

**The Big Data Regulator, Rebooted:
Why and How the FDA Can and Should Disclose Confidential Data on Prescription Drugs**

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Abstract:

Medicines are complex products, and it is often extraordinarily difficult to know whether they cure or kill. The FDA holds an enormous reservoir of data on these medicines, data that sheds light on that precise question, and yet the agency currently discloses only a trickle to researchers, doctors, patients, and the public at large. This paper explains why and how the FDA can and should “reboot” its disclosure rules to disclose much more data on safety and efficacy of prescription drugs, to protect patients, advance science, and safeguard democracy. Though the need for this data is clearer than ever, last Term a Supreme Court case threatened the viability of one existing tool through which independent researchers have historically obtained clinical data from the FDA: Freedom of Information Act (FOIA) requests. We present a wealth of new evidence about the urgency of the problem together with a novel argument for proactive data disclosure—what we term “data publicity”—that can be achieved without any legislative reform. We provide a roadmap to data publicity that navigates the two main challenges to data sharing: protecting the privacy of individuals who participate in trials and defeating the claims that companies make that this data is and should remain confidential. Along the way, we show that trade secrecy law does not create an impossible barrier to disclosure, contrary to the view of the pharmaceutical industry. Our analysis illuminates a broader problem that is woven through the regulatory state in our information age: corporations urge us to buy their products and services because they are technologically innovative, yet increasingly they hide the inner workings of those technologies from us. The model we offer here could, we suggest, become a template for other regulatory agencies to permit meaningful democratic oversight of industry and revitalize the agencies themselves in an age of information capitalism.

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Introduction

Few issues are more important to us than the quality and safety of our medicines. At any given moment, about half of America is taking a prescription drug,¹ and medicines represent a startling 2% of total US GDP each year.² But there is a structural problem at the heart of our system for the development and assessment of medicines – a problem of secrecy in the age of big data.

Medicines are complex products, and it is often extraordinarily difficult to know whether they hurt or help. This can often only be known after clinical trials, whose conduct and interpretation are highly complex. These trials are today typically (particular at later stages) conducted by companies with extraordinarily strong financial interests in the outcomes of the trials.³ This, of course, is a key justification for our drug regulatory system: independent experts who have the public's interest at heart are needed to examine and validate data about the effects of medicines.⁴ But our drug regulatory bodies are under-resourced, and recent examples show that outside expert analysis can shed extraordinarily important insights into concealed risks of medicines.

The painkiller Vioxx, promoted as safer than aspirin, offers a stark case. The drug was a blockbuster, earning \$2 billion each year for Merck, before being abruptly removed from the market because it caused heart attacks, strokes, and heart failure.⁵ The evidence only became known to outside experts through litigation. Later independent research showed that signals of the risks of the drug were present in the data 3½ years before the drug was withdrawn from the market.⁶ But that evidence did not reach doctors or patients because the data was not consistently published or made available to the scientific community.⁷ It is estimated that tens of thousands of people died as a result.⁸

¹ Shelly Hagan, *Nearly One in Two Americans Takes Prescription Drugs: Survey*, BLOOMBERG (May 8, 2019), <https://www.bloomberg.com/news/articles/2019-05-08/nearly-one-in-two-americans-takes-prescription-drugs-survey>

² *National Health Expenditures 2017 Highlights*, CMS, <https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/Downloads/highlights.pdf> (last visited Jan. 25, 2020).

³ Applied Clinical Trials Editors, *Sizing Up the Clinical Research Market*, APPLIED CLINICAL TRIALS (Mar. 1, 2010), <http://www.appliedclinicaltrials.com/print/213683?page=full> (estimating that industry funds approximately 90% of the clinical trials conducted for investigational drugs and devices).

⁴ Amy Kapczynski, *Dangerous Times: The FDA's Role in Information Production, Past and Future*, 102 MINN. L. REV. 2357 (2018), <https://scholarship.law.umn.edu/mlr/130>.

⁵ Joseph S. Ross et. al, *Pooled Analysis of Rofecoxib Placebo-Controlled Clinical Trial Data: Lessons for Postmarket Pharmaceutical Safety Surveillance*, 169 ARCHIVES OF INTERNAL MED. 1976, 1976 (2009).

⁶ *Id.*; see also Yale Univ. Collaboration for Research Integrity and Transparency, WHAT'S IN YOUR MEDICINE CABINET 35 (Feb. 2018), https://law.yale.edu/sites/default/files/area/center/crit/document/crit_policy_paper_february_2018_3rd_edition.pdf.

⁷ *Id.*

⁸ David J Graham et al., *Risk of Acute Myocardial Infarction and Sudden Cardiac Death in Patients Treated with Cyclo-oxygenase 2 Selective and Non-Selective Non-Steroidal Anti-inflammatory Drugs: Nested Case-Control Study*, 365 LANCET 475, 480 (2005); see also Carolyn Abraham, *Vioxx took deadly toll: study*, Globe & Mail, Jan.

Data secrecy also causes harm by undermining our health care system: It prevents us from making the best allocation of scarce resources, and obscures avenues for systematic reform created by the light that data sharing can shed on institutional practices at FDA and in industry.

There is, accordingly, emerging consensus that researchers and the public need better access to clinical trial data, to allow for the independent assessments that can help keep both the industry and regulators honest and accountable.⁹ What is missing is an effective legal and regulatory framework for the release of this data. For several years, working closely with medical researchers and a legal team, we have worked to maximize the potential of existing strategies for clinical trial data disclosure, and this paper sets out the key insight developed through that work: If researchers are to have systematic access the clinical trial data needed to help spot unsafe and ineffective medicines, the FDA will have to make clinical trial data available proactively.

We set out here the case that the agency can, consistent with existing law, do that, and a description of how it can do so while navigating the two main challenges to data sharing: protecting the privacy of individuals who participate in trials and navigating the claims that companies make that this data is and should remain confidential. Drawing on examples of successful data sharing in other countries, and at other agencies, we also show that the process can be done effectively and with manageable resource implications. Our central contribution is to bring a wealth of new evidence about the significance of the problem together with an updated argument for proactive disclosure that can be achieved without legislative reform.¹⁰ We show

25, 2005, <https://www.theglobeandmail.com/life/vioxx-took-deadly-toll-study/article1113848/> (last visited Feb 8, 2020) (estimating “anywhere from 39,000 to 61,000 deaths in the United States could be linked to Vioxx”).

⁹ Inst. of Med. of the Nat’l Academies, SHARING CLINICAL TRIAL DATA: MAXIMIZING BENEFITS, MINIMIZING RISK (2015), <https://www.nap.edu/catalog/18998/sharing-clinical-trial-data-maximizing-benefits-minimizing-risk>.

¹⁰ The most important existing analysis of the problem dates to the late 1970s, in an article by Robert Halperin. Robert M. Halperin, *FDA Disclosure of Safety and Effectiveness Data: A Legal and Policy Analysis*, 1979 DUKE L.J. 286 (1979). He argued for a similar outcome, though with significantly less evidence available about the nature of the problem. Other notable analyses were published around this time by Pendergast and McGarity & Shapiro. See William R. Pendergast, *The Responsibility of the FDA to Protect Trade Secrets*, 27 FOOD DRUG. COSM. L. J. 366 (1972); McGarity & Shapiro, *The Trade Secret Status of Health and Safety Testing Information: Reforming Agency Disclosure Policies*, 93 HARV. L. REV. 837 (1980). Two Supreme Court decisions undercut the specific arguments and avenues for proactive disclosure that Halperin’s proposal relied on: *Chrysler v. Brown* (1979) and *Ruckelshaus v. Monsanto* (1984). *Chrysler Corp. v. Brown*, 441 U.S. 281, 294 (1979); *Ruckelshaus v. Monsanto*, 467 U.S. 986, 1008-09 (1984). We describe below why these decisions do not actually preclude proactive disclosure of safety and efficacy data, as there exist alternative authorities and avenues for disclosure. Other scholars have called more recently for more disclosure of clinical trial data, but do not discuss the many legal and practical barriers, as well as arguments to overcome them, to the extent that we do here. See, e.g., Rebecca S. Eisenberg, *The Role of the FDA in Innovation Policy*, 13 MICH. TELECOMM. & TECH. L. REV. 345 (2007); Matthew Herder, *Toward a Jurisprudence of Drug Regulation*, 42 J.L. MED. & ETHICS 244 (2014); Mustafa Ünlü, *It is Time: Why the FDA Should Start Disclosing Drug Trial Data*, 16 MICH. TELECOMM. & TECH. L. REV. 511 (2010); Rebecca S. Eisenberg, *Data Secrecy in the Age of Regulatory Exclusivity*, in THE LAW AND THEORY OF TRADE SECRECY 467 (Rochelle C. Dreyfuss, and Katherine J. Strandburg, eds., 2011); Peter Doshi and Tom Jefferson, *Disclose Data Publicly, Without Restriction*, 45 J.L. MED. & ETHICS 42 (2017); Joshua M. Sharfstein et al., *Blueprint for Transparency at the U.S. Food and Drug Administration: Recommendations to Advance the Development of Safe and Effective Medical Products*, J. L. MED. & ETHICS (2018); Amy Kapczynski & Jeanie Kim, *Clinical Trial Transparency: The FDA Should and Can Do More*, 45 J. L. MED. & ETHICS 33.

the flaws in arguments made by industry and some scholars, who have suggested that meaningful proactive disclosure is prohibited under U.S. federal statute¹¹ or, if permitted, will require expensive compensation to industry for violation of its intellectual property.¹² We show that the time is ripe for proactive disclosure, in part because of the U.S. Supreme Court’s 2019 decision in *Food Marketing Institute v. Argus Leader Media (FMI)*, which both confirmed federal agencies’ authority to disclose information proactively and threatened the viability of what is currently the primary means through which independent researchers obtain clinical data from the FDA: Freedom of Information Act (FOIA) requests.¹³

The paper is centrally aimed at solving an important public health problem, but it also contributes to two broader literatures. The first is the literature on transparency and the implications of freedom of information laws. “Transparency” as an ideal has been rightly criticized recently as having taken on a formalistic, decontextual quality, one that does not appropriately recognize that “freedom” at times requires more than unfettered, standardless exchange,¹⁴ and that does not appreciate how freedom of information laws can be weaponized to undermine public interests.¹⁵ We show here that the implications of data sharing turn on – and should be sensitive to – a broader political economic context. Data sharing can serve public interests here because of a wider ecology that includes researchers (often publicly funded) with the necessary resource to analyzing the data, and publications and norms (here, of the “open science” tradition in academic medicine) that help generate and validate important new insights and challenge false claims. Data itself does not generate these insights, and constraints on how data is used are as important as freedoms if data sharing is to work well.

In addition, we argue that data use agreements will be an important component of data disclosure in our “big data” age. These provide a means to navigate issues of privacy and commercial interest – issues that can otherwise shut down data sharing, rightly or wrongly -- and a mechanism for other publicly-minded conditions to be developed and imposed.¹⁶ Decontextualized demands for “openness” have also gained traction in recent decades,¹⁷ and

¹¹ Jeffrey K. Francer and Natalie A. Turner, *Responsible Clinical Trial Data Sharing: Medical Advancement, Patient Privacy, and Incentives to Invest in Research*, 8 J. HEALTH & LIFE SCI. L. 63, 92 (2014) (“Federal law consistently has protected the confidentiality of companies’ non-public clinical trial information provided to FDA as part of the new drug approval process, including study reports, protocols, and raw safety and effectiveness data.”); Amy Westergren, *The Data Liberation Movement: Regulation of Clinical Sharing in the European Union and the United States*, 38 HOUS. J. INT’L L. 887, 909 (2016). See also Eisenberg, *Data secrecy*, *supra* note [TK] at 488-89 (while not explicitly suggesting that proactive disclosure is currently prohibited by law, suggesting statutory reform to permit proactive disclosure).

¹² Erika Lietzan, *A New Framework for Assessing Clinical Data Transparency Initiatives*, 18 MARQ. INTELL. PROP. L. REV. 33 (2014).

¹³ *Food Mktg. Inst. v. Argus Leader Media*, 139 S. Ct. 2356 (2019).

¹⁴ David E. Pozen, *Transparency’s Ideological Drift*, 128 YALE L. J. 100 (2018); Philip Mirowski, *The future(s) of open science*, 48 SOC. STUD. SCI. 171 (2018); Mary D. Fan, *Private Data, Public Safety: A Bounded Access Model of Disclosure*, 94 N.C. L. REV. 161, 197 (2015).

¹⁵ Pozen, *supra* note [TK]; Margaret B. Kwoka, *FOIA, Inc.*, 65 DUKE L.J. 1361, 1388 (2016).

¹⁶ See Fan, *supra* note [TK], at 198 (proposing “expert-oriented bounded access” to government agency-held data pursuant to data protection plans as a way to permit experts to make meaningful use of that data while insulating agencies from legal risk).

¹⁷ See Amy Kapczynski, *The Law of Information Capitalism*, YALE L. J. (forthcoming 2020).

might suggest that we need unfettered data exchange in every instance, exchange that treats all parties – including companies – equally. We argue instead that the FDA should prioritize health researchers over industry, and that it should use data use agreements to ensure those researchers protect legitimate public interests. These contracts are possible only with proactive disclosure and are inconsistent with reactive FOIA requests, and here we join other scholars in suggesting that the future of FOIA, if it is to achieve its aims, lies in the development of robust proactive disclosure systems. In part to mark these distinctions, we call what we seek here not data transparency, but data “publicity.” The term as we use it, which calls upon early progressive traditions, marks the need for attention to context and resources if data sharing is to serve the public.¹⁸

We also seek to contribute to the broader literature on the future of the regulatory state and the conditions of democracy broadly understood. We live today in an extraordinarily information-intensive age. Decades of dramatic advances in technologies for information processing have transformed the core of the modern economy, and enabled the emergence of massively complex new industries and firms. This means that not only pharmaceuticals, but also products like cars, insurance, airplanes, and phones are far more informationally-intensive today than they were twenty years ago. Informationally intensive products and systems are complex, difficult to understand and evaluate, and can change very rapidly.¹⁹ Where systems are improperly or fraudulently designed – think here about Volkswagen’s deceptive emissions testing, or Boeing’s defective automated flight software for the 737 MAX – they generate serious social and individual harms. Regulators face growing challenges in this environment, and we need structures to allow the public to hold both regulators and the industry accountable. Yet the same barriers that appear in this context – centrally, issues of privacy, corporate claims to trade secrecy and confidentiality, and the difficulties with reactive data release models (FOIA especially) in a context where we need comprehensive and complex data sets to reach real understanding – will appear, we suggest, throughout the administrative state. Our paper thus has lessons, we think, for a wide variety of regulators and issues, from consumer product regulation to environmental regulation to the regulation of algorithms and software.²⁰

This paper contains three Parts. In Part I, we describe the need for clinical trial data publicity, and offer an overview of the specific types of data that researchers and watchdogs need to access. We offer a brief sketch of the political economy of health data, to provide a basis for the claim that data sharing here can advance knowledge and serve public interests. We also describe why much of this data is in the ordinary course treated as secret, and why existing legal avenues for public disclosure of clinical data (such as FOIA) fail to create sufficient disclosure. We need proactive disclosure of safety and efficacy data by the FDA: data publicity.

¹⁸ Pozen, *supra* note [TK], at 148 (noting that “[t]he progressives in the early 1900s spoke of “publicity,” rhetorically tethering their efforts to the notion of a public and its needs and demands”).

¹⁹ As Julie Cohen has pointed out, “Industrial-era regimes of economic regulation presumed well-defined industries, ascertainable markets and choices, and relatively discrete harms amenable to clear description and targeted response. The shift to an informational political economy has disrupted those presumptions.” JULIE COHEN, *The Regulatory State in the Information Age*, in *BETWEEN TRUTH AND POWER: LAW IN AN AGE OF INFORMATION CAPITALISM* 170 (2019).

²⁰ As we will describe, accountability cannot be achieved by data access alone, because resources and expertise are also needed. These resources in some places exist, and in other places would have to be developed.

Part II explains how the FDA could implement the proactive data disclosure we need. We show that, contrary to the conventional wisdom and the (usual) view of the FDA itself, federal law does not prohibit the FDA from disclosing most clinical trial safety and efficacy²¹ data. Properly understood, federal law authorizes expansive proactive release of information, particularly where safety is a concern. The FDA’s current regulations and other interpretations of certain statutes will, however, need to be rescinded or revised. We describe why the agency should prioritize disclosure to the public, researchers, and journalists over disclosure to industry, and disclose all relevant data for all FDA-approved drugs. We argue that the FDA should establish data use agreements to prohibit or discourage commercial use and protect individual privacy; open access as a model is a poor fit here for reasons we describe. We also anticipate and rebut some legal and economic arguments likely to be raised by the pharmaceutical industry, including the contention that disclosure will require the FDA to pay expensive compensation under the Takings Clause.

We conclude, in Part III, with two points. First, recognizing that the agency faces its own temptations toward secrecy,²² we sketch how Congress could legislate the right result for public health if the FDA does not take the appropriate steps. Second, we draw lessons from this example for the broader industrial and regulatory context. Companies broadly have incentives to obscure negative data about their products, and regulators – often under-resourced and on the losing end of an arms race with industry – are commonly tempted to obscure their own failures, particularly once regulatory decisions have been made that might put the public at risk. The problem we describe in pharmaceuticals, and the needed response, will, we argue, reiterate across many different industries and regulators, because it has structural sources. The FDA is a paradigmatic “big data” regulatory agency, but far from the only one, and systematic proactive disclosure by the FDA could serve as a model for how other data-intensive regulatory agencies, present and future, can translate and protect values of democracy in our data-intensive age.

Part I: The Data the FDA Must Disclose, and Why the FDA Must Disclose It Proactively

A. The Need for Clinical Trial Publicity

In the United States, no drug may be sold until a company firsts submit to the FDA studies that show that it is safe and efficacious. Though not widely appreciated, FDA’s primary

²¹ We use the term “efficacy” broadly to cover any and all evidence that drugs work as intended—that is, that they have provide some therapeutic benefit for some intended use. We thus use “efficacy” to cover both evidence of therapeutic benefit under controlled laboratory conditions and evidence of therapeutic benefit under less-than-ideal real-world conditions. Some in the medical literature use the term “efficacy” more narrowly, to refer only to evidence generated under controlled laboratory conditions, and the term “effectiveness” to refer to real-world evidence. *See, e.g.,* Edzard Ernst and M. H. Pittler, Letter to the Editor, *Efficacy or effectiveness?*, 260 J. OF INTERNAL MED. 488 (2006).

²² As Justice Breyer pointed out in his *FMI* dissent, there is a “temptation, common across the private and public sectors, to regard as secret all information that need not be disclosed, . . . for reasons no better than convenience, skittishness, or bureaucratic inertia.” *FMI*, 139 S. Ct. at 2368 (Breyer, J., dissenting).

function in this context is to generate and validate information.²³ It gives companies reason to produce not only positive but also negative information about their products, and to share data with regulators who can validate it.²⁴

The clinical studies (also known as clinical trials) that drug companies submit to the FDA typically take years and many millions of dollars to conduct, and occur in a variety of stages. After laboratory and pre-clinical tests, a drug proceeds to studies in humans, which are divided into three phases: phase 1 trials, typically small and used to evaluate toxicity and dosage; larger phase 2 trials, used to gather more information about safety and to begin to explore efficacy; and phase 3 trials where the drug is tested in larger groups to determine whether it has benefits that outweigh the harms for the proposed use, and to examine adverse events in a larger population.²⁵ Phase 4 trials are those done after marketing, to study longer term safety and effectiveness and study outstanding questions not resolved at approval.²⁶ Information gathered in this process is of enormous significance to public health, but is not routinely shared or made available to researchers. Traditionally, data remains with the entity that conducts and/or sponsors the study, and outside reviewers have little opportunity to access it.²⁷

This capsule summary of the various phases of clinical studies illuminates an important but sometimes neglected fact of pharmaceuticals—“safety” and “efficacy” of medicines cannot be determined independently of one another and must be understood together. No drug is without side effects, and medicines can also harm indirectly by displacing alternative remedies. A drug is considered acceptably “safe” only if its known therapeutic benefits outweigh its known harms.²⁸ This weighing of benefits and harms is invariably specific to a particular use in a particular patient population²⁹—for example, for slowing tumor growth in people with metastatic, non-squamous, non-small cell lung cancer, or for improving physical function in adult patients with moderately to severely active rheumatoid arthritis. The link between safety

²³ Kapczynski, *Dangerous Times*, *supra* note [TK], at 2357-58 (describing the common arguments that FDA operates as a “certifier” of information, or paternalistically to protect the public from dangerous products, and describing why instead its framework statutes establish it as primarily addressing a problem of information production and validation); *see also* Rebecca S. Eisenberg, *The Role of the FDA in Innovation Policy*, 13 MICH. TELECOMM. & TECH. L. REV. 345, 370 (2007).

²⁴ Kapczynski, *Dangerous Times*, *supra* note [TK], at 2363-64 (describing the problem, and noting that competitors have insufficient incentive to generate this data because of free rider problems).

²⁵ *Step 3: Clinical Research, Clinical Research Phase Studies*, FDA, https://www.fda.gov/patients/drug-development-process/step-3-clinical-research#Clinical_Research_Phase_Studies (last visited Jan. 25, 2020).

²⁶ Phase 4 trials are also called postmarket or postmarketing trials.

²⁷ Joseph S. Ross, Richard Lehman & Cary P. Gross, *The Importance of Clinical Trial Data Sharing: Toward More Open Science*, 5 CIRCULATION: CARDIOVASCULAR QUALITY & OUTCOMES 238-240 (2012).

²⁸ *FDA's Drug Review Process: Continued*, FDA,

<https://www.fda.gov/drugs/drug-information-consumers/fdas-drug-review-process-continued> (last visited Feb. 7, 2020) (“Once a new drug application is filed, an FDA review team—medical doctors, chemists, statisticians, microbiologists, pharmacologists, and other experts—evaluates whether the studies the sponsor submitted show that the drug is safe and effective for its proposed use. No drug is absolutely safe; all drugs have side effects. ‘Safe’ in this sense means that the benefits of the drug appear to outweigh the known risks.”)

²⁹ *See, e.g., Spectrum Pharm., Inc. v. Burwell*, 824 F.3d 1062, 1069 (D.C. Cir. 2016) (“FDA’s approval of a drug application shows that the agency concluded that the drug in its anticipated form is safe and effective *for the indication sought*.” (emphasis added))

and efficacy means that a drug that is shown to be entirely ineffective – that is, that has no therapeutic benefits – is per se “unsafe.” Because safety can only be understood in relation to efficacy, and vice versa, we refer to “safety and efficacy data” collectively throughout this paper. We do not distinguish two separate types of data—“safety data” and “efficacy data”—but instead refer to all the data that sheds light on drugs’ risks and benefits.

Recent attention to the problem of secrecy of safety and efficacy data has begun to document the extent of the issue, and its implications. We now know, for example, that many clinical trials are not published in a timely fashion.³⁰ Publication bias is also a deep problem: Negative studies are also significantly less likely to be published than positive ones, and when trials *are* published, key information may be omitted, or the study’s results mischaracterized.³¹ One recent article compared FDA’s summary reviews of trials with the published literature for antidepressant drugs, and showed that very few of the trials the FDA considered negative were published, while almost all of the positive trials were published.³² Of the few negative studies published, moreover, most were misleadingly described in print as instead having positive results.³³ This publication bias creates significant problems for doctors, who commonly consult the published literature to advise their prescribing, but also for the studies that guide clinical practice more broadly. For example, the gold standard in meta-research, the Cochrane Group, conducts reviews of important medicines to aggregate and determine the balance of the evidence and its implications for prescribing. Review teams typically only have access to the published literature, and the results and recommendations of their reviews have been reversed in rare cases when teams have been able to access more complete data sets.³⁴

The implications for patients of hidden data can be grave. In its few years on the market, Vioxx, for example, was estimated to have caused 88,000 to 140,000 serious cardiac events, leading to tens of thousands of deaths.³⁵ Because of data that was revealed only in litigation, we

³⁰ Joseph S. Ross et al., *Publication of NIH Funded Trials Registered in ClinicalTrials.gov: Cross-Sectional Analysis*, 344 BRIT. MED. J. d7292 (2012), available at <https://www.bmj.com/content/344/bmj.d7292> (“Despite recent improvement in timely publication, fewer than half of trials funded by NIH are published in a peer reviewed biomedical journal indexed by Medline within 30 months of trial completion.”).

³¹ An-Wen Chan et al., *Empirical Evidence for Selective Reporting of Outcomes in Randomized Trials: Comparison of Protocols to Published Articles* 291 JAMA 2457 (2004).

³² Erick H. Turner et al., *Selective Publication of Antidepressant Trials and Its Influence on Apparent Efficacy*, 358 NEW ENG. J. MED. 252, 256 (2008) (table showing 37 (97%) unpublished negative studies and one (3%) unpublished positive study).

³³ *Id.* (table showing sixteen (67%) unpublished negative studies, five (21%) published negative studies that conflict with FDA decision, and three (12%) published negative studies that agree with FDA decision).

³⁴ Tom Jefferson, et al., *Neuraminidase Inhibitors for Preventing and Treating Influenza in Healthy Adults and Children*, COCHRANE DATABASE SYST. REV. CD008965 (Apr. 2014), available at <https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD008965.pub4/full>; Tom Jefferson et al., *Neuraminidase Inhibitors for Preventing and Treating Influenza in Healthy Adults: Systematic Review and Meta-Analysis*, 339 BRIT. MED. J. b5106 (2009), available at <https://www.bmj.com/content/339/bmj.b5106>. The researchers were only able to access the data after years of requests and a public campaign for the release of the data conducted by the British Medical Journal.

