

THE DATA LIBERATION MOVEMENT: * REGULATION OF CLINICAL TRIAL DATA SHARING IN THE EUROPEAN UNION AND THE UNITED STATES

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* Lynn Hudson, Co-Chair of the Institute of Medicine’s workshop on clinical trial data sharing, noted her excitement at being a part of the “data liberation movement.” Frank Rockhold & Lynn Hudson, *Sharing Clinical Research Data: A Workshop, Session III: Standardization and Governance*, INST. OF MED., (Oct. 4, 2012).

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I. INTRODUCTION

There are currently over 200,000 studies registered on clinicaltrials.gov,¹ and 4,000 new studies take place in the European economic area each year.² Clinical trials yield thousands of pages of valuable safety and efficacy data.³ The trial's sponsor submits that data to a regulatory body, like the U.S. Food and Drug Administration (FDA) in the United States or the European Medicines Agency (EMA) in the European Union, to obtain approval to market a drug, biologic, vaccine, or other therapeutic health product to the public.⁴ Clinical trial data submitted to support a marketing application could be pooled and re-analyzed to benefit the public,⁵ but only if the data are made available for those uses. Historically, pharmaceutical manufacturers were unwilling to share the raw data they generated in clinical trials, and the policies of the United States and the European Union enabled that secrecy.

However, right now, clinical trial data are the subject of an international discussion about government transparency, public health, and scientific innovation that threatens the data exclusivity that the drug industry has typically enjoyed.⁶

1. *Trends, Charts, and Maps*, NAT'L INSTS. OF HEALTH, <https://www.clinicaltrials.gov/ct2/resources/trends> (last visited Jan. 18, 2016).

2. *Clinical Trials in Human Medicines*, EUR. MEDS. AGENCY, http://www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/general_content_000489.jsp&mid=WC0b01ac058060676f (last visited Jan. 16, 2015).

3. G. Lee Skillington & Eric M. Solovy, *The Protection of Test and Other Data Required by Article 39.3 of the TRIPS Agreement*, 24 NW. J. INT'L L. & BUS. 1, 7 (2003).

4. See *id.* at 6-7 (explaining the drug approval process generally from preclinical trials to human trials to eventual approval or denial of a marketing application); see also *How Drugs Are Developed and Approved*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved> (last visited Jan. 18, 2016) (explaining the drug approval process, including data collection and submission, using the drug calcitonin as an example); *Clinical Trials in Human Medicines*, *supra* note 2 ("The European Medicines Agency relies on the results of clinical trials carried out by pharmaceutical companies to reach its opinions on the authorisation of medicines.").

5. See *infra* Section III (discussing the potential benefits of Non-Summary Data sharing).

6. See *infra* Sections III (discussing how an incident pertaining to the drug Vioxx led to a push for greater data sharing) and IV (briefly discussing transparency laws in the United States and European Union, and explaining that while both bodies protect the

Industry is under increasing pressure to provide outside scientists access to detailed, patient-level clinical trial data, as well as the protocols followed to collect data and the analytic tools used to interpret its meaning, for the sake of innovation and for the good of public health.⁷

This comment will focus on the role that regulatory bodies in the European Union and United States are playing in making data sharing a compulsory resultant of the marketing approval process. Each has taken action to increase the amount of data available to the public through governmental agencies.⁸ The discussion will explore and compare the paths to increased data sharing taken by the European Union, through the EMA, and the United States, through the FDA. It will show that the evolution of the EMA's early reactive data sharing rules into proactive, patient-level data sharing policies was founded on a public health argument that is not available to the FDA.

Part II will follow the evolution of data sharing regimes. Part III will put the data-sharing discussion into the context of its real world implications through an evaluation of some justifications for increased sharing as well as potential risks. Finally, Part IV compares the transparency laws governing release of data in the European Union and the United States to discern their similarities and critical differences. The purpose of this comment is to show that the FDA is constrained by U.S. law in a way that the EMA is unconstrained and to discuss the distribution of risk in the data sharing systems that are emerging in the European Union and the United States.

II. BACKGROUND

Between 1997 and 2008, a global push for greater disclosure of information relating to clinical trials led to policy changes at

commercial interests of companies submitting data in a marketing application, the European Union has implemented a process of balancing those interests with the public good that could be achieved if the data were disclosed to the public).

7. Nicholette Zeliadt & Roxanne Khamsi, *Four Models of Clinical Trial Data Offered in New Report*, 20 NATURE MED. 224, 224 (2014).

8. The clinical trial data sharing policies of both the European Union and the United States will be discussed in detail in Section II and IV of this paper.

the World Health Organization (WHO), the World Medical Association (WMA), the EMA, and the FDA and to the creation of three clinical trial registries. As a result of these efforts, the public gained access to basic information about a study.⁹

In the United States, the National Institutes of Health (NIH) established the country's first clinical trial database, *clinicaltrials.gov*, in February of 2000, under authority granted to it by the U.S. Congress in the Food and Drug Administration Modernization Act (FDAMA).¹⁰ The FDAMA requires reporting of "a description of the purpose of each experimental drug, patient eligibility criteria for participation in the trial, a description of the location of clinical trial sites, and a point of contact for those wanting to enroll in the trial."¹¹ In addition, in 2002, the FDA published a guidance document suggesting reporting of four categories of data: (1) Descriptive Information; (2) Recruitment Information; (3) Location and Contact Information; and (4) Administrative Data.¹²

These categories encompass descriptive information about the study itself, rather than data produced by the study. "Descriptive information" includes general information about the study, its design, the intervention being tested, and the condition or disease it is meant to treat.¹³ "Recruitment information" includes the status of participant recruitment, e.g. "recruiting" or "no longer recruiting," along with study enrollment eligibility criteria.¹⁴

Similarly, the WHO worked to make general clinical trial information available on a global scale. Participants in a 2004 Ministerial Summit on Health Research called for the WHO to

9. See 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 SCIS. L. 63, 79-80, 87 (2014) (outlining information made available to the public in the United States through *clinicaltrials.gov*, and discussing the WHO's efforts to make databases from a variety of countries available in one portal).

10. U.S. FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY: INFORMATION PROGRAM ON CLINICAL TRIALS FOR SERIOUS OR LIFE-THREATENING DISEASES AND CONDITIONS 1-2 (2002), <http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126838.pdf>.

11. 42 U.S.C. § 282(j)(2)(A) (2012).

