trials: Old Problem Assumes New Urgency in the Age of Immunotherapy*, 39 AM. SOC'Y CLINICAL ONCOLOGY EDUC. 3(2019).

⁹⁹ See e.g. Mahvash Hussain-Gambles et al., *Why Ethnic Minority Groups Are Under-Represented in Clinical Trials: A Review of the Literature*, 12 HEALTH SOC. CARE COMMUNITY 382 (2004), <https://pubmed.ncbi.nlm.nih.gov/15373816/> (discussing minority under-representation in the United Kingdom);

¹⁰⁰ Carolyn Y. Johnson, *Large U.S. Covid-19 Vaccine Trials Are Halfway Enrolled, But Lag on Participant Diversity*, WASH. POST (Aug. 27, 2020), <https://www.washingtonpost.com/health/2020/08/27/large-us-covid-19-vaccine-trials-are-halfway-enrolled-lag-participant-diversity/>

¹⁰¹ Hala T. Borno et al., *Covid-19 Disparities: An Urgent Call for Race Reporting and Representation in Clinical Research*, Contemp Clin Trials Commun. (2020), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7391979/> (surveying clinical trials focusing on products other than vaccines).

¹⁰² U.S. FOOD & DRUG ADMIN., *Pfizer-BioNTech COVID-19 Vaccine Letter*, <https://www.fda.gov/media/144412/download>

¹⁰³ MODERNA, *Moderna Announces First Participant Dosed in NIH-led Phase 1 Study of mRNA Vaccine (mRNA-1273) Against Novel Coronavirus* (Mar. 16, 2020), <https://investors.modernatx.com/news-releases/news-release-details/moderna-announces-first-participant-dosed-nih-led-phase-1-study>

later expanded.¹⁰⁴ On December 14, 2020, Pfizer reported a total enrollment of 44,863 volunteers in 150 sites across six countries, including the United States.¹⁰⁵ By then, 43,004 volunteers (95.9% of the trial population) had received the second shot.¹⁰⁶ At that point, demographic data relative to the United States indicated that 13% of volunteers were Latinx, 10% were Black, 6% were Asian and 1.3% were Native American.¹⁰⁷ Although, Pfizer's announcement did not specify this information at the time, these numbers imply that 69.7% of the volunteers in the Pfizer/BioNTech vaccine trial in the United States did not belong to racial or ethnic minorities, for an overall diversity rate of 30.3%.¹⁰⁸

Moderna's vaccine clinical trial, which took place across sites in over twenty states in the United States,¹⁰⁹ drew from a somewhat smaller volunteer pool (30,000 participants) and displayed a slightly higher diversity rate. Just over a month before submitting its emergency use authorization application to the FDA, Moderna released a report on phase 3 trials for its vaccine candidate, which at that point had met its enrollment goal of 30,000 volunteers in several sites across the United States.¹¹⁰ By October 22, 2020, a total of 25,654 participants had received the second dose of the vaccine.¹¹¹ Demographic data showed that 20% of volunteers were Latinx, 10% were Black or African American, 4% were Asian, 63% were White, and all other races and ethnicities accounted for 3% of the trial population.¹¹² These numbers put the diversity rate almost 7 points above Pfizer/BioNTech's, at 37%.

Yet neither Moderna nor Pfizer/BioNTech's diversity targets and near-final diversity enrollment are satisfactory according to experts. In August 2020, Moderna used social media to promote its "diversity & inclusion" plan for COVID-19 trials, noting that their vaccine candidate

¹⁰⁴ See Matthew Herper, *Pfizer and BioNtech Announce Plan to Expand Covid-19 Vaccine Trial*, STAT (Sept. 12, 2020), <https://www.statnews.com/2020/09/12/pfizer-and-biontech-announce-plan-to-expand-covid-19-vaccine-trial/>

¹⁰⁵ PFIZER, *Our Progress in Developing an Investigational Covid-19 Vaccine*, (Dec. 14, 2020), <https://www.pfizer.com/science/coronavirus/vaccine>

¹⁰⁶ *Id.*, *ib.*

¹⁰⁷ *Id.*, *ib.*

¹⁰⁸ *Id.*, *ib.* (listing diversity rates for participants in the Pfizer/BioNTech clinical trial).

¹⁰⁹ MODERNA, *Moderna Cove Study*, at 2 https://www.modernatx.com/sites/default/files/content_documents/2020-COVE-Study-Enrollment-Completion-10.22.20.pdf (reporting data relative to October 21, 2020), at 6.

¹¹⁰ MODERNA, *Moderna's Fully Enrolled Phase 3 COVE Study of mRNA-1273*, <https://www.modernatx.com/cove-study>

¹¹¹ *Id.*, *ib.*

¹¹² MODERNA, *Moderna Cove Study*, at 2 https://www.modernatx.com/sites/default/files/content_documents/2020-COVE-Study-Enrollment-Completion-10.22.20.pdf (reporting data relative to October 21, 2020).

was being tested in “nearly 100 sites with representative demography.”¹¹³ Shortly thereafter, however, the company had to slow down the enrollment process because it was not able to recruit enough participants from racial and ethnic minorities.¹¹⁴ Facing similar problems, Pfizer expanded its target enrollment from 30,000 to 40,000 volunteers.¹¹⁵ Pfizer’s press release specifically noted that the expansion was driven by the goal to “increase trial population diversity.”¹¹⁶ In the context of this specific trial, diversity efforts were also focused on including younger populations in order to garner data on volunteers as young as age 16, as well as populations with certain conditions, such as chronic HIV and Hepatitis C.¹¹⁷

The examples of Pfizer/BioNTech and Moderna within the context of the COVID-19 vaccine race are especially relevant given the fact that their vaccine candidates were the first to enter the United States market, but these companies are by no means the only ones facing diversity problems in vaccine clinical trials. A representative for Velocity Clinical Research, an organization involved in COVID-19 vaccine trials in multiple locations across the United States,¹¹⁸ reported similar enrollment problems, describing instructions to slow down volunteer recruitment in a way that tersely illustrates the magnitude of the problem: “Some of our sites, bluntly, are situated in a largely white population [sic]. We have had sites in those places that were told, ‘You need to stop now and only recruit from minorities.’”¹¹⁹

Moderna’s data on the progression of clinical trial enrollment is similarly illustrative:

¹¹³ TWITTER (Aug. 21, 2020), https://twitter.com/moderna_tx/status/1296942996592746498

¹¹⁴ Eric Broodman, *Among People of Color Asked to Join Covid-19 Vaccine Trials, Worries About Inequities Run Deep*, STAT (Sept. 25), <https://www.statnews.com/2020/09/25/among-people-of-color-asked-to-join-covid-19-vaccine-trials-worries-about-inequities-run-deep/>

¹¹⁵ *Id.*, *ib.*

¹¹⁶ Pfizer, *Press Release: Pfizer and BioNtech Propose Expansion of Pivotal COVID-19 Vaccine Trial* (Sept. 12, 2020), <https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-propose-expansion-pivotal-covid-19>

¹¹⁷ *Id.*, *ib.*

¹¹⁸ VELOCITY CLINICAL RESEARCH, <https://velocityclinical.com>

¹¹⁹ Broodman, *Among People of Color Asked to Join Covid-19 Vaccine Trials, Worries About Inequities Run Deep*, *supra* note 114.