³⁵ David J Graham et al., *Risk of Acute Myocardial Infarction and Sudden Cardiac Death in Patients Treated with Cyclo-oxygenase 2 Selective and Non-Selective Non-Steroidal Anti-inflammatory Drugs: Nested Case-Control Study*, 365 LANCET 475, 480 (2005); see also Carolyn Abraham, *Vioxx took deadly toll: study*, Globe & Mail, Jan.

now know that when Merck, early in the development process, learned that the drug might have negative cardiovascular side effects, it did not design studies to measure this risk, and it manipulated the published data to hide the problem.³⁶ The drug Paxil offers another example: the antidepressant was marketed by GlaxoSmithKline for five years for use in pediatric populations, but never approved for that indication.³⁷ It became popular for this use – with over two million prescriptions in children a year – on the basis of a medical journal article that claimed that the medicine was “generally well tolerated and effective” in young patients.³⁸ In fact, the drug increased the risk of suicidal thinking and suicide in young people.³⁹ When independent researchers were given access to the study that underlay the published article, they found that the study did not support efficacy in adolescents, and showed the risks quite clearly.⁴⁰

Clinical trial publicity can do more than facilitate the discovery of unknown safety problems and improper industry practices. It can also help affirm the credibility of studies that are conducted properly, and prevent the risk that studies will be duplicated because investigators are unaware they were conducted before. Because patients undergo risks in clinical trials, the scientific community has an obligation to make the best possible use of the results.⁴¹

Data sharing can, in addition, help improve treatment guidelines, and prevent wasteful spending by governments and insurers. For example, by pooling IPD from a wide range of settings, malaria researchers were recently able to revise treatment guidelines for children. They estimated that a small dosage increase in one drug would significantly cut the risk of treatment failure, and still cure 95% of cases, saving both resources and lives in the process.⁴²

Drug prices and overall spending on “innovative” new drugs have ballooned in recent years, sometimes without evidence that these expensive treatments provide meaningful

25, 2005, <https://www.theglobeandmail.com/life/vioxx-took-deadly-toll-study/article1113848/> (last visited Feb 8, 2020) (estimating “anywhere from 39,000 to 61,000 deaths in the United States could be linked to Vioxx”).

³⁶ Harlan Krumholz et al., *What Have We Learnt from Vioxx?*, 334 BRIT. MED. J. 120, 120 (2007); Janice Hopkins Tanne, *Merck Used Ghostwriters and Selective Data in Vioxx Publications*, JAMA Says. 336 BRIT. MED. J. 849 (2008).

³⁷ An “indication” is a method of using a given drug in a particular patient population. Omudhome Ogbu, *Indications for Drugs (uses), Approved vs. Non-approved*, MEDICINENET (Jay Marks, ed.), https://www.medicinenet.com/indications_for_drugs_approved_vs_non-approved/views.htm (last visited Jan. 26, 2020).

³⁸ Peter Doshi, *No Correction, No Retraction, No Apology, No Comment: Paroxetine Trial Reanalysis Raises Questions About Institutional Responsibility*, 351 BRIT. MED. J. h4629, 1 (2015), available at <https://www.bmj.com/content/351/bmj.h4629>.

³⁹ U.S. Food and Drug Administration, *FDA Talk Paper T03-43: FDA Statement Regarding the Anti-Depressant Paxil for Pediatric Population*, (June 19 2003), available at <https://ahrp.org/fda-statement-regarding-anti-depressant-paxil-for-children/> (last visited Jan. 27, 2020).

⁴⁰ Joanna Le Noury et al., *Restoring Study 329: Efficacy and Harms of Paroxetine and Imipramine in Treatment of Major Depression in Adolescence*, 351 BRIT. MED. J. h4320 (2015), available at <https://www.bmj.com/content/351/bmj.h4320>.

⁴¹ Jeffrey M. Drazen, *Sharing Individual Patient Data from Clinical Trials*, 372 NEW ENG. J. MED. 201 (2015); see also Doshi and Jefferson, *Disclose Data Publicly*, *supra* note [TK].

⁴² The Effect of Dosing Regimens on the Antimalarial Efficacy of Dihydroartemisinin-Piperaquine: A Pooled Analysis of Individual Patient Data, 10 PLOS MED e1001564 (2013), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3848996/> (last visited Feb 8, 2020), at 10-11.

therapeutic benefits over older, cheaper alternatives.⁴³ Two stark examples: In the 2000s and early 2010s, governments around the world spent billions stockpiling oseltamivir (Tamiflu) and zanamivir (Relenza) to fight seasonal and pandemic flu viruses; after years of digging, a group of researchers associated with the Cochrane Collaboration obtained unpublished clinical trial data and, in 2014, revealed that these expensive drugs failed to prevent the spread of the flu, reduce hospital admissions, or minimize complications.⁴⁴ Eteplirsen (Exondys 51), a drug approved by the FDA in 2016 for treatment of a rare form of muscular dystrophy, costs close to \$1 million per year per patient,⁴⁵ yet an exhaustive independent analysis of eteplirsen's cost effectiveness by the independent Institute for Clinical and Economic Review (ICER) concluded that there was no concrete evidence of clinical benefit or cost-effectiveness at any price, let alone \$1 million.⁴⁶ In other disease areas, like cancer, drugs of similarly dubious therapeutic value are sending drug spending soaring.⁴⁷ In some cases, companies deliberately obscure evidence that only a narrow population will benefit from a drug, as was the case, for example, with a Genentech drug for lung cancer, erlotinib (Tarceva). The company knew – but hid – the fact that it only helped a narrow group of patients with a particular mutation, causing the government to waste substantial sums (and patients to experience side effects) that could not be justified by the data.⁴⁸ For decades now, independent analysts have sought greater access to clinical data to permit fuller weighing of the true risks and benefits of prescription drugs and more accurate identification of the drugs actually worth paying for.⁴⁹

⁴³ Alison Kodjak, *Prescription Drug Costs Driven By Manufacturer Price Hikes, Not Innovation*, NPR (January 7, 2019), <https://www.npr.org/sections/health-shots/2019/01/07/682986630/prescription-drug-costs-driven-by-manufacturer-price-hikes-not-innovation> (“The skyrocketing cost of many prescription drugs in the U.S. can be blamed primarily on price increases, not expensive new therapies or improvements in existing medications as drug companies frequently claim, a new study shows.”), citing Inmaculada Hernandez, *The Contribution of New Product Entry Versus Existing Product Inflation in the Rising Costs of Drugs*, 38 HEALTH AFFAIRS 76 (2019).

⁴⁴ Richard Van Noorden, *Report Disputes Benefit of Stockpiling Tamiflu*, NATURE (Apr. 10, 2014), <https://www.nature.com/news/report-disputes-benefit-of-stockpiling-tamiflu-1.15022> (citing Tom Jefferson, et. al, *Neuraminidase Inhibitors for Preventing and Treating Influenza in Healthy Adults and Children*, COCHRANE DATABASE SYST. REV. CD008965 (Apr. 2014)).

⁴⁵ Katie Thomas and Reed Abelson, *The \$6 Million Drug Claim*, N.Y. TIMES (Aug. 25, 2019), <https://www.nytimes.com/2019/08/25/health/drug-prices-rare-diseases.html>.

⁴⁶ Kyle Blankenship, *Want Bang for Your Buck? Don't Look to Sarepta's Pricey DMD Therapy Exondys*, ICER SAYS, FIERCE PHARMA (May 23, 2019), <https://www.fiercepharma.com/pharma/want-bang-for-your-buck-don-t-look-to-sarepta-s-pricey-dmd-therapy-exondys-icer-says> (citing Inst. for Clinical and Econ. Rev., DEFLAZACORT, ETEPLIRSEN, AND GOLODIRSEN FOR DUCHENNE MUSCULAR DYSTROPHY: EFFECTIVENESS AND VALUE (Jul. 2019), https://icer-review.org/wp-content/uploads/2018/12/ICER_DMD_Evidence-Report_071119.pdf).

⁴⁷ Tito Fojo et al., *Unintended Consequences of Expensive Cancer Therapeutics—The Pursuit of Marginal Indications and a Me-too Mentality That Stifles Innovation and Creativity: The John Conley Lecture* 140 JAMA OTOLARYNGOL HEAD NECK SURGERY 1225 (2014); Tracy Rupp and Diana Zuckerman, *Quality of Life, Overall Survival, and Costs of Cancer Drugs Approved Based on Surrogate Endpoints*, 177 JAMA INTERNAL MED. 276 (2017); Peter B. Bach, *Insights Into the Increasing Costs of Cancer Drugs*, 17 CLINICAL ADVANCES IN HEMATOLOGY & ONCOLOGY 287 (2019).

⁴⁸ Yale Univ. Collaboration for Research Integrity and Transparency, *WHAT'S IN YOUR MEDICINE CABINET*, *supra* note [TK] at 17; Melody Petersen, *This \$7,800-A-Month Cancer Drug Caused Rashes and Rarely Worked. Now Trump Could Make FDA Approvals Even Easier*, L.A. TIMES (Feb. 3, 2017), <https://www.latimes.com/business/la-fi-fda-tarceva-approval-20170204-htmlstory.html>.

⁴⁹ See, e.g., Nat'l Inst. for Health Care Mgmt. Research and Educ. Found., *CHANGING PATTERNS OF PHARMACEUTICAL INNOVATION* 18 (May 2002), <https://nihcm.org/pdf/innovations.pdf> (“This report has shown a disparity between spending and clinical value, with a large increase in recent spending attributable to line extensions

Finally, secrecy harms our health care system by making it more difficult to identify problems in both regulatory and industry practice. For example, when independent researchers are given access to the FDA's data and permitted to validate the agency's work, they may detect failures and spur socially beneficial reform. For example, between 2012 and 2019, a group of researchers at Johns Hopkins, in part with our assistance, obtained detailed internal agency data on the FDA's Risk Evaluation and Mitigation Strategy (REMS) for powerful, dangerous, highly addictive fast-acting fentanyl products.⁵⁰ The Hopkins researchers showed, based on this data, that the REMS program was not working well, and that these drugs were being widely prescribed to patients for whom the risk of addiction and overdose was unacceptably high, thus exacerbating the opioid epidemic.⁵¹ The Hopkins researchers' investigation quickly sparked high-profile media coverage,⁵² attention from Congress,⁵³ a hearing at the FDA,⁵⁴ and, ultimately, agency changes to the REMS, which tightened prescribing rules to reduce inappropriate use.⁵⁵ Data publicity can shed light on bad practices in industry too – practices that are constantly evolving. For example, data released in conjunction with lawsuits helped show the emergence of the “ghostwriting” phenomenon (where companies pay prominent researchers to put their names on studies in which they have played no part),⁵⁶ and also gave evidence of so-called “seeding trials,” where companies engage in otherwise prohibited marketing under the guise that they are running clinical trials.⁵⁷

providing no significant clinical improvement over older medications. To make cost effective decisions, they will need to increase their understanding of the relative value of pharmaceutical alternatives . . .”).

⁵⁰ Jeffrey E. Rollman et al., *Assessment of the FDA Risk Evaluation and Mitigation Strategy for Transmucosal Immediate-Release Fentanyl Products*, 321 JAMA 676, 677 (2019). The researchers obtained this data via a years-long Freedom of Information Act (FOIA)-based investigation with the assistance of the author AK and others at Yale's Collaboration for Research Integrity and Transparency. See Yale Law School, *MFIA/CRIT Team Supports Johns Hopkins Investigation of FDA Oversight of Fentanyl Products*, YLS TODAY NEWS (Feb. 22, 2019), <https://law.yale.edu/yls-today/news/mfiacrit-team-supports-johns-hopkins-investigation-fda-oversight-fentanyl-products>.

⁵¹ *Id.*

⁵² See, e.g., Emily Baumgaertner, *F.D.A. Did Not Intervene to Curb Risky Fentanyl Prescriptions*, N.Y. TIMES (Aug. 2, 2018), <https://www.nytimes.com/2018/08/02/health/fda-fentanyl-opioid-epidemic-overdose-cancer.html>.

⁵³ See, e.g., Letter from Hon. Edward Markey, U.S. Senator, to Hon. Scott Gottlieb, Commissioner, FDA (Aug. 17, 2018), available at <https://www.markey.senate.gov/imo/media/doc/FDA%20REMS%20and%20fentanyl%2008.17.18.pdf>.

⁵⁴ See, e.g., G. Caleb Alexander, Testimony for the Record Submitted to the U.S. Food and Drug Administration for the Joint Meeting of the Drug Safety and Risk Management Advisory Committee and the Anesthetic and Analgesic Drug Products Advisory Committee, Dkt. No. FDA-2018-N-1917 (Aug. 3, 2018), <https://int.nyt.com/data/documenthelper/123-fda-opioid-overdose-cancer/4be5694a2729eb5b522d/optimized/full.pdf>.

⁵⁵ See Press Release, Commissioner Scott Gottlieb, Statement from FDA Commissioner Scott Gottlieb, M.D. on New Steps to Strengthen Agency's Safety Requirements Aimed at Mitigating Risks Associated with Transmucosal Immediate-Release Fentanyl Products (Mar. 27, 2019), <https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-new-steps-strengthen-agencys-safety-requirements-aimed>.

⁵⁶ The PLoS Medicine Editors, *Ghostwriting: The Dirty Little Secret of Medical Publishing That Just Got Bigger*, 6 PLOS MEDICINE e1000156 (2009).

⁵⁷ Kevin P. Hill et al., *The ADVANTAGE Seeding Trial: A Review of Internal Documents*, 149 ANN INTERN MED 251 (2008). For more bad practices in the pharmaceutical industry, see Alexander C. Egilman et al., *Confidentiality Orders and Public Interest in Drug and Medical Device Litigation*, 180 JAMA INTERN MED 292–299 (2020).

As these examples show, a robust ecology of researchers and organizations exists that have been able, in high-stakes instances, to generate important new health insights, and connect those insights to changes in practice. This is the result of a broader political economy that includes not just industry-funded researchers, but a robust tradition of public and academic health research. Over decades, with hundreds of billions of dollars of support from public funders like the NIH, academic science has evolved a network of institutions and practices, from academic journals, to norms about conflict of interest, to norms of priority and disclosure that underpin the “open science” model.⁵⁸ This is critical because extracting insights from clinical trial data is an enormously time- and resource-intensive exercise, and one that requires dedication to scientific craft. Even given this rather favorable context, there are challenges for data sharing, and additional resources might be needed as more data is made available.

The private sector lacks incentives to do the work of fighting secrecy and independently evaluating the safety and efficacy of each other’s drugs. Originator companies face serious conflict of interest issues. For-profit competitors face free rider dynamics and misaligned incentives: competitors might benefit if a successful, beneficial drug is forced off the market.⁵⁹

When to share safety and efficacy data on prescription drugs? The right time is at the moment of FDA approval, or very shortly thereafter. The deadly and costly regulatory failures we describe above, such as rofecoxib (Vioxx), oseltamivir (Tamiflu), and fentanyl, highlight a major drawback of our current system: if relevant data reaches independent researchers, it usually does so *years* after approval, by which time much damage has already been done. When it comes to data publicity, late is better than never, but not much. Safety and efficacy data is most valuable in the weeks and months that immediately after approval of a new drug, as it is during this time that various stakeholders make important decisions: insurers decide whether to place the new drug on their formularies,⁶⁰ medical associations update treatment guidelines, and individual prescribers and patients decide whether the new drug is right for them. Secrecy and delayed transparency currently impose huge, largely hidden costs on our health care system: injuries, death, and billions of dollars of unnecessary spending. The costs saved by averting just one regulatory failure on the scale of Vioxx—which cost Merck billions,⁶¹ and insurers and injured patients even more—would more than cover the costs of creating and maintaining the data publicity plan we propose here. Effective data publicity could create a virtuous feedback loop: if useful safety and efficacy data were made available at the time of approval, the

⁵⁸ See Amy Kapczynski, *Order without Intellectual Property: Open Science in Influenza*, 102 Cornell L. Rev. 1539 (2017); Fan, *supra* note [TK] at 199 (describing public health researchers and suggesting that “trained professionals such as researchers who are ethically obligated to comply with datause and protection safeguards and attorneys who are ethically bound to abide by limitations on disclosure” are best “suited to maximize the value of disclosure by using their expertise to detect potential threats to public safety”).

⁵⁹ Amy Kapczynski & Talha Syed, *The Continuum of Excludability and the Limits of Patents*, 122 Yale L. J. 1900, 1923 (on negative information and industry incentives); Kapczynski, *Dangerous Times*, *supra* note [TK] at 2363 (similar).

⁶⁰ “Formularies,” Health Affairs Health Policy Brief, September 14, 2017. DOI: 10.1377/hpb20171409.000177.

⁶¹ Lewis Krauskopf, *Merck agrees to pay \$4.85 billion in Vioxx settlement*, REUTERS, November 9, 2007, <https://www.reuters.com/article/us-merck-vioxx-settlement-idUSL0929726620071109> (last visited Feb 10, 2020).

ecosystem of researchers reviewing and interpreting this data would grow larger and stronger, and their insights and recommendations would reinforce the value of data publicity.

Which data to share? There are several different categories of data that are needed to bring benefits to patients, clinicians, researchers, and insurers. Clinical trial data can be thought of as falling into three broad categories: metadata (which is data about the data – including protocols, statistical analysis plans, and analytic code); summary data (which is any summary that highlights and explains key results, from summaries made by companies and regulators, to summaries in the published literature); and individual participant data (which including raw data collected from trial participants, including in executable data sets and adverse event reports).⁶² Each form of data is important. While data on unapproved drugs is also important for research (for example, because it can speed up research on the same or similar compounds), our focus here is on the data needed to assess the quality of drugs that are currently on the market, because this data is of particularly urgent interest for patients and providers.⁶³

Metadata is needed to understand how to interpret the data produced by the trial. The most important such data is the study protocols, which set forth how investigators plan to proceed, include a statistical analysis plan, and identify the endpoints the study will evaluate. They are important to secondary researchers because only with access to protocols can one put participant level data in context, and determine whether investigators remained true to their plan. This is critical, because a common source of misleading data is selective reporting of clinical trial outcomes. If investigators publish only some prespecified outcomes, or change them even in subtle ways, they can make a drug falsely appear to have more significant effects.⁶⁴ As one example, after a study is conducted, it is almost inevitable that one will be able to find some pattern in the data if one “dredges” for one: this is the result of the test for statistical significance, which is conventionally established when there is a less than 5% likelihood that an outcome was the result of chance.⁶⁵ This means that one in every 20 comparisons that one makes with a data set will produce falsely “significant” results – so that if one repeatedly tests data for associations

⁶² Inst. of Med. of the Nat’l Academies, SHARING CLINICAL TRIAL DATA: MAXIMIZING BENEFITS, MINIMIZING RISK (2015), <https://www.nap.edu/catalog/18998/sharing-clinical-trial-data-maximizing-benefits-minimizing-risk>.

⁶³ For a more comprehensive list of types of data that the FDA could and should make available, see Joshua M. Sharfstein et al., *Blueprint for Transparency at the U.S. Food and Drug Administration: Recommendations to Advance the Development of Safe and Effective Medical Products*, 45 J. L. MED. & ETHICS 7 (2018) <https://doi.org/10.1177/1073110517750615>. We do not mean to suggest that important clinical data on unapproved products—in Investigational New Drug (IND) applications, in unapproved New Drug Applications (NDAs) and Biologic License Applications (BLAs), in complete response letters from the FDA, and so on—should not be disclosed proactively. However, the legal case for their proactive disclosure traverses different questions, putting these forms of data beyond the scope of this paper. Among the differences, some of the FDA’s existing statutory authority to disclose clinical data is limited to approved products, and claims of confidentiality may be stronger as to data on unapproved products. We note, however, that the strategy of release under a data use agreement could address concerns about the need for legitimate protection of confidences for other forms of clinical trial data, as well as data from other industries.

⁶⁴ John PA Ioannidis et al., *Outcome Reporting Bias in Clinical Trials: Why Monitoring Matters*, 356 BRIT. MED. J. j408 (2017), available at <https://www.bmj.com/content/356/bmj.j408>.

⁶⁵ James L. Mills, *Data Torturing*, 329 NEW ENG. J. MED. 1196, 1997 (1993). The phenomenon of study investigators “dredging” data to identify correlations that appear statistically significant is also referred to as “p-hacking.” Christie Aschwanden, *We’re All ‘P-Hacking’ Now*, WIRED (Nov. 26, 2019), <https://www.wired.com/story/were-all-p-hacking-now/>.

with, say, occupation, zodiac sign, hair color, zip code – one will readily be able to produce a positive result, but that result cannot be treated as reliable.⁶⁶ Although it is poor scientific practice, it is in fact rare for investigators to fully report all of their outcomes and justify any deviations from their protocols in publications.⁶⁷ This was a key part of the Paxil story: on re-analysis it was learned that all of the planned study endpoints were negative, but the authors who published the initial misleading study simply switched to different outcomes that showed better results.⁶⁸

Two kinds of summary data are not generally public, but are critical for research validation: clinical study reports (CSRs), and internal assessments done by the FDA, including scientific reviews generated by individual reviewers or teams. A clinical study report is a sizeable report, often running into the thousands of pages, prepared by a manufacturer and submitted to the FDA to summarize the clinical investigations conducted on humans.⁶⁹ Such reports are not now routinely disclosed by the FDA,⁷⁰ though they have been made available in FOIA litigation, including litigation over Gilead’s Hepatitis C drug, sofosbuvir, in which one of the authors participated.⁷¹ The European Medicines Association (EMA) has adopted a process for disclosing CSRs with minimal redactions, although its implementation has been suspended.⁷² When such CSRs have been made available they have led to important new insights into risks

⁶⁶ *Id.*

⁶⁷ Ioannides et al., *supra* note __.

⁶⁸ See Yale Univ. Collaboration for Research Integrity and Transparency, PROMOTING TRANSPARENCY IN CLINICAL RESEARCH: WHY AND HOW 9 (Nov. 2017), https://law.yale.edu/sites/default/files/area/center/crit/crit_white_paper_november_2017_best_promoting_transparency_in_clinical_research_why_and_how.pdf.

⁶⁹ Sharfstein et al, *supra* note [TK].

⁷⁰ The FDA announced in January 2018 that it would begin a pilot program to release portions of CSRs for FDA-approved drugs: “the study report body, the protocol and amendments, and the statistical analysis plan for each of the participating product’s pivotal studies.” Press Release, Commissioner Scott Gottlieb, Statement from FDA Commissioner Scott Gottlieb, M.D. on New Steps FDA is Taking to Enhance Transparency of Clinical Trial Information to Support Innovation and Scientific Inquiry Related to New Drugs (Jan. 16, 2018), <https://www.fda.gov/news-events/press-announcements/fda-commissioner-scott-gottlieb-md-new-steps-fda-taking-enhance-transparency-clinical-trial>. The program depended on industry consent, and the FDA promised it would “continue to protect patient privacy, trade secret, and confidential commercial information in the CSRs [it] release[d] as part of the pilot.” *Id.* The FDA’s pilot program was discontinued in June 2019 after only one industry sponsor – Janssen – agreed to participate. See Zachary Brennan, *FDA Plots Shift Away From CSR Pilot to Forge New Transparency on Drug Approval Process*, RAPS (June 26, 2019), <https://www.raps.org/news-and-articles/news-articles/2019/6/fda-plots-shift-away-from-csr-pilot-to-forge-new-t>.

⁷¹ Yale Law School, *GHJP Closes Two-Year FOIA Case Against Drug Manufacturer*, YLS TODAY NEWS (Sept. 19, 2017), <https://medicine.yale.edu/news-article/15794/>.

⁷² *Clinical Data Publication*, EUROPEAN MED. AGENCY, <https://www.ema.europa.eu/en/human-regulatory/marketing-authorisation/clinical-data-publication> (last visited Jan. 28, 2020); Till Bruckner, *European Medicines Agency Backtracks on Transparency Pledges, Restricts Access to Key Documents*, TRANSPARIMED (Aug. 19, 2018), <https://www.transparimed.org/single-post/2018/08/19/European-Medicines-Agency-backtracks-on-transparency-pledges-restricts-access-to-key-drug-safety-documents>. More on the EMA’s clinical data sharing policy *infra* § II.B.

that have led to new black-box warnings (the most serious kind), and in some jurisdictions to the withdrawal of medicines.⁷³

FDA reviewers undertake careful analysis of medicines before they are approved,⁷⁴ and the published assessments of senior FDA officials and of individual scientific review teams within the FDA—clinical/medical, toxicological, statistical, chemical, etc.—can also provide important indications of difficulty or concern.⁷⁵ (These assessments are published as part of the “approval package” that the FDA publishes on the “Drugs@FDA” site⁷⁶ every time it approves a new drug or new indication of an existing drug.) The assessments contain a variety of important information not often found in the medical literature, such as details from clinical trial protocols and statistical analysis plans, more complete sets of efficacy endpoints and adverse events, comparisons of FDA versus sponsor analyses of the same data, important details about postmarketing study requirements, and each individual FDA reviewer’s (or review team’s) view on whether the drug application should be approved.⁷⁷ Without summary evidence of this kind, researchers are less likely to know where they might want to dig deeper.⁷⁸

⁷³ Yale Univ. Collaboration for Research Integrity and Transparency, PROMOTING TRANSPARENCY, *supra* note [tk] at 12-13 (describing this with respect to the diabetes drug rosiglitazone (Avandia)).

⁷⁴ For a minority of drugs, the FDA convenes a panel of outside experts—an “advisory committee”—to advise on whether to approve the drug. The FDA releases advisory committee materials (after a FOIA case required it of them), which reveal the basis of evidence that those experts use to make a recommendation on approval. See Peter Lurie & Allison Zieve, *Sometimes the Silence Can Be like the Thunder: Access to Pharmaceutical Data at the FDA*, 69 LAW AND CONTEMP. PROBS. 85, 91 (Summer 2006) for description of advisory committee materials and the FOIA case. The FDA discloses these materials pursuant to the Federal Advisory Committee Act, 5 U.S.C. App. 2. See 21 C.F.R. § 314.430(d)(1). Advisory committee materials typically include some metadata and summary data, which has proven valuable to independent researchers. See, e.g., Clifford J. Rosen, *The Rosiglitazone Story—Lessons From an FDA Advisory Committee Meeting*, 357 NEW ENG. J. MED. 844 (2007); Aaron S. Kesselheim and Jerry Avorn, *Approving a Problematic Muscular Dystrophy Drug: Implications for FDA Policy*, 316 JAMA 2357 (2016). However, advisory committees are convened only occasionally, to consider specific questions on a relatively small of drugs, and the data disclosed is also incomplete.

⁷⁵ See Lisa M. Schwartz and Steven Woloshin, *Lost in Transmission – FDA Drug Information That Never Reaches Clinicians*, 361 NEW ENG. J. MED. 1717, 1719 (2009); Herder, *Toward a Jurisprudence*, *supra* note 24 at 256; Matthew Herder, Christopher Morten, and Peter Doshi, *Integrated Drug Reviews at the US Food and Drug Administration—Legal Concerns and Knowledge Lost*, JAMA INTERNAL MED. (forthcoming March 2020).