12. U.S. FOOD & DRUG ADMIN, *supra* note 10, at 3.

13. *Id.*

14. *Id.*

facilitate “a platform linking a network of international clinical trial registers to ensure a single point of access and the unambiguous identification of trials.”¹⁵ A 2005 World Health Assembly Resolution expanded on that idea.¹⁶ Participant nations called for better access to clinical trial information for patients, families, patient groups, and others.¹⁷ In 2005, the WHO established the International Clinical Trial Registry Platform (ICTRP).¹⁸ The data stored in the ICTRP is similar to the trial information found on clinicaltrials.gov; it includes generalized information about the purpose of the trial and the sponsor.¹⁹

In the European Union, the EudraCT and European Clinical Trials Databases were developed to collect clinical trial information for use by regulators and for release to the public.²⁰ Regulation (EC) No. 726/2004 created the EMA and called for a publicly accessible database to contain certain information about approved drugs.²¹ Additionally, the database was to “include references to data on clinical trials currently being carried out or already completed.”²² In 2009, the European Commission released a list of data fields from the EudraCT database that would be made public.²³ As in the United States, the European

15. WORLD HEALTH ORG., REPORT FROM THE MINISTERIAL SUMMIT ON HEALTH RESEARCH 32 (2005), http://www.who.int/rpc/summit/documents/summit_report_final2.pdf.

16. World Health Org., Fifty-Eighth World Health Assembly: Resolutions and Decisions Annex, 126-27, WHA58/2005/REC/1 (2005), http://apps.who.int/gb/ebwha/pdf_files/WHA58-REC1/English/A58_2005_REC1-en.pdf. [hereinafter WHA Resolution].

17. WORLD HEALTH ORG., *supra* note 15, at 32; WHA Resolution, *supra* note 16, at 127.

18. WORLD HEALTH ORG., *supra* note 15, at 35.

19. *International Clinical Trials Registry Platform: WHO Data Set*, WORLD HEALTH ORG., <http://www.who.int/ictrp/network/trds/en/> (last visited Feb. 11, 2016).

20. *Clinical Trials in Human Medicines*, *supra* note 2.

21. Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 Laying Down Community Procedures for the Authorisation and Supervision of Medicinal Products for Human and Veterinary Use and Establishing A European Medicines Agency, arts. 1, 57(1)(d), 2004 O.J. (L 136) 1 (EC).

22. *Id.* art. 57(2).

23. List of Fields Contained in the ‘EudraCT’ Clinical Trials Database to be Made Public, in Accordance with Article 57(2) of Regulation (EC) No 726/2004 and Its Implementing Guideline 2008/C168/02, ENTR/F/2/SF D (2009) 3687, at 2-5 (EC) (Feb. 4, 2009) [hereinafter Commission Guidance on Disclosure of EudraCT Data].

Union disclosed general categories of information relating to the sponsor, the investigational product, and the clinical trial.²⁴

The need for greater transparency was recognized outside of government. In 2008, the Fifty-Ninth WMA conference amended the Declaration of Helsinki (Declaration) to include two new principles that related to clinical trial information.²⁵ The WMA is an independent international organization representing physicians.²⁶ Its Declaration is a statement of ethical principles for medical research involving human subjects.²⁷ After 2008, the Declaration included, in Section 19, an expression of the WMA's perspective that registration of clinical trials is an ethical imperative: "Every clinical trial must be registered in a publicly accessible database before recruitment of the first subject."²⁸

Eventually, publication of general information about clinical trials gave way to publication of summary results information. At the time the European Commission's 2009 guidance was published, the EudraCT system did not contain results information.²⁹ However, the commission made it clear that summary results data would be released to the public once that information actually became available in EudraCT.³⁰ In 2012, the European Commission provided for the release of some summary results information,³¹ and, as of July 2014, EudraCT's programming has been updated to fully implement summary

24. *Id.*

25. WHA Resolution, *supra* note 16; Karmela Krleža-Jerić & Trudo Lemmens, *7th Revision of the Declaration of Helsinki: Good News for the Transparency of Clinical Trials*, 50 CROAT. MED. J. 105, 106 (2009).

26. *About the WMA*, WORLD MED. ASS'N, <http://www.wma.net/en/60about/index.html> (last visited Jan. 16, 2015).

27. WORLD MED. ASS'N, DECLARATION OF HELSINKI: ETHICAL PRINCIPLES FOR MEDICAL RESEARCH INVOLVING HUMAN SUBJECTS ¶ 1 (2008).

28. *Id.* ¶ 35.

29. Commission Guidance on Disclosure of EudraCT Data, *supra* note 23, at 8.

30. *Id.*

31. Commission Guideline — Guidance on Posting and Publication of Result-Related Information on Clinical Trials in Relation to the Implementation of Article 57(2) of Regulation (EC) No 726/2004 and Article 41(2) of Regulation (EC) No 1901/2006, 2012 O.J. (C 302) 7, 8 [hereinafter Commission Guidelines].

results sharing.³² EudraCT's summary results fields are mostly identical to those found in clinicaltrials.gov.³³

The Food Drug Administration Amendments Act (FDAAA), passed in 2007, mandated the publication of summary results information on clinicaltrials.gov.³⁴ It expanded the types of trials that must be reported in the database and increased the scope of information that trial sponsors are required to submit.³⁵ The FDAAA requires the FDA to adopt rules implementing the expanded results sharing requirements by 2010. However, the FDA did not propose a rule under the FDAAA until 2014,³⁶ and, as of this writing, no final rule has been promulgated. The NIH, the body that maintains the database, modified clinicaltrials.gov in 2008 to enable the implementation of the FDAAA.³⁷ In spite of a regulatory void, some sponsors began submitting results data in 2008.³⁸

This movement to share summary results data is now giving way to a movement to share raw, participant-level data. There is a call to share not only raw data but the study plans and methods of analysis that constitute the context in which those data were collected and evaluated (Non-Summary Data).³⁹

32. *Clinical Trials – Directive 2001/20/EC*, EUR. COMMISSION, http://ec.europa.eu/health/human-use/clinical-trials/directive/index_en.htm#ct3 (last visited Mar. 6, 2015) (“As of 21 July 2014, the clinical trial results posted by sponsors in the EudraCT line with the Guideline 2012/C302/03 will become available to the public. This date corresponds to the finalization of the programming of the database”)

33. Commission Guidelines, *supra* note 31, at 8.

34. Food Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, § 801(a)(2), 121 Stat. 823, 904 (2007) (codified at 42 U.S.C. § 282(j)).

35. *Id.* § 801.

36. Clinical Trials Registration and Results Submission, 79 Fed. Reg. 69,566, 69,566-68 (Nov. 21, 2014) (noting that the statutory authority for the regulation is the 2007 FDAAA).

37. Clinical Trials Registration and Results Submission, 79 Fed. Reg. 69,566, 69,566 (Nov. 21, 2014) (to be codified at 42 C.F.R. pt. 11).

38. *Clinicaltrials.gov to Include Basic Results Data*, NAT'L LIBR. MED. TECH. BULL. (Oct. 21, 2008), http://www.nlm.nih.gov/pubs/techbull/so08/so08_clinicaltrials.html.

39. *See, e.g.*, INST. OF MED. OF THE NAT'L ACADS., SHARING CLINICAL TRIAL DATA 7 (2015), http://www.nap.edu/catalog.php?record_id=18998 (calling for drug manufacturers to share safety and effectiveness data, protocols, statistical analysis, and statistical tools).