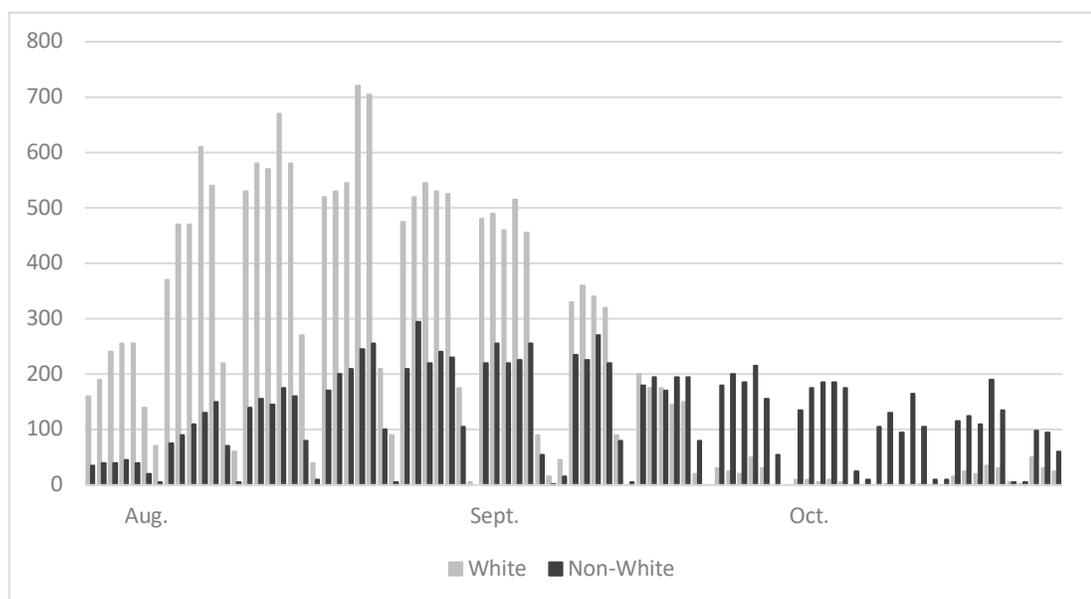


Figure 1: Moderna COVID-19 vaccine clinical trials enrollment, July 27, 2020 through October 21, 2020¹²⁰

The graph shows that during the first half of the enrollment period, White participants were being recruited at rates that more than doubled those of non-White participants.¹²¹ And perhaps even more tellingly, once diversity issues were flagged and the company began slowing down recruitment, it did not increase diversity by increasing recruitment among non-White populations, but rather by maintaining non-White recruitment at the same levels while drastically reducing recruitment of White participants and eventually bringing it close to a halt.¹²²

Nevertheless, this strategy can scarcely be said to have worked. Consider the case of enrollment of Black or African American volunteers for the Moderna vaccine trial. In August, when concerns about diversity in COVID-19 vaccine clinical trials began being voiced more forcefully,¹²³ the Moderna trial had enrolled only 7% Black or African American volunteers.¹²⁴ By mid-September that number had gone up to 13%.¹²⁵ Yet, as noted above, once enrollment was

¹²⁰ Adapted from MODERNA, *Moderna Cove Study*, *supra* note 109, at 5.

¹²¹ *Id.*, *ib.*

¹²² *Id.*, *ib.*

¹²³ See e.g. Johnson, *supra* note 100; Cohen, *infra* note 128.

¹²⁴ Broodman, *Among People of Color Asked to Join Covid-19 Vaccine Trials, Worries About Inequities Run Deep*, *supra* note 114.

¹²⁵ *Id.*, *ib.*

completed the overall percentage of Black participants had dropped to 10%.¹²⁶ This number – as well as the overall diversity numbers in COVID-19 vaccine clinical trials – are far from the ones cited by public health experts as needed to accomplish the intertwined goals of accurately reflecting the racial and ethnic make-up of the United States and generating more granular data for purposes of regulatory review and vaccine trust-building.¹²⁷

The specific demographic burden of COVID-19 poses even more challenges from the perspective of minority representation in vaccine clinical trials. The director of the National Institute of Allergy and Infectious Diseases, Dr. Anthony Fauci, has noted that, given the disproportionately higher toll of COVID-19 on minorities, clinical trials for COVID-19 vaccines should enroll a significantly larger percentage of minority volunteers than other types of trials.¹²⁸ Dr. Fauci suggested that, in the specific case of COVID-19 vaccines, minority enrollment should in fact be twice as high as the percentage of minorities in the United States population,¹²⁹ which commentators relying on the most recent U.S. Census Bureau data calculated to translate into a goal of 66.4% minority enrollment in COVID-19 vaccine clinical trials.¹³⁰ While it is important that the representativity goals articulated by Dr. Fauci are far higher than the standards typically used in vaccine clinical trials – and in no way required by the FDA in assessing vaccine clinical trial data – the point remains that minority representation remains low as a feature of clinical trials in general, and vaccine clinical trials in particular. Dr. Fauci’s approach is also not an isolated one, with other members of the scientific community agreeing that, given both the historical underrepresentation of minority populations in clinical trials and the burden of COVID-19 on minorities, it is necessary to oversample minority populations in vaccine trials.¹³¹

The Government Accountability Office, a non-partisan government United States agency,¹³² issued a report in November 2020 finding that, albeit successful in generating data on

¹²⁶ See *Moderna Cove Study*, *supra* note 112 (providing data on 25,654 out of 30,000 trial participants, which represents 85.5% of total enrollment).

¹²⁷ See e.g. Elizabeth Cohen, *Despite Effort, Enrollment of Minorities for Coronavirus Vaccine Trial is Lagging*, CNN (Aug. 22, 2020), <https://www.cnn.com/2020/08/22/health/coronavirus-moderna-minorities-lag/index.html>

¹²⁸ *Id.*, *ib.*

¹²⁹ *Id.*, *ib.*

¹³⁰ *Id.*, *ib.*

¹³¹ Johnson, *supra* note 100.