⁷⁶ *Drugs@FDA: FDA-Approved Drugs*, FDA, <https://www.accessdata.fda.gov/scripts/cder/daf/> (last visited Jan. 27, 2020).

⁷⁷ Herder, Morten & Doshi, *supra* n. [TK]; Schwartz & Woloshin, *supra* n. [TK].

⁷⁸ *Id.* In June 2019, the FDA announced that it plans to discontinue publication of the assessments of individual reviewers and review teams and shift to publication of a single consolidated “integrated review” that combines the assessments of all FDA reviewers. See FDA Notice, *New Drugs Regulatory Program Modernization: Improving Approval Package Documentation and Communication*, 84 FR 30733 (June 27, 2019), <https://www.regulations.gov/document?D=FDA-2019-N-2012-0001>. The FDA’s announcement has sparked outcry from independent researchers in medicine and law. See Herder, Morten & Doshi, *Integrated Drug Reviews*, *supra* note [TK]; Comment from Peter Doshi et al. re: Docket No. FDA-2019-N-2012 (“New Drugs Regulatory Program Modernization: Improving Approval Package Documentation and Communication”) (Aug. 23, 2019), available at <https://www.regulations.gov/contentStreamer?documentId=FDA-2019-N-2012-0010&attachmentNumber=1&contentType=pdf>. We believe that the FDA should resume publication of complete reviews of individual FDA reviewers and review teams as part of its “rebooted” disclosure policy.

Finally, granular, specific individual patient-level data is also extremely valuable to researchers. This includes raw data collected for each patient in the trials, and to be practically usable must be made available in executable (analysis-ready) form (i.e. in a form that can be analyzed using appropriate analytic software, such as Excel).⁷⁹ Granular data of this sort is rarely available to researchers, but pilot projects that have made it available on a voluntary basis have proven that there is both demand for the data, and that important research insights can be gleaned from reanalysis of patient-level data.⁸⁰ For example, researchers reviewed previously unavailable individual patient data from 33 clinical trials of the once-blockbuster, now deprecated⁸¹ drug rosiglitazone (Avandia) and identified serious discrepancies between the safety profile embedded in that that individual patient data and what had previously been revealed in summary data, including significantly higher risk of myocardial infarction (heart attack).⁸² The most important individual patient data emerge from the “pivotal” trials that are used to support approval of the drug. Individual adverse event reports and other post-market data are also valuable, but the need is less pressing, as these data are currently available in aggregate form from the FDA.⁸³

A consensus is emerging among medical experts that more data sharing is essential to protect health,⁸⁴ and patients widely support more sharing as well.⁸⁵ Data sharing also supports the FDA’s primary purpose: the agency’s primary information production function is negated if much of the information produced under its influence remains unavailable to researchers.⁸⁶ Many new initiatives to promote data sharing have emerged and shown that more access to data

⁷⁹ Perry Nisen and Frank Rockhold, *Access to Patient-Level Data from GlaxoSmithKline Clinical Trials*, 369 NEW ENG. J. MED. 475, 476 (2013) (describing these two kinds of patient-level data, raw and analysis-ready, and GSK’s efforts to make them more available to researchers).

⁸⁰ Joseph S. Ross et al., *Overview and Experience of the YODA Project with Clinical Trial Data Sharing After 5 Years*, 5 NATURE (Nov. 27, 2018), available at <https://www.nature.com/articles/sdata2018268> (noting 100 requests for data, and requests for almost 70% of all trials available on the site, with 13% already resulting in a publication); see also Matthew Herder et al., “An Open Letter in Support of FDA’s Clinical Study Report Pilot Project,” Jan. 16, 2019, <https://cspinet.org/sites/default/files/attachment/FDA-CSR-pilot-open-letter-FINAL.pdf> (describing the benefits of sharing clinical study reports, which contain individual patient data, with researchers).

⁸¹ Steven E. Nissen, *The rise and fall of rosiglitazone*, 31 EUR HEART J 773–776 (2010).

⁸² Joshua D. Wallach et al., *Updating insights into rosiglitazone and cardiovascular risk through shared data: individual patient and summary level meta-analyses*, 368 BRIT. MED. J. 17078 (2020), <https://www.bmj.com/content/368/bmj.17078> (last visited Feb 6, 2020).

⁸³ As we describe *infra* § II.B, individual adverse event reports are difficult to anonymize and may not be of great importance given the availability of the aggregate information from the FDA.

⁸⁴ IOM, *SHARING CLINICAL TRIAL DATA*, *supra* note 9; http://www.who.int/medicines/ebola-treatment/data-sharing_phe/en/; WHO, *DEVELOPING GLOBAL NORMS FOR SHARING DATA AND RESULTS DURING PUBLIC HEALTH EMERGENCIES* (Sept. 2015), http://www.who.int/medicines/ebola-treatment/data-sharing_phe/en/; Hudson, Kathy L. Hudson and Francis S. Collins, *Sharing and Reporting the Results of Clinical Trials* 313 JAMA 355 (2015) (describing the NIH view); Darren B. Taichman et al., *Sharing Clinical Trial Data: A Proposal From the International Committee of Medical Journal Editors*, 374 NEW ENG. J. MED. 384 (2016); Aaron S. Kesselheim and Michelle M. Mello, *Confidentiality Laws And Secrecy In Medical Research: Improving Public Access To Data On Drug Safety*, 26 HEALTH AFFAIRS 483 (2007); Drazen, *Sharing Individual Patient Data*, *supra* note [TK]; Ross et al., *YODA Project*, *supra* note [TK].

⁸⁵ Michelle M. Mello, Van Lieou and Steven N. Goodman, *Clinical Trial Participants’ Views of the Risks and Benefits of Data Sharing*, 378 NEW ENGL. J. MED. 2202 (2018).

⁸⁶ Kapczynski, *Dangerous Times: The FDA’s Role in Information Production, Past and Future*, *supra* n. [TK].

can facilitate better science, and protect patients.⁸⁷ But existing approaches have not yet solved the problem.

B. FOIA and Other Approaches Are Insufficient

There are existing sources of clinical trial data, but none are comprehensive or responsive enough to provide the necessary access and accountability.

1. ClinicalTrials.gov

Existing law requires anyone who conducts a Phase 2, 3, or 4 clinical trial of an FDA-approved drug or medical device to disclose information on that trial via the public ClinicalTrials.gov website, which is administered by the National Institutes of Health (NIH).⁸⁸ Each trial must be registered before it begins and must report a summary of trial results when completed.⁸⁹ Since 2017, drug companies and other trial sponsors have been required to submit full trial protocol documents, a valuable resource to researchers, who use the protocols to understand and critique how trials are designed, run, and analyzed.⁹⁰ But compliance with ClinicalTrials.gov requirements is spotty, especially when it comes to reporting results after trials are completed: only about two-thirds of completed trials had reported results as of 2019, according to multiple studies, raising concerns that drug companies and other trials sponsors are selectively reporting some results and withholding others.⁹¹ While NIH and FDA have discretion to use legal tools against noncompliant trial sponsors to enforce compliance with results reporting, including large fines, NIH and FDA have never used these tools, and few observers expect them to begin anytime soon.⁹² Even if NIH and FDA began meaningful enforcement of results reporting and missing trial result were made available, ClinicalTrials.gov would remain insufficient for some researchers, because the results reported there do not contain

⁸⁷ Ross et al., *YODA Project*, *supra* note 74; Deborah A. Zarin et al., *10-Year Update on Study Results Submitted to ClinicalTrials.gov*, 381 NEW ENG. J. MED. 1966 (2019).

⁸⁸ 42 U.S.C. § 282(j); 42 C.F.R. Part 11.

⁸⁹ For a summary of ClinicalTrials.gov and trial sponsors' reporting requirements, *see* Zarin et al., *supra* note [TK], at 1968.

⁹⁰ Zarin et al., *supra* n. [TK], at 1966.

⁹¹ Zarin et al., *supra* n. [TK], at 1969 (reporting that, as of May 2019, 66% of completed trials had reported results); Nicholas J DeVito, Seb Bacon & Ben Goldacre, *Compliance with legal requirement to report clinical trial results on ClinicalTrials.gov: a cohort study*, 395 *The Lancet* 361, 365 (2020) (reporting that, as of September 16, 2019, 63.8% of completed trials had reported any results); Jennifer E. Miller, et al. *Measuring Clinical Trial Transparency: an Empirical Analysis of Newly Approved Drugs and Large Pharmaceutical Companies*, 7 *BRIT. MED. J. OPEN* e017917 (2017), available at <https://bmjopen.bmj.com/content/7/12/e017917> (estimating, as of mid-2016, that only 71% of trials of new drugs approved by the FDA in 2014 subject to mandatory results reporting had actually reported results on time to ClinicalTrials.gov), at 5-6; *Who's Sharing Their Clinical Trial Results?*, FDA TRIALS TRACKER, <http://fdaaa.trialstracker.net/> (last visited Jan. 25, 2020) (website tracking compliance with ClinicalTrials.gov reporting requirements, which estimated a reporting rate of about 68% as of January 2020); Charles Piller, *FDA and NIH Let Clinical Trial Sponsors Keep Results Secret and Break the Law*, *SCIENCE* (Jan. 13, 2020), <https://www.sciencemag.org/news/2020/01/fda-and-nih-let-clinical-trial-sponsors-keep-results-secret-and-break-law> (concluding that “[f]ew trial sponsors have consistently [reported results to ClinicalTrials.gov], even after a 2007 law made posting mandatory for many trials registered in the database.”).

⁹² *See, e.g.*, Piller, *supra* n. [TK] (“NIH and FDA officials do not seem inclined to apply that pressure.”).

complete metadata or summary data and typically report no individual patient data at all.⁹³ For these reasons, the ClinicalTrials.gov website is an inadequate source of safety and efficacy data, useful and important as it is.⁹⁴

2. Litigation and Voluntary Data Sharing

In the U.S., a small but vital stream of safety and efficacy data on prescription drugs is unearthed via discovery in tort and other litigation.⁹⁵ But only a subset of drugs become the subject of litigation, and the relevant data often remains secret pursuant to protective or sealing orders.⁹⁶

While some companies have voluntarily committed to clinical trial data sharing, and efforts by independent and academic researchers to expand voluntary data sharing, such as the Good Pharma Scorecard⁹⁷ are gaining traction, a majority of drug companies still decline to share their data fully.⁹⁸ Gaps may be particularly likely where the data is most consequential, and in notable cases companies have refused to disclose despite repeated requests and even legal action initiated by researchers.⁹⁹

3. Foreign Drug Regulators

What about foreign medicines regulators? They do provide some very useful information, but not everything that American researchers need. The two leading foreign sources of data on drugs are the European Medicines Agency (EMA) in the European Union and Health Canada in Canada. Like the U.S., both the EMA and Health Canada disclose a small but highly useful set of summary data and metadata upon the approval of new drugs and upon

⁹³ *Scientific Information*, U.S. NAT'L LIBRARY OF MED., <https://clinicaltrials.gov/ct2/manage-recs/how-report#ScientificInformation> (last visited Jan. 29, 2020) (defining data reported on ClinicalTrials.gov).

⁹⁴ The same is true of the FDA assessments published on the FDA's Drugs@FDA website as part of a drug's approval package (described *supra* § I.A): some important metadata and summary data is disclosed, but not comprehensively, and not enough to prevent cases like those described above.

⁹⁵ Aaron S. Kesselheim and Jerry Avorn, *The Role of Litigation in Defining Drug Risks*, 297 JAMA 308 (2007); Alexander C. Egilman et al., *Confidentiality Orders and Public Interest in Drug and Medical Device Litigation*, JAMA INTERNAL MED. (Oct. 28, 2019), available at <https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2753427>.

⁹⁶ *Id.*

⁹⁷ *Good Pharma Scorecard*, BIOETHICS INTERNATIONAL, <https://bioethicsinternational.org/good-pharma-scorecard/> (last visited Jan. 28, 2020).

⁹⁸ See Jennifer Miller, *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), available at <https://www.bmj.com/content/366/bmj.14217> (As of Spring 2018, only "25% of large pharmaceutical companies fully met the data sharing standard," although "the proportion increased to 33% when companies were given an opportunity to improve their policies and practices.").

⁹⁹ The drug company Sarepta Therapeutics provides a vivid example. It has refused to share data on its FDA-approved drug eteplirsen with an independent journalist despite years of FOIA litigation. See *infra* n. [TK] and surrounding text and Charles Seife, *Is the Food and Drug Administration Withholding Drug Trial Data to Protect the Corporate Secrets of Pharmaceutical Companies?*, SCIENTIFIC AMERICAN (Feb. 2018), <https://www.scientificamerican.com/article/is-the-fda-withholding-data-about-a-controversial-drug-to-protect-its-manufacturer/>.

approval of new uses of existing drugs, summarizing clinical data at a high level explaining the agencies' approval decisions.¹⁰⁰ EMA goes further than the FDA in disclosing useful summary data and metadata insofar as it discloses information on why it *refuses* to approve drugs, just as it does when it approves them.¹⁰¹

Both the EMA and Health Canada recently began laudable efforts to proactively disclose more detailed summary data and some individual patient data. Though neither is a comprehensive source of data, these efforts offer unparalleled access to data on a relatively small number of drugs. In 2015 the EMA implemented a proactive disclosure policy, Policy 0070, which disclosed highly useful summary data and metadata—including trial protocols, clinical study reports, clinical summaries, documentation of statistical methods, clinical overviews, which provide critical analysis of the trial data—as well as a relatively small amount of individual patient data¹⁰² for drug applications submitted to the EMA from 2015 onward.¹⁰³ The EMA made data for over 130 drugs available,¹⁰⁴ and, in early 2020, the CJEU upheld the legality of the policy over legal challenges from industry.¹⁰⁵ But the policy has stalled in practice: it was suspended in August 2018 as the EMA prepared to move from London to Amsterdam in the lead-up to Brexit¹⁰⁶ and remains suspended as of writing.¹⁰⁷ Thus, while Policy 0070 got off to a strong start, we have yet to see if and when it will resume.

In Canada, a proactive disclosure policy modeled on the EU's launched in early 2019 and is off to a promising start. In March 2019, Health Canada began disclosing a set of safety and efficacy data similar to EMA Policy 0070, which includes trial protocols, clinical study reports,

¹⁰⁰ See, generally, Herder, *Toward a Jurisprudence*, *supra* note [TK]; Sammy Almashat and Michael Carome, *Withholding Information on Unapproved Drug Marketing Applications: The Public Has a Right to Know*, 45 J.L. MED. & ETHICS 46 (2017).

¹⁰¹ Herder, *Toward a Jurisprudence*, *supra* note [TK] at 246. The U.S. FDA once promised to do the same. When Scott Gottlieb was appointed Commissioner of the FDA in 2017, he announced that he would lead an effort to disclose complete response letters (which contain important safety and efficacy data, and the FDA's analysis of the data). When Gottlieb resigned in 2019, he admitted that the effort had stalled and failed. See Sarah Karlin-Smith, *Gottlieb Pushes Forward on FDA Transparency*, POLITICO (Sept. 18, 2017), <https://www.politico.com/tipsheets/prescription-pulse/2017/09/18/gottlieb-pushes-forward-on-fda-transparency-222340>; Sarah Karlin-Smith and Sarah Oweremohle, *Up This Week: Breast Implant Safety*, POLITICO (Mar. 25, 2019), <https://www.politico.com/newsletters/prescription-pulse/2019/03/25/up-this-week-breast-implant-safety-414932> (“Is trying to increase transparency around complete response letters the best use of the finite public resource [I] have?”).

¹⁰² Typically in the form of narrative descriptions of individual patients appearing in the text of clinical study reports. See Jean-Marc Ferran and Sarah Nevitt, *European Medicines Agency Policy 0070: An Exploratory Review of Data Utility in Clinical Study Reports for Academic Research*, 19 BRIT. MED. RESEARCH METHODOLOGY (Nov. 2019) at 2, available at <https://bmcmmedresmethodol.biomedcentral.com/articles/10.1186/s12874-019-0836-3>.

¹⁰³ Ferran & Nevitt, *supra* note [TK] at 2; *Clinical Data Publication*, *supra* note [TK].

¹⁰⁴ Barbara Mantel, *Canada's Decision to Make Public More Clinical Trial Data Puts Pressure on FDA*, NPR (Oct. 11, 2019), <https://www.npr.org/sections/health-shots/2019/10/11/769348119/canadas-decision-to-make-public-more-clinical-trial-data-puts-pressure-on-fda>.

¹⁰⁵ *Clinical Data Publication*, *supra* note [tk].

¹⁰⁶ Peter Doshi, *EMA Scales Back Transparency Initiatives Because of Workload*, 362 BRIT. MED. J. k3513 (2018), available at <https://www.bmj.com/content/362/bmj.k3513>.

¹⁰⁷ *Clinical Data Publication*, *supra* note [tk].

clinical summaries, documentation of statistical methods, and clinical overviews.¹⁰⁸ Health Canada also announced that it would release historical data on earlier-approved drugs “upon receipt of a request from the public and within the limits of [the agency’s] administrative capacity.”¹⁰⁹ Proactive disclosure has proceeded gradually: as of December 2019, data from only about 20 drugs had been posted¹¹⁰; Health Canada has said it will prioritize release of data on first-in-class drugs in 2019 before expanding to all new drug submissions in 2020 or 2021.¹¹¹

But reliance on foreign sources of information on prescription drugs—European, Canadian, or other—will always be an imperfect solution, as drugs are often approved in the U.S. first before they are approved anywhere else,¹¹² and some drugs are never approved anywhere but the U.S.¹¹³ For example, one study of orphan drugs showed that 26% of orphan drugs approved in the U.S. as of 2012 were not approved in Canada,¹¹⁴ and some common medicines, including artemisinin (anti-malarial) and ivermectin (anti-parasitic), are not approved by Health Canada.¹¹⁵ We also do not know if companies submit the same data to different regulatory agencies – and it is plausible that the FDA, which is the most robust drug regulatory agency in the world, has more data, particularly in controversial cases, than do other regulators. Even if Health Canada’s or the EMA’s data disclosure policies expand to cover all drugs approved in those jurisdictions, Americans would be much better served by disclosure by our own regulatory agency.

¹⁰⁸ *Guidance Document on Public Release of Clinical Information: Profile Page*, HEALTH CANADA, <https://www.canada.ca/en/health-canada/services/drug-health-product-review-approval/profile-public-release-clinical-information-guidance.html> (last visited Jan. 28, 2020).

¹⁰⁹ *2.2 Clinical Information in Drug Submissions*, HEALTH CANADA, <https://www.canada.ca/en/health-canada/services/drug-health-product-review-approval/profile-public-release-clinical-information-guidance/document.html#s2.2> (last visited Jan. 28, 2020).

¹¹⁰ *Search for Clinical Information on Drugs and Medical Devices*, HEALTH CANADA, <https://clinical-information.canada.ca/search/ci-rc> (last visited Jan. 28, 2020).

¹¹¹ *3.3 Information Schedule for the Proactive Disclosure of Clinical Information in Drug Submissions and Medical Device Applications*, HEALTH CANADA, <https://www.canada.ca/en/health-canada/services/drug-health-product-review-approval/profile-public-release-clinical-information-guidance/document.html#s3.3> (last visited Jan. 28, 2020).

¹¹² Nicholas S. Downing et al., *Regulatory Review of Novel Therapeutics — Comparison of Three Regulatory Agencies*, 366 NEW ENG. J. MED. 2284 (2012); <https://www.nejm.org/doi/full/10.1056/NEJMsa1200223>; Nicholas S. Downing et al., *Regulatory Review of New Therapeutic Agents — FDA versus EMA, 2011–2015*, 376 NEW ENG. J. MED. 1386 (2017).

¹¹³ For example, the controversial Duchenne muscular dystrophy drug eteplirsen was approved in the United States in 2016 but not approved in Europe, Canada, or elsewhere. See Mark Terry, *Going its Own Way, European Regulators Reject Sarepta’s Exondys 51 for DMD*, BIOSPACE (Sept. 21, 2018), <https://www.biospace.com/article/going-its-own-way-european-regulators-reject-sarepta-s-exondys-51-for-dmd-fda/>.

¹¹⁴ Matthew Herder, *Some Numbers behind Canada’s Decision to Adopt an Orphan Drug Policy: US Orphan Drug Approvals in Canada, 1997–2012*, 11 HEALTHCARE POLICY 70 (2016), available at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4872554/pdf/policy-11-070.pdf>.

¹¹⁵ Adam R. Houston et al., *Why Some Essential Medicines are Unavailable in Canada: It Shouldn’t Take a Crisis to Spur Sensible Reforms that Improve Access to Essential Medicines*, POLICY OPTIONS POLITIQUES (Jul. 4, 2017), <https://policyoptions.irpp.org/magazines/july-2017/why-some-essential-medicines-are-unavailable-in-canada/>.

4. The Freedom of Information Act

That leaves the Freedom of Information Act (FOIA) as the most important approach for independent researchers to obtain clinical data on FDA-approved drugs.¹¹⁶ As we show in the remainder of this subpart, FOIA is frustrating and inadequate for that purpose. FOIA at the FDA has four key flaws: FOIA requests are (1) reactive and require the requester to know precisely what information she seeks before she asks, (2) slow, (3) resource intensive, and (4) highly deferential to industry. We discuss each of these four flaws in more detail below and share a few details of our first-hand experience with FOIA requests to the FDA. Though we focus specifically here on the limits of FOIA to obtain safety and efficacy data from the FDA, we believe the lessons we draw have wider application for FOIA throughout the federal government, as most of the problems we identify are systemic, as we discuss briefly at the end of this subpart.

On its plain text, FOIA might seem a reasonable way to obtain safety and efficacy data from the FDA. FOIA generally requires a federal agency to make information—“records”—within its possession “promptly available” to “any person”¹¹⁷ who requests that information.¹¹⁸ A naïve researcher might reasonably file a FOIA request with the FDA for all of the safety and efficacy data it possesses on a drug of interest and eagerly await the FDA’s “prompt” release of that data, as contemplated by the statute.

Our naïve researcher is very likely to be disappointed. First, the FDA would almost certainly object to the request for “all” safety and efficacy data as overbroad and refuse to fulfill it on that basis. The statute asks requesters to “reasonably describe[]” the records they seek.¹¹⁹ Agencies have interpreted this statutory language as permitting them to refuse to process FOIA requests unless those requests identify with “specificity” or “particularity” the individual records sought, and courts have upheld this practice.¹²⁰ Even if specific, readily identifiable records are requested, the FDA may also refuse to process a FOIA request it deems “unduly burdensome,”

¹¹⁶ 5 U.S.C. § 552. “FOIA requests are generally the only avenue available to consumer groups, researchers, and physicians seeking to access information not released by the FDA.” Aaron S. Kesselheim and Michelle M. Mello, *Confidentiality Laws And Secrecy In Medical Research: Improving Public Access To Data On Drug Safety*, 26 HEALTH AFFAIRS 483 (2007). See also Lurie and Zieve, *Sometimes the Silence Can Be like the Thunder*, *supra* note 68 at 89 (identifying advisory committee materials and FOIA requests as the two approaches “that have provided the greatest access to pharmaceutical data”). For other analysis of FOIA at the FDA, see Laurence Tai, *A Tale of Two Transparency Attempts at FDA*, 69 FOOD & DRUG L.J. 423, 423 (2013); Amy Kapczynski and Jeanie Kim, *Clinical Trial Transparency: The FDA Should and Can Do More*, 45 J.L. MED. & ETHICS 33 (2017); Mathew Herder, *Reviving the FDA’s Authority to Publicly Explain Why New Drug Applications Are Approved or Rejected*, 178 JAMA INTERNAL MED. 1013, 1013 (2018); Alexander C. Egilman et al., *Systematic overview of Freedom of Information Act requests to the Department of Health and Human Services from 2008 to 2017*, 4 RESEARCH INTEGRITY AND PEER REV. 26 (2019).

¹¹⁷ For purposes of making a FOIA request, a “person” can be any individual or organization, commercial or noncommercial, citizen or noncitizen, located anywhere in the world. See 1 West’s Fed. Admin. Prac. § 709 (“Freedom of Information Act—Procedure for requests”).

¹¹⁸ 5 U.S.C. § 552.

¹¹⁹ 5 U.S.C. § 552(a)(3).

¹²⁰ See, e.g., *Assassination Archives & Research Center v. CIA*, 720 F. Supp. 217, 219 (D.D.C. 1989) (“[I]t is the requester’s responsibility to frame requests with sufficient particularity to ensure that searches are not unreasonably burdensome, and to enable the searching agency to determine precisely what records are being requested.”).

another agency practice that courts have upheld.¹²¹ Thus, to ensure processing, a FOIA requester must request a limited set of specific, clearly defined data. The requester generally cannot simply ask for data from a particular clinical trial but should identify the precise metadata, summary data, and individual patient data she needs to perform an independent analysis of each trial. This creates an information asymmetry problem, the “requester’s paradox”: how can a requester request a specific record if she does not know how to describe the record, for example because she is unaware it exists?¹²²

Second, if the FDA did process our requester’s request, FDA would take months, or more likely years, to release any information to our researcher. Between 2008 and 2017, FDA took more than 60 days to fulfill most FOIA requests, even those deemed simple.¹²³ Requests for clinical trial data contained in INDs, NDAs, and BLAs are routinely assigned to the complex queue,¹²⁴ where processing times are longer still – an average of 127 days in 2018, by the FDA’s own estimates,¹²⁵ with about 15% of requests on the complex queue taking over 400 days to process.¹²⁶ In our own experience making and litigating FOIA requests to the FDA,¹²⁷ obtaining clinical data from the FDA takes years, years spent negotiating page-by-page with the FDA over release of individual documents, interspersed with long stretches of waiting. While expedited processing is theoretically available, by regulation the FDA grants expedited processing only to requesters who demonstrate an imminent threat to life or safety or an urgent need to inform the public of actual or alleged agency misconduct,¹²⁸ a difficult standard rarely met in practice.¹²⁹ The FDA FOIA office is backlogged, with over 3,000 FOIA requests outstanding at the end of 2018.¹³⁰ Kwoka has shown that this backlog is attributable to the enormous number of FOIA requests that FDA receives from commercial rather than nonprofit or media requesters.¹³¹

¹²¹ See, e.g., *AFGE, Local 2782 v. U.S. Dep’t of Commerce*, 907 F.2d 203, 209 (D.C. Cir. 1990) (“An agency need not honor a request that requires ‘an unreasonably burdensome search,’” even if the records are requested “with sufficient precision to enable the agency to identify them.” (quoting *Goland v. CIA*, 607 F.2d 339, 353 (D.C.Cir.1978))).