III. RISKS AND BENEFITS OF SHARING NON-SUMMARY DATA

Proponents for Non-Summary Data sharing cite principled and practical advantages that are grounded in government transparency and public health. Independent scientists can use raw clinical trial data to discover earlier endpoints for drug testing,⁴⁰ conduct patient-level meta-analyses for safety and efficacy,⁴¹ and act as a check on regulators.⁴² All of these uses have the potential to make the public safer.⁴³

The risks involved in clinical trial participation could be reduced. Locating indicators of a drug's effectiveness earlier in the clinical trial process could shorten the length of trials and reduce the time it takes to get treatment options to patients.⁴⁴ If the answer to a research question is apparent from existing data, drug manufacturers could forego a clinical trial,⁴⁵ and prevent the repetition of doomed trials on new groups of participants.⁴⁶

40. See Availability of Masked and De-Identified Non-Summary Safety and Efficacy Data – Request for Comments, 78 Fed. Reg. 33,421, 33,422 (June 4, 2013) (discussing an evaluation of Hepatitis C studies that led to the discovery that a twelve-week endpoint was as predictive as waiting until twenty four weeks and suggesting that independent scientists could do the same analysis if raw data were made widely available).

41. See Francer & Turner, *supra* note 9, at 69-71 (outlining the safety and efficacy benefits of outside analyses of patient-level data).

42. See *id.* at 70 (noting that researchers are less likely to suppress relevant data from regulators if they know qualified researchers will be checking their work); Michelle M. Mello et al., *Preparing for Responsible Sharing of Clinical Trial Data*, 369 NEW ENG. J. MED. 1651, 1652-53 (2013).

43. See STEVE OLSON & AUTUMN S. DOWNEY, SHARING CLINICAL RESEARCH DATA 9 (2013) (arguing that increased safety is an ethical argument for increased data transparency); see also Mello et al., *supra* note 42, at 1,653 (“Because of the public health benefits of well-designed analyses of participant-level data . . .”).

44. See Mello et al., *supra* note 42, at 1,652 (listing speed in innovation and operational efficiencies in conducting clinical trials among the benefits of sharing data); Availability of Masked and De-Identified Non-Summary Safety and Efficacy Data - Request for Comments, 78 Fed. Reg., at 33,422 (“Analysis of data from multiple clinical and preclinical studies has been used to identify potentially valid endpoints for clinical trials, understand the predictive value of preclinical models, clarify how medical products work in different diseases, and inform development of novel clinical designs and endpoints to the benefit of patients.”).

45. Mello et al., *supra* note 42, at 1,653.

46. See Clinical Trials Registration and Results Submission, 79 Fed. Reg. 69,566, 69,573 (Nov. 21, 2014) (noting that sharing data regarding failed studies would “reduces inadvertent and unnecessary duplication of clinical studies.”).

Therapies could be tailored for effectiveness and safety. A single clinical trial utilizes a small groups of participants, which results in data with limited analytical utility. Mass data sharing across studies enables patient-level meta-analyses on large groups of participants to identify the risks and benefits of certain therapies for certain groups of individuals with greater specificity. That kind of analysis would optimize treatment decisions and prevent unnecessary harm.⁴⁷

Further, analyses of larger pools of data facilitate the discovery of safety issues unobservable in smaller groups,⁴⁸ which could have big public health implications.⁴⁹ The drug Vioxx provides a useful example. In 1999, the FDA approved Vioxx, a non-steroidal anti-inflammatory drug, for marketing as a painkiller.⁵⁰ In 2004, Merck, the drug's manufacturer, pulled Vioxx off of the market when the drug was linked to heart complications and stroke in its users.⁵¹ A later study of the Vioxx case indicated that if the data of 100 million Vioxx users had been monitored for complications, the risk of heart attack would have been discovered in just two to three months.⁵²

Greater data sharing enables scientists outside of the drug manufacturer and unconstrained by the limited resources of a government agency to search for safety indicators and test the validity of the data used to justify approval of drugs released onto

47. See Francer & Turner, *supra* note 9, at 71 (noting that meta-analyses of data led to the discovery that aspirin could be used to prevent heart attacks and that the dangers of using high doses of erythropoietin to treat certain renal patients who were anemic could have been detected earlier if data had been pooled).

48. See Mello et al., *supra* note 42, at 1,653 ("Pooling of these data . . . may detect safety problems unobservable in smaller samples.").

49. See *id.* (explaining that increased data sharing can allow detection of safety and efficacy issues that are not detectable in smaller groups).

50. Letter from Robert J. DeLap, Director, Office of Drug Evaluation, Center for Drug Evaluation and Research, to Robert E. Silverman, Senior Director, Regulatory Affairs, Merck Research Laboratories (May 20, 1999) (approving Vioxx for treatment of acute pain).

51. Alex Berenson, et al., *Despite Warnings, Drug Giant Took Long Path to Vioxx Recall*, N.Y. TIMES (Nov. 14, 2004), <http://www.nytimes.com/2004/11/14/business/despite-warnings-drug-giant-took-long-path-to-vioxx-recall.html?>

52. Transcript of Food and Drug Administration Sentinel Network Public Meeting – March 7, 2007, at 70 (Mar. 7, 2007) (statement of Richard Platt), <http://www.fda.gov/downloads/Safety/FDAsSentinelInitiative/UCM116513.pdf>.

the market.⁵³ Re-analysis of clinical trial data is a desirable goal considering clinical trial data can be riddled with inaccuracy and inconsistency, and the apparent clarity of summary data might be misleading.⁵⁴ The Director of Clinicaltrials.gov noted data issues in studies reported to the United States' clinical trial registry:

[T]he experience at ClinicalTrials.gov has shown that protocols are often vague, are not always followed, or in some cases may not even exist. In addition, summary data are not always readily available even for trials that have already been published. For many trials, no one can explain the structure of the trial or the analysis of the data, said Zarin. What we learned is there is not an objective, easy- to-describe route from the initial participant-level data to the summary data. Many people and many judgments are involved.⁵⁵

But, for data disclosure to work, the benefits have to be balanced with the potential harms. As discussed below, data sharing might harm both industry and the public.

A major criticism from industry is that releasing data threatens the commercial interests of the company that invested in data collection, and that is no small investment. While cost estimates vary,⁵⁶ A Tufts Center for the Study of Drug Development study released in 2014 estimates that the “average pre-tax industry cost per new prescription drug approval (inclusive of failures and capital costs) \$2,558 million,” or nearly \$2.6 billion.⁵⁷ Drug development costs have consistently increased

53. Aaron Xavier Fellmeth, *Secrecy, Monopoly, and Access to Pharmaceuticals in International Trade Law: Protection of Marketing Approval Data Under the TRIPs Agreement*, 45 HARV. INT'L L.J. 443, 475-76 (2004) (explaining that drug companies are incentivized to not disclose unfavorable results or exaggerate efficacy to regulatory agencies, and without third party examination those issues might not be discovered).

54. OLSON & DOWNEY, *supra* note 43, at 30.

55. *Id.* (internal quotations omitted).