¹³² U.S. GOV’T ACCOUNTABILITY OFF, <https://www.gao.gov/about/>

vaccine candidates in record time, the COVID-19 vaccine clinical trials lacked transparency.¹³³ In particular, the report noted that the sponsors of the clinical trials provided little information on the collection and analysis of safety and efficacy data for population sub-groups, including racial and ethnic minorities:

[COVID-19 vaccine] clinical trial protocols provide limited details on how the vaccine developers will analyze their safety and efficacy data, specifically for population subgroups (e.g., the elderly, people with comorbidities, or racial/ethnic groups) or sample sizes needed for such subgroup analyses. Unless vaccine developers collect sufficient data for a subgroup analysis, it may not be possible to identify the potential for different safety or efficacy results for one or more subgroups, even if vaccine candidates are found safe and effective in the aggregate for the general population.¹³⁴

This chronic under-representation of minority populations in vaccine clinical trials feeds into larger vaccine trust problems, explored in Part II.B, which contribute towards vaccine hesitancy, leading individuals indicated for a vaccine to forego vaccination, sometimes even in cases in which the vaccine can be administered at no direct cost to the patient.¹³⁵ But it is important to note here that disparities in racial and ethnic representation in data collection and generation during vaccine clinical trials are then compounded by other types of systemic disparities that pervade the vaccine development and distribution ecosystem.

The mistrust experienced by minorities with regard to medical research and the ways in which clinical trials have been conducted for decades vastly exceeds the domain of COVID-19 vaccines. A study following the administration of H1N1 vaccines in Los Angeles County at free vaccination clinics during the 2009 swine flu pandemic found “[w]ide racial/ethnic disparities in vaccination rates,” especially among Black populations.¹³⁶ Outside the context of pandemic

¹³³ U.S. GOV'T ACCOUNTABILITY OFF., GAO-21-207, *Federal Efforts Accelerate Vaccine and Therapeutic Development, but More Transparency Needed on Emergency Use Authorizations* (Nov. 17, 2020) [hereinafter GAO Report].

¹³⁴ *Id.*, at 17.

¹³⁵ See e.g. Rueben C. Warren et al., *Trustworthiness before Trust — Covid-19 Vaccine Trials and the Black Community*, 383 N. ENGL. J. MED. e121 (2020); William Wan, *Coronavirus Vaccines Face Trust Gap in Black and Latino Communities, Study Finds*, WASH. POST (Nov. 23, 2020), <https://www.washingtonpost.com/health/2020/11/23/covid-vaccine-hesitancy/>;

¹³⁶ Alonzo Plough et al., *Pandemics and Health Equity: Lessons Learned from the H1N1 Response in Los Angeles County*, 17 J. PUB. HEALTH MGMT. & PRAC. 20 (2011),

vaccines, data gleaned over the years from seasonal flu vaccination provide a useful glimpse into disparities at the vaccine distribution and access levels.¹³⁷ Vaccination rates among adult populations have historically been lower among Black, Hispanic, and American Indian or Alaska Native populations than among White populations.¹³⁸ The lower rates are attributable to multiple factors, including lower insurance rates and logistical hurdles.¹³⁹ However, trust deficits in the healthcare system and in medical research leading to the commercialization of new vaccines – and, more broadly, pharmaceutical products in general – remain a contributing factor of lower vaccine uptake among minority communities.¹⁴⁰

Mistrust in the process leading to the commercialization of COVID-19 vaccines – both in the clinical trials and in FDA review of clinical trial data, as explained in Part II.B – led to the announcement that several entities which do not play a role in drug regulation in the United States were forming task forces or panels to perform ad hoc reviews of any COVID-19 vaccines authorized or approved by the FDA.¹⁴¹

Responding to concerns about both minority under-representation and FDA review of COVID-19 vaccines, the National Medical Association (NMA) announced the creation of a task force composed of Black doctors to review COVID-19 vaccines and drugs.¹⁴² The National Medical Association is a professional and scientific organization founded in 1895 to respond to problems posed by Jim Crow laws and other mechanisms of racial segregation leading to the disenfranchisement of Black Americans.¹⁴³ It began “representing African American physicians and health professionals in the United States” at a time in which the membership in the American

https://journals.lww.com/jphmp/Abstract/2011/01000/Pandemics_and_Health_Equity___Lessons_Learned_From.4.aspx

¹³⁷ See e.g. Samantha Artiga et al., *Racial Disparities in Flu Vaccination: Implications for COVID-19 Vaccination Efforts*, KFF (Sept. 15, 2020), <https://www.kff.org/policy-watch/racial-disparities-flu-vaccination-implications-covid-19-vaccination-efforts/>

¹³⁸ See CTRS. DISEASE CONTROL & PREVENTION, *Flu Vaccination Coverage, United States, 2019–20 Influenza Season* (2020), <https://www.cdc.gov/flu/fluview/coverage-1920estimates.htm> (providing vaccination data on the most recent influenza season).

¹³⁹ Artiga et al, *supra* note 137.

¹⁴⁰ *Id.*, *ib.* See also Washington, *Medical Apartheid*, *supra* note 58; Brandt, *Racism and Research*, *supra* note 58.

¹⁴¹ See Eric Broodman, *Not Trusting the FDA, Black Doctors’ Group Creates Panel to Vet Covid-19 Vaccines*, STAT (Sept. 21, 2020), <https://www.statnews.com/2020/09/21/black-doctors-group-creates-panel-to-vet-covid19-vaccines/>

¹⁴² NAT’L MED. ASS’N, NMA FORMS COVID-19 TASK FORCE TO TAKE THE POLITICS OUT OF VACCINE DEVELOPMENT (Sept. 21, 2020) [hereinafter NMA Announcement], <https://www.nmanet.org/news/527978/NMA-Forms-COVID-19-Task-Force-Take-the-Politics-Out-of-Vaccine-Development.htm>

¹⁴³ NAT’L MED. ASS’N, ABOUT US, https://www.nmanet.org/page/About_Us

Medical Association was denied to non-White physicians,¹⁴⁴ and today it has over 30,000 members.¹⁴⁵ In August 2020, the NMA approved a resolution to create a COVID-19 taskforce, which included doctors affiliated with federal public health institutions at the core of the response to COVID-19, like the Centers for Disease Control and Prevention (CDC), the vaccine advisory group responsible for federal vaccination recommendations (the Advisory Committee on Immunization Practices, or ACIP), as well as representatives of medical professional organizations, such as the Infectious Disease Society of America and the Pediatric Infectious Disease Society.¹⁴⁶ The task force was charged with helping “address questions and concerns about efficacy, safety, and allocation of COVID-19 vaccines and therapeutics.”¹⁴⁷ The NMA specifically framed the formation of the task force as prompted by concerns that diminishing “public trust in the FDA that will adversely affect participation in clinical trials, especially in the African-American community.”¹⁴⁸

The NMA’s taskforce was not the only case in which players normally extraneous to the FDA’s drug and vaccine review process announced interventions designed to act as a check on FDA review of COVID-19 clinical trial data. In late September 2020, citing politicization of the review of COVID-19 vaccine clinical trial data, the governor of New York announced that the state would independently review any COVID-19 vaccines approved by the FDA before allowing them to be distributed across the state.¹⁴⁹ In October 2020, the governor of California announced the formation of the California COVID-19 Scientific Safety Review Workgroup, formed by “California physician scientists” to “independently review the safety and efficacy of any vaccine that receives FDA approval for distribution.”¹⁵⁰ And in October 2020, the states of Washington,

¹⁴⁴ *Id.*, HISTORY, <https://www.nmanet.org/page/History>

¹⁴⁵ *Id.*, ABOUT US, *supra* note 143.