¹²² See, e.g., Ari Schwartz, *Using Open Internet Standards to Provide Greater Access in a Post-9/11 World*, 2 I/S: J. L. POL’Y 125, 128 (2005) (“[T]he ‘requester’s paradox’: how can I know to request a specific document, when I don’t even know that the document exists?”).

¹²³ Egilman et al., *Systematic overview of Freedom of Information Act requests*, *supra* note [TK], at 4.

¹²⁴ Telephone call by Christopher Morten with Darshini Satchi, FDA FOIA Office (November 13, 2019) (notes on file with author).

¹²⁵ *HHS Fiscal Year 2018 Freedom of Information Annual Report*, HHS, <https://www.hhs.gov/foia/reports/annual-reports/2018/index.html> (last visited Jan. 27, 2020).

¹²⁶ *Id.* (685 of 4,446 processed complex requests had a response time of over 400 days).

¹²⁷ Yale Law School, *GHJP Closes Two-Year FOIA Case*, *supra* note [tk]; *Sarepta*, YALE LAW SCHOOL MEDIA FREEDOM & INFORMATION ACCESS CLINIC, <https://law.yale.edu/mfia/projects/open-data/sarepta> (last visited Jan. 25, 2020).

¹²⁸ 21 C.F.R. § 20.44(a).

¹²⁹ *HHS Fiscal Year 2018 Freedom of Information Annual Report*, HHS, <https://www.hhs.gov/foia/reports/annual-reports/2018/index.html> (indicating that in Fiscal Year 2018, FDA denied 449 requests for expedited processing and granted zero).

¹³⁰ *Id.*

¹³¹ Margaret B. Kwoka, *FOIA, Inc.*, 65 DUKE L.J. 1361, 1388 (2016).

Third, our requester will likely find that FOIA is not only slow but resource intensive. Successful use of FOIA to obtain clinical data from the FDA requires money and some legal sophistication.¹³² Even FOIA requests processed without litigation may require the help of a lawyer to negotiate document productions. The FDA charges fees for searching, reviewing, and duplicating documents that can run to the tens of thousands of dollars for large productions of data.¹³³

Fourth, and perhaps most important, whatever data FDA does release to our researcher is likely to be heavily redacted, out of deference to industry, and therefore of limited value. The FDA, and some (but not all) courts, have adopted the view that most of the safety and efficacy data on FDA-approved drugs held by the FDA is the exclusive “property”—so-called “commercial or financial information that is privileged or confidential,” often shortened to “confidential commercial information” (CCI)—of the drug companies that submit those data,¹³⁴ at least in the several years following FDA approval.¹³⁵ The FDA has adopted, by rule, an expansive definition of CCI: “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.”¹³⁶ Under one of FOIA’s nine exemptions to FOIA’s background rule of mandatory disclosure, any agency may withhold CCI

¹³² See David E. Pozen *Freedom of Information Beyond the Freedom of Information Act*, 165 U. Pa. L. Rev. 1097, 1113 (2017) (noting that effective use of FOIA requires “the wherewithal to negotiate with FOIA staff and to litigate denials under unfavorable conditions”); Seth F. Kreimer, *The Freedom of Information Act and the Ecology of Transparency*, 10 U. PA. J. CONST. L. 1011, 1020 (2008) (“To press a recalcitrant administration for disclosure under FOIA requires time, money, and expertise.”).

¹³³ *FOIA Fees*, FDA, <https://www.fda.gov/regulatory-information/freedom-information/foia-fees> (last visited Jan. 29, 2020). While fee waivers are available, see 21 C.F.R. § 20.46, the burden is on the requester to prove eligibility (demanding further legal expertise), and there is no guarantee the FDA will grant the waiver.

¹³⁴ See 21 C.F.R. §§ 20.61(b) (defining CCI broadly, to cover “valuable data”), 20.61(c) (promising not to disclose CCI to FOIA requesters), 314.430(b), (c), (e) (promising to keep secret most of the safety and efficacy data in New Drug Applications (for small molecule drugs)); 601.51(b), (c), (e) (same for Biologics License Applications (for biologic drugs)); *Judicial Watch, Inc. v. Food & Drug Admin.*, 449 F.3d 141, 148, 149 (D.C. Cir. 2006) (holding that “[e]xemption 4 extends to at least some information contained in INDs and NDAs,” although “[e]xemption 4 does not categorically exempt all information in INDs and NDAs”); *Citizens Comm’n on Human Rights v. Food & Drug Admin., Eli Lilly & Co.*, No. 92-cv-5313, 1993 WL 1610471, at *9 (C.D. Cal. May 10, 1993), *aff’d in part, remanded in part sub nom. Citizens Comm’n on Human Rights v. Food & Drug Admin.*, 45 F.3d 1325 (9th Cir. 1995) (holding that “research data and results [in an NDA for an FDA-approved drug] were properly withheld from plaintiff pursuant to Exemption 4 of the FOIA”); *but see Teich v. FDA*, 751 F. Supp. 243, 253 (D.D.C. 1990) (holding that preclinical data on breast implants did not qualify as CCI); *Pub. Citizen Health Research Grp., v. FDA*, 964 F. Supp. 413, 415-16 (D.D.C. 1997) (suggesting that a clinical trial protocol was not CCI); *cf. Public Citizen Health Research Group v. Dep’t of Health, Educ. & Welfare*, 477 F. Supp. 595, 605 (D.D.C. 1979) (holding that medical documents that contained “no data concerning fees, payment schedules, or other commercial arrangements [and] . . . no information about secret formulas or rare treatment methods” were not CCI).

¹³⁵ FDA rules do permit the FDA to disclose publicly all safety and effectiveness data on a small molecule drug once the drug goes generic, or as of the date the drug could go generic. 21 C.F.R. §314.430(f). No corresponding rule appears to exist for biologic and biosimilar drugs. Section 314.430(f) is required by statute; it implements a provision of the Hatch-Waxman Act. Section 104 of the Hatch-Waxman Act, 98 Stat. 1597 (1984) (codified as amended at 21 U.S.C. § 355(1)). Yet, as Eisenberg has noted, “industry has successfully resisted a plain meaning interpretation of this provision,” and the FDA does not regularly disclose additional safety and efficacy data even when a drug goes generic, or as of the date the drug could go generic. Eisenberg, *The Role Of The FDA*, *supra* note [TK] at 381.

¹³⁶ 21 C.F.R. § 20.61(b).

from a FOIA requester,¹³⁷ and the same FDA rule, 21 CFR § 20.61, not only permits withholding of CCI but *prohibits* the agency from disclosing data deemed CCI to FOIA requesters.¹³⁸ The same rule also permits submitters to designate data and other information CCI upon submission.¹³⁹ If the FDA receives a FOIA request for such data, the FDA must notify the submitter and permit the submitter to propose withholding of that data before it released to the FOIA requester.¹⁴⁰ This gives drug companies, not agency officials, the first opportunity to decide which clinical data on their products to disclose and which to keep secret. While the FDA has an obligation to independently verify the submitters' proposed withholding and redaction,¹⁴¹ it does not always do so,¹⁴² perhaps because of limited agency resources, the agency's deep backlog of FOIA requests, or a desire to avoid confrontation with industry "partners." Between 2008 and 2017, the FDA cited FOIA exemption 4—the CCI exemption—more often than any other to withhold information from FOIA requesters.¹⁴³

The problem of FDA deference to industry's view of what constitutes CCI grew worse in June 2019 with the Supreme Court's decision in *Food Marketing Institute v. Argus Leader*.¹⁴⁴ *FMI* upended decades of settled precedent on the meaning of the term "confidential" under the relevant exemption of FOIA, significantly expanding the scope of information and data withholdable as CCI.¹⁴⁵ Before *FMI*, withholdable CCI had generally been limited to information and data whose disclosure would cause substantial competitive harm to the submitter,¹⁴⁶ a definition sufficiently narrow to permit some determined FOIA requesters to obtain some (incomplete) safety and efficacy data on FDA-approved drugs.¹⁴⁷ *FMI* eliminated

¹³⁷ FOIA "exemption 4." 5 U.S.C. § 552(b)(4).

¹³⁸ 21 C.F.R. § 20.61(c); *see also* 21 C.F.R. § 20.82(b).

¹³⁹ 21 C.F.R. § 20.61(d).

¹⁴⁰ 21 C.F.R. § 20.61(e). This rule implements a Reagan-era executive order requiring federal agencies to notify submitters of CCI before disclosing it. E.O. 12,600.

¹⁴¹ 21 C.F.R. § 20.61(e).

¹⁴² In a number of FOIA cases, the FDA has initially withheld documents under exemption 4, deeming them CCI, only to release them later as non-CCI, upon court order or negotiation with the FOIA requester. *See, e.g., Seife v. Food & Drug Admin.*, No. 17-CV-3960 (JMF), 2019 WL 1382724, at *2, *3 (S.D.N.Y. Mar. 27, 2019) (holding that "FDA's redactions [under exemption 4] are overbroad" and ordering FDA to "re-review and, as necessary re-redact, the documents that are in dispute"); *AIDS Healthcare Foundation v. Food & Drug Admin.*, No. 11-cv-07925 (C.D. Cal. Aug. 6, 2013) (order re: defendant's motion for summary judgment), slip op. at 21 (holding that FDA "has failed to demonstrate that the safety and efficacy records that have been withheld are 'confidential' financial and commercial records" and "order[ing] the FDA to produce complete and unredacted copies of the safety and efficacy records to" the FOIA requester); Public Citizen, *Public Citizen HRG v. FDA (Bextra)*, <https://www.citizen.org/litigation/public-citizen-hrg-v-fda-bextra/> (explaining that Public Citizen made a FOIA request to the FDA for certain metadata concerning the drug valdecoxib (Bextra), which was initially withheld but then released after Public Citizen filed a complaint); *Pub. Citizen Health Research Group v. Food & Drug Admin. (Schering)*, 185 F.3d 898, 903 (D.C. Cir. 1999) (ordering release of documents from an IND application, IND No. 18113, that had been withheld by FDA under FOIA exemption 4, because the FDA had not shown that exemption 4 applied); *see also, generally, Lurie & Zieve, Sometimes the Silence*, *supra* note [TK].

¹⁴³ Egilman et al., *Systematic overview of Freedom of Information Act requests*, *supra* note [TK], at 4 (Table 3).

¹⁴⁴ *Food Mktg. Inst.*, 139 S. Ct. 2356 (2019).

¹⁴⁵ *Id.* at 2366.

¹⁴⁶ *See Nat'l Parks & Conservation Assn. v. Morton*, 498 F.2d 765 (D.C. Cir. 1974).

¹⁴⁷ *See supra* note [TK] [citing successful FOIA cases – note beginning "In a number of FOIA cases, the FDA has initially withheld documents under exemption 4 . . ."]

the substantial competitive harm requirement¹⁴⁸ and held that information or data that is merely “customarily kept private, or at least closely held, by the person imparting it” may qualify as CCI and thus for withholding.¹⁴⁹

FMI's focus on what the individual submitter “customarily ke[eps] private” or “closely held” raises a troubling prospect for the future of FOIA at the FDA: anything that drug companies subjectively deem secret may qualify as CCI and thus qualify for withholding from FOIA requesters, thwarting future researchers who seek this data. This would make FOIA less useful than ever. It is true that the Supreme Court left open the question of whether information or data that is merely “customarily kept private, or at least closely held, by the person imparting it” constitutes CCI, or whether the information or data must also be subject to “some assurance that it will remain secret” to the submitter from the agency that receives the submission to qualify.¹⁵⁰ But while this open question may provide FOIA requesters with a glimmer of hope, the fact that the FDA has long had regulations on the books promising the secrecy of data in drug applications may moot this potential second element of the *FMI* test.¹⁵¹ (We explain in Part II.A that despite all this, the FDA possesses authority to disclose *proactively* safety and efficacy data that qualifies as CCI, authority that is confirmed rather than undermined by *FMI*.)

A brief example drawn from the authors' own experience may illuminate how these four problems together make FOIA difficult for researchers. In December 2016, investigative journalist Charles Seife filed a targeted FOIA request for clinical data, agency records, and correspondence concerning the drug eteplirsen (Exondys 51), which is marketed by Sarepta Therapeutics and which was approved by the FDA for treatment of Duchenne muscular dystrophy earlier in 2016.¹⁵² Seife became interested in eteplirsen because of the controversial circumstances of its approval; in his words, the FDA “overruled its own scientific advisers, rejected the recommendations of its review panel, triggered a formal internal dispute process, and apparently sparked the resignation of one senior official and the retirement of another.”¹⁵³ Sarepta now charges close to \$1,000,000 per patient per year for eteplirsen¹⁵⁴ despite the fact that, even as of 2019, it had yet to generate any persuasive evidence that the drug actually

¹⁴⁸ *Food Mktg. Inst.*, 139 S. Ct. at 2363.

¹⁴⁹ *Id.*

¹⁵⁰ *Id.*

¹⁵¹ The Supreme Court also left open the question of whether new statutory language introduced in the FOIA Improvement Act of 2016, requiring that an agency prove that it “reasonably foresees that disclosure would harm an interest protected by” the FOIA exemption to justify withholding, heightens the standard for withholding for FOIA requests filed after 2016. 5 U.S.C. § 552(a)(8)(A). This statutory text, not yet construed by any court cases in connection with exemption 4, provides an alternative basis for FOIA requesters to argue that FOIA exemption 4 cannot possibly cover anything and everything that regulated entities subjectively deem secret upon submission to a regulator. *See, e.g.*, Memorandum of Law in Support of Plaintiff's Combined Cross-Motion for Summary Judgment and in Opposition to Defendants' Motions for Summary Judgment at 11, *Seife v. Food & Drug Admin.*, No. 1:17-cv-03960 (S.D.N.Y. Nov. 4, 2019).

¹⁵² *See* Exhibit 1 to Complaint, *Seife v. Food & Drug Admin.*, No. 1:17-cv-03960 (S.D.N.Y. May 25, 2017).

¹⁵³ Charles Seife, *FDA Documents Reveal Depths of Internal Rancor Over Drug's Approval Process*, UNDARK (Aug. 2, 2017), <https://undark.org/2017/08/02/fda-eteplirsen-janet-woodcock/>.

¹⁵⁴ *See* Thomas and Abelson, *supra* note [TK].

works.¹⁵⁵ Seife’s 2016 FOIA request was narrowly targeted and sought a specific subset of clinical data—Clinical Study Reports, protocols and protocol amendments, statistical analysis plans and plan amendments, and documents of regulatory communications—from two specific clinical trials of eteplirsen.¹⁵⁶ The FDA denied Seife expedited processing and placed his request “in the complex processing queue,” meaning a potentially years-long wait for documents.¹⁵⁷ With legal help from Yale’s Collaboration for Research Integrity and Transparency and Media Freedom and Information Access Clinic, with which both authors are affiliated, Seife filed a FOIA suit against the FDA in the Southern District of New York in May 2017.¹⁵⁸ As of writing, almost three years later, most of the data Seife seeks remains secret,¹⁵⁹ despite eteplirsen’s clinical significance and major financial implications, and despite hundreds of hours of pro bono legal assistance. Sarepta has intervened in the suit as co-defendant, and Seife continues to litigate. Sarepta and FDA continue to argue that the clinical data Seife seeks can be withheld from Seife and other members of the public, under the Supreme Court’s new *FMI* test.¹⁶⁰

The flaws we have identified in FOIA are not at all unique to FDA, though they are perhaps particularly severe there. Margaret Kwoka,¹⁶¹ David Pozen,¹⁶² and others¹⁶³ have

¹⁵⁵ Inst. for Clinical and Economic Review, *ICER Publishes Evidence Report on Treatments for Duchenne Muscular Dystrophy* (Jul. 11, 2019), https://icer-review.org/announcements/dmd_evidence_report/ (last visited Jan. 29, 2020).

¹⁵⁶ See *supra* note [TK – citing complaint in *Seife v. FDA*] at 4.

¹⁵⁷ *Id.*

¹⁵⁸ Complaint, *Seife v. Food & Drug Admin.*, No. 1:17-cv-03960 (S.D.N.Y. May 25, 2017).

¹⁵⁹ The parties negotiated a document production, completed over 2017 and 2018, of over 35,000 pages of data and discussion thereof, which Seife and counsel painstakingly reviewed. See Charles Seife, *Is the Food and Drug Administration Withholding Drug Trial Data to Protect the Corporate Secrets of Pharmaceutical Companies?*, 318 SCI. AM. 38, 38 (2018). Seife is unable to make effective use of much of the data because of extensive redactions.

¹⁶⁰ See Sarepta Therapeutics, Inc.’s Memorandum of Law in Opposition to Plaintiff’s Combined Cross-Motion for Summary Judgment and Reply in Further Support of its Supplemental Motion for Summary Judgment, *Seife v. Food & Drug Admin.*, No. 1:17-cv-03960 (S.D.N.Y. Dec. 5, 2019); Defendants’ Memorandum of Law in Opposition to Plaintiff’s Renewed Cross-Motion for Summary Judgment and Reply Brief in Further Support of Defendants’ Renewed Motion for Summary Judgment, *Seife v. Food & Drug Admin.*, No. 1:17-cv-03960 (S.D.N.Y. Dec. 5, 2019).

¹⁶¹ See Kwoka, *FOIA, Inc.*, *supra* note [TK]; Margaret B. Kwoka, *Inside FOIA, Inc.*, 126 YALE L.J. F. 265 (2016); Margaret B. Kwoka, *First-Person FOIA*, 127 YALE L.J. 2204 (2018).

¹⁶² Pozen, *Transparency’s Ideological Drift*, *supra* note [TK]; David E. Pozen, *Freedom of Information Beyond the Freedom of Information Act*, 165 U. PA. L. REV. 1097 (2017); David E. Pozen, *The Leaky Leviathan: Why the Government Condemns and Condone Unlawful Disclosures of Information*, 127 HARV. L. REV. 512 (2013); David E. Pozen, *Deep Secrecy*, 62 STAN. L. REV. 257 (2010).

¹⁶³ For other important recent work, see David C. Vladeck, *Information Access—Surveying the Current Legal Landscape of Federal Right-to-Know Laws*, 86 TEX. L. REV. 1787 (2008); Michael Herz, *Law Lags Behind: FOIA and Affirmative Disclosure of Information*, 7 CARDOZO PUB. L. POL’Y & ETHICS J. 577 (2009); collected essays in TROUBLING TRANSPARENCY: THE HISTORY AND FUTURE OF FREEDOM OF INFORMATION (David E. Pozen & Michael Schudson, eds., 2018); MARK FENSTER, *THE TRANSPARENCY FIX: SECRETS, LEAKS, AND UNCONTROLLABLE GOVERNMENT INFORMATION* (2017); Laurence Tai, *Fast Fixes for FOIA*, 52 HARV. J. ON LEGIS. 455 (2015); Jennifer Shkabatur, *Transparency With(out) Accountability: Open Government in the United States*, 31 YALE L. & POL’Y REV. 79 (2012); Michele Bush Kimball, *Shining the Light from the Inside: Access Professionals’ Perceptions of Government Transparency*, 17 COMM. L. & POL’Y 299 (2012); Seth F. Kreimer, *The Freedom of Information Act and the Ecology of Transparency*, 10 U. PA. J. CONST. L. 1011 (2008). Practitioners may find the FOIA Wiki administered by the Reporters Committee for Freedom of the Press a helpful resource. FOIA WIKI, https://foia.wiki/wiki/Main_Page (last visited Jan. 24, 2020).

analyzed the law and practice of FOIA across the entire federal government, exploring on its limitations, pitfalls, values, and political economy. Pozen has criticized FOIA as “a distinctively ‘reactionary’ form of transparency.”¹⁶⁴ We will not reiterate these authors’ thoughtful critiques in any depth except to highlight that FOIA is not only bad for researchers; it is bad for the FDA. FOIA impedes the core work of FDA, as it consumes resources and employee time that could be used to other ends.¹⁶⁵ The costs are high: between 2008 and 2017, the FDA spent \$305 million on FOIA, \$2,653 per request.¹⁶⁶ Only a trivial fraction of these costs is recovered through user fees.¹⁶⁷ Shifting to an alternative disclosure system that reduces the number and complexity of the FOIA requests that FDA processes could save tens of millions of dollars – dollars that could be used to create and sustain that alternative disclosure system.

C. The FDA Must Disclose Safety and Efficacy Data Proactively

Because FOIA is insufficient, the FDA needs an alternative disclosure system. Proactive disclosure by the FDA is the best way to break the current logjam and free the safety and efficacy data currently locked inside the FDA. This is consistent with what critics of the limits of FOIA have called for more generally, though the problem here is still more acute, because confidential commercial information and patient privacy arguments compound the general problems with FOIA when industry and datasets are the targets.¹⁶⁸

To date, the FDA has lacked the will to try proactive disclosure.¹⁶⁹ By 2006, Lurie and Zieve would remark that the FDA’s tradition of disclosure lagged the rest of the Department of

¹⁶⁴ Pozen, *Freedom of Information Beyond the Freedom of Information Act*, *supra* note [TK], at 1097.

¹⁶⁵ *Id.* at 1123-31.

¹⁶⁶ Egilman et al., *Systematic Overview of Freedom of Information Act Requests to the Department of Health and Human Services from 2008 to 2017*, *supra* note TK, at 4.

¹⁶⁷ *Id.* (showing that HHS as a whole spent \$446.4 million on FOIA and recovered just \$8.5 million in fees between 2008 and 2017).

¹⁶⁸ Kwoka has argued that “[t]argeted, strategic affirmative disclosure . . . provides one of the most promising avenues for alleviating the privatization of FOIA and returning public information to its anticipated democratic use.” Kwoka, *FOIA Inc.*, *supra* note [TK], at 1429. Pozen has similarly argued that “[t]he most scalable approach (or family of approaches) to transparency policy, and the most plausible substitute for the traditional FOIA model, is affirmative disclosure. Rather than wait for a request for specific records to be filed, whole categories of records deemed appropriate for release can be posted online or otherwise published on a regular schedule.” Pozen, *Freedom of Information Beyond the Freedom of Information Act*, *supra* note [TK], at 1149.

¹⁶⁹ O’Reilly and Fisher have explained how then-FDA Commissioner Frank Young and other FDA officials intervened during negotiation and passage of the Hatch-Waxman Act in 1984 to express the view that the Act does not expand the agency’s obligation to disclose safety and efficacy data, despite statutory language mandating that “[s]afety and efficacy data” “be made available to the public, upon request,” under various circumstances. James T. O’Reilly, *Knowledge Is Power: Legislative Control of Drug Industry Trade Secrets*, 54 U. Cin. L. Rev. 1, 20–21 (1985); Jane A. Fisher, Disclosure of Safety and Effectiveness Data under the Drug Price Competition and Patent Term Restoration Act, 41 FOOD DRUG COSM. L.J. 268 (1986). By 2006, Lurie and Zieve would remark that the FDA’s tradition of disclosure lagged the rest of HHS. Peter Lurie & Allison Zieve, *Sometimes the Silence Can Be like the Thunder: Access to Pharmaceutical Data at the FDA*, 69 L. & CONTEMP. PROBS. 85, 96 (Summer 2006). Tai observed in 2013 that the FDA had created, through regulation, self-imposed obstacles to proactive disclosure (discussed *infra* § II.B) not demanded by statute. Tai, *A Tale of Two Transparency Attempts at FDA*, *supra* note [TK], at 429.

Health and Human Services (HHS).¹⁷⁰ What is different now? For one, there is growing enthusiasm among both academics and policy makers to examine and challenge corporate influence over regulatory agencies and to bolster those agencies' power, integrity, and accountability.¹⁷¹ Political will for real reform may be building: as of writing, leading presidential contenders have called for greater information disclosure and reduced industry influence at FDA.¹⁷²

Moreover, the legal case for proactive disclosure has become both stronger and more urgent since May 2019, when the Supreme Court decided *FMI*.¹⁷³ While *FMI* has dealt further damage to the already broken FOIA system, as noted above, the decision contained a little-noticed silver lining: it confirmed that agencies have authority to disclose information to the public even when that information is protected by FOIA exemption 4. (We discuss this authority in Part II.A.) To be clear, we don't propose to eliminate FOIA; we propose merely to create a separate, more robust proactive disclosure regime alongside it. In Part II, we show how data disclosure at the FDA can and should be "rebooted" to include proactive disclosure.

Part II: Rebooting the Big Data Regulator

A. The FDA Has the Authority It Needs To Disclose Safety and Efficacy Data

Some commentators, especially in industry, have suggested that release of clinical trial data and other evidence of the risks and benefits of prescription drugs is simply illegal, whether because of the absence of authority to disclose or because of actual prohibition by statute.¹⁷⁴ The

¹⁷⁰ Lurie & Zieve, *supra* note [TK].

¹⁷¹ See, e.g., Pozen, *Transparency's Ideological Drift*, *supra* n. [TK]; Amy Kapczynski, *The Lochnerized First Amendment and the FDA: Toward a More Democratic Political Economy*, 118 COLUM. L. REV. F. 179 (2018); Amy Sinden, *The Cost-Benefit Boomerang*, AMERICAN PROSPECT (July 25, 2019), <https://prospect.org/economy/cost-benefit-boomerang>; K. Sabeel Rahman, *The New Utilities: Private Power, Social Infrastructure, and the Revival of the Public Utility Concept*, 39 CARDOZO L. REV. 1621, 1669 (2018).

¹⁷² Sheila Kaplan, *Elizabeth Warren Calls on Former F.D.A. Chief to Quit Pfizer Board*, N.Y. TIMES (July 2, 2019), <https://www.nytimes.com/2019/07/02/health/elizabeth-warren-scott-gottlieb-pfizer.html> (call for reduced industry influence on FDA); Leahy, Sanders, Welch Urge FDA to Swiftly Resolve Critical Drug Recall, BERNIE SANDERS, U.S. SENATOR FOR VERMONT (Oct. 18, 2019), <https://www.sanders.senate.gov/newsroom/press-releases/leahy-sanders-welch-urge-fda-to-swiftly-resolve-critical-drug-recall> (calling for greater disclosure by FDA); Sanders Places Hold on FDA Nominee, BERNIE SANDERS, U.S. SENATOR FOR VERMONT (Jan. 26, 2016), <https://www.sanders.senate.gov/newsroom/press-releases/sanders-places-hold-on-fda-nominee> (call for reduced industry influence on FDA).