56. Skillington & Solovy, *supra* note 3, at 8.

57. J.A. DiMasi et al., *Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs*, 40 J. HEALTH & ECON. 20 (2016). The study results were released as a webcast that is available through the Center's website. Tuft Center for the Study of Drug Dev., *November 18, 2014: Cost Study Press Event Webcast*, TUFTS CTR. STUDY OF DRUG DEV.

about eight percent annually in the last decade,⁵⁸ and there is little indication that costs will level out or begin to drop anytime in the near future, if the status quo is maintained. A continued source of cost is money invested in products that never make it to market.⁵⁹ The cost of developing investigational products that eventually fail must be absorbed into the price of products purchased by consumers.⁶⁰

Right now data exclusivity ensures that the time and money a private company invests in research and development will pay off when a drug gets to market.⁶¹ There is concern that data sharing will result in a loss of secrecy that will level the competitive playing field that makes drug development lucrative.⁶² A competitor could use available data to be the first to market in a country in which the data generator has not sought approval or discover a new indication for a drug that the data originator could have discovered to recoup the cost of investment.⁶³

There is further concern about the quality of the science that might come out of wide participant-level data sharing. Competitors or independent scientists could cherry pick big data sets with malicious intent.⁶⁴ Poor quality reanalysis could result in unnecessary health scares and diminish confidence in the regulatory drug approval process.⁶⁵

(Nov. 18, 2014), http://csdd.tufts.edu/news/complete_story/cost_study_press_event_webcast.

58. Skillington & Solovy, *supra* note 3, at 8.

59. *Id.*

60. *Id.*

61. *Id.* at 10.

62. *See, e.g.*, Pharmaceutical Research and Manufacturers of America, Comments to Docket No. FDA-2013-N-0271: Availability of Masked and Deidentified Non-Summary Safety and Efficacy Data; Request for Comments, 13-14 (July 24, 2013), <https://www.regulations.gov/contentStreamer?documentId=FDA-2013-N-0271-0003&attachmentNumber=1&disposition=attachment&contentType=pdf> [hereinafter PhRMA Comments] (noting that patient-level data sharing, of even masked and de-identified data, would likely reduce incentives to invest in biopharmaceutical innovation).

63. Skillington & Solovy, *supra* note 3, at 10.

64. Peter Doshi et al., *The Imperative to Share Clinical Study Reports: Recommendations from the Tamiflu Experience*, 9 PLOS MED., no. 4, 2012, at 1, 5, <http://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1001201>.

65. Franer & Turner, *supra* note 9, at 76.

Also, participant-level data sharing could compromise the privacy interests of research participants.⁶⁶ Sharing individual data creates opportunities for participant identification.⁶⁷ Identifying information might accidentally remain attached to data when it is released,⁶⁸ a person's identity might be ascertainable from de-identified data alone,⁶⁹ or the identities of subjects might be revealed through data re-identification techniques.⁷⁰ Re-identification techniques evolve, making the requirements for true de-identification hard to pin down.⁷¹

Though the risks of Non-Summary Data sharing might not be insurmountable,⁷² it may be that industry is better able to manage the risks than government agencies.⁷³ However, government agencies arguably have a duty to release clinical trial data in spite of the commercial interests at stake if disclosure would benefit public health.⁷⁴

In the past, the EMA and FDA have played parallel roles, critical in increasing the transparency of clinical trial information.⁷⁵ But each agency operates within distinctive legal frameworks that can produce disparate outcomes. The following section will outline and compare the policy approaches taken and

66. Hans-Georg Eichler et al., *Open Clinical Trial Data for All? A View from Regulators*, 9 PLOS MED., no. 4, 2012, at 1, 1, [http://www.plosmedicine.org/article/](http://www.plosmedicine.org/article/fetchObject.action?uri=info:doi/10.1371/journal.pmed.1001202&representation=PDF)fetchObject.action?uri=info:doi/10.1371/journal.pmed.1001202&representation=PDF.

67. *Id.*

68. *Id.*

69. *See id.* (noting that there is still a small risk that individual participants can be identified from anonymized datasets, particularly if the clinical trial was for an ultra-rare disease treatment).

70. Francer & Turner, *supra* note 9, at 72-73.

71. *See id.* (illustrating that the FDA's advanced notice of proposed rulemaking process discussed the challenges created by the evolving technology and increasingly available amount of data).

72. Eichler et al., *supra* note 66, at 1.

73. Francer & Turner, *supra* note 9, at 99.

74. *See, e.g.*, Sergio Bonini et al., *Transparency and the European Medicines Agency – Sharing of Clinical Trial Data*, 371 N. ENG. J. MED. 2,452, 2,454 (2014) (“[P]ublic health interests must outweigh any private intellectual or commercial interest.”); Trudo Lemmens & Candice Telfer, *Access to Information and the Right to Health: The Human Rights Case for Clinical Trials Transparency*, 38 AM. J.L. & MED. 63, 89 (2011) (arguing that shared, public access to clinical trial data is a component of a right to health).

75. *Supra* Part II.

legal regimes established in the United States and the European Union for both reactive and proactive data sharing.

IV. THE PATH TO NON-SUMMARY DATA SHARING

A. *Introduction*

Reactive data sharing is release of information at the request of some entity or person to that entity or person, and proactive data sharing is release of information before a request is made to the general public.⁷⁶ EMA and FDA policies on reactive and proactive data sharing arise in part from transparency law affecting each agency. In the European Union, reactive data sharing policy evolved into proactive data sharing through a particular public good provision found in E.U. transparency law that is absent in similar laws in the United States. As a result, the FDA has failed to transition its compulsory data-sharing program from summary to Non-Summary Data sharing while the EMA was compelled to initiate compulsory proactive Non-Summary Data sharing in the European Union for public health reasons.

B. *Transparency Laws*

Both the FDA and EMA have a limited duty to release information in reaction to requests for documents made under transparency laws that require regulators to provide documents to the public.⁷⁷ Those transparency laws contain certain exceptions that protect clinical trial data from disclosure in the European Union, until 2010, and continue to protect Non-Summary Data from disclosure in the United States today.

Underlying both sets of laws is a policy that favors disclosure with few exceptions. The European Union's regulation regarding public access to documents from the European Parliament, Council, and Commission (Transparency Regulation) states that

76. EUR. INFO. SOC'Y GRP., REPORT OF THE MEETING OF THE PERSONAL IDENTITY GROUP MEETING ON DATA SHARING AND GUIDANCE 5 (2004), <http://www.eurim.org.uk/activities/pi/040908dsreport.pdf>.