¹⁴⁶ NMA Announcement, *supra* note 142.

¹⁴⁷ *Id.*, *ib.*

¹⁴⁸ *Id.*, *ib.*

¹⁴⁹ Michael Gold & Jesse McKinkley, *New York Will Review Virus Vaccines, Citing Politicization of Process*, N.Y. TIMES (Sept. 24, 2020), <https://www.nytimes.com/2020/09/24/nyregion/new-york-coronavirus-vaccine.html>

¹⁵⁰ See CA. DPT. PUB. HEALTH, *Scientific Safety Review Workgroup*, <https://www.cdph.ca.gov/Programs/CID/DCDC/Pages/COVID-19/Scientific-Safety-Review-Workgroup.aspx>; CAL. OFF. GOV., *Governor Newsom Names Scientific Safety Review Workgroup to Advise State on COVID-19 Vaccines* (Oct. 19, 2020), <https://www.gov.ca.gov/2020/10/19/governor-newsom-names-scientific-safety-review-workgroup-to-advise-state-on-covid-19-vaccines/>

Oregon and Nevada joined California's Review Workgroup.¹⁵¹ Although the Review Workgroup eventually endorsed the COVID-19 vaccine sponsored by Pfizer/BioNTech to which the FDA granted the first vaccine emergency use authorization,¹⁵² the formation of multiple state-level bodies charged with reviewing FDA vaccine authorizations speaks to the overall trust deficit currently experienced in the United States in connection with vaccine clinical trials – at least within the context of accelerated data production and regulatory review of vaccines as a major public health crisis unfolds.

It is possible, indeed probable, that some of the factors that contributed to distrust of emerging COVID-19 vaccines are specific to the ways in which the federal response to the pandemic preparedness and response was perceived as defective by the general public and abundantly criticized by public health experts.¹⁵³ As such, some of the events that colored public perceptions of COVID-19 vaccines are likely to remain idiosyncratic to the current pandemic. Yet, vaccine trust deficits have long been partly rooted in public perceptions of how vaccine clinical trial data is generated and assessed. In addition to affecting the scientific and regulatory processes, longstanding holes in the vaccine data infrastructure resulting from under-collection of information relative to minority populations pose challenges to vaccine trust that have long characterized vaccine R&D and that – absent more forceful corrective interventions – will persist beyond the COVID-19 pandemic.

B. DATA SHARING: ENABLING SCRUTINY AND FOLLOW-ON INNOVATION

Even if imperfectly collected, data generated during vaccine clinical trials provides valuable clues not only to regulatory entities exercising their gatekeeping functions, but also to the

¹⁵¹ CAL. OFF. GOV., *Western States Join California's Scientific Safety Review Workgroup to Ensure Safety of COVID-19 Vaccine* (Oct. 27, 2020), <https://www.gov.ca.gov/2020/10/27/western-states-join-californias-scientific-safety-review-workgroup-to-ensure-safety-of-covid-19-vaccine/>

¹⁵² CAL. OFF. GOV., *Summary of Findings* (Dec. 12, 2020), <https://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/COVID-19/Scientific-Safety-Review-Workgroup-Recommendations-December-2020.pdf>

¹⁵³ See e.g. Drew Altman, *Understanding the US Failure on Coronavirus*, 370 BRIT. MED J. m3417 (2020), <https://www.bmj.com/content/370/bmj.m3417>; Eric C. Schneider, *Failing the Test — The Tragic Data Gap Undermining the U.S. Pandemic Response*, 383 N. ENGL. J. MED. 299 (2020), <https://www.nejm.org/doi/full/10.1056/nejmp2014836>

scientific community and, ultimately, the public at large.¹⁵⁴ However, not all data collected during vaccine clinical trials can be scrutinized or used for follow-on research endeavors. On the one hand, there has long been evidence of significant under-reporting of data gathered during vaccine clinical trials.¹⁵⁵ On the other, data that is disclosed in a specific context may be treated as secret or proprietary vis-à-vis third parties – the most common scenario involving clinical trial data disclosed to a regulatory agency in connection with an application to market a new vaccine.¹⁵⁶ Together, these two types of restrictions have combined to erect significant hurdles to the free flow of data and scientific knowledge about newly developed vaccines.

As far as the reporting and publication of vaccine clinical trial data is concerned, law and practice have long been poorly aligned. As seen above, the Declaration of Helsinki established that medical researchers had a duty to make the results of studies involving human subjects publicly available.¹⁵⁷ Yet, studies have repeatedly found that the results of vaccine clinical trials are routinely published after a considerable delay, and in many cases are not published at all.¹⁵⁸ These two phenomena have been documented in both the case of vaccines developed when a pandemic compresses vaccine development and testing timelines and outside the context of pandemics or other highly disruptive public health crises.¹⁵⁹

The case of vaccine clinical trial data generated during the 2009 H1N1 swine flu pandemic is instructive. These vaccines developed in a timeline that was even more compressed than the

¹⁵⁴ See *infra* note 93 and accompanying text.

¹⁵⁵ See *infra* notes 160-171 and accompanying text.

¹⁵⁶ See *infra* note 178 and accompanying text.

¹⁵⁷ Declaration of Helsinki, *supra* note 71.