¹⁷³ *Food Mktg. Inst.*, 139 S. Ct. at 2356.

¹⁷⁴ See, e.g., Jeffrey K. Francer & Natalie A. Turner, *Responsible Clinical Trial Data Sharing: Medical Advancement, Patient Privacy, and Incentives to Invest in Research*, 8 J. HEALTH & LIFE SCI. L. 63, 92 (2014) ("Federal law consistently has protected the confidentiality of companies' non-public clinical trial information provided to FDA as part of the new drug approval process, including study reports, protocols, and raw safety and effectiveness data."); Joseph G. Milner, *Sunlight and Other Disinfectants: Disclosure Obligations under the Federal Securities and Drug Regulatory Regimes*, 72 FOOD & DRUG L.J. 141, 141 (2017) ("[A] trio of federal statutes requires FDA to keep sensitive information submitted by drug companies confidential."); Biotechnology Industry Organization (BIO), Comment Letter on FDA's Proposed Rule Regarding Availability for Public Disclosure and Submission to FDA for Public Disclosure of Certain Data and Information Related to Human Gene Therapy or Xenotransplantation (Jan. 18, 2001), available at <https://www.bio.org/advocacy/letters/disclosure-information>;

FDA itself has sometimes,¹⁷⁵ but inconsistently,¹⁷⁶ adopted this view. This view is mistaken, as we explain. Proactive disclosure is, in fact, legal under existing law. That is, the FDA already has statutory authority to release many varieties of data about pharmaceuticals, including metadata, summary data (aggregate data), and executable (analysis-ready) data from clinical trials as well as certain real-world evidence gathered by the FDA.

1. Federal Law Does Not Protect the Secrecy of Safety and Efficacy Data

Agencies have the right to release data in their possession unless specifically prohibited by law.¹⁷⁷ FOIA is not itself a limit to disclosure; while certain FOIA exemptions *permit* agencies to withhold information from requesters, no FOIA exemption (standing alone) *requires* agencies to withhold.¹⁷⁸ Agencies' proactive disclosure power was formally recognized by

Pharmaceutical Research and Manufacturers of America (PhRMA), Comment Letter on Draft Proposals for Public Comment Regarding Disclosure Policies of the U.S. Food and Drug Administration (Docket No. FDA-2009-N-0247) (Jul. 20, 2010), available at <https://www.regulations.gov/contentStreamer?documentId=FDA-2009-N-0247-0252&attachmentNumber=1&contentType=pdf>. Lietzan has argued that disclosure by the FDA of safety and efficacy data is not outright prohibited but should require compensation under the Takings Clause. See Lietzan, *supra* note [TK]. As we explain, *infra* § II.D, this is incorrect.

¹⁷⁵ See Richard A. Merrill, *The Architecture of Government Regulation of Medical Products*, 82 VA. L. REV. 1753, 1792 n.122 (1996) (noting that “FDA has consistently taken the legal position that unpublished safety and effectiveness data submitted as part of an NDA are confidential and cannot be released to the public or used to support another manufacturer’s NDA”); see also, generally, Erika Lietzan, *A New Framework for Assessing Clinical Data Transparency Initiatives*, *supra* note [TK], at 51-53 (2014) (collecting examples of FDA expressing the view that it has no discretion to release safety and efficacy data).

¹⁷⁶ See, e.g., Availability for Public Disclosure and Submission to FDA for Public Disclosure of Certain Data and Information Related to Human Gene Therapy or Xenotransplantation,” 66 Fed. Reg. 4688 (proposed Jan. 18, 2001) (expressing the view that FDA has authority to disclose proactively, inter alia, certain safety and efficacy information); Robert Temple & Gordon W. Pledger, *The FDA’s Critique of the Anturane Reinfarction Trial*, 303 NEW ENG. J. MED. 1488 (1980) (FDA publication criticizing a drug company’s safety and efficacy claims and apparently disclosing to the public previously secret details of one of the drug company’s clinical trials).

¹⁷⁷ This principle has been recognized repeatedly by the Supreme Court. See *infra* n. [TK – next footnote]. It has also been recognized repeatedly by the executive branch, including the Solicitor General of the United States (under President Trump) and President Obama. See Brief for the United States as Amicus Curiae Supporting Petitioner at 32, *Food Marketing Institute v. Argus Leader*, No. 18-481 (U.S.) (Because “[FOIA] does ‘not limit an agency’s discretion to disclose information,’ ‘even if a district court’s order requiring disclosure under FOIA is stayed pending appeal, the government could simply release the records itself, rendering any appeal moot,’ and ‘nothing in an appeal by a nongovernment person could prevent the agency’s disclosure of its own records.’” (quoting *Chrysler*, 441 U.S. at 292, 294); Presidential Memorandum for Heads of Executive Departments and Agencies Concerning the Freedom of Information Act, 74 Fed. Reg. 4683 (Jan. 21, 2009) (“The presumption of disclosure should be applied to all decisions involving FOIA. The presumption of disclosure also means that agencies should take affirmative steps to make information public.”); Attorney General Holder’s Memorandum for Heads of Executive Departments and Agencies Concerning the Freedom of Information Act, 74 Fed. Reg. 51879 (Oct. 8, 2009) (“I strongly encourage agencies to make discretionary disclosures of information. An agency should not withhold records merely because it can demonstrate, as a technical matter, that the records fall within the scope of a FOIA exemption.”).

¹⁷⁸ The Supreme Court has explained repeatedly that agencies’ proactive disclosure authority extends not just to information *outside* the scope of the FOIA exemptions but to information *within* these exemptions, including FOIA exemption 4. FOIA exemption 4 merely *permits* agencies to withhold “trade secrets and commercial or financial information obtained from a person and privileged or confidential.” 5 U.S.C. 552(b)(4). In *Chrysler v. Brown*, the Court squarely held that FOIA exemption 4 is an “exception to the disclosure mandate of the FOIA and not a limitation on agency discretion.” *Chrysler*, 441 U.S. at 291 n.11. “[T]he FOIA by itself protects the submitters’ interest in confidentiality only to the extent that this interest is endorsed by the agency collecting the information.”

Congress in the federal “housekeeping statute,”¹⁷⁹ codified at 5 U.S.C. § 301, which grants all federal agencies general authority to disclose information in their possession.¹⁸⁰

Existing limits on the FDA’s disclosure of safety and efficacy data on prescription drugs primarily arise from two concerns: patient privacy and trade secrecy.¹⁸¹ Patient privacy is a

Id. at 293. “Congress did not limit an agency’s discretion to disclose information when it enacted the FOIA.” *Id.* at 294. In *Ruckelshaus v. Monsanto*, the Court concluded that even if certain health, safety, and environmental data about pesticides submitted to the EPA were trade secrets, the Federal Government had the authority to disclose that data, as long as it did not provide assurances to the company that it would not do so. *Ruckelshaus v. Monsanto*, 467 U.S. 986, 1004-05, 1008-09 (1984). The Supreme Court’s recent decision in *FMI* again confirms, albeit with little fanfare, that federal agencies possess discretion to disclose proactively material that falls within the scope of FOIA exemption 4. *Food Mktg. Inst.*, 139 S. Ct. at 2362. In *FMI*, respondent Argus Leader’s argued that the petitioner’s “injury is not redressable because a favorable ruling would merely restore the government’s discretion to withhold the requested data under Exemption 4, and it might just as easily choose to provide the data anyway.” *Id.* The Court dismissed this argument not by questioning the agency’s (USDA’s) discretionary authority to disclose the requested data but instead by relying on the agency’s *Monsanto*-esque assurances that it would not exercise that authority unless compelled to do so by court order. *Id.* As such, *FMI* implicitly acknowledged the agency’s discretion to disclose information eligible for withholding under FOIA exemption 4.

¹⁷⁹ *Chrysler*, 441 U.S. at 309 n.39.

¹⁸⁰ “The head of an Executive department or military department may prescribe regulations for the government of his department, the conduct of its employees, the distribution and performance of its business, and the custody, use, and preservation of its records, papers, and property.” 5 U.S.C. § 301. Section 301 further states that it “does not authorize withholding information from the public or limiting the availability of records to the public” and thus appears to embody and codify the background principle that agencies can, at will, make information in their possession available to the public, even absent a specific authorizing regulation. *Id.* In *Chrysler*, the Supreme Court named section 301 as a source of authority for agencies to create proactive disclosure regulations. *Chrysler*, 441 U.S. at 309 n.40 (“This does not mean, of course, that disclosure regulations promulgated on the basis of § 301 are ‘in excess of statutory jurisdiction, authority, or limitations’ for purposes of the APA, 5 U.S.C. § 706(2)(C). It simply means that disclosure pursuant to them is not ‘authorized by law’ within the meaning of § 1905.”); *see also id.* at 320 n.2 (Marshall, J., concurring) (“[T]he courts below must determine on remand whether § 1905 covers the types of information respondents intended to disclose. Disclosure of those documents not covered by § 1905 would, under the Court’s holding, be ‘in accordance with law.’”). Certain circuit decisions can be read to suggest that 5 U.S.C. § 301, as a “housekeeping” statute, does not provide agencies’ “substantive” authority to craft regulations and policies concerning disclosure. *See, e.g., In re Bankers Trust Co.*, 61 F.3d 465, 470 (6th Cir. 1995); *Exxon Shipping Co. v. Dep’t of Interior*, 34 F.3d 774, 777 (9th Cir. 1994). However, these decisions uniformly address and criticize agency efforts to withhold information from discovery under the alleged authority of § 301, in contravention of the statute’s explicit command that “[t]his section does not authorize withholding information from the public or limiting the availability of records to the public.” 5 U.S.C. § 301. These decisions do not hold that an agency cannot promulgate rules for proactive disclosure under the authority of § 301. *See Gen. Eng’g, Inc. v. N.L.R.B.*, 341 F.2d 367, 374 n.10 (9th Cir. 1965) (the housekeeping statute is not “a convenient blanket to hide anything Congress may have neglected or refused to include under specific secrecy laws”). Agencies promulgated proactive disclosure regulations under the authority of section 301 at least as recently as the 1960s and 70s—*see, e.g., Sears Roebuck & Co. v. Eckerd*, 575 F.2d 1197 (7th Cir. 1978); *Chrysler Corp. v. Schlesinger*, 565 F.2d 1172 (3d Cir. 1977)—and there is nothing in *Chrysler* or subsequent cases that appears to prevent agencies from doing so in the future.

¹⁸¹ *See, e.g., Food & Drug Admin., FDA’s Clinical Data Summary Pilot Program: Questions Frequently Asked by Industry* (May 2, 2018), available at <https://www.fda.gov/drugs/development-approval-process-drugs/fdas-clinical-data-summary-pilot-program-questions-frequently-asked-industry> (“FDA will redact information as we currently do when processing these types of documents in response to Freedom of Information Act (FOIA) requests or when posting an action package. This means that FDA will redact selected portions of the CSRs for trade secrets, confidential commercial information, and personal privacy information.”). Both of these concerns are formally reflected in FOIA. FOIA includes distinct exemptions for trade secrets and CCI (5 U.S.C. § 552(b)(4)), and for personal privacy (5 U.S.C. § 552(b)(6)). These exemptions permit, but not require, agencies to withhold

widely accepted value,¹⁸² and one we share. Patient privacy is a vital concern any time clinical data is shared, and the risk of violation of patient privacy is particularly critical when individual patient data is released. Patient privacy concerns are pronounced when the patient population is stigmatized, as in trials of medical abortion drugs or treatments for sexually transmitted infections, and privacy is harder to protect where the clinical study size is small or the disease is rare. The FDA currently, and properly, exempts from disclosure any data “which constitutes a clearly unwarranted invasion of personal privacy,”¹⁸³ and the agency discloses safety and efficacy data only after the data has been “deidentified” to remove information that readily identifies individual patients, to protect patient privacy.¹⁸⁴ As explained in Part § II.B, the FDA’s rules and practices on deidentification appear reasonable, and should be incorporated into the “rebooted” data publicity regime we propose. Existing protocols for deidentification make the practice a viable one for the agency and for researchers.¹⁸⁵ (As we discuss below, reidentification is a potential concern, and data use agreements can and should be used to forbid it.)¹⁸⁶

We do, however, disagree with the FDA’s stance on trade secrecy, and that stance currently is the central obstacle to meaningful public access to safety and efficacy data on prescription drugs.¹⁸⁷ The FDA’s professed concern over trade secrecy arises from two distinct federal trade secrecy statutes that govern the FDA—section 301(j) of the Food, Drug, and Cosmetic Act (FDCA), codified at 21 U.S.C. § 331(j), and the Trade Secrets Act (TSA), codified at 18 U.S.C. §§ 1905-1909—but the FDA’s concern also implicates other sources of trade secrecy law, including FOIA and the Uniform Trade Secrets Act (UTSA) and other state-level trade secrecy law.¹⁸⁸ We consider each and show that none of these sources of law creates an impassable barrier to data publicity.

The first statute—section 301(j) of the FDCA—is no barrier to safety and efficacy data publicity at all. Section 301(j) only prohibits “revealing, other than to the Secretary or officers or employees of the Department, or to the courts when relevant in any judicial proceeding under this chapter, any information acquired . . . concerning any method or process which as a trade

information by the exemptions. *See supra* note [TK – n. beginning “The Supreme Court has explained, decade after decade, . . .”].

¹⁸² U.S. DEP’T OF HEALTH, EDUCATION, & WELFARE, THE BELMONT REPORT: ETHICAL PRINCIPLES AND GUIDELINES FOR THE PROTECTION OF HUMAN SUBJECTS OF RESEARCH (1979), available at <https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/read-the-belmont-report/index.html>.

¹⁸³ 21 C.F.R. § 20.63. *See also* 21 C.F.R. § 20.82(b)(2).

¹⁸⁴ *See infra* § II.B.

¹⁸⁵ *See id.*

¹⁸⁶ *See id.*

¹⁸⁷ *See supra* n. [TK – the one citing Merrill and Lietzan].

¹⁸⁸ The FDA itself has, at times, conflated section 301(j) of the FDCA, the TSA, and FOIA exemption 4. *See, e.g.*, 39 Fed. Reg. 44,602, 44,612 (1974) (“[I]t is not feasible or practical to determine the differences, if any, between the confidentiality provisions in 18 U.S.C. 1905 and 21 U.S.C. 331(j), and the Freedom of Information Act. If there are any differences, they are extremely subtle and small. Accordingly, the Commissioner intends, for practical reasons of daily administration of the law, to regard the coverage of these provisions as identical.”).

secret is entitled to protection.”¹⁸⁹ Contrary to the FDA’s prevailing view that this section covers some safety and efficacy data,¹⁹⁰ the statutory language is limited to manufacturing information—information “concerning any method or process”—and no court has ever construed section 301(j) to cover safety or efficacy data. The Tenth Circuit has held that section 301(j) “is arguably narrower than [the already narrowly construed trade secret provision of FOIA] Exemption 4 in that it is limited to information relating to methods or processes whereas Exemption 4 applies to all trade secret information.”¹⁹¹

The second statute—the TSA¹⁹²—requires somewhat more extensive analysis, but ultimately it, too, creates no legitimate barrier to disclosure of the safety and efficacy data we describe above.¹⁹³ The TSA is a criminal statute that prohibits federal employees from disclosing certain confidential information when not “authorized by law”:

Whoever, being an officer or employee of the United States or of any department or agency thereof, . . . publishes, divulges, discloses, or makes known in any manner or to any extent not authorized by law any information coming to him in the course of his employment or official duties or by reason of any examination or investigation made by, or return, report or record made to or filed with, such department or agency or officer or employee thereof, which information concerns or relates to the trade secrets, processes, operations, style of work, or apparatus, or to the identity, confidential statistical data, amount or source of any income, profits, losses, or expenditures of any person, firm, partnership, corporation, or association; . . . shall be fined under this title, or imprisoned not more than one year, or both; and shall be removed from office or employment.¹⁹⁴

¹⁸⁹ 21 U.S.C. § 331(j). Heled has observed that FDCA section 301(j) poses an obstacle to the FDA’s disclosure of biologics manufacturing information and has suggested that Congress consider amending it. Yaniv Heled, *The Case for Disclosure of Biologics Manufacturing Information*, 47 J. L. MED. ETHICS 54, 63 (2019).

¹⁹⁰ See, e.g., 65 Fed. Reg. 64,607, 64,612 (2000) (“FDA will not disclose any information from postmarketing study reports that is considered a trade secret as defined in § 20.61(a) and section 301(j) of the act (21 U.S.C. 331(j))”); 39 Fed. Reg. 44,602, 44,612, 44,633 (1974) (stating that “[u]nder the Federal Food, Drug, and Cosmetic Act, . . . the safety and effectiveness data for new drugs and new animal drugs, including antibiotic drugs for veterinary use, fall within the trade secrets exemption and thus are not available for public disclosure unless the applicant has previously made the information public or the drug has been disapproved or withdrawn from the market or the drug has reached the stage where it may be marketed without submission of such data to the agency for approval” and that “[e]ven if [disclosure of trade secrets and CCI] would be in the public interest, in order to protect the public health, and even if the Commissioner wishes as a matter of discretion to release such material, such disclosure cannot lawfully be undertaken.”); see also *supra* note [TK - the one citing Merrill and Lietzan].

¹⁹¹ *Anderson v. Dep’t of Health & Human Servs.*, 907 F.2d 936, 951 (10th Cir. 1990). The court went on to say, “[t]his . . . is probably a distinction without much of a difference since we have defined trade secret to be limited to a secret ‘used for the making, preparing, compounding, or processing of trade commodities.’” *Id.*; cf. *Public Citizen Health Research Group v. FDA*, 704 F.2d 1280, 1287 n. 19 (proffering, in dicta, a narrow interpretation of section 301(j)). See also Richard S. Fortunato, Note, *FDA Disclosure of Safety and Efficacy Data: The Scope of Section 301(j)*, 52 FORDHAM L. REV. 1280, 1283 (1984) (explaining why section 301(j) should be construed narrowly); McGarity & Shapiro, *supra* note [TK], at 886-87 (same).

¹⁹² 18 U.S.C. §§ 1905-1909.

¹⁹³ *Supra* § I.A.

¹⁹⁴ 18 U.S.C. § 1905.

Passed decades ago, the penalties contemplated by the TSA—fines, imprisonment, and removal—have apparently never been applied.¹⁹⁵ The reach of the act is critically confined by its text: disclosure of trade secrets is permissible whenever “authorized by law.” In our view the FDA’s statutory authority to make rules for disclosure is broad enough to establish such authority, meaning that the agency need not evaluate whether the data in question is a trade secret for the purposes of the Act. The data use agreements we advise would also permit the agency to rule out by contract behavior that would violate trade secrecy law, and thus should also insulate regulators from any challenge under the TSA. However, agencies will undoubtedly be more likely to release information that they believe does not rise to the level of trade secret protection, so we first explain here why clinical trial data will not generally be protected by trade secrecy law generally or as regards the TSA specifically.

Two questions arise when assessing the scope of the TSA: the first is whether clinical trial data can ever be considered trade secrets, even under the most expansive understanding of that term, and the second is whether the TSA incorporates a narrow or broad definition of “trade secret”. As to the former, state trade secrecy laws today, grounded in the UTSA and common law, sweep relatively broadly and protect any information that is secret, is subject to reasonable efforts to maintain its secrecy, and that confers a competitive advantage on its owner.¹⁹⁶ However, the safety and efficacy data we seek will generally have little or no direct value to competitors and thus will confers minimal or no competitive advantage to the company on whose behalf the FDA is currently maintaining secrecy. Courts have held that most safety and efficacy data from clinical trials has no demonstrable competitive value.¹⁹⁷ As regards individual patient-level data, competitors cannot use “subject-specific data to demonstrate the safety or effectiveness of other products,” because “[t]he slightest change in the pharmaceutical formulation or dosage” from an existing drug to a new one renders the data unacceptable for approval of the new drug.¹⁹⁸ Incomplete but nonetheless informative summaries of the much of the same safety and efficacy data must already be disclosed via ClinicalTrials.gov and the FDA’s Drugs@FDA website,¹⁹⁹ blunting whatever adverse competitive impact disclosure of the complete set of safety and efficacy data could have. The courts have ruled that clinical trial

¹⁹⁵ Milgram on Trade Secrets, Sec. 12.02 n. 8.

¹⁹⁶ See Restatement (Third) of Unfair Competition; UTSA § 1.4.

¹⁹⁷ See, e.g., *Public Citizen Health Research Group v. FDA*, 704 F. 2d at 1290 & n.28 (holding that “not every bit of information submitted to the government by a commercial entity qualifies for protection under Exemption 4” and citing, approvingly, *Public Citizen Health Research Group v. Department of Health, Educ. & Welfare*, 477 F. Supp. at 605, which held medical documents that contained “no data concerning fees, payment schedules, or other commercial arrangements [and] ... no information about secret formulas or rare treatment methods,” did not constitute “commercial information”); *AIDS Healthcare Foundation v. Food & Drug Admin.*, supra note [TK], at 21 (holding that “FDA has not established a likelihood that disclosure of the data summaries and analyses withheld under Exemption 4 would cause substantial competitive injury to Gilead”); see also *Teich v. FDA*, 751 F. Supp. 243, 253 (D.D.C. 1990) (holding that preclinical data on breast implants did not qualify as CCI); *Pub. Citizen Health Research Grp. v. FDA*, 964 F. Supp. 413, 415-16 (D.D.C. 1997) (suggesting that a clinical trial protocol was not CCI).

¹⁹⁸ *Public Citizen Health Research Group v. FDA*, 2000 WL 34262802, No. Civ.A. 99–0177(JR) (D.D.C. Jan. 19, 2000).

¹⁹⁹ See *supra* § I.B. Some courts have held, in the FOIA context, that when federal law requires publication of certain information (e.g., publication of clinical trial results on ClinicalTrials.gov), that information should be deemed public by operation of law, even if not actually published in practice. See, e.g., *Inner City Press v. Bd. of Governors*, 463 F.3d 239, 249 (2d Cir. 2006).

protocols can in general be released by the FDA, concluding that they do not meet the definition of CCI (more capacious even than trade secrets) under FOIA exemption 4. By the time a drug is approved, years have likely passed since the clinical trials relied on for approval were designed, increasing the likelihood that details of the design of those trials have been disclosed through other means and decreasing their competitive value.

Industry has attempted to block past proposals to disclose some safety and efficacy data by suggesting that even if the FDA could prevent competitors from taking advantage of that data within the U.S., freerides would nonetheless be able to copy the disclosed data and resubmit it to foreign drug regulators to support approval of competitor products there.²⁰⁰ This foreign freeriding concern is not convincing, in our view.²⁰¹ First, if a “resubmitted” company is the first to seek to register a particular drug in a particular foreign jurisdiction, meaning that no data has been submitted to the same regulator by the original submitter to the FDA, then presumably the original submitter decided not to compete in that jurisdiction, effectuating little or no competitive harm. Second, over 70 nations provide data exclusivity protection,²⁰² including all of the world’s most profitable markets for pharmaceuticals²⁰³; if the original submitter has sought registration in any of these nations, then resubmission of data will be prohibited under that nation’s data exclusivity laws.²⁰⁴ Third, as we explain below,²⁰⁵ the data made available through our data publicity scheme will almost certainly be redacted to some extent and thus may not be accepted by the foreign regulator, thereby discouraging resubmission. Fourth, the FDA can data use agreements to prohibit resubmission to other drug regulators and impose stringent penalties for breach.

²⁰⁰ See, e.g., Comments of the Pharmaceutical Research and Manufacturers of America (PhRMA) on Draft Proposals For Public Comment Regarding Disclosure Policies of the U.S. Food and Drug Administration (Docket No. FDA-2009-N-0247), Jul. 20, 2010, at 30 (alleging that disclosure “of safety and efficacy data [will cause] grave competitive harm to the research-based biopharmaceutical industry[] and subsequently damage incentives to take new products through the costly drug approval process. . . . [T]hese data could be used to support approval in virtually every other country in the world, even after redaction of trade secret information.”), available at <https://www.regulations.gov/contentStreamer?documentId=FDA-2009-N-0247-0252&attachmentNumber=1&contentType=pdf>.

²⁰¹ See Amy Kapczynski *The interaction between open trial data and drug regulation in selected developing countries*, Paper commissioned by the Committee on Strategies for Responsible Sharing of Clinical Trial Data (2014), available at <http://www.nationalacademies.org/hmd/~media/Files/Report%20Files/2015/SharingData/KapczynskiPaper.pdf>.

²⁰² Data exclusivity: Encouraging development of new medicines – IFPMA, <https://www.ifpma.org/resource-centre/data-exclusivity-encouraging-development-of-new-medicines/> (last visited Feb 8, 2020).

²⁰³ See Biggest Pharmaceutical Markets In The World By Country, WorldAtlas, <https://www.worldatlas.com/articles/countries-with-the-biggest-global-pharmaceutical-markets-in-the-world.html> (last visited Feb 8, 2020) (listing the U.S., Japan, China, Germany, France, Brazil, Italy, UK, Canada, and Spain as the largest markets for pharmaceuticals).

²⁰⁴ Not all countries have data exclusivity laws, and all countries ought, under principles of national sovereignty and avoidance of giving U.S. law extraterritorial effect, to decide for themselves whether data exclusivity laws are appropriate. We note, however, that we are not aware of a drug regulator in any country that requires submission of more than summary data but does not, at the same time, provide some kind of provide data exclusivity. Thus, we are not aware of any country where disclosure of individual patient data and the other data we contemplate, *supra* § I.A, where resubmission could cause serious competitive harm.

²⁰⁵ *Infra* § II.B.