77. Freedom of Information Act, 5 U.S.C. § 552(a)(1) (2012); Council Regulation 1049/2001, art. 1(4), 2001 O.J. (L 145) 43 (EC).

it promotes a general policy of wide access to documents,⁷⁸ tempered by three exceptions.⁷⁹ The most notable exception for this discussion allows an agency to refuse to release information if it would undermine the commercial interests of the data producer.⁸⁰ The European Union's general policy and the allowable exceptions were codified by the EMA in their own Rules for the Implementation of Regulation (EC) No 1049/2001 on Access to EMEA Documents,⁸¹ which preserves the policy of wide access and carries over the Transparency Regulation's three exceptions.⁸²

Similarly, the FDA is obligated to release documents under the U.S. Freedom of Information Act (FOIA).⁸³ The FOIA was enacted to give the public a check on agency action, which is, perhaps unsurprisingly, why the general policy underlying the Act, like the E.U.'s Transparency Regulation, is wide disclosure.⁸⁴ It also contains enumerated exemptions that shield certain documents from release.⁸⁵ Like the E.U.'s Transparency

78. Council Regulation 1049/2001, art. 1(4), 2001 O.J. (L 145) 43 (EC) (granting among the "fullest" possible access while still considering the legal limitations).

79. *Id.* art. 4(1)-(3).

80. *Id.* art. 4(2) (refusing access to documents undermining commercial interest unless public interest requires otherwise).

81. Compare Council Regulation 1049/2001, art. 1(4), 2001 O.J. (L 145) 43 (EC), with Rules for the Implementation of Regulation (EC) No 1049/2001 on Access to EMEA Documents, art. 1(1), EMEA/MB/203359/2006 Rev 1 Adopted (Dec. 19, 2006) ("The scope of this Decision is to ensure the widest possible access [to agency documents.]").

82. Compare Council Regulation 1049/2001, art. 1(4), 2001 O.J. (L 145) 43 (EC), with Rules for the Implementation of Regulation (EC) No 1049/2001 on Access to EMEA Documents, arts. 3(1)-(3), EMEA/MB/203359/2006 Rev 1 Adopted (Dec. 19, 2006).

83. FOIA requires that "[e]ach agency make available to the public" certain categories of information outlined in the Act. 5 U.S.C. § 552 (2012). For information on FOIA requests directed to the FDA, see generally *Freedom of Information*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/RegulatoryInformation/foi/default.htm> (last updated Oct. 6, 2014).

84. See *Pub. Citizen v. U.S. Dep't of Health & Human Servs.*, 975 F. Supp. 2d, 81, 93 (D.C. Cir. 2013) ("Congress enacted FOIA as means to open agency action to the light of public scrutiny.") (citing *Am. Civil Liberties Union v. U.S. Dep't of Justice*, 655 F.3d 1, 5 (D.C. Cir. 2011)) (internal quotations omitted).

85. 5 U.S.C. § 552(b) (2012). The FDA codified the requirements of FOIA in its own public information regulation, 21 C.F.R. § 20 (2015).

Regulation, FOIA contains an exemption for information in which the data originator has a commercial interest.⁸⁶

Those similarities aside, the European Union's rules, and, subsequently, the EMA's own transparency rules contain a balancing test that is absent in U.S. law. If the commercial interests of the data producer are undermined by disclosure, then, in both countries, the public's right to that information must yield to the rights of the data producer; however, unique to the EMA transparency rules and absent from FOIA, is a mandate that the commercial interest must be balanced against the public good that would result from release of information otherwise protected by the commercial interest exception.⁸⁷

The discussion below seeks to highlight how this balancing rule, applied in the context of reactive data release, became the catalyst for the European Union's transition to proactive Non-Summary Data sharing, and, through comparison, investigate how the FDA is constrained from passing proactive Non-Summary Data sharing policies of its own.

C. *EMA Policy on Reactive Non-Summary Data Sharing*

The EMA's first step toward Non-Summary Data sharing came in November of 2010 when it released its Policy on Access to Documents (Related to Medicinal Products for Human and Veterinary Use).⁸⁸ This is a reactive policy of disclosure;⁸⁹ a member of the public can request any documents, including Non-Summary Data, involved in the EMA's decision-making process for authorizing a given drug for marketing in the European

86. 5 U.S.C. § 552(b)(4) (exempting from FOIA's disclosure requirements information that is "commercial or financial information obtained from a person and privileged or confidential").

87. *Decision of the European Ombudsman Closing His Inquiry into Complaint 2560/2007/BEH Against the European Medicines Agency*, EUROPEAN OMBUDSMAN, ¶¶ 33, 35 (Nov. 24, 2010), <http://www.ombudsman.europa.eu/cases/decision.faces/en/5459/html.bookmark> [hereinafter *Decision of the European Ombudsman*].

88. *See European Medicines Agency Policy on Access to Documents (Related to Medicinal Products for Human and Veterinary Use)*: Policy/0043, EUR. MEDS. AGENCY, EMA/110196/2006 (Dec. 1, 2010) [hereinafter *EMA Policy on Access to Documents*] (discussing the EMA's policy to embrace openness of operation for accessing documents).

89. Bonini et al., *supra* note 74, at 2,453.

Union.⁹⁰ This policy is a revision to the EMA's Rules motivated by a well-publicized complaint brought against the EMA by a non-profit research collaborative when the EMA refused to grant two of the organization's researchers access to data requested under the Rules.⁹¹

The data requested involved Non-Summary Data related to placebo-controlled trials of two anti-obesity drugs.⁹² The researchers wanted to re-evaluate the safety and efficacy data the drug manufacturer submitted in its marketing application to re-assess the safety of these drugs in light of new data that had been obtained since the products went on the market.⁹³ The EMA's refusal resulted in a years-long dispute process involving the European Ombudsman.⁹⁴

The Ombudsman found that the EMA's Rules did not preclude the EMA from releasing the requested Non-Summary Data.⁹⁵ When it refused the researchers' request, the EMA relied on article 3(2)(a) of the Rules, which allows the EMA to refuse disclosure of information if such disclosure would undermine the protection of a party's commercial interests, unless there is an overriding public interest in disclosure.⁹⁶

Case law gives the commercial interest exception greater specificity: An agency invoking the commercial interest exception is required to assess "(i) whether access to the document would

90. *EMA Policy on Access to Documents*, *supra* note 88, § 4.1; Bonini et al., *supra* note 74, at 2,454.

91. Peter Götzsche & Anders Jørgensen, *Opening up Data at the European Medicines Agency*, 342 BRIT. MED. J. 1,184, 1,184-86 (2011).

92. *Id.* at 1,184.

93. *See, e.g., id.* (describing Peter Götzsche & Anders Jørgensen's efforts to access unpublished trial reports from the EMA); *Questions and Answers on the Review of Orlistat-Containing Medicines*, EUR. MEDS. AGENCY, EMA/CHMP/113837/2012 Rev. 1 (Apr. 24, 2012) (reviewing the approved drug orlistat upon possible risks of severe liver injury); *Questions and Answers on the Recommendation to Suspend the Marketing Authorisation of Acomplia (Rimonabant)*, EUR. MEDS. AGENCY, EMEA/537153/2008 (Oct. 23, 2008) (advocating suspension of the marketed drug rimonabant after concerns of psychiatric side effects on patients).

94. Hans-Georg Eichler, *Presentation at the Institute of Medicine Workshop: Clinical Trial Data Sharing: A Workshop* at 0:30-2:30, EUR. MEDS. AGENCY, <http://youtu.be/nUJ5GJQTRZc?t=1m8s>.