¹⁵⁸ See Lamberto Manzoli et al., *Non-Publication and Delayed Publication of Randomized Trials on Vaccines: Survey*, 348 BRIT. MED. J. 3058 (2014), <https://www.bmj.com/content/348/bmj.g3058> (reporting publication delays and lack of publication of clinical trial data for vaccines developed both during and outside the context of a pandemic); Christopher W. Jones & Timothy F. Platts-Mills, *Delayed Publication of Vaccine Trials*, 348 BRIT. MED. J. 3259 (2014), <https://www.bmj.com/content/348/bmj.g3259> (similarly addressing both contexts); John P. A. Ioannidis et al., *Publication Delay of Randomized Trials on 2009 Influenza A (H1N1) Vaccination*, 6 PLOS ONE e28346 (2011), <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0028346> (presenting a case study focused solely on data from trials for H1N1 vaccines, which took place in response to the 2009 swine flu pandemic). Studies have also found that not all clinical trials are registered. See e.g. Scott M. Lassman, *Clinical Trial Transparency: A Reassessment of Industry Compliance with Clinical Trial Registration And Reporting Requirements in the United States*, 7 BRIT. MED. J. OPEN e015110 (2017), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5623439/>; Jennifer Miller et al., *Sharing of Clinical Trial Data and Results Reporting Practices Among Large Pharmaceutical Companies: Cross Sectional Descriptive Study and Pilot of a Tool to Improve Company Practices*, 366 BRIT. MED. J. 14217 (2019), <https://www.bmj.com/content/366/bmj.14217>

¹⁵⁹ See *infra* note 160 and accompanying text.

timeline for the first COVID-19 vaccines: the strain of influenza that caused the 2009 pandemic was identified in April and the FDA approved four H1N1 vaccines in September of the same year.¹⁶⁰ Yet publication of clinical trial data lagged considerably: of the 73 vaccine trials that took place between 2009 and 2010, only 21 had published data by June 2011, almost two years after FDA approval of the vaccines.¹⁶¹ This represents less than a third (29%) of the trial universe for vaccine candidates developed and tested in a situation of heightened public health need.¹⁶² The results of most H1N1 vaccine clinical trials remained unpublished.¹⁶³

The same is true outside the context of pandemics.¹⁶⁴ A study conducted by Lamberto Manzoli and colleagues surveyed 384 randomized vaccine clinical trials enrolling over 404,758 participants.¹⁶⁵ In addition to surveying H1N1 vaccine clinical trials, this study also included vaccines developed and tested outside pandemic contexts: human papillomavirus, meningococcal, pneumococcal, and rotavirus vaccines.¹⁶⁶ The study found that, on average, only half of vaccine clinical trials were published after a median of 26 months from completion of the trial.¹⁶⁷ Publication was defined as cases in which “one or more of the main outcomes appeared in a peer reviewed journal, either online or in print.”¹⁶⁸ Almost two-thirds of the data relative to participants in randomized vaccine clinical trials was not published in peer-reviewed literature.¹⁶⁹

¹⁶⁰ See Jones & Platts-Mills, *Delayed Publication of Vaccine Trials*, *supra* note 158; Robert Roos, *FDA Approves Four Companies' H1N1 Vaccines*, CIDRAP (Sept. 15, 2009), <https://www.cidrap.umn.edu/news-perspective/2009/09/fda-approves-four-companies-h1n1-vaccines>

¹⁶¹ Ioannidis., *Publication Delay of Randomized Trials on 2009 Influenza A (H1N1) Vaccination*, *supra* note 158; Manzoli, *supra* note 165.

¹⁶² Ioannidis, *ib.*

¹⁶³ *Id.*, *ib.*

¹⁶⁴ Manzoli, *supra* note 158.

¹⁶⁵ *Id.*, *ib.*

¹⁶⁶ *Id.*, *ib.*

¹⁶⁷ *Id.*, *ib.*

¹⁶⁸ *Id.*, *ib.*

¹⁶⁹ *Id.*, *ib.* Some of the trials not published in peer-review publications shared results through the national registry of clinical trials, ClinicalTrials.gov. See *supra* note 75 and accompanying text. The combined percentage of vaccine clinical trials publishing in peer-review and ClinicalTrials.gov was 61%. *Id.*, *ib.* Studies in non-vaccine domains have similarly found that a significant percentage of clinical trials remains unpublished. See e.g. Joseph S. Ross, *Publication of NIH Funded Trials Registered in Clinicaltrials.Gov: Cross Sectional Analysis*, 344 BRIT. MED. J. 7292 (2012) (finding that a third of registered NIH-funded trials are still unpublished after a median of 51 months following trial completion).

Delayed publication and lack of publication of vaccine clinical trial data produces detrimental effects that extend beyond the context of follow-on research.¹⁷⁰ As Kay Dickersin and Drummond Rennie noted in a 2003 study evaluating the implementation of the clinical trial registration requirements introduced by the 1997 Food and Drug Administration Modernization Act: “if the knowledge gained [through clinical trials] is never reported, the trust between patients and investigators and that between patients and research ethics review boards are both damaged.”¹⁷¹

In addition to these problems, segments of the vaccine data infrastructure often remain inaccessible to many players in the vaccine innovation ecosystem – from researcher to follow-on innovators in biopharma to activists in the health space – for relatively long periods of time. These cases encompass situations in which data collected during vaccine clinical trials has been reported and submitted for independent review, but is not made available outside the regulatory context.¹⁷²

Sponsors of drugs and vaccines are required to submit data to regulatory agencies across the world in standardized ways in the form of clinical study reports (CSR).¹⁷³ These reports tend to contain more data than what is disclosed through other channels, such as publication in peer-review literature.¹⁷⁴ However, not all the information contained in the clinical study reports submitted by drug and vaccine sponsors to regulatory entities is made publicly available.¹⁷⁵ As further detailed in Part III, the European drug regulator has in recent years taken steps to promote

¹⁷⁰ See e.g. Trudo Lemmens & Candice Telfer, *Access to Information and the Right to Health: The Human Rights Case for Clinical Trials Transparency*, 38 AM. J. L. & MED. 63 (2012) (making the case for greater clinical trial data registration and reporting from a human rights perspective).

¹⁷¹ Kay Dickersin & Drummond Rennie, *Registering Clinical Trials*, 290 J. AM. MED. ASS’N. 516 (2003), <https://pubmed.ncbi.nlm.nih.gov/12876095/>

¹⁷² See *infra* notes 178-183 and accompanying text.

¹⁷³ U.S. FOOD & DRUG ADMIN., *E3 Structure and Content of Clinical Study Reports* (1996), <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/e3-structure-and-content-clinical-study-reports>; 61 Fed. Reg. 37,320 (July 17, 1996) (providing context on FDA guidance on clinical study reports issued in accordance with the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use). See also Beate Wieseler et al., *Impact of Document Type on Reporting Quality of Clinical Drug Trials: A Comparison of Registry Reports, Clinical Study Reports, and Journal Publications*, 344 BRIT. MED. J. D8141 (2012), <https://pubmed.ncbi.nlm.nih.gov/22214759/>; Tom Jefferson et al., *When to Include Clinical Study Reports and Regulatory Documents in Systematic Reviews*, 23 BRIT. MED. J. EVID. BASED MED 210 (2018), <https://pubmed.ncbi.nlm.nih.gov/30309870/>

¹⁷⁴ Ho, *Avoiding the TRIPS Trap*, *supra* note 93, at 17.