What safety and efficacy data might have legitimate competitive value and thus qualify as a trade secret under a broad state law definition? The EMA offers helpful guidance here: it has explained that, for purposes of EU law, only data that bears “innovative features” qualifies for secrecy (under the EMA’s doctrine of CCI).²⁰⁶ An EMA advisory committee enumerated examples of the relatively few subcategories of safety and efficacy data likely to bear such features, which include new assay methodologies for biomarkers, methods to pursue newly validated endpoints, and novel trial designs that streamline and make more economical proof of efficacy.²⁰⁷ Public Citizen’s Health Research Group has endorsed the EMA advisory committee’s list as illustrative of the rare circumstances under which safety and efficacy data might qualify for protection as a trade secret or CCI,²⁰⁸ and we do the same. We agree with the EMA and with Public Citizen that the safety and efficacy data in routine drug applications generated via established clinical protocols will likely contain no “innovative features” at all and thus not qualify for secrecy, whatever the definition of trade secret or CCI applied.²⁰⁹

Also pertinent is the question of the scope of the TSA’s definition of “trade secrets.” The language of the TSA is superficially broad, encompassing, *inter alia*, confidential information relating to “trade secrets,” “operations,” and “style of work,” but the statute was adopted in 1948, in an era when the most influential statement of trade secrecy protection was the First Restatement of Torts. The First Restatement is commonly understood to have defined a narrower scope for trade secrecy law than did the USTA or the Restatement (Third) of Unfair Competition, both elaborated in the 1980s.²¹⁰ It states clearly that trade secrets are protected as a matter of commercial morality and not property,²¹¹ and because of this different basis in protection, as well as certain specific exclusions (see section 759), trade secrecy law in this earlier period was substantially narrower than it is today.²¹² The TSA also codifies a handful of older federal anti-disclosure statutes, each narrowly focused on protecting closely-held

²⁰⁶ EUROPEAN MEDICINES AGENCY, EXTERNAL GUIDANCE ON THE IMPLEMENTATION OF THE EUROPEAN MEDICINES AGENCY POLICY ON THE PUBLICATION OF CLINICAL DATA FOR MEDICINAL PRODUCTS FOR HUMAN USE 48 (Mar. 2, 2016), https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/external-guidance-implementation-european-medicines-agency-policy-publication-clinical-data_en-0.pdf.

²⁰⁷ CLINICAL TRIAL ADVISORY GROUP ON RULES OF ENGAGEMENT (CTAG3), ADVICE TO THE EUROPEAN MEDICINES AGENCY ON RULES OF ENGAGEMENT FOR ACCESSING CLINICAL TRIAL DATA 1 (Apr. 4, 2013), https://www.ema.europa.eu/en/documents/other/ctag3-advice-european-medicines-agency-rules-engagement-accessing-clinical-trial-data-final-advice-4_en.pdf.

²⁰⁸ See Sarah Sorscher and Michael Carome, *Submission of comments on 'Policy 0070 on publication and access to clinical-trial data'*, <https://www.citizen.org/wp-content/uploads/migration/2163.pdf>.

²⁰⁹ See *supra* notes [TK – preceding 3 notes].

²¹⁰ See, e.g., Edmund W. Kitch, *The Expansion of Trade Secrecy Protection and the Mobility of Management Employees: A New Problem for the Law*, 47 S. C. L. REV. 659 (1995).

²¹¹ Restatement, *supra* note [TK], section 757 (“The suggestion that one has a right to exclude others from the use of his trade secret because he has a right of property in the idea has been frequently advanced and rejected. The theory that has prevailed is that the protection is afforded only by a general duty of good faith and that the liability rests upon breach of this duty; that is, breach of contract, abuse of confidence or impropriety in the method of ascertaining the secret.”).

²¹² The First Restatement excluded ephemeral and negative information, for example. See *id.* The Restatement also made clear, mirroring with the TSA, that “[a] privilege to disclose may also be given by the law . . . in order to promote some public interest.” *Id.* section 757, cmt. (d).

manufacturing and financial information shared with government employees.²¹³ As the Supreme Court has said, “[t]he Trade Secrets Act is not a guarantee of confidentiality to submitters of data.”²¹⁴ In construing the TSA narrowly, the Supreme Court aligns with Levine, Lyndon, and other commentators, who have argued that “trade secrets” and other purportedly confidential information should receive narrow and thin protection in public law contexts, as when information is submitted to government agencies or created by private industry with public money.²¹⁵ Because the TSA governs the entire federal administrative state, appropriately narrow interpretation of the scope of the TSA has great importance not just for drugs but for data publicity and democratic accountability across the federal government, with implications from criminal justice²¹⁶ to federal agencies’ growing use of algorithmic decisionmaking²¹⁷ to the safety of food and our environment.²¹⁸

²¹³ See *Chrysler*, 441 U.S. at 296-98 (tracing history of TSA); Mark Q. Connelly, *Secrets and Smokescreens: A Legal and Economic Analysis of Government Disclosures of Business Data*, 1981 WIS. L. REV. 207, 230. [can expand cite – revisit research by YLS librarians]

²¹⁴ *Ruckelshaus v. Monsanto*, 467 U.S. at 1008-09. See also *Public Citizen Health Research Group v. FDA*, 704 F.2d at 1289 (“When the question of defining proprietary information appears in the public context of whether health and safety data submitted to an agency should be publicly disclosed, the interests of the public in disclosure and the protection of innovation incentives pose important considerations which the common law definition was not designed to handle. The Restatement approach, with its emphasis on culpability and misappropriation, is ill-equipped to strike an appropriate balance between the competing interests of regulated industries and the general public. Therefore, lumping health and safety testing data with all other types of proprietary information is inherently suspect.”).

²¹⁵ David S. Levine, *Secrecy and Unaccountability: Trade Secrets in Our Public Infrastructure*, 59 FLA. L. REV. 135, 191-92 (2007) (“[T]he commercial definition of a trade secret could be narrowed, as in the FOIA trade secret exemption, to only apply to information that is actually used in commerce or where its disclosure would pose an immediate threat to the security of the infrastructure itself. In this way, the information that would be protected from disclosure would be less than that covered by the current all-encompassing definition, and would reflect more respect for the legitimate needs of the public.”); Mary L. Lyndon, *Secrecy and Access in an Innovation Intensive Economy: Reordering Information Privileges in Environmental, Health, and Safety Law*, 78 U. COLO. L. REV. 465, 498 (2007) (explaining the characteristics that “environmental, health, and safety” data (such as data on the safety and efficacy of drugs) must have to qualify as proper trade secrets). See also David S. Levine, *The People’s Trade Secrets*, 18 MICH. TELECOMM. & TECH. L. REV. 61 (2011); David S. Levine, *The Impact of Trade Secrecy on Public Transparency*, in *THE LAW AND THEORY OF TRADE SECRECY* (Rochelle C. Dreyfuss and Katherine J. Strandburg, eds., 2011), at 438 (proposing, *inter alia*, “to narrow the definition of a trade secret in the public infrastructure context”); Peter S. Menell, *Tailoring a Public Policy Exception to Trade Secret Protection*, 105 CALIF. L. REV. 1 (2017). Feldman and Graves have separately argued, persuasively, that a different sort of pharmaceutical data—data on the true prices paid for pharmaceuticals—should not be protected, as a trade secret, from disclosure by regulators. Robin Feldman and Charles Graves, *Naked Price and Pharmaceutical Trade Secret Overreach*, Yale Journal of Law & Technology (Forthcoming); UC Hastings Research Paper No. 354. Available at SSRN: <https://ssrn.com/abstract=3426225> or <http://dx.doi.org/10.2139/ssrn.3426225>. While Feldman and Graves address some federal trade secrecy law, including FOIA and the TSA, they focus their analysis on state drug pricing transparency proposals and state trade secrecy law.

²¹⁶ See, e.g., Rebecca Wexler, *Life, Liberty, and Trade Secrets: Intellectual Property in the Criminal Justice System*, 70 STAN. L. REV. 1343 (2018).

²¹⁷ See, e.g., Hannah Bloch-Wehba, *Access to Algorithms*, Fordham Law Review, *forthcoming* (2019).

²¹⁸ See, e.g., Mary L. Lyndon & David S. Levine, Comment Letter on Proposed Bureau of Land Management Rule Providing Trade Secret Protection to Chemical Information in the Hands of Fracking Entities (Aug. 23, 2013), https://papers.ssrn.com/sol3/papers.cfm?abstract_id=2363284; Julie E. Zink, *When Trade Secrecy Goes Too Far: Public Health and Safety Should Trump Corporate Profits*, 20 VAND. J. ENT. & TECH. L. 1135, 1162 (2018).

Perhaps with a sense of this history, the Supreme Court has many times suggested that the TSA is narrower in scope than state trade secrecy laws. For example, in *Ruckelshaus v. Monsanto*, certain “health and safety data” concerning a pesticide submitted by Monsanto to the EPA was deemed by the Court to be a trade secret under Missouri state law²¹⁹ but not protected by the TSA’s prohibition on unauthorized disclosure.²²⁰ Just last year, the Supreme Court reaffirmed a narrow construction of the TSA, albeit implicitly, in *FMI*, where it held that the scope of the TSA must be narrower than FOIA exemption 4, which provides agencies discretion to withhold trade secrets and CCI.²²¹ The narrow scope of the TSA, properly construed, is yet further reason to think that the safety and efficacy data on prescription drugs that we defined above²²² is not covered by the statute. The Supreme Court’s decision in *Ruckelshaus v. Monsanto* suggests that, under the TSA, a regulatory agency may disclose any “health and safety” data submitted by “an industry that long has been the focus of great public concern and significant government regulation,” “absent an express promise” of confidentiality on the part of the agency²²³; surely safety and efficacy on prescription drugs data qualifies as such. Indeed, on two occasions, it appears the FDA has done just that and disclosed discrete non-public safety and efficacy data on FDA-approved drugs when doing so served the public interest.²²⁴ (To our

²¹⁹ 467 U.S. at 1001-02.

²²⁰ *Id.* at 1008-09 (“[T]he Trade Secrets Act is not a guarantee of confidentiality to submitters of data, and, absent an express promise, Monsanto had no reasonable, investment-backed expectation that its information would remain inviolate in the hands of EPA. In an industry that long has been the focus of great public concern and significant government regulation, the possibility was substantial that the Federal Government, which had thus far taken no position on disclosure of health, safety, and environmental data concerning pesticides, upon focusing on the issue, would find disclosure to be in the public interest.”).

²²¹ *FMI*, 139 S. Ct. at 2362. (“[A ruling favorable to the withholding agency] would merely restore the government’s discretion to withhold the requested data under Exemption 4, and it might just as easily choose to provide the data anyway.”). A 1983 decision of the DC Circuit, *Public Citizen Health Research Group v. FDA*, also endorses, in dicta, a construction of the TSA as narrow in scope. 704 F.2d 1280, 1287 (reasoning that “health and safety data submitted to the FDA” would not meet the definition of “trade secrets under the federal TSA (citing *United States ex rel. Norwegian Nitrogen Products Co. v. United States Tariff Commission*, 6 F.2d 491, 495 (D.C.Cir.1925), vacated as moot, 274 U.S. 106 (1927), which construed a predecessor statute to the TSA)). Oddly, the DC Circuit has elsewhere held that the TSA is broad in scope, possibly even broader than FOIA exemption 4. *See, e.g., CNA Fin. Corp. v. Donovan*, 830 F.2d 1132, 1151-52 (D.C. Cir. 1987) (“It is our considered view, therefore, that the scope of the [Trade Secrets] Act is at least co-extensive with that of Exemption 4 of FOIA, and that, in the absence of a regulation effective to authorize disclosure, the Act prohibits OFCCP from releasing any information in CNA’s affirmative action programs and EEO-1 reports that falls within Exemption 4.”). However, the D.C. Circuit has subsequently suggested the view, later reaffirmed by the Supreme Court in *FMI*, that the TSA must be narrower than FOIA exemption 4, such that some material covered by exemption 4 can be released at the agency’s discretion. *See Pub. Citizen Health Research Group v. Food & Drug Admin. (Schering)*, 185 F.3d 898, 903 (D.C. Cir. 1999) (certain information in investigational new drug applications “may be withheld if the agency carries its burden under Exemption 4 of the FOIA” (emphasis added)). The Seventh Circuit has long taken a narrow view of the TSA, consistent with the holdings of *Ruckelshaus v. Monsanto* and *FMI*. *See Gen. Elec. Co. v. Nuclear Regulatory Comm’n*, 750 F.2d 1394, 1402 (7th Cir. 1984) (“Exemption 4 is broadly worded, and it is hard to believe that Congress wanted seekers after information to stub their toes on a rather obscure criminal statute almost certainly designed to protect that narrower category of trade secrets — secret formulas and the like — whose disclosure could be devastating to the owners and not just harmful. So if the Reed Report is not protected by exemption 4, even more clearly is it not protected by section 1905 either.”).

²²² *Supra* § I.A.

²²³ 467 U.S. at 1008.

²²⁴ In 1980, the FDA published a letter in the *New England Journal of Medicine* criticizing an article a drug company had published in the same journal. The drug company’s article suggested that a clinical trial proved that

knowledge, the FDA faced no litigation or other negative consequences in the wake of these actions.) Should the FDA officially adopt the broader view that safety and efficacy data is not protected by the TSA, it would be in good international company, as Health Canada and the EMA have recently expressed the view that clinical data simply cannot be deemed a trade secret or CCI, with minimal exceptions.²²⁵

2. The FDA Can Protect Its Data Publicity Regime with an Authorizing Regulation

On the best view of the matter, federal law does not protect the secrecy of safety and efficacy data, but the pharmaceutical industry does not share this view.²²⁶ Our experience in FOIA litigation has established that individual drug companies will fight strenuously to keep clinical data secret,²²⁷ whether out of legitimate concern over trade secrecy or for less legitimate reasons, such as concerns about impact of negative information on sales or approval.²²⁸ Thus we turn to the second critical feature of the TSA. The FDA can legally disclose safety and efficacy data *even if* that data is deemed a trade secret, so long as the FDA makes the disclosure pursuant to an authorizing regulation with proper “force of law.” This feature of the TSA is a powerful shield, as an authorizing regulation could formally implement the FDA’s data publicity regime and simultaneously insulate the agency from liability and protracted litigation. (Data use agreements that limit who uses data and how those users use that data will further shield the FDA, as we describe below.²²⁹)

an already-approved drug (Anturane) was safe and effective for an as-yet unapproved (off label) method of use. The FDA’s letter provided a detailed critique of the trial and the drug company’s claims and apparently disclosed to the public previously secret data from the trial—data that should have qualified as CCI under the FDA’s definition. *See* FDA, *The FDA’s Critique of the Anturane Reinfarction Trial*, 303 NEW ENG. J. MED. 1488 (1980). In *Public Citizen Health Research Group v. Food & Drug Administration*, No. 04-304 (D.D.C. Feb. 26, 2004), the FDA settled a FOIA litigation and released NDA documents concerning unapproved uses of the FDA-approved drug valdecoxib (Bextra) that may have been deemed CCI, at least at the time of the litigation. (This case is described in Lurie & Zieve, *supra* note [TK].)

²²⁵ *See, e.g., Clinical Data Publication*, EUROPEAN MED. AGENCY, <https://www.ema.europa.eu/en/human-regulatory/marketing-authorisation/clinical-data-publication> (last visited Jan. 28, 2020) (“The Agency considers that, in general, clinical data cannot be considered CCI but in limited circumstances study reports may contain CCI, which can be redacted.”) (EMA); *European Medicines Agency policy on publication of clinical data for medicinal products for human use*, EUROPEAN MED. AGENCY, https://www.ema.europa.eu/en/documents/other/european-medicines-agency-policy-publication-clinical-data-medicinal-products-human-use_en.pdf at 3, 4 (“clinical data cannot be considered CCI,” except in “limited circumstances” “where disclosure may undermine the legitimate economic interest” of the submitter”); Matthew Herder, *Transparency by Sleight of Hand?* (Jan. 3, 2018), CRITICAL Thinking Blog, <https://law.yale.edu/centers-workshops/collaboration-research-integrity-and-transparency-crit/critical-thinking-blog/transparency-sleight-hand> (last visited Feb. 13, 2020) (“once Health Canada makes a regulatory decision . . . unpublished safety and efficacy drug data is [confidential business information] no more”).

²²⁶ *Supra* n. [TK – n. citing Francer and Turner]

²²⁷ *See supra* § I.B.4 (describing experience with FOIA).

²²⁸ *See, e.g., Public Citizen Health Research Grp. v. FDA*, 704 F.2d at 1291 n.30 (observing that industry may fear disclosure because it can cause “customer or employee disgruntlement” and “embarrassing publicity attendant upon public revelations concerning, for example, illegal or unethical payments to government officials or violations of civil rights, environmental or safety laws”).

²²⁹ *Infra* § II.B.

The TSA prohibits disclosure of trade secret information only when that disclosure is “not authorized by law.”²³⁰ As the then-governing Restatement (Torts) affirmed, trade secrets were considered disclosable when the public interest required it. “Authorization by law” to disclose trade secrets protected by section 1905 exists when an agency disclosure regulation is promulgated under a grant of Congressional authority via statute.²³¹ Congress has granted the FDA the requisite authority to disclose data on the safety and effectiveness of pharmaceuticals through two distinct statutes. The first authorizing statute is the general purpose rulemaking provision of the Food, Drug, and Cosmetics Act (FDCA), codified at 21 U.S.C. § 371(a), which grants FDA blanket “authority to promulgate regulations for the efficient enforcement of” the FDCA,²³² including the FDCA’s mandate to “protect the public health by ensuring that . . . human and veterinary drugs are safe and effective.”²³³ The second authorizing statute is a subsection of the Food and Drug Administration Amendments Act of 2007 (FDAAA), codified at 21 U.S.C. § 355(r),²³⁴ which expanded²³⁵ the FDA’s already broad mandate to disclose

²³⁰ 18 U.S.C. § 1905.

²³¹ *Chrysler*, 441 U.S. at 301, 302 (“The legislative power of the United States is vested in the Congress, and the exercise of quasi-legislative authority by governmental departments and agencies must be rooted in a grant of such power by the Congress and subject to limitations which that body imposes.”); *see also Qwest Commc’ns Int’l Inc. v. F.C.C.*, 229 F.3d 1172, 1177 (D.C. Cir. 2000) (interpreting *Chrysler* and holding that the relevant question is “whether [a] reviewing court could reasonably conclude that the statutory grant of authority contemplated the regulations providing for release of information”).

²³² The FDA has expressed a justifiably expansive view of its powers under section 701(a), stating that it “gives FDA general rulemaking authority to issue regulations for the efficient enforcement of the [FDCA].” FDA Proposed rule, “Availability for Public Disclosure and Submission to FDA for Public Disclosure of Certain Data and Information Related to Human Gene Therapy or Xenotransplantation,” 66 FR 4688, 4694. The FDA explicitly recognized that section 371 authorizes it to disclose even information protected by the TSA. “FDA’s issuance of this proposed rule is authorized under 21 U.S.C. § 371 even if the information to be disclosed could be considered confidential commercial information covered by Exemption 4 and within the scope of protection of the Trade Secrets Act (18 U.S.C. 1905).” 66 FR 4688, 4694. A broad interpretation of the FDA’s power to regulate under section 701(a) has been endorsed by courts. *See Nat’l Ass’n of Pharmaceutical Mfrs. v. FDA*, 637 F.3d 877, 889 (2d Cir. 1981) (holding that 21 U.S.C. § 371(a) confers power to make substantive regulations that are binding); *Pharmaceutical Mfrs. v. Food & Drug Admin.*, 484 F. Supp. 1179, 1183 (D. Del. 1980) (holding that 371(a) “has been broadly construed to uphold a wide variety of assertions of regulatory power,” so long as regulations promulgated under 371(a) “effectuate a Congressional objective expressed elsewhere in the [FDCA]”); *see also United States v. Nova Scotia Food Products Corp.*, 568 F. 2d 240, 246 (2d Cir. 1977) (holding generally that “[w]hen agency rulemaking serves the purposes of the statute, courts should refuse to adopt a narrow construction of the enabling legislation which would undercut the agency’s authority to promulgate such rules.”). The FDA ultimately withdrew the proposed rule (“Availability for Public Disclosure and Submission to FDA for Public Disclosure of Certain Data and Information Related to Human Gene Therapy or Xenotransplantation”), but did not repudiate its interpretation of FDCA section 701(a). *See* 67 FR 33040, 33045 (withdrawing the proposed rule without comment).

²³³ 21 U.S.C. § 393(b)(2)(B).

²³⁴ Pub. L. No. 110-85, 121 Stat. 823 (codified at various points of Titles 21 and 42 of the U.S. Code).

²³⁵ *See supra* § I.B (explaining, *inter alia*, FDAAA’s mandate to disclose safety and efficacy data through ClinicalTrials.gov and approval packages); *see also* Andrew C. von Eschenbach, *The FDA Amendments Act: Reauthorization of the FDA*, 63 FOOD & DRUG L.J. 579, 581 (2008) (describing FDAAA as “massive legislation” informed by a “spirit of transparency”); Brandon Powell, *Silence Is Not the Best Medicine: Requiring Disclosure of Clinical Trial Data for Abandoned Drugs*, 33 J. LEGAL MED. 571, 582 (2012) (explaining how FDAAA expanded mandatory public disclosure of clinical trial results).

information on drug safety.²³⁶ As explained above,²³⁷ drug safety and drug efficacy are inexorably linked, and the mandate of section 355(r) to publicize “information about drugs” and “drug safety information” should be understood to encompass both safety and efficacy—that is, data on drugs’ benefits as well as their harms.²³⁸ Each of these authorizing statutes empowers the FDA to promulgate an authorizing regulation, with force of law, to permit or require disclosure of safety and efficacy data without risk of criminal liability under the TSA.²³⁹ In other words, the FDA need not agonize over the question of whether specific safety and efficacy data does or not qualify for protection as a trade secret; so long as an appropriate authorizing regulation is in place, the FDA can act on the assumption that all this data is a trade secret for purposes of the TSA, and disclose it anyway.²⁴⁰

²³⁶ 21 U.S.C. § 355(r)(1) compels the Secretary of HHS to “improve the transparency of information about drugs and allow patients and health care providers better access to information about drugs by developing and maintaining an Internet Web site” that “improves communication of drug safety information to patients and providers.” Congress did not cabin the proper scope of HHS’s authority (or that of its delegee, FDA) to disclose of drug safety information but instead explicitly extended discretion to define and disclose “other material determined appropriate by the Secretary.” 21 USC § 355(r)(2)(B)(vii). While the phrase “other material determined appropriate by the Secretary” has not, at time of writing, been interpreted by any court, it seems clear that Congress intended to authorize HHS (and its delegee, the FDA) to disclose information protected as a “trade secret” or as “confidential commercial information.” In another subsection of the same section of FDAAA (subsection (l)), written at the same time, Congress explicitly withheld authorization to disclose information that qualifies as a trade secret or CCI, but Congress did not withhold this authorization in subsection (r). Compare § 355(r), which places no limits on disclosure, with 21 U.S.C. § 355(l), the provision of FDAAA that requires “[p]ublic disclosure of safety and effectiveness data and action package[s]” but which explicitly “does not authorize the disclosure of any trade secret, confidential commercial or financial information, or other matter listed in section 552(b) of title 5.”

²³⁷ *Supra* § I.A.

²³⁸ Other subsections of 21 U.S.C. § 355 confirm the link between safety and efficacy. For example, section 355(d) empowers the FDA to deny approval of an application if that application fails to show the drug is safe *for its intended therapeutic use*. 21 U.S.C. § 355(d) (focusing on whether “such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof”).

²³⁹ According to the Supreme Court, an “authorizing” pro-disclosure regulation, for purposes of the TSA, must have “force and effect of law.” *Chrysler*, 441 U.S. at 301. Assuming it is promulgated with proper process, a disclosure regulation has the requisite force and effect of law so long as there is “a nexus between the regulations and some delegation of the requisite legislative authority by Congress.” *Id.* at 304. The nexus standard is permissive: “[t]he pertinent inquiry is whether under any of the arguable statutory grants of authority the . . . disclosure regulations . . . are reasonably within the contemplation of that grant of authority.” *Id.* at 306; *see also id.* at 308 (“This is not to say that any grant of legislative authority to a federal agency by Congress must be specific before regulations promulgated pursuant to them can be binding on courts in a manner akin to statutes. What is important is that the reviewing court reasonably be able to conclude that the grant of authority contemplates the regulations issued.”); *Parkridge Hospital, Inc. v. Califano*, 625 F.2d 719, 724 (6th Cir. 1980) (holding that a statute that provided, generally, that “no disclosure . . . shall be made except as the Secretary may by regulations prescribe” met the *Chrysler* nexus standard). FDCA section 701(a) and 21 U.S.C. § 355(r) easily meet this standard. The Second Circuit has specifically held that section 701(a) meets the *Chrysler* nexus standard, and thus disclosure regulations promulgated under that statutory provision have “force and effect of law” and authorize disclosure under the TSA. *See Nat’l Ass’n of Pharmaceutical Mfrs. v. FDA*, 637 F.3d at 889.

²⁴⁰ In addition, the FDA’s determinations that particular clinical data does or does not qualify as CCI or a trade secret will likely be entitled to deference upon judicial review. *See CNA Financial Corp. v. Donovan*, 830 F.2d 1132, 1155 (extending deference to an agency’s determination that certain data qualified as CCI); *cf. Am. Sumatra T. Corp. v. SEC*, 110 F.2d, 121 (D.C. Cir. 1940) (approving an agency’s decision to keep certain commercial information confidential and noting that “if the conclusion reached [by the agency] is just as likely to be correct as incorrect, it is our duty to let it stand.”).

We outline below the data publicity regime that the FDA should create through regulation.²⁴¹ We close this subpart by observing that when FDA creates regulations authorizing and implementing disclosure of safety and efficacy data, it can and should concomitantly rescind a set of existing regulations that currently neuter the agency’s proactive disclosure power. The FDA should revise its overbroad definition of CCI²⁴² to match the EMA’s²⁴³ and clarify that only safety and efficacy data that has genuinely “commercial or financial” character qualifies as CCI. The FDA must rescind 21 CFR § 20.61(c), which unnecessarily surrenders the agency’s discretionary disclosure authority and makes a sweeping promise that “[d]ata and information submitted or divulged to the Food and Drug Administration which fall within the definitions of a trade secret or confidential commercial or financial information are not available for public disclosure.”²⁴⁴ The FDA should also rescind scattered rules that promise secrecy for specific submissions of safety and efficacy data.²⁴⁵

B. A Roadmap to Rebooting the FDA’s Disclosure Rules

We have explained that the FDA has all the statutory authority it needs to proactively disclose safety and efficacy data on pharmaceuticals. The only step required to reboot the FDA’s data disclosure is for the agency to promulgate and implement, pursuant to that statutory authority, a relatively simple authorizing set of rules that establish procedures for proactive disclosure. We provide here a high-level roadmap to effective proactive clinical data disclosure rules, including what we believe are four key features:

- (1) Prospectively disclosing data on all newly approved drugs;
- (2) Retrospectively disclosing historical data on a limited number of important drugs;
- (3) Requiring industry to submit its clinical data in redacted, publicly disclosable form, to minimize burden on the FDA; and

²⁴¹ *Infra* § II.B.