95. *Decision of the European Ombudsman*, *supra* note 87, ¶ 88, § B.

96. *Id.* ¶ 27.

specifically and actually undermine the protected interest and (ii) whether there is no overriding public interest in disclosure. That assessment must be apparent from the reasons underpinning the decision.⁹⁷ In his proposal for a friendly resolution, the Ombudsman was unconvinced that the EMA had shown that disclosure of the requested documents would *specifically and actually undermine* the commercial interests of the data originator.⁹⁸ This was in spite of the fact that he recognized the potential commercial interests at stake: “[T]he Ombudsman understood that the that clinical study reports contain the full details of the clinical development programme, which represents the most substantial part, both in terms of time and cost, in the development of a medicinal product.”⁹⁹

Later, after reviewing the files withheld by the EMA, the Ombudsman failed to find that they contained any intellectual property, trade secrets, or commercial confidences at all.¹⁰⁰ Relevant to the Ombudsman’s decision was that the files did not contain information about the composition or formulae of the products under trial, manufacturing or control processes of the drugs, or the marketing or development strategies of the company.¹⁰¹

While the case turned on the Ombudsman’s decision that the files did not contain protected information, the Ombudsman went to opine that there existed an overriding public interest in disclosure.¹⁰² The Ombudsman found that the complainants’ had raised health concerns that would establish an overriding public interest in disclosure *even if the information fell within the commercial interest exception*.¹⁰³

97. *Id.* ¶ 28 (citing MyTravel Group v. Commission, Case No. T-403/05, [2008] ECR II-2027, ¶ 33) (emphasis added).

98. *Id.* ¶ 30.

99. *Id.* ¶ 32.

100. *Id.* ¶¶ 75–80.

101. *Id.* ¶¶ 78–79.

102. *Id.* ¶¶ 32–34.

103. *Id.* ¶¶ 32–34; *see also* Gotzsche & Jørgensen, *supra* note 91, at 1,185.

D. The EMA and Proactive Non-Summary Data Sharing

The Ombudsman brought about a sea change in the transparency policy of the EMA.¹⁰⁴ The EMA adopted the position clinical trial data is not commercial confidential information.¹⁰⁵ The notion that the public interest in the health and safety benefits of data disclosure must outweigh the intellectual and commercial interests of private parties guided the EMA's transparency policy changes.¹⁰⁶ Regulators saw the EMA's 2010 policy as the first step in a two-step process of allowing the widest possible access to documents.¹⁰⁷ The 2010 policy is reactive, but proactive disclosure was always the ultimate goal.¹⁰⁸

In 2014, the EMA published the European Medicines Agency Policy on Publication of Clinical Data for Medicinal Products for Human Use.¹⁰⁹ This policy requires the proactive publication of clinical trial data submitted to the EMA as part of marketing application or as part of a post-marketing monitoring effort.¹¹⁰ Data are not published until after the marketing application is approved, and commercially confidential information can be withheld, but generally the EMA does not view trial data as commercial confidential information.¹¹¹ To protect trial participants, all data will be de-identified.¹¹² To protect against re-identification and to prevent misuse of data, the EMA will release data in various forms with varying degrees of restricted access.¹¹³ Some require user agreements under which the user

104. Eichler, *supra* note 94, at 1:30–2:10; *Opening the Doors to Clinical Trial Data*, ALZFORUM (Nov. 15, 2013), <http://www.alzforum.org/news/community-news/opening-doors-clinical-trial-data>.

105. Eichler, *supra* note 94, at 1:30 - 2:10.

106. Bonini et al., *supra* note 74, at 2,454.

107. *Id.* at 2,452 (“It represents the first step in implementing the principle of allowing the widest possible access to data”)

108. *Id.* at 2,453.

109. The Policy became effective on January 1, 2015. European Medicines Agency Policy on Publication of Clinical Data for Medicinal Products for Human Use, EUR. MEDS. AGENCY, EMA/240810/2013 (Oct. 2, 2014).

110. *Id.* at 2-4.

111. *Id.* at 4, 8.

112. *Id.* at 7.

113. *Id.* at 3-6.

agrees to certain terms of use.¹¹⁴ Terms will forbid re-identification of data or attempting to use data to gain commercial advantage by using the work of the data originator.¹¹⁵

E. The FDA Policies and Reactive Non-Summary Data Sharing

Like, article 3(2)(b) of the Rules, FOIA's fourth category of exempt information allows an agency to withhold "trade secrets and commercial or financial information obtained from a person and [is] privileged or confidential."¹¹⁶ Courts interpret exemption four as a necessary benefit conferred on private parties that cooperate with regulatory bodies by disclosing data.¹¹⁷ In the case of a party who is compelled to provide data to an agency by statute, the assurance of confidentiality is considered necessary to ensure that the data provider will be willing to share good data.¹¹⁸ The implication is that, if a private party is concerned about the safety of its commercial interests, that concern might affect the quality of the dataset it provides.¹¹⁹ Exemption four intentionally favors the interests of the data originator.¹²⁰

It seems that Non-Summary Data are well protected by exemption four. The court applies a robust definition of "commercial" that encompasses any document in which a data provider has a commercial interest,¹²¹ and the FDA is not required to balance the commercial interest of the drug manufacturer against the public good.¹²²

114. *Id.* at 5, 10-11, 13-14.

115. *Id.* at 6.

116. 5 U.S.C. § 552(b)(4) (2012).

117. *Critical Mass Energy Project v. Nuclear Regulatory Comm'n*, 975 F.2d 871, 873 (D.C. Cir. 1992) (citing *Nat'l Parks & Conservation Ass'n v. Morton*, 498 F.2d 765, 770 (D.C. Cir. 1974)).

118. *Id.* at 878.

119. *Id.* at 877-78.

120. *Id.* at 873.

121. *Pub. Citizen v. U.S. Dep't of Health & Human Servs.*, 975 F. Supp. 2d 81, 100 (D.C. Cir. 2013).

122. *Compare* Council Regulation 1049/2001, art. 4(2), 2001 O.J. (L 145) 43 (EC) (stipulating that exception two is applied unless there is an overriding public interest in disclosure), *with* Freedom of Information Act, 5 U.S.C. § 552(b)(4) (which does not contain a similar public interest provision).

The term commercial is not defined in FOIA or its legislative history.¹²³ The courts give the word its ordinary meaning,¹²⁴ which they interpret to be fairly broad. “Not every bit of information submitted to the government by a commercial entity qualifies for protection under exemption four. . . .”¹²⁵ “Information is commercial if, in and of itself, it serves a commercial function or is of a commercial nature.”¹²⁶ Exemption four shields documents that represent sensitive commercial information, such as customer lists, profit and loss reports, inventories, and development plans.¹²⁷ Another definition of commercial draws information in which the data provider has a commercial interest under exemption four’s protection.¹²⁸ For example, because safety and effectiveness data are instrumental in gaining approval of a product, the data originator has a commercial interest in them.¹²⁹ These data are not commercial in nature, but relate to the commercial interests of the provider.¹³⁰

Aside from being commercial, to get the protection of exemption four, data must also be confidential.¹³¹ The *National Parks* two-part test, applied by courts to evaluate the confidentiality of information that the submitter was required to provide the government, provides that information is confidential when disclosure would: 1) impair the agency’s ability to get information in the future, or; 2) cause substantial competitive

123. *Pub. Citizen*, 975 F. Supp. 2d at 99.