¹⁷⁵ See e.g. Hilda Bastian, *What the systematic review of HPV vaccine clinical study reports does, and does not, reveal: commentary on Jørgensen et al.*, 7 SYST. REV. 117 (2018), <https://pubmed.ncbi.nlm.nih.gov/32106882/> (exploring this problem in the context of vaccine clinical study reports).

the disclosure of both CSR data and information often not contained in clinical study reports, as is the case of individual patient data.¹⁷⁶

In the United States, The FDA has long treated most of the data submitted by sponsors – including vaccine data – as proprietary or quasi-proprietary, either by virtue of existing legal frameworks regulating trade secrecy and other types of confidential information, as well as FDA’s expansive approach to the concept of protected data.¹⁷⁷

Data submitted to the FDA that qualifies as a trade secret cannot be disclosed by the agency.¹⁷⁸ The law defines a trade secret as “any commercially valuable plan, formula, process, or device that is used for the making, preparing, compounding, or processing of trade commodities and that can be said to be the end product of either innovation or substantial effort.”¹⁷⁹ Disclosure of data protected as a trade secret by an officer or employee of the FDA is punishable by a fine and removal from office or employment, and may result in imprisonment for up to a year.¹⁸⁰

The prohibition on disclosure extends to commercial and financial information deemed “privileged or confidential,” which the law defines as “valuable data or information which is used in one's business and is of a type customarily held in strict confidence or regarded as privileged and not disclosed to any member of the public by the person to whom it belongs.”¹⁸¹

Data generated during clinical trials has long been treated by the FDA as proprietary information, and specifically as a trade secret. The Food, Drug and Cosmetic Act (FDCA) in § 331(j) prevents the FDA from disclosing “any method or process” that qualifies as a trade secret.¹⁸² In regulations issued in the 1970s, the Agency determined that “safety and effectiveness data for new drugs (...) fall within the trade secrets exemption and thus are not available for public disclosure,” a position it has maintained ever since.¹⁸³

¹⁷⁶ Ho, *Avoiding the TRIPS Trap*, *supra* note 93, at 18. See also Anna L. Davis & James Dabney Miller, *The European Medicines Agency and Publication of Clinical Study Reports: A Challenge for the US FDA*, 317 J. AM. MED. ASS’N. 905 (2017), <https://pubmed.ncbi.nlm.nih.gov/28241281/#affiliation-1>

¹⁷⁷ But see Peter Doshi, *FDA to Begin Releasing Clinical Study Reports in Pilot Programme*, 360 BRIT. MED. J. k294, (2018), <https://pubmed.ncbi.nlm.nih.gov/29363507/>.

¹⁷⁸ 21 C.F.R. § 20.61 (c).

¹⁷⁹ 21 C.F.R. § 20.61 (a).

¹⁸⁰ 18 U.S.C. § 1905.

¹⁸¹ 21 C.F.R. § 20.61 (b)(c).

¹⁸² 21 U.S.C. § 331(j).

¹⁸³ 39 Fed. Reg. 44,602, 44,633. See also 42 Fed. Reg. 3,094.

Several legal commentators, however, have disagreed with FDA's interpretation of § 331(j) in the FDCA. Rebecca Eisenberg has made the case that "it is by no means obvious from the statutory language that 'any method or process which as a trade secret is entitled to protection' includes data from clinical trials."¹⁸⁴ Christine Galbraith has noted that some of the defining characteristics of clinical trials make them a poor fit for trade secrecy frameworks: "A fundamental tenet of trade secret law is that protection exists only as long as the information is kept confidential. The very nature of a clinical trial is quite public in many respects, making maintenance of complete secrecy fairly difficult."¹⁸⁵ And Arti Rai has argued that the passage of the Hatch-Waxman Act in 1984 further eroded FDA's policy stance on clinical trial data by setting up a pathway for the approval of generic drugs that allows for FDA disclosure of data to follow-on innovators or the public in general, as long as the period of regulatory exclusivities attached to the reference drug has expired.¹⁸⁶

In addition to the ongoing debate about FDA's interpretation of the legal status of data submitted by drug and vaccine sponsors seeking market authorization, the mere existence of a filing of an investigational new drug application (IND) for a biologic – the regulatory category vaccines belong to – cannot be disclosed or acknowledged by the FDA.¹⁸⁷ And even in the cases of information disclosed by sponsors as part of a submission to clinical trial registries, that information is not standardized, effectively allowing companies to often provide vague information.¹⁸⁸

While the FDA announced some changes in connection with the authorization and approval of COVID-19 drugs and vaccines,¹⁸⁹ a report issued by the Government Accountability Office in

¹⁸⁴ Rebecca S. Eisenberg, *The Role of the FDA in Innovation Policy*, 13 MICH. TELECOMM. & TECH. L. REV. 345, 380 (2007) (also acknowledging that "the longstanding administrative practice would make it difficult to adopt a narrower reading of the provision at this point") *Id.*, *ib.*

¹⁸⁵ Christine Galbraith, *Dying to Know: A Demand for Genuine Public Access to Clinical Trial Results Data*, 78 MISS. L. J. 705, 753 (2009).

¹⁸⁶ Arti K. Rai, *Risk Regulation and Innovation: The Case of Rights-Encumbered Biomedical Data Silos*, 92 NOTRE DAME L. REV. 1645, 1656-57 (2017). See also 21 U.S.C. § 355(l)(1), (1)(E) (2012).

¹⁸⁷ 21 C.F.R. § 601.50 (a). See also *id.* 601.50 (c) (carving out an exception for individuals who have experienced an adverse effect in connection with administration of the biologic covered by an investigational new drug application).

¹⁸⁸ See Debora Zarin et al., *Issues in the Registration of Clinical Trials*, 297 J. AM. MED. ASS'N. 2112 (2007), <https://pubmed.ncbi.nlm.nih.gov/17507347/>. See also Miller, *supra* note 158 (further describing transparency issues in the reporting of clinical trial data).

¹⁸⁹ See e.g. U.S. FOOD & DRUG ADMIN., *COVID-19 Update: FDA's Ongoing Commitment to Transparency for COVID-19 EUAs* (Nov. 17, 2020), <https://www.fda.gov/news-events/press-announcements/covid-19-update-fdas-ongoing-commitment-transparency-covid-19-euas>

November 2020 found that, at least in the case of COVID-19 therapeutic products, FDA had not always been transparent in disclosing data supporting emergency authorizations for non-vaccine products, “because the agency has not uniformly disclosed information from its scientific review of the safety and effectiveness data at the time of each authorization.”¹⁹⁰ Similarly, some problems related to timely disclosure of information or data were reported in connection with COVID-19 vaccine clinical trials.¹⁹¹ For example, Pfizer – the first vaccine sponsor to receive an emergency use authorization in the United States – delayed the release of the amended vaccine clinical trial protocol.¹⁹² And another pharmaceutical company, AstraZeneca, was criticized for being too slow to share negative results from its COVID-19 vaccine candidate clinical trials.¹⁹³

Recently, other jurisdictions have adopted measures designed to increase transparency and access to both clinical trial data and other types of information relative to new drugs and vaccines.¹⁹⁴ The Essay now surveys an example of a data policy adopted during the COVID-19 pandemic by one of these jurisdictions as a blueprint for implementing measures that help mitigate some of the problems – albeit only on the data disclosure side – of the vaccine data infrastructure.