²⁴² 21 C.F.R. § 20.61(b). *See supra*, § I.B.4. While the FDA’s current rule defining CCI is overbroad, its rule defining trade secrecy is appropriately narrow. *See* 21 C.F.R. § 20.61(a).

²⁴³ *See supra* § II.A.1.

²⁴⁴ The FDA should also rescind 21 C.F.R. § 20.82(b)(1), which similarly promises that any information that meets the FDA’s definition of CCI or a trade secret will not be disclosed. Once these regulations have been rescinded, the FDA will have no legal obligation to provide the companies that submit safety and efficacy data with notice or an opportunity to be heard before proactively disclosing that data. *See Pharm. Manufacturers Ass’n v. Weinberger*, 401 F. Supp. 444, 447 (D.D.C. 1975) (denying request for preliminary injunction to provide notice and an opportunity to be heard). Executive Order 12600 requires FDA and other executive agencies to notify submitters when agencies receive FOIA requests for submitted information that may qualify for protection under FOIA exemption 4, but the Order does not require notification in the event that the same information is disclosed through other legal avenues. Exec. Order No. 12600, 52 Fed. Reg. 23781, 3 C.F.R., 1987 Comp., p 235.

²⁴⁵ *See* Sharfstein et al., *Blueprint for Transparency*, *supra* note [tk], at 8 n.7 (listing specific anti-disclosure rules that govern different types of applications submitted to the FDA). For example, 21 C.F.R. § 314.430 specifically requires the FDA to treat all safety and efficacy data submitted in supplemental new drug applications (sNDAs) as secret unless and until the FDA approves the sNDA. *See* 21 C.F.R. § 314.430(a) (defining “supplements” (i.e., sNDAs) as “applications” for purposes of the rule), 21 C.F.R. § 314.430(b) (“FDA will not publicly disclose the existence of an application or abbreviated application before an approval letter is sent to the applicant under 314.105 or tentative approval letter is sent to the applicant under 314.107, unless the existence of the application or abbreviated application has been previously publicly disclosed or acknowledged.”). This creates an unnecessary barrier to disclosure, and a harmful one, as sNDAs often contain data on the safety and efficacy of “off-label” uses of FDA-approved drugs, which may affect thousands, even millions, of patients. *See* Lurie & Zieve, *supra* note [TK]; Almshat & Carome, *supra* note [TK].

- (4) Requiring users to make data requests and enter into data use agreements, to prevent misuse of sensitive data.

These four features are intended to ensure effective clinical trial publicity while assuaging the two chief concerns that have historically limited the FDA's data disclosure: patient privacy and trade secrecy.

The fourth feature—requiring users of data to make data requests and enter into data use agreements—may not be strictly necessary, but we believe this feature will be highly valuable. Data use agreements will not only help to protect patient privacy and relieve any lingering concerns over trade secrecy but will also increase flexibility, reduce administrative costs, and limit the agency's potential legal liability.

1. Prospective Disclosure of Data on All Newly Approved Drugs

Going forward, the FDA should disclose the safety and efficacy data we described above²⁴⁶ for all the drugs it approves, small molecule and biologic. Disclosure should occur on the day of approval, or immediately after, for the reasons presented above²⁴⁷: it is in the months immediately after approval that safety and efficacy data is most useful. Of course, the FDA should also disclose later-collected safety and efficacy data collected from studies of already-approved products, including Phase 4 studies and Phase 2 and 3 studies submitted to support approval of new indications.

Given that the costs of preparing data for disclosure will be borne by industry, not the FDA,²⁴⁸ we see no reason for the FDA to limit disclosure of data to only a subset of approved drugs, such as those that are controversial or best-selling. Disclosing data for all FDA-approved drugs will ensure that all patients have access to information about the drugs they are putting in their bodies, regardless of whether the drug is a blockbuster taken by millions of patients or an orphan drug used by only a handful. Access to broad data sets, incorporating data from many different drugs, will also permit some of the promised benefits of big data, including machine learning and other applications of artificial intelligence, to emerge.²⁴⁹

2. Retrospective Disclosure of Historical Data on a Limited Number of Highly Important Drugs

What to do with the enormous trove of data that the FDA currently possesses on already-approved drugs? Should this historical data be disclosed? We believe that at least some should. Retrospective disclosure of this sort involves practical and legal obstacles that prospective disclosure does not. Our analysis of the primary potential legal hurdle—the Takings Clause—is

²⁴⁶ *Supra* § I.A.

²⁴⁷ *Id.*

²⁴⁸ *See infra* § II.B.

²⁴⁹ Jennifer Bresnick, FDA: Real-World Data, Machine Learning Critical for Clinical Trials, HEALTH IT ANALYTICS (Jan. 31, 2019), <https://healthitanalytics.com/news/fda-real-world-data-machine-learning-critical-for-clinical-trials>; P. Shah, F. Kendall, S. Khozin et al., *Artificial Intelligence and Machine Learning in Clinical Development: A Translational Perspective*, 2 NPJ DIGITAL MED. 69 (2019), available at doi:10.1038/s41746-019-0148-3.

presented below.²⁵⁰ As we explain below, takings claims will be surmountable. The bigger hurdle to retrospective disclosure will likely be practical, not legal: locating, formatting, and redacting data for public disclosure would be expensive and time-consuming for the agency. We propose the FDA could begin by retroactively disclosing data from a relatively small number of drugs—perhaps 10-20 per year. These drugs could be selected based on their aggregate public health significance (e.g., by numbers of prescriptions or by impact on overall disease burden), economic importance (e.g., top drugs by revenue), specific concerns over safety or efficacy, or other factors FDA deems appropriate. The drugs could be selected by experts within the FDA or by an expert advisory committee.

3. Industry Must Submit Its Clinical Data in Redacted, Publicly Disclosable Form

In explaining the need for clinical trial publicity, we traced some of the enormous costs that data secrecy currently imposes on patients, payers, and the public at large. Shifting from secrecy to data publicity would produce correspondingly large cost savings, as well as benefits to human health and to medical science. Yet we acknowledge that creating and maintaining a data publicity program could impose costs on the FDA. To minimize those costs, the FDA can and should place the burden of preparing data for public disclosure on industry.

The FDA can, by regulation, require industry to submit redacted versions of all submissions of clinical trial data, with (genuine) trade secrets, confidential commercial information, and sensitive individual patient data redacted. Federal statute authorizes the FDA to dictate the specific format in which drug companies submit clinical data,²⁵¹ and the FDA has issued detailed guidance that does just that.²⁵² Moreover, the FDA already asks drug companies to help prepare clinical trial data sets in redacted form, in case they become subject to disclosure through FOIA: the FDA requires them to submit clinical trial records with “names and other information which would identify patients or research subjects” redacted²⁵³ and further encourages them to redact trade secrets and CCI.²⁵⁴ The FDA proposed shifting the burden of redaction to industry in a (more modest) past proactive disclosure plan.²⁵⁵ And the FDA would

²⁵⁰ See *infra* § II.C.2.

²⁵¹ See 21 U.S.C. §§ 355(k), 379k-1.

²⁵² FOOD & DRUG ADMIN., PROVIDING REGULATORY SUBMISSIONS IN ELECTRONIC FORMAT – STANDARDIZED STUDY DATA: GUIDANCE FOR INDUSTRY (Dec. 2014), <https://www.fda.gov/media/82716/download> and FOOD & DRUG ADMIN., PROVIDING REGULATORY SUBMISSIONS IN ELECTRONIC FORMAT – SUBMISSIONS UNDER SECTION 745A(A) OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT: GUIDANCE FOR INDUSTRY (Dec. 2014), <https://www.fda.gov/media/88120/download> (guidance documents establishing requirements for electronic submission of standardized clinical and nonclinical study data under section 745A(a) of the FDCA (21 U.S.C. § 379k-1)). The FDA currently requires all submissions adhere to data standard (format) developed in collaboration with the nonprofit Clinical Data Interchange Standards Consortium (CDISC). See FOOD & DRUG ADMIN., STUDY DATA STANDARDS: WHAT YOU NEED TO KNOW (Sept. 2017), <https://www.fda.gov/media/98907/download>. This standard is useful to outside researchers, so no further manipulation of the data is required.

²⁵³ 21 C.F.R. § 20.63(b). However, this requirement seems, in practice, to fall short of requiring full deidentification of individual patient data, as the FDA regularly redacts additional information to protect patient privacy.

²⁵⁴ 21 C.F.R. § 20.61(d).

²⁵⁵ In 2001, the FDA proposed regulations to require sponsors of trials to “submit information . . . in redacted version for public disclosure, removing all information that would be defined as trade secret or personal information whose disclosure would constitute a clearly unwarranted invasion of privacy, and certain confidential commercial

not be alone if it required this now: the European Medicines Agency and Health Canada both require submission of data in both unredacted (for agency use) and redacted (for public disclosure) forms, such that the regulators need merely to review and approve the data before releasing it.²⁵⁶ Requiring industry to do the redaction, and then ensuring it has been done correctly, is consistent with the FDA's primary function in regulating medicines: specifying and validating the information that drug companies generate and disclose on their products.²⁵⁷ The FDA could give the redaction requirement real teeth: it could reject submissions wherein data is incompletely or incorrectly redacted, and it could threaten to place ongoing trials on clinical hold if sponsors do not comply.²⁵⁸ The costs imposed on industry to prepare these redactions would be non-zero but reasonable; in 2001, FDA estimated the cost of redacting data in one IND application to prepare it for public disclosure at approximately \$124,000 (in 2001 dollars).²⁵⁹

The FDA has been described in recent years as an agency squeezed by political, industry, and patient pressures and short on staff and resources.²⁶⁰ Creating and maintaining a data publicity program will require staff and resources, but we think the burden will be reasonable if redaction, the most time-consuming step, is shouldered primarily by industry. Indeed, switching from reactive disclosure through FOIA to data publicity may produce substantial cost savings. As noted above, the FDA currently spends about \$30 million per year fulfilling FOIA requests, about \$3,000 per request.²⁶¹ A significant portion of the FOIA requests fielded by the FDA are

information. Each submission for public disclosure would be accompanied by a statement, signed by a responsible person, that the information has been suitably redacted." 66 Fed. Reg. 4688, 4703.

²⁵⁶ See, e.g., *Clinical Data Publication*, EUROPEAN MEDS. AGENCY, <https://www.ema.europa.eu/en/human-regulatory/marketing-authorisation/clinical-data-publication#preparing-the-data-for-publication-section> (last visited Jan. 24, 2020) ("Clinical reports must be anonymised to prevent patients and professionals who participated in clinical trials from being identified . . ."); *External guidance on the implementation of the European Medicines Agency policy on the publication of clinical data for medicinal products for human use*, EUROPEAN MEDS. AGENCY, https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/external-guidance-implementation-european-medicines-agency-policy-publication-clinical-data_en-1.pdf (describing a two-process in which a drug company first submits proposed redactions, which are reviewed in a "consultation process" with the EMA, then submits a final redacted document package); *Public Release of Clinical Information: guidance document*, HEALTH CANADA, <https://www.canada.ca/en/health-canada/services/drug-health-product-review-approval/profile-public-release-clinical-information-guidance/document.html#s4.4> ("4.4 Submission of Annotated Documents with Proposed CBI Redaction(s) and Anonymization").

²⁵⁷ Kapczynski, *Dangerous Times*, *supra* note [TK], at 2359.

²⁵⁸ In its 2001 proposal to disclose safety and efficacy data from human gene therapy and xenotransplantation trials, the FDA proposed to place pending INDs on clinical hold if sponsors failed to submit data in the correct, redacted form for public disclosure. 66 Fed. Reg. 4688, 4692, 4697.

²⁵⁹ *Id.* at 4701.

²⁶⁰ Editorial, *The F.D.A. in Crisis: It Needs More Money and Talent*, N.Y. TIMES (Feb. 3, 2008), <https://www.nytimes.com/2008/02/03/opinion/03sun1.html>; Matthew Herder, *Pharmaceutical Drugs of Uncertain Value, Lifecycle Regulation at the US Food and Drug Administration, and Institutional Incumbency*, MILBANK QUARTERLY (2019). Past transparency initiatives at the FDA have failed, at least in part, for lack of resources and enthusiasm on the part of agency personnel. See Tai, *A Tale of Two Transparency Attempts at FDA*, *supra* note [TK] at 443; Karlin-Smith & Owerhohle, *supra* note [TK] (quoting the former head of the FDA, Scott Gottlieb in asking "Is trying to increase transparency around complete response letters the best use of the finite public resource [sic] have?").

²⁶¹ Egilman et al., *Systematic Overview*, *supra* note [TK] at 4.

for clinical data on approved products,²⁶² and making this data available through alternative means should reduce the volume of FOIA requests and the costs incurred by processing them. Money and employee time that the FDA saves on FOIA could be reallocated toward implementing and maintaining the proactive disclosure system.

How, exactly, should industry redact its data? We have explained above²⁶³ how the FDA should follow the lead of the EMA and revise its regulatory definitions of trade secrecy and CCI to clarify that clinical data generally qualifies as neither, unless it happens to have some innovative feature. As to individual patient data, which implicates the privacy of those patients, balancing the benefits of data sharing against the risks to patients whose data is shared is a profound and difficult question, and one we do not attempt to resolve conclusively here.²⁶⁴ However, we note that deidentification of individual patient data through redaction personal identifiers (such as names) and quasi-identifiers (such as birthdate and zip code) can reduce the risk of identification of individual patients, though not eliminate it entirely.²⁶⁵ The FDA already has a rule that requires “names or other information which would identify” individual patients be deleted before records are publicly disclosed,²⁶⁶ and the FDA has long experience with redacting individual patient information before disclosing clinical data.²⁶⁷ The FDA’s 2018 clinical data summary pilot program provides a helpful template for deidentification,²⁶⁸ as do Health Canada’s²⁶⁹ and the EMA’s²⁷⁰ guidance on deidentification of clinical data.

²⁶² For example, Kwoka has documented that the FDA’s single highest-volume FOIA request is a for-profit company called FOI Services, Inc., which files hundreds of requests per year, and that a focus of these requests is data from NDAs. Kwoka, *FOIA Inc.*, *supra* n. [TK], at 1388-89.

²⁶³ *Supra* § II.A.

²⁶⁴ See generally I. Glenn Cohen and Michelle Mello, *Big Data, Big Tech, and Protecting Patient Privacy*, 322(12) JAMA 1141 (2019); W. Nicholson Price and I. Glenn Cohen, *Privacy in the age of medical big data*, 25 NAT MED 37 (2019); Efthimios Parasidis, Elizabeth Pike & Deven McGraw, *A Belmont Report for Health Data*, 380 NEW ENGLAND JOURNAL OF MEDICINE 1493–1495 (2019); I. Glenn Cohen, Holly Fernandez Lynch, Effy Vayena, Urs Gasser, *Big Data, Health Law, and Bioethics*, Cambridge University Press, 2018. For a detailed analysis of deidentification in practice, see Khaled El Emam & Bradley Malin, *Concepts and Methods for De-Identifying Clinical Trial Data*, in *Sharing Clinical Trial Data* 231–32 (2015).

²⁶⁵ See, e.g., Adam Tanner, *Strengthening Protection of Patient Medical Data* 11-12 (The Century Found., Jan. 10, 2017), <https://production-tcf.imgix.net/app/uploads/2017/01/11165252/strengthening-protection-of-patient-medical-data-1.pdf>; Liangyuan Na, Cong Yang, Chi-Cheng Lo et al., *Feasibility of Reidentifying Individuals in Large National Physical Activity Data Sets From Which Protected Health Information Has Been Removed With Use of Machine Learning*, 1(8) J. AM. MED. ASS’N NETWORK OPEN e186040 (2018), doi:10.1001/jamanetworkopen.2018.6040.

²⁶⁶ 21 C.F.R. § 20.63(a); see also 5 U.S.C. § 552a.

²⁶⁷ For an overview, see *The FDA and Personal Privacy Information*, 2 Food & Drug Admin. § 22:51 (2019).

²⁶⁸ *FDA’s Clinical Data Summary Pilot Program: Questions Frequently Asked by Industry*, FDA (May 2, 2018), <https://www.fda.gov/drugs/development-approval-process-drugs/fdas-clinical-data-summary-pilot-program-questions-frequently-asked-industry> (noting personal privacy information (PPI) to be redacted before disclosure).

²⁶⁹ *Public Release of Clinical Information: Guidance Document* section 6, GOV’T OF CAN. (Mar. 12, 2019), <https://www.canada.ca/en/health-canada/services/drug-health-product-review-approval/profile-public-release-clinical-information-guidance/document.html> - s6.

²⁷⁰ EUROPEAN MEDICINES AGENCY, EXTERNAL GUIDANCE ON THE IMPLEMENTATION OF THE EUROPEAN MEDICINES AGENCY POLICY ON THE PUBLICATION OF CLINICAL DATA FOR MEDICINAL PRODUCTS FOR HUMAN USE (Oct. 15, 2018), https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/external-guidance-implementation-european-medicines-agency-policy-publication-clinical-data_en-3.pdf.

Deidentification is not a panacea. As AI grows more powerful and more data on each of us is collected, aggregated, and traded by corporations, reidentification becomes more likely and more deeply problematic.²⁷¹ We might reasonably fear, for example, insurers reidentifying individual people from a clinical trial in patients with chronic disease, to deny coverage to those whose treatment costs are likely to be highest,²⁷² or residential landlords using reidentification to discriminate against potential renters with health conditions like HIV.²⁷³ Reidentification is also a dynamic problem; bad actors may adapt around technical safeguards to prevent reidentification. Where particular forms of individual patient data are particularly susceptible to reidentification, such as individual adverse event reports for drugs that treat rare diseases,²⁷⁴ the risk might be so great that the data should not be disclosed at all. But past experience with clinical data disclosure shows that reidentification can be discouraged, and its harms reduced, through imposition of data use agreements, which contractually prohibit reidentification and other unauthorized use.²⁷⁵ These agreements form the fourth key feature of data publicity that we describe here, and we turn to them now.

4. Data Requests and Data Use Agreements

Some safety and efficacy data can be disclosed to the public without restriction, as it does not implicate patient privacy or other protected interests. (The same data can and should be released to FOIA requesters in the same way.) This is particularly true for certain high-level metadata and summary data, like clinical study reports (with minimal redactions to excise manufacturing information or individual information about patients) and internal assessments prepared by the FDA.

But open access the wrong solution for more sensitive data. The FDA should limit access to data that is more sensitive, whether because it implicates patient privacy, risk of competitors' misuse, or perhaps some other legitimate interest, in two ways. First, the FDA should disclose sensitive data only upon receipt of a "data request" from the prospective user. Each request should be reviewed by the FDA. In this review, the FDA could confirm that a given requester is credible, capable of making and intends to use the data for a legitimate purpose, such as meta-analysis of clinical trials to be published in the medical literature. The FDA can and should

²⁷¹ See generally Shoshana Zuboff, *THE AGE OF SURVEILLANCE CAPITALISM* (2019); see also Sharon Hoffman, *Citizen Science: The Law and Ethics of Public Access to Medical Big Data*, 30 *Berkeley Tech. L.J.* 1741 (2015) (describing a growing risk of reidentification of health data specifically).

²⁷² Specialty credit rating agencies already create and sell health reports on individual people. Ann Carrns, *Consumers Can Check on Data Beyond Their Credit Reports*, N.Y. TIMES (Jan. 15, 2014), <https://www.nytimes.com/2014/01/15/your-money/consumers-can-check-on-data-beyond-their-credit-reports.html>.

²⁷³ Noah Remnick, *Suit Accuses Landlord of Discriminating Against Tenant With AIDS*, N.Y. TIMES (June 23, 2015), <https://www.nytimes.com/2015/06/24/nyregion/suit-accuses-landlord-of-discriminating-against-tenant-with-aids.html>.

²⁷⁴ K. Tucker, J. Branson, M. Dilleen et al., *Protecting Patient Privacy When Sharing Patient-Level Data From Clinical Trials*, 16 *BMC MED. RES. METHODOLOGY* 77 (2016), doi:10.1186/s12874-016-0169-4.

²⁷⁵ El Emam & Malin, *supra* note [TK].

prioritize requests from noncommercial requesters, which would both conserve agency resources and advance policy goals like prompt communication of drug risks to patients and prescribers.²⁷⁶

Second, whenever the FDA grants a data use request, the agency should require the requester to sign a legally binding data use agreement that would prohibit, *inter alia*, unauthorized dissemination of the data, commercial use, and reidentification of individual patients.²⁷⁷ These agreements are common in the world of clinical data sharing and have been used successfully by the European Medicines Agency (under Policy 0070),²⁷⁸ the NIH (for access to the Biologic Specimen and Data Repository Information Coordinating Center (BioLINCC)),²⁷⁹ and the Yale Open Data Access (YODA) Project, among others.²⁸⁰ The precise language of the data use agreement, and the specific terms and conditions imposed, are left to the agency, but YODA's data use agreement provides exemplary conditions, such as a prohibition on using the data "in pursuit of litigation or for commercial interests," a prohibition on distribution of the data to third parties, a prohibition on reidentification of individuals, an obligation to disseminate findings through the peer-reviewed medical literature, and an obligation to immediately report any "unexpected or serious safety findings" to health and regulatory authorities.²⁸¹

²⁷⁶ If the FDA promulgates its proactive disclosure regulations under the authority delegated by 21 U.S.C. § 355(r), there is textual support for privileging access by patients and doctors over other users of the data, such as commercial users. "[T]he Secretary shall improve the transparency of information about drugs and allow patients and health care providers better access to information about drugs by developing and maintaining an Internet Web site that . . . improves communication of drug safety information to patients and providers." 21 U.S.C. § 355(r)(1).

²⁷⁷ See, e.g., *How Can Covered Entities Use and Disclose Protected Health Information for Research and Comply with the Privacy Rule?*, NATIONAL INSTITUTES OF HEALTH, https://privacyruleandresearch.nih.gov/pr_08.asp ("An agreement into which the covered entity enters with the intended recipient of a limited data set that establishes the ways in which the information in the limited data set may be used and how it will be protected." The agreement may include "[s]tipulations that the recipient will [n]ot use or disclose the information other than permitted by the agreement or otherwise required by law[,] [u]se appropriate safeguards to prevent the use or disclosure of the information, except as provided for in the agreement, and require the recipient to report to the covered entity any uses or disclosures in violation of the agreement of which the recipient becomes aware, [h]old any agent of the recipient (including subcontractors) to the standards, restrictions, and conditions stated in the data use agreement with respect to the information[,] [and] [n]ot identify the information or contact the individuals."). In endorsing proactive sharing of safety and efficacy data subject to some restrictions on the use of that data, we align with Lietzan. While she has expressed a generally more industry-protective view of clinical trial data sharing and proposes compensating industry, we agree with her conclusion that "[t]he public policy arguments together point to controlled sharing with non-profit researchers to advance general scientific knowledge, including our understanding of approved medicines." Lietzan, *supra* n. [TK], at 39.

²⁷⁸ *European Medicines Agency policy on publication of clinical data for medicinal products for human use*, EUROPEAN MED. AGENCY, *supra* note [TK].

²⁷⁹ Sean A. Coady, George A. Mensah, Elizabeth L. Wagner, Miriam E. Goldfarb, Denise M. Hitchcock & Carol A. Giffen, *Use of the National Heart, Lung, and Blood Institute Data Repository*, 376 NEW ENG. J. MED. 1849 (2017), <https://www.nejm.org/doi/full/10.1056/NEJMsa1603542>.

²⁸⁰ J. Ross, J. Waldstreicher, S. Bamford et al., *Overview and Experience of the YODA Project with Clinical Trial Data Sharing after 5 Years*, 5 SCI. DATA 180268 (2018), doi:10.1038/sdata.2018.268. YODA's template data use agreement is available here: <http://yoda.yale.edu/data-use-agreement>.

²⁸¹ *Yale University Open Data Access (YODA) Project Procedures to Guide External Investigator Access to Clinical Trial Data*, <https://yoda.yale.edu/sites/default/files/files/YODA%20Project%20Data%20Release%20Procedures%20February%202019.pdf>.

A major benefit is reducing the risk of competitive harm to the company that submitted the data to the FDA. Eisenberg has observed that industry has long asserted that competitors with access to clinical data may freeride and submit that data in support of their own drug applications to the FDA or to foreign regulators.²⁸² As we explained above,²⁸³ we disagree that safety and efficacy data has genuine competitive value and qualifies for legal protection as a trade secret, but in any event, there are clear practical benefits to imposition of binding, enforceable data use agreements that threaten significant monetary and other penalties for unauthorized commercial use. By prohibiting commercial use, the FDA would hedge its bets, protect its working relationships with the companies that submit clinical data, limit litigation over the proper scope of trade secrecy protection, and minimize any obligation to pay compensation under the Takings Clause.²⁸⁴ It would also discourage commercial requests for data through the data publicity regime, reducing administrative burden.

At the same time, data use agreements could impose affirmative obligations on users of data—for example, obligations to complete data analysis promptly and share the findings with the public. These affirmative obligations would ensure that data publicity provides real benefits to the public and actually promotes accountability and democracy.

C. The FDA Can Defend Its Proactive Disclosure Regime

If the FDA adopts the proactive data publicity regime we propose, it will undoubtedly be met with industry resistance. Past proposals by the FDA to begin even modest proactive disclosure of safety and efficacy data were met with a barrage of criticism and threatened legal challenges.²⁸⁵ We have already addressed one of the most important of these challenges above²⁸⁶—the notion that disclosure of clinical data will threaten patient privacy. Industry’s two main remaining arguments are a policy argument—disclosure will erode incentives to innovate—and a legal one—disclosure will violate the Takings Clause of the Fifth Amendment. Neither withstands scrutiny.

1. Incentives to Innovate

²⁸² Eisenberg, *Data secrecy in the age of regulatory exclusivity*, *supra* note [TK] at 489.

²⁸³ *Supra* § II.A.

²⁸⁴ *See infra* § II.C.