124. *Pub. Citizen Health Research Grp. v. Food & Drug Admin.*, 704 F.2d 1,280, 1,290 (D.C. Cir. 1983).

125. *Id.*

126. *Pub. Citizen*, 975 F. Supp. 2d at 99 (quoting *Nat’l Ass’n of Homebuilders v. Norton*, 309 F.3d 26, 38 (D.C. Cir. 2002)).

127. *See Pub. Citizen Health Research Grp.*, 704 F.2d at 1,290 (implying that the court recognizes a valid commercial interest in such information and recognizing that other types of information may be protected by exemption four); *see also Pub. Citizen*, 975 F. Supp. 2d at 99-100 (looking at the range of information held exempt from disclosure under exemption four by courts).

128. *Pub. Citizen Health Research Grp.*, 704 F.2d at 1,290.

129. *Id.*

130. *Id.*

131. Freedom of Information Act, 5 U.S.C. § 552(b)(4) (2012).

harm to the entity that submitted the information.¹³² The kind of substantial competitive harm envisioned in exemption four is harm that results from disclosure that gives “competitors . . . valuable insights into the operational strengths and weaknesses of a [company], while [its competitors] could continue in the customary manner of ‘playing their cards close to their chest.’”¹³³

A successful argument for confidentiality shows that competitive harm would result from disclosure because the data are related to the business of the drug manufacturer or the drug development plans of the manufacturer.¹³⁴ For example, in one case it was found that the disclosure of data from an abandoned investigational new drug application would cause substantial competitive harm when the originator was developing successor drugs based on the abandoned clinical trial data, the target illness was not relatively well-controlled by existing products, and a number other companies were developing the same class of drug.¹³⁵ As such, it seems substantial competitive harm could result if a competitor could obtain all the data in a new drug application and use it to support their own application.¹³⁶

Once the data in a marketing application is found to be exempt from disclosure, public good arguments cannot defeat that exemption. The FOIA does not contain a provision that requires an agency to balance private interests against the greater public good.¹³⁷ In other words, if requested information falls within

132. *Critical Mass Energy Project v. Nuclear Regulatory Comm’n*, 975 F.2d 871, 873 (D.C. Cir. 1992) (citing *Nat’l Parks & Conservation Ass’n v. Morton*, 498 F.2d 765, 770 (D.C. Cir. 1974)).

133. *Pub. Citizen Health Research Grp.*, 185 F.3d 898, 905 (D.C. Cir. 1999) (citing *Nat’l Parks & Conservation Ass’n v. Kleppe*, 547 F.2d 673, 684 (D.C. Cir. 1976)).

134. *See id.* (discussing the business risks of sharing information that support a finding of competitive harm; *see also Critical Mass Energy Project*, 975 F.2d at 878-80 (holding that commercial information voluntarily given to the government is “confidential” for the purposes of exemption four if it is of the type of information which would customarily not be released because of the potential for competitive harm in the industry)).

135. *Pub. Citizen Health Research Grp.* 185 F.3d at 900, 903, 905.

136. *Webb v. Dep’t of Health & Human Servs.*, 696 F.2d 101, 103 (D.C. Cir. 1982).

137. *Compare* Council Regulation 1049/2001, art. 4(2), 2001 O.J. (L 145) 43 (EC) (stipulating that the exception two is applied unless there is an overriding public interest

exemption four, the agency can withhold that information without further considering the public good that could result from disclosure.¹³⁸ One court found that avoiding risk to human health was not the public interest promoted by FOIA.¹³⁹ The court noted that the complainant's "consequentialist approach to public interest in disclosure is inconsistent with the balance of private and public interests the Congress struck in Exemption 4."¹⁴⁰ The court identified the "relevant public interest" underlying FOIA: "if through disclosure the public would learn something directly about the workings of government, then the information should be disclosed unless it comes within a specific exemption."¹⁴¹

F. FDA and Proactive Non-Summary Data Sharing

The justifications for release of information based on the public good that the Ombudsman found compelling would fall flat in a U.S. court.¹⁴² At the same time, the Ombudsman applied a limited definition of commercial that is narrower than the definition used in U.S. courts. In spite of the legal challenges such a policy would face in the United States, the FDA did propose a rule for proactive sharing raw, patient-level data.¹⁴³

The FDA tried to get around the commercial interest of the data originator in its 2013 proposed rule. The FDA issued a request for comment on a system of proactive sharing of masked

in disclosure), *with* Freedom of Information Act, 5 U.S.C. § 552(b) (which does not contain a similar public interest provision).

138. See, e.g., *Pub. Citizen Health Research Grp.*, 185 F.3d, at 904 (noting that it was not open to complainant to make assertions that disclosure of data from failed trials would bring about public good in the form of preventing future risky tests).

139. *Id.*

140. *Id.* (internal citations omitted).

141. *Id.*

142. See *Opening the Doors to Clinical Trial Data*, *supra* note 104 ("The Ombudsman ruled in 2010 that public health concerns regarding drugs on the market take precedence over commercial confidentiality . . ."); see also *Pub. Citizen Health Research Grp.*, 185 F.3d at 904 (clarifying that in the balance between public and private interests, "the public interest side of the balance is not a function of . . . any potential negative consequences disclosure may have for the public.").

143. Availability of Masked and De-Identified Non-Summary Safety and Efficacy Data - Request for Comments, 78 Fed. Reg. 33,421, 33,421-23 (June 4, 2013).

and de-identified data.¹⁴⁴ The proposal indicated the agency would not classify masked data, data that is no longer linked to a product or a manufacturer, as commercial information or trade secrets.¹⁴⁵ On this view, raw data are instantiated with commercial value based on a competitor's ability to identify the type of drug being tested or the maker of that drug.¹⁴⁶ Industry players opposed the FDA's proposal,¹⁴⁷ and, ultimately, the FDA did not promulgate a rule compelling masked, patient-level data sharing.

In 2014, the FDA finally proposed a rule implementing the data expansion provisions of the FDAAA. The proposed rule would require clinical trial sponsors or their designees to include certain summary outcome and adverse event data in the *clinicaltrials.gov* database.¹⁴⁸ The FDA's proposed rule, if finalized, would apply to interventional, controlled trials of drugs, biologics, or devices, regardless of whether the product under study has been licensed, approved, or cleared by the FDA.¹⁴⁹

V. CONCLUSION

While this does represent an expansion of proactive reporting requirements in the United States,¹⁵⁰ the FDA's program is meager compared to the EMA's new proactive reporting regime. But the FDA is limited by U.S. law. While the EMA could lean on

144. *Id.* at 33,421.