III. TOWARDS A RICHER VACCINE CLINICAL TRIAL DATA INFRASTRUCTURE

So far, the Essay has highlighted some of the most salient and longstanding problems affecting the vaccine clinical trial data infrastructure. It has also surveyed some of the legislative efforts adopted from the mid-twentieth century onwards to improve the ways in which vaccine clinical trial data is both collected and shared. The shortcomings of current frameworks, however, indicate that further action continues to be necessary on these two fronts.

¹⁹⁰ GAO Report, *supra* note 133, at 20.

¹⁹¹ See Jennifer E. Miller et al., *Far More Transparency is Needed for Covid-19 Vaccine Trials*, STAT (Nov. 5, 2020), <https://www.statnews.com/2020/11/05/transparency-is-needed-for-covid-19-vaccine-trials/>

¹⁹² *Id.*, *ib.*

¹⁹³ *Id.*, *ib.*

¹⁹⁴ See e.g. Cynthia M. Ho, *Avoiding the TRIPS Trap*, *supra* note 93, at 5. See also EUR. MED. AGENCY, *European Medicines Agency Policy on Publication of Clinical Data for Medicinal Products for human Use*, Policy 70, EMA/144064/2019 (Mar. 21, 2019), https://www.ema.europa.eu/en/documents/other/european-medicines-agency-policy-publication-clinical-data-medicinal-products-human-use_en.pdf; Health Canada, *Public Release of Clinical Data- Guidance Document* (Mar.12, 2019), <https://www.canada.ca/en/health-canada/services/drug-health-product-review-approval/profile-public-release-clinical-information-guidance/document.html>

Many of the interventions required to address the systemic problems explored throughout the Essay will necessarily have to occur on prolonged timelines, and require concerted efforts from different players in the vaccine development and deployment ecosystem. For example, addressing overall under-representation issues in vaccine clinical trials implies tackling intertwined yet fundamentally different problems, from logistical hurdles ranging from transportation and childcare arrangements, to existing implicit biases against racial and ethnic minority patients held by a majority of healthcare providers,¹⁹⁵ just to name a few areas. Moreover, efforts to improve representation of racial and ethnic minorities in vaccine clinical trials cannot be detached from efforts needed in connection with under-representation of minorities in clinical trials involving other medical products.

But while improving vaccine clinical trial data collection and sharing remains a long-term, multi-prong proposition, there are some more immediate fixes available to regulators and policymakers that would progressively enrich the vaccine clinical data infrastructure. As the COVID-19 pandemic exposed some of the holes in this infrastructure, it also provided the impetus for institutional players like the European Medicines Agency (EMA) and the FDA to respond to ongoing vaccine data-related problems, particularly with regard to the disclosure of clinical trial data.

Following years of criticism for lack of transparency of its clinical trial data sharing policy,¹⁹⁶ the EMA started publishing clinical trial data submitted by drug and vaccine sponsors in 2016 as part of an effort to render the regulatory review process more transparent.¹⁹⁷ The amount of information made publicly available by the Agency according to this new policy vastly surpassed its previous practices, as well as the standard at the FDA.¹⁹⁸ For each drug or vaccine application, the new policy mandated the disclosure of the clinical overview of the product, the

¹⁹⁵ See e.g. William J. Hall et al., *Implicit Racial/Ethnic Bias Among Health Care Professionals and Its Influence on Health Care Outcomes: A Systematic Review*, 105 Am. J. Pub. Health e60 (2015), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4638275/> (finding that “[m]ost health care providers appear to have implicit bias in terms of positive attitudes toward Whites and negative attitudes toward people of color”).

¹⁹⁶ See e.g. Tracy Hampton, *European Drug Agency Under Fire: Critics Charge That Trial Data Are Too Inaccessible*, 306 J. AM. MED. ASS’N. 593, (2011), <https://pubmed.ncbi.nlm.nih.gov/21828315/>

¹⁹⁷ See EUR. MED. AGENCY, *Clinical Data Publication*, <https://www.ema.europa.eu/en/human-regulatory/marketing-authorisation/clinical-data-publication>. See also ID., *External Guidance on the Implementation of the European Medicines Agency Policy on the Publication of Clinical Data for Medicinal Products for Human Use* (2018), <https://www.ema.europa.eu/en/human-regulatory/marketing-authorisation/clinical-data-publication>.

¹⁹⁸ See Davis & Miller, *supra* note 176.

clinical summary, study reports associated with individual clinical studies, the study protocol, the sample case report form used to record information on an individual patient, and information on the statistical methods employed to evaluate the data collected during clinical trials.¹⁹⁹

Nevertheless, the EMA suspended this new data disclosure policy in December 2018, shortly before relocating from London to Amsterdam in the wake of the Brexit vote.²⁰⁰ While the Agency committed to reinstating the policy after the move was completed, it announced a delay in 2020 citing the onset of the COVID-19 pandemic as the cause.²⁰¹ As of January 2021 the policy remains suspended.²⁰² However, during the early stages of the COVID-19 pandemic there were repeated calls for the Agency to share more information about clinical trial data submitted in connection with applications for COVID-19 drugs and vaccines.²⁰³ In response, in May 2020 the EMA announced the adoption of an *ad hoc* data policy for COVID-19 products, including vaccines.²⁰⁴ The *ad hoc* policy not only restored the publication of clinical trial data for approved COVID-19 products, but also the expedited and increased disclosure of other types of information about experimental and approved COVID-19 products.²⁰⁵ For example, the additional information now made available for COVID-19 products includes the expedited publication of product

¹⁹⁹ EUR. MED. AGENCY, *Clinical Data Publication*, *supra* note 197. See also EUR. MED. AGENCY, *Common Technical Document for the Registration of Pharmaceuticals for Human Use: Organisation Of Common Technical Document* (2004), https://www.ema.europa.eu/en/documents/scientific-guideline/ich-m-4-common-technical-document-registration-pharmaceuticals-human-use-organisation-ctd-step-5_en.pdf (describing the content of each one of these types of documents).