²⁸⁵ *See, e.g.*, Letter from Robert A. Long, Jr., Partner, Covington & Burling, to Food & Drug Admin. in re: Docket Nos. 2004P-0171/CP and 2003P-0176/CP 4–5, 8–10, 15–17 (July 13, 2005), <https://web.archive.org/web/20170211011252/http://www.fda.gov/ohrms/dockets/dockets/03p0176/03p-0176-c000003-01-vol3.pdf>; Pharmaceutical Research and Manufacturers of America (PhRMA), Comment Letter on FDA Transparency Task Force Initiative (Aug. 7, 2009), <https://www.fdanews.com/ext/resources/files/archives/f/FDA-2009-N-0247-0107.1.pdf>; Pharmaceutical Research and Manufacturers of America (PhRMA), Comment Letter on Proposed FDA Disclosure Policies (July 20, 2010), <https://beta.regulations.gov/document/FDA-2009-N-0247-0252> and Biotechnology Industry Organization (BIO), Comment Letter on Proposed FDA Disclosure Policies (July 20, 2010), <https://beta.regulations.gov/document/FDA-2009-N-0247-0251>; J. Castellani, *Are Clinical Trial Data Shared Sufficiently Today? Yes*, 347 BRIT. MED. J. f1881 (2013) (opinion piece by the President and CEO of PhRMA).

²⁸⁶ *Supra* § II.B.

The pharmaceutical industry has repeatedly protested that disclosure of safety and efficacy data would be bad public policy because, whatever the benefits, disclosure would permit later market entrants to “free ride” on an innovator company’s data and thereby undermine incentives to develop new drugs.²⁸⁷ For example, in 2010, PhRMA (one of the two leading industry trade organizations) submitted comments to the FDA alleging that “[i]mplementation of [an FDA proposal to consider release of non-summary (raw) safety and effectiveness data within INDs, BLAs, and NDAs] could cause grave competitive harm to the research-based biopharmaceutical industry— and subsequently damage incentives to take new products through the costly drug approval process.”²⁸⁸

The pharmaceutical industry makes these arguments despite the absence of any study showing conclusively that clinical data secrecy provides significant incentives to innovate. Whatever the FDA’s disclosure policy, it is clear that drug companies will continue to generate and submit clinical trial data to the FDA for as long as they continue to develop drugs, because the FDA continues to require that data to approve new drugs and new indications of existing drugs; generation and submission of clinical trial data is thus a non-negotiable condition of participation in the marketplace. While the pharmaceutical industry argues that fewer companies will choose to participate in the marketplace at all, for fear of free-riders, we are skeptical. As Eisenberg,²⁸⁹ Price & Rai,²⁹⁰ and Heled²⁹¹ have observed, innovative prescription drugs are already protected by patents and by an elaborate set of FDA-granted exclusivities.²⁹² In addition, the ANDA and ABLA processes already permit—indeed, encourage—a kind of free-riding on clinical data, as they allow follow-on drug manufacturers to obtain FDA approval on the basis of a relatively small evidence bases by relying on the data generated for an already-approved reference product, the FDA.²⁹³ As Herder has argued, disclosure of safety and efficacy data may

²⁸⁷ *Supra* note [TK – note citing Letter from Robert A. Long, etc.]. See also Bruce N. Kuhlik, *The Assault on Pharmaceutical Intellectual Property*, 71 U. CHI. L. REV. 93 (2004).

²⁸⁸ Pharmaceutical Research and Manufacturers of America (PhRMA), Comment Letter on Proposed FDA Disclosure Policies (July 20, 2010), *supra* note [tk], at 30. PhRMA’s comments continued, “With respect to data in approved applications, no aspect of United States law would prevent a competitor from re-submitting these ‘full reports’ to support approval of a subsequent NDA for its own drug. Moreover, these data could be used to support approval in virtually every other country in the world, even after redaction of trade secret information. Even if the data were not used to support approval of another product they would provide competitors with relevant insight into how to develop other, competitive products.” *Id.*

²⁸⁹ Rebecca S. Eisenberg, *Patents, Product Exclusivity, and Information Dissemination: How Law Directs Biopharmaceutical Research and Development*, 72 FORDHAM L. REV. 477 (2003); Peter Zweifel, *Reexamining Drug Regulation from the Perspective of Innovation Policy*, 160 J. INSTITUTIONAL & THEORETICAL ECON. 126 (2004); *Patents and Regulatory Exclusivity*, in OXFORD HANDBOOK ON THE ECONOMICS OF THE BIOPHARMACEUTICAL INDUSTRY 167-98 (P. Danzon & S. Nicholson, eds., 2012.).

²⁹⁰ W. Nicholson Price II & Arti K. Rai, *Manufacturing Barriers to Biologics Competition and Innovation*, 101 IOWA L. REV. 1024, 1028 (2015) (proposing disclosure of biologic drug manufacturing currently protected as trade secrets).

²⁹¹ Yaniv Heled, *Parents vs. Statutory Exclusivities in Biological Pharmaceuticals-Do We Really Need Both?*, 18 MICH. TELECOMM. TECH. L. REV. 419 (2012), available at <http://www.mttir.org/voleighteen/heled.pdf>.

²⁹² *Frequently Asked Questions on Patents and Exclusivity*, FOOD & DRUG ADMIN. (May 2, 2018), <https://www.fda.gov/drugs/development-approval-process-drugs/frequently-asked-questions-patents-and-exclusivity>.

²⁹³ 21 U.S.C. § 355 & 42 U.S.C. § 262. See also Eisenberg, *The Role Of The FDA In Innovation Policy*, *supra* note [TK] at 381 (“This concern about free riders using publicly available data to get approval to sell a generic product in

accelerate, not harm, innovation by reducing wasteful development of unsuccessful drug candidates.²⁹⁴ In any event, the FDA can and should limit any harm to drug companies' incentives to innovate by imposing data use agreements like those we have proposed, which would prohibit competitors from making copycat use of the data.²⁹⁵ Finally, we observe that, as explained above,²⁹⁶ publicizing more information on the risks and benefits of drugs may discourage spending on "innovative" new treatments that provide no meaningful therapeutic advantage over older, cheaper alternatives; as such, data publicity could be a *useful* disincentive for this sort of innovation and push drug companies to focus more resources on generating bigger therapeutic breakthroughs.

Conceptually, we might also view the data that drug companies generate on prescription drugs as emerging from a kind of public-private partnership between industry and the FDA; to deprive the public of access to data that the public pays to create would be unfair.²⁹⁷ We might also view disclosure of safety and efficacy data as a reasonable quid pro quo: if drug companies want to sell their products in the enormously profitable U.S. market,²⁹⁸ they must consent to disclosure of clinical data on those products.²⁹⁹ The pharmaceutical industry's enthusiastic exploitation of the patent system is another choice that requires (or arguably should require) disclosure of clinical data as a quid pro quo.³⁰⁰

competition with a pioneer drug was arguably more substantial prior to the Hatch-Waxman Act than it is today. Under current law, generic competitors are effectively permitted to rely upon data previously submitted to the FDA for a bioequivalent product through the use of an ANDA once the statutory periods of data exclusivity have expired.”).

²⁹⁴ Herder, *Toward a Jurisprudence of Drug Regulation*, *supra* n. [TK], at 248.

²⁹⁵ See *supra* § II.B.

²⁹⁶ *Supra* § I.A.

²⁹⁷ See Kapczynski, *Dangerous Times*, *supra* note [TK]. Others have explained that information that is submitted to regulatory agencies by private industry and/or generated with public dollars may not deserve protection as a trade secret. See Levine, *The People's Trade Secrets*, *supra* note [tk]; Levine, *Secrecy and Unaccountability: Trade Secrets in Our Public Infrastructure*, *supra* note [Tk]; Lyndon, *Secrecy and Access in an Innovation Intensive Economy: Reordering Information Privileges in Environmental, Health, and Safety Law*, *supra* note [tk], at 498.

²⁹⁸ In 2018, over a third of global pharmaceutical revenues were generated in the United States. *Global Pharma Spending Will Hit \$1.5 Trillion in 2023, Says IQVIA*, PHARM. COM. (Jan. 29, 2019), <https://pharmaceuticalcommerce.com/business-and-finance/global-pharma-spending-will-hit-1-5-trillion-in-2023-says-iqvia/>.

²⁹⁹ FDA does already disclose some clinical data upon approval of a drug. See *infra* § I.B.

³⁰⁰ Many commentators have questioned the practical quality and value of patent disclosure, pharmaceutical patents very much included. See generally, e.g., Colleen V. Chien, *Contextualizing Patent Disclosure*, 69 VAND. L. REV. 1849, 1850-51 (2016) (overviewing justification for patent system as an incentive to encourage innovators to disclose technical information to public); Jeanne C. Fromer, *Dynamic Patent Disclosure*, 69 VAND. L. REV. 1715 (2016); Lisa Larrimore Ouellette, *Do Patents Disclose Useful Information?*, 25 HARV. J.L. & TECH. 531 (2012); Sean B. Seymore, *The Teaching Function of Patents*, 85 NOTRE DAME L. REV. 621, 626 (2010); Jeanne C. Fromer, *Patent Disclosure*, 94 IOWA L. REV. 539 (2009). For more detailed analysis of pharmaceutical patents, see Gregory N. Mandel, *The Generic Biologics Debate: Industry's Unintended Admission that Biotech Patents Fail Enablement*, 11 VA. J.L. & TECH. 8 (2006); Janet Freilich, *Prophetic Patents*, 53 U.C. DAVIS L. REV. 663 (2019); Yaniv Heled, *Patents v. Statutory Exclusivities in Biological Pharmaceuticals - Do We Really Need Both*, 18 MICH. TELECOMM. & TECH. L. REV. 419 (2012). One might conceivably view sharing of clinical data as a fair trade for patents on methods of using prescription drugs.

Effects on incentives to innovate may not actually be industry's main concern. Drug companies may simply wish to avoid the release of data showing that their products are ineffective or unsafe. As the D.C. Circuit has observed, drug companies' reluctance to allow the FDA to disclose clinical data on prescription drugs sometimes arises not from a legitimate fear of competitors making use of that data but instead "the embarrassing publicity attendant upon public revelations concerning, for example," violations of safety laws.³⁰¹

2. Takings

Drug companies that submit safety and efficacy data from clinical trials of prescription drugs to the FDA have generally argued that these data are trade secrets protected by the Takings Clause of the Fifth Amendment and that disclosure without the submitter's consent constitutes a regulatory taking payment of "just compensation."³⁰² In fact, the FDA will likely owe little or no compensation under the Takings Clause if it begins proactive disclosure of safety and efficacy data. For *prospective* disclosure—i.e., for disclosure of safety and efficacy data submitted to the FDA *after* the agency implements new proactive disclosure rules—the analysis is simple: the Takings Clause does not apply. In *Ruckelshaus v. Monsanto*, the leading Supreme Court case on the application of the Takings Clause to data submitted to federal regulatory agencies, the Court held that agency disclosure of industry-submitted information can constitute a taking *if and only if* the agency first provided an assurance of secrecy.³⁰³ As soon as the FDA ceases assuring industry that future submissions of safety and efficacy data will be kept secret, all future takings claims will be foreclosed.³⁰⁴

³⁰¹ *Public Citizen Health Research Group v. FDA*, 704 F.2d 1280, 1291, n.30 (D.C. Cir 1983).

³⁰² For example, in 2010 the FDA's Transparency Task Force proposed to begin disclosing some metadata and summary data on safety and efficacy of prescription drugs. FOOD & DRUG ADMIN., FDA TRANSPARENCY INITIATIVE: DRAFT PROPOSALS FOR PUBLIC COMMENT REGARDING DISCLOSURE POLICIES OF THE U.S. FOOD AND DRUG ADMINISTRATION (May 2010), <http://www.lb7.uscourts.gov/documents/02c51292.pdf>. PhRMA subsequently submitted comments alleging that "[e]ven if statutory and regulatory changes were made to allow FDA to implement the Task Force's recommendations, disclosure of trade secrets and confidential commercial information currently in FDA's hands or developed in reliance on the current statutory and regulatory scheme would constitute an unconstitutional taking requiring payment of just compensation." Pharmaceutical Research and Manufacturers of America (PhRMA), Comment Letter on Proposed FDA Disclosure Policies (July 20, 2010), *supra* note [tk].

³⁰³ 467 U.S. at 1011 ("[T]he statute also gave Monsanto explicit assurance that EPA was prohibited from disclosing publicly, or considering in connection with the application of another, any data submitted by an applicant if both the applicant and EPA determined the data to constitute trade secrets. Thus, with respect to trade secrets submitted under the statutory regime in force between the time of the adoption of the 1972 amendments and the adoption of the 1978 amendments, the Federal Government had explicitly guaranteed to Monsanto and other registration applicants an extensive measure of confidentiality and exclusive use. This explicit governmental guarantee formed the basis of a reasonable investment-backed expectation." (citation omitted)). *See also id.* at 1008 ("[A]s long as Monsanto is aware of the conditions under which the data are submitted, and the conditions are rationally related to a legitimate Government interest, a voluntary submission of data by an applicant in exchange for the economic advantages of a registration can hardly be called a taking."); *id.* at 1013 ("[W]e hold that EPA's consideration or disclosure of data submitted by Monsanto to the agency prior to October 22, 1972, or after September 30, 1978, does not effect a taking.").

³⁰⁴ *See* Pamela Samuelson, *Principles for Resolving Conflicts between Trade Secrets and the First Amendment*, 58 HASTINGS L.J. 777, 809 (2006) ("While proponents of the trade-secrets-as-property conception tend to invoke *Ruckelshaus* as supporting the property concept, a fuller review of the Court's ruling demonstrates that trade secret interests are balanced against other societal interests, and sometimes the larger societal interests override trade secret interests. The strong property right theory that Monsanto propounded was soundly trounced in *Ruckelshaus*.").

The takings analysis for *retrospective* disclosure—i.e., for disclosure of safety and efficacy submitted to the FDA *before* the agency implements new proactive disclosure rules—is more complex but still favors the agency. To the extent that safety and efficacy data (as broadly defined above³⁰⁵) qualifies as a trade secret for purposes of the Takings Clause,³⁰⁶ disclosure of this data may not constitute a taking when the public interest in disclosure is balanced against the submitter’s interest in secrecy. *Ruckelshaus v. Monsanto*, as an initial matter, turned on the data in question qualifying as trade secrecy under state law, and as we have described, we believe that clinical trial data generally will not so qualify.³⁰⁷ If a court deemed that the FDA did disclose a trade secret, this disclosure still would not amount to a compensable taking unless there was interference with “reasonable investment-backed expectations.”³⁰⁸ The Court has elsewhere held that a crucial aspect of the character of the governmental action is the “nature of the State’s interest” and that a strong, legitimate public interest tips in favor of finding no taking.³⁰⁹ As

³⁰⁵ *Supra* § I.A.

³⁰⁶ It is not entirely clear, even in the wake of *Ruckelshaus v. Monsanto*, that all safety and efficacy data constitutes a “trade secret” for purposes of the Takings Clause. In the takings analysis, information qualifies as a “trade secret” protected by the Clause if it meets the relevant state law definition of a trade secret. *See, e.g., Ruckelshaus v. Monsanto*, 467 U.S. at 1001 (applying the relevant Missouri state law definition of a trade secret, which incorporated the definition found in the Restatement (First) of Torts). In *Ruckelshaus v. Monsanto*, the parties stipulated that “much” (though apparently not all) “of the information, research, and test data that Monsanto” had submitted to the EPA “contain[ed] or relat[ed] to trade secrets as defined by the Restatement of Torts.” *Id.* at 1001-02. Scholars have argued that under the Restatement and state law definitions of a trade secret, information that is submitted to regulatory agencies by private industry will not always qualify for protection as a trade secret. *See* Levine and Lyndon, *supra* note [TK]. In Part § II.A, *supra*, we explained that a few subcategories of clinical data that have genuine “commercial or financial” character and some innovative quality, such as new assay methodologies for biomarkers, properly qualify as confidential commercial information (CCI). In our view, it is, at most, these subcategories of clinical data that meet the definition of a trade secret found in the Restatement (First) of Torts, under which a trade secret must “differ[] from other secret information in a business . . . in that it is not simply information as to single or ephemeral events in the conduct of the business” and must instead be “a process or device for continuous use in the operation of the business.” Restatement (First) of Torts § 757, cmt. b.

³⁰⁷ Strangely, the EPA stipulated that the data in *Ruckelshaus v. Monsanto* was at least partly protected by the relevant state trade secret law, and that state law treated trade secrets as property, though there is some doubt that this is true. *See* Pamela Samuelson, *Information as Property: Do Ruckelshaus and Carpenter Signal a Changing Direction in Intellectual Property Law*, 38 CATH. U. L. REV. 365, 378-79 (1988).

³⁰⁸ 467 U.S. at 1005 (citations omitted). The court observed that there is no “set formula” for determining when regulatory action constitutes a taking but focused on investment-backed expectations, noting two other relevant factors too: “the character of the governmental action, [and] its economic impact.” *Id.*

³⁰⁹ *Keystone Bituminous Coal Ass’n v. DeBenedictis*, 480 US 470, 488 (1987) (“In *Pennsylvania Coal* the Court recognized that the nature of the State’s interest in the regulation is a critical factor in determining whether a taking has occurred, and thus whether compensation is required.” (citing *Pennsylvania Coal Co. v. Mahon*, 260 U. S. 393, 415 (1922))). In *Philip Morris, Inc. v. Reilly*, the First Circuit, sitting en banc, held that a Massachusetts state law requiring disclosure the ingredient lists in cigarettes was a taking because the state had failed to show a legitimate public interest in disclosure. 312 F.2d 24, 44, 46 (1st Cir. 2002) (stating that the court simply was “not convinced that the Disclosure Act, particularly the provisions about which the tobacco companies complain, really helps to promote public health” and concluding that disclosure constituted a taking because “the character of the government action determines the case. The Disclosure Act causes the tobacco companies to lose their trade secrets, entirely, and appellants advance no convincing public policy rationale to justify the taking itself.”). Setting aside the question of whether *Philip Morris* was correctly decided, the facts of *Philip Morris* are readily distinguishable insofar as the FDA can articulate a convincing public policy rationale to justify disclosure of safety and efficacy data on prescription drugs—*see supra* § I.A—and, indeed, already has in some instances. *See* FDA’s proposed rule on public disclosure of data on Human Gene Therapy and Xenotransplantation, *supra* n. [TK], at 4,692 (“The agency

explained above, the public interest in disclosure of safety and efficacy data on prescription drugs is strong. In addition, the economic impact of disclosure could be limited through use of data use agreements that prevent competitor drug companies from making use of the data.³¹⁰ As such, courts may well conclude that disclosure by the FDA of safety and efficacy data submitted under an expectation of secrecy effects no taking at all.³¹¹

Even if courts do deem disclosure of safety and efficacy a taking, the “just compensation” due will likely be minimal. Under the takings doctrine, the purpose of “just compensation” is to make the takee whole,³¹² and the amount of just compensation is typically (though not always) the “fair market value” of the taken property.³¹³ As explained above the FDA can use data use agreements to limit access by commercial users of data and prevent competitive uses.³¹⁴ In addition, while we are not aware of the FDA or other commentators having made the argument, it seems plausible to us that the data exclusivity periods that the FDA already grants drug companies upon new approvals—three years of market exclusivity upon approval of a new indication based on new clinical investigation, five years upon approval of a new (small molecule) chemical entity, seven years for a new orphan drug, twelve years for a new biologic, and so on³¹⁵—constitute sufficient “just compensation” to satisfy the Takings Clause.

Part III: Conclusion and Extrapolation

There is mounting evidence that we need comprehensive access to clinical trial data to protect our health. Today, researchers and clinicians can only rarely access to the data that they need to validate the efficacy and safety of medicines and guide clinical practice. This state of affairs has already contributed to the deaths of tens of thousands of people, and will continue to put us all at risk until steps are taken to proactively disclose this data. Regulators in Canada and the EU have taken halting steps in this direction, showing that it can be done, but leaving gaps that only the US FDA can fill. Here, we show how an administration committed to

believes that there is great benefit in having human gene therapy and xenotransplantation products scrutinized, as they are being developed, by individuals with a wide variety of perspectives, including scientists from different disciplines, biomedical ethicists, patient advocacy organizations, and the general public, because of the unique blend of proposed benefit as well as potential risk to society that these products possess.”).

³¹⁰ See *supra* § II.B & C.1.

³¹¹ See Fan, *supra* note [TK], at 200 (arguing that limiting disclosure of confidential data to researchers subject to strict limits on data use “renders disclosure nonpublic, averting Fifth Amendment takings concerns”); cf. *Exxon Corp. v. FTC*, 589 F.2d 582, 589 (D.C. Cir. 1978) (holding that limited disclosure of alleged trade secrets to a Congressional committee did not constitute public disclosure, did not “impair the value of the trade secrets involved,” and did not implicate the due process clause).

³¹² *United States v. 564.54 Acres of Land*, 441 U.S. 506, 511 (1979).

³¹³ *Id.* See also *Fla. Rock Indus. v. United States*, 18 F.3d 1560, 1569 (Fed. Cir. 1994) (“[T]he amount of just compensation should be proportional to the value of the interest taken as compared to the total value of the property . . .”). For an analysis of the proper calculation of “just compensation” in takings cases, see Katrina Miriam Wyman, *The Measure of Just Compensation*, 41 U.C. DAVIS L. REV. 239 (2008); Christopher Serkin, *The Meaning of Value: Assessing Just Compensation for Regulatory Takings*, 99 NW. U. L. REV. 677, 678, 682 (2005); Glynn S. Lunney, Jr., *Compensation for Takings: How Much is Just?*, 42 CATH. U. L. REV. 721, 725 (1993).

³¹⁴ The FDA could also amend its regulations governing approval of drug applications to clarify that it will not approve “copycat” new drug applications filed with “borrowed” clinical data. See Lietzan, *supra* n. [TK], at 82.

³¹⁵ *Frequently Asked Questions on Patents and Exclusivity*, *supra* note [TK] (3-, 5-, and 7-year exclusivities); 42 U.S.C. § 262(k)(7)(A) (12-year exclusivity).

healthcare reform and corporate accountability could reboot the FDA and establish a proactive data sharing system that would plausibly more than pay for itself, and that would benefit the public's health.

Our goal is to supplement and strengthen the FDA's credibility and authority in this context, and the features we propose —features like shifting the burden of redaction to industry and data use agreements that prohibit commercial use—are intended to serve that goal. There is, of course, a risk that the agency will not act.³¹⁶ If the FDA does not act, Congress can and should. Congress has already acted recently to expand access to certain health, by mandating that the FDA publish approval packages³¹⁷ and postmarket drug safety information (i.e., adverse event data)³¹⁸ on its website. Congress could do the same with the safety and efficacy data we describe.³¹⁹

Our analysis also helps point to a broader problem that is woven through the regulatory state in our information age. Commerce and industry are increasingly informational, making access to data essential to understand the implications of a wide range of products, from self-driving cars to environmental chemicals to complex financial instruments. The same dynamics we trace here – the incentives industry has to hide data *even as it relies on this data to claim that its products will benefit the public* – are in fact pervasive. Whether it is Boeing, touting the safety of its planes, or Monsanto, urging the safety of its weed-killer, companies have pervasive incentives to claim virtue for their products but obscure the data that would enable third parties to validate their claims. Regulators will often be in possession of relevant data but have limits – resources, person power, and conflicts of their own – that mean that the real benefits of this data cannot be leveraged unless outside parties have access. But those seeking access to corporate data in other areas are likely to face the same obstacles we address here: the cost and complexity of FOIA and the problems of the new *FMI* standard; the tendency of agencies to overprotect corporate data, treating as confidential or trade secrets data that may not meet that definition;³²⁰ and the inability to overcome corporate opposition and privacy concerns without proactive disclosure – and disclosure that can create limits as well as enable access.

³¹⁶ As Justice Breyer observed in his dissent in *FMI v. Argus Leader*, there is a “temptation, common across the private and public sectors, to regard as secret all information that need not be disclosed, . . . for reasons no better than convenience, skittishness, or bureaucratic inertia.” *Food Marketing Institute*, 139 S. Ct. at 2368 (Breyer, J., dissenting). See also Kreimer, *The Ecology of Transparency*, *supra* n. [tk] and Seth F. Kreimer, *The Ecology of Transparency Reloaded*, in *TROUBLING TRANSPARENCY: THE FREEDOM OF INFORMATION ACT AND BEYOND* (David Pozen & Michael Schudson eds., Columbia 2018).

³¹⁷ FDAAA Title IX sec. 916, codified at 21 U.S.C. § 355(l).

³¹⁸ FDAAA section [TK], codified at 21 U.S.C. § 355(r).

³¹⁹ If Congress decides to legislate in this arena, it could helpfully clear up any lingering uncertainty about the boundaries of 18 U.S.C. § 1905 (the TSA) and 21 U.S.C. § 331(j) (section 301(j) of the FDCA) by mandating release of the specific types of safety and efficacy data we have defined – see *supra* § I.A – notwithstanding these sections. Congress could also ensure that both the FDA and drug companies cooperate with a mandatory data publicity regime by amending the provisions that concern approval of new drugs, 21 U.S.C. § 355 (NDAs) and 42 U.S.C. § 262 (BLAs), to make submission of redacted, publicly disclosable data a precondition of approval and to require FDA disclosure within some defined time period, such as within 30 days of approval.

³²⁰ For an example of broad deference to trade secrets, see 47 C.F.R. § 0.457(d) (FCC). [add other sources]

The model we offer here, of data publicity subject to data use agreements, could, we suggest, become a template for other agencies. Our analysis of the TSA and takings law are also generalizable and can help support data publicity more broadly than in just the pharmaceutical context. There will be, of course, fact specific questions about where and when disclosure is warranted – and even circumstances where calls for transparency will be disingenuously mobilized to harm the public.³²¹ We leave it to others to take what is useful from our analysis to explore the need for and avenues to data publicity elsewhere in the regulatory state.

³²¹ See, e.g., *Comments on Proposed Rule, Strengthening Transparency in Regulatory Science*, 83 Fed. Reg. 18,786 (Docket ID No. EPA-HQ-OA-2018-0259), <https://www.scribd.com/document/385677020/Letter-from-Harvard-leaders-to-EPA-s-Andrew-Wheeler-on-proposed-science-policy> (academic letter describing the problems with an EPA “transparency” proposal that would have undermined access to reliable climate science).