145. *See id.* at 33,423 (indicating that sharing raw, de-identified, and masked data under this proposal will not result in sharing a trade secret or commercial information).

146. *See id.* (suggesting different strategies for masking data to protect commercial interest).

147. *See* PhRMA Comments, *supra* note 62, at 2 (discussing PhRMA's concerns regarding the possibility the proposal might chill the development of new medicinal products). PhRMA is a body that represents over fifty of the world's largest pharmaceutical companies. *Member Companies*, PhRMA, <http://www.phrma.org/about/member-companies> (last visited Jan. 18, 2016).

148. *See* 79 Fed. Reg. 69,566 (2014) for the notice of proposed rulemaking.

149. The FDA's proposed rule would extend the reporting requirements to unapproved applicable clinical trials. *Id.* at 69,567. *See also Summary of HHS/NIH Proposals to Enhance Transparency of Clinical Trial Results*, NAT'L INSTS. HEALTH (Nov. 19, 2014), http://www.nih.gov/news/health/nov2014/od-19_summary.htm [hereinafter *Summary of HHS/NIH Proposals*] (explaining the broad application of the proposed rule).

150. *Summary of HHS/NIH Proposals*, *supra* note 149.

public health justifications for release of Non-Summary Data, the FDA simply cannot.

The good news is that the wheels of data sharing are moving. Ultimately, it will be up to industry in the United States to create an atmosphere of sharing. There is an effort to reduce the culture of distrust that is pervasive in the pharmaceutical industry in order to foster sharing at the industry level.¹⁵¹ To that end, the Institute of Medicine of the National Academies (IOM) released a report sponsored by industry players and government agencies that recommends data sharing practices.¹⁵² Prior to the IOM's report, PhRMA and the European Federation of Pharmaceutical Industries and Associations (EFPIA) adopted a set of Principles for Responsible Data Sharing (Principles) in and between the United States and the European Union.¹⁵³ The Principles encourage member companies to share scientific information, including patient-level data and study protocols, from clinical trials on patients in the United States and European Union with qualified researchers through individual agreements.¹⁵⁴ Member companies are expected to implement the Principles' data sharing plan through company level policies.¹⁵⁵ The Principles require companies to appoint an independent scientific review committee to decide the merits of research proposals submitted by independent scientists.¹⁵⁶ An approved proposal is a candidate for data sharing.¹⁵⁷

However, there are some limitations to the kind of sharing the Principles will produce.¹⁵⁸ For example, the Principles only

151. INST. OF MED. OF THE NAT'L ACADS., *supra* note 39, at 156.

152. *Id.* at 80-82.

153. PhRMA & EFPIA, PRINCIPLES FOR RESPONSIBLE CLINICAL TRIAL DATA SHARING: OUR COMMITMENT TO PATIENTS AND RESEARCHERS (2013).

154. *Id.* princ. 1.

155. *Id.*

156. *Id.*

157. *Id.*

158. For examples of how medical organizations have implemented the PhRMA & EFPIA Principles, see generally *Clinical Trials Data and Information Sharing*, ABBVIE, <http://www.abbvie.com/research-innovation/clinical-trials-data-and-information-sharing/home.html> (last visited Feb. 7, 2016) (sharing clinical trial data only after a drug has been approved) and *Clinical Trials Data Sharing*, CELGENE, <https://www.celgene.com/research-development/clinical-trials/clinical-trials-data-sharing>

require data sharing after market approval of a product or indication.¹⁵⁹ Also, companies can elect to decide what data to share at the company level rather than at the independent committee level.¹⁶⁰

The IOM recommendations provide an alternative framework for Non-Summary Data sharing. IOM advocates sharing data from a wide variety of projects, not just those that resulted in approved drugs.¹⁶¹ IOM recommends sharing a whole suite of Non-Summary Data; raw data, study protocols, statistical analyses, and analytical tools.¹⁶² IOM notes that there are examples of successful, industry level data collaborative groups.¹⁶³

While industry appears to be taking a step toward greater data sharing, it cannot be denied that these are piecemeal efforts that create a patchwork of different repositories, standards for disclosure, and methods for obtaining access. Maybe all that has been achieved in the United States is dumping the contents of small silos of data into bigger silos. The European Union has achieved something more robust.

As the European Union gets closer to complete disclosure, it is worth noting that the results of their document disclosure program revealed that few data requestors were the sort that data transparency initiatives aim to reach.¹⁶⁴ Instead of reaching patient groups, independent researchers, and concerned physicians, a large portion of requestors were competitor pharmaceutical companies and lawyers seeking evidence in

(last visited Feb. 7, 2016) (accepting data requests from “qualified researchers” and making exceptions only after evaluating the “scientific validity” of the request).

159. PHRMA & EFPIA, *supra* note 153.

160. *See, e.g., Clinical Trials Data and Information Sharing, supra* note 158 (explaining the process by which Abbvie, upon request, conducts an internal review of a clinical trial before deciding whether to share the data).

161. *See* INST. OF MED. OF THE NAT'L ACADS., *supra* note 39, at 8-12 (recommending that providers share metadata, summaries, and the full data package for all clinical trials, regardless of the regulatory outcome).

162. *Id.* at 96-105.

163. *See, e.g., id.* at 18, 20 (discussing the success of the YODA collaborative).

164. *See* Bonini et al., *supra* note 74, at 2,454 (arguing that the low number of patients and patient associations making requests shows a need for more effective communication about the transparency policy).

failure to warn cases.¹⁶⁵ The European Union's policy led to three lawsuits against the EMA, two of which were resolved between the EMA and the complaining party.¹⁶⁶

As Non-Summary Data sharing systems take shape in the European Union and the United States, a host of legal and practical challenges will emerge.¹⁶⁷ The EMA will be forced to protect the commercial and personal information that are threatened when data is released to the public. That will be difficult considering de-identification is a moving target,¹⁶⁸ and the parties who have sought data from the EMA so far have been those who are likely seeking a peak at a competitor's work to gain a market advantage.¹⁶⁹

While the United States has shifted the burden of protecting the private interests of drug manufacturers and research participants to private industry players, it is unclear whether or not the industry can be trusted to engage in robust data sharing. Arguably, the FDA is shirking a duty to promote transparency and public health by leaving Non-Summary Data sharing to interested industry parties who have fought for data secrecy in the past. But it appears, without some assistance from Congress to overcome the legal hurdles to robust Non-Summary Data sharing, the FDA is limited in its ability to be part of the global data sharing movement.

165. *Id.* at 2,452-53.

166. *Id.*

167. *See id.* at 2,454 (characterizing the implementation of data sharing systems as a learning process in which public health and private commercial interests must be balanced).

168. Francer & Turner, *supra* note 9, at 72-74 (arguing that it has become increasingly difficult to ensure that trial data will not be re-identifiable after it is shared).

169. *See* Bonini et al., *supra* note 74, at 2,452 (offering statistics showing that the largest percentage of approved data requests is made up of requests from within the pharmaceutical industry). The author speculates that competition is the motive for the entities mentioned in this article.