²⁰⁰ EUR. MED. AGENCY, *Clinical Data Publication*, *supra* note 197. See also ID., *Relocation to Amsterdam*, <https://www.ema.europa.eu/en/about-us/history-ema/relocation-amsterdam>. See also Zachary Brennan, *Brexit Impact: EMA Suspends Publication of Clinical Trial Data*, RAPS (Aug. 15, 2018), <https://www.raps.org/news-and-articles/news-articles/2018/8/brexit-impact-ema-suspends-publication-of-clinica>

²⁰¹ EUR. MED. AGENCY, *Clinical Data Publication*, *supra* note 197 (noting that, as of January 2021, the clinical trial data sharing policy “remains suspended due to ongoing business continuity linked to the COVID-19 pandemic”).

²⁰² *Id.*, *ib.*

²⁰³ See e.g. IQWiG, *Open Letter to the European Medicines Agency* (May 14, 2020), <https://www.iqwig.de/en/press/press-releases/all-clinical-trial-data-on-covid-19-medicines-and-vaccines-should-be-published-on-the-day-of-marketing-authorisation.13015.html> (providing the letter submitted to the EMA by the Institute for Quality and Efficiency in Healthcare, an independent drug and medical device review organization created in Germany in 2004). See IQWiG, *Legal foundations of IQWiG*, <https://www.iqwig.de/en/about-us/responsibilities-and-objectives-of-iqwig/legal-foundations-of-iqwig.2952.html>

²⁰⁴ See EUR. MED. AGENCY, *European Medicines Agency Response to IQWiG on Transparency of COVID-19 Related Activities*, https://www.ema.europa.eu/en/documents/other/european-medicines-agency-response-iqwig-transparency-covid-19-related-activities_en.pdf

²⁰⁵ ID., *Transparency: Exceptional Measures for COVID-19 Medicines*, <https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/treatments-vaccines/transparency-exceptional-measures-covid-19-medicines>

applications and assessment reports, as well as the disclosure of information that the EMA does not typically share under its standard policy, such as the publication of the full body of the risk management plan for a given product instead of the publication of only the summary of the plan, as was usual under its standard data policy.²⁰⁶ In the specific case of vaccines, the EMA began publishing monthly safety updates for approved COVID-19 vaccines, something it does not do with other types of vaccines under the standard data policy.²⁰⁷ Moreover, the Agency is also releasing additional safety information about vaccines on an *ad hoc* basis.²⁰⁸

The following chart summarizes some of the main changes between the standard policy and the COVID-19 ad hoc policy adopted by the EMA.

	Standard Policy	Policy for COVID-19 Products
Scientific advice	No information is published	Publication of list of products that have received scientific advice or guidance
Marketing authorization applications	Active substance and therapeutic area disclosed on monthly list ²⁰⁹	Announcement of application published within one day
Product information	Published in all E.U. languages with the product assessment report ²¹⁰	English version published within one day of favorable opinion from Committee for Medicinal Products for Human Use
Publication of European Public Assessment Report (EPAR)	Not published until at least two weeks after marketing authorization is issued	Published within three days of marketing authorization
Updates to EPAR	Updates published	Updates expedited for “major” changes
Risk Management Plan (RMP)	Summary of RMP published	Full body of RMP published
Clinical trial data	Publication suspended; set to resume after COVID-19 pandemic	Clinical trial data published after marketing authorization is issued. Additional trial data published if “major” changes occur

²⁰⁶ *Id.*, *ib.*

²⁰⁷ *Id.*, *ib.*

²⁰⁸ *Id.*, *ib.*

²⁰⁹ *Id.*, *Medicines Under Evaluation*, <https://www.ema.europa.eu/en/medicines/medicines-under-evaluation> (providing the monthly list of medicines under evaluation by the EMA).

²¹⁰ *Id.*, *European Public Assessment Reports: Background and Context*, <https://www.ema.europa.eu/en/medicines/what-we-publish-when/european-public-assessment-reports-background-context>

Application for extension of indication	Information not published	Announcement of application published within one day
Monthly safety updates for vaccines	Information not published	Published monthly for approved COVID-19 vaccines. Additional information provided on ad hoc basis

Figure 2: EMA's Standard Data Policy Versus COVID-19 Data Policy²¹¹

The quick adoption of the COVID-19 ad hoc data policy by the EMA shows how regulators can be more responsive to informational and transparency deficits in the vaccine data infrastructure – and to similar deficits affecting other types of medical products. This responsiveness is especially critical in the case of emerging vaccines. As seen in Part I.B, one of the most significant features of the COVID-19 vaccine race is that, unlike R&D focused on other COVID-19 medical products, it relies on a form of technology that, although studied for over a decade, is essentially new.²¹² Cutting-edge science, follow-on improvements and perceptions of medical products resulting from these scientific processes are all predicated on a robust and transparent flow of information and data. Moving forward, the data policy adopted by the EMA for COVID-19 products can and should be regarded as a starting point towards the building of a richer and more transparent data infrastructure.

To be sure, the steps taken by the EMA to increase data disclosure during the pandemic happened on the heels of a policy reversal that greatly decreased the amount of information available about drugs, vaccines and other medical products outside the COVID-19 space.²¹³ Although this reversal is meant to be temporary, it also calls attention to the difficulties regulators face in broadening the disclosure of clinical trial data and other types of drug- and vaccine-related information. While EMA's policy reversal appears to have been at least partly rooted in its adjustment to Brexit, there are hurdles that are more generalizable to drug regulators across the world. As Cynthia Ho has recently pointed out, efforts to increase data disclosure by national regulatory agencies often bring data-related debates into the realm of intellectual property

²¹¹ Adapted from ID., *Transparency: Exceptional Measures for COVID-19 Medicines*, *supra* note 205 (Jan. 5, 2020 version).

²¹² *Infra* notes 85-89 and accompanying text.

²¹³ See *supra* note 200 and accompanying text.

negotiations, which in turn fall back on trade law channels to resolve international disputes, thus complicating the political economy of this area.²¹⁴

Finally, it is important to note that the solution surveyed here addresses only one subset of problems in the vaccine data infrastructure. On their own, efforts to improve disclosure frameworks leave data generation, collection and publication problems untouched. This Essay has highlighted a range of shortcomings in the vaccine data infrastructure as it relates to the production of data about new vaccines, and concludes by pointing towards an existing example of the implementation of measures that addresses one of these shortcomings. Amidst the pressures posed by the pandemic on the scientific and regulatory communities, the adoption of the COVID-19 data policy at the EMA shows a path forward. Many other improvements are still necessary in the area of data disclosure alone, beginning with the adoption of more permanent data policies in Europe and, hopefully, beyond.

²¹⁴ See Ho, *supra* note 93, at 2-3.