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INCREASING TRANSPARENCY OF CLINICAL TRIAL DATA IN THE UNITED STATES AND THE EUROPEAN UNION

I. THE STATUS OF CLINICAL TRIALS DATA

The Internet is becoming “the greatest source of health information” for most consumers, which reinforces the importance of making online information about clinical trials accessible in a reliable, unbiased format.¹ Non-reporting and distorted reporting of clinical trials impede the betterment of scientific knowledge and public health.² Therefore, proper reporting of clinical trial results on the Internet is an essential step to ensure the research community and providers “. . . fully understand the benefits . . . [and] potential consequences of taking a certain drug.”³

There have been increasing demands for public transparency, such as the Declaration of Helsinki, which states the need for complete disclosure of clinical trial data.⁴ Clinical trial data is research meant to “contribute to *generalizable* knowledge” as set forth in the Belmont Report,⁵ and the research community has an obligation to share that data with trial participants.⁶ Hoarding data will cause researchers to “duplicate efforts,

1. James M. Wood & Roxanne M. Gariby, *Hoarding Away Science: Towards a More Transparent View of Health and Online Registries for Independent Postmarket Drug Research*, 60 FOOD & DRUG L.J. 547, 548 (2005).

2. See generally World Health Organization (WHO), *WHO Calls for Increased Transparency in Medical Research* (2015), <http://www.who.int/mediacentre/news/notes/2015/medical-research-transparency/en/>.

3. Wood & Gariby, *supra* note 1, at 548. The 2010 Consolidated Standards of Reporting Trials (CONSORT) Statement has motivated the international community to “[improve] the reporting quality for . . . trials.” Kenneth F. Schulz et al., *CONSORT 2010 Statement: Updated Guidelines For Reporting Parallel Group Randomised Trials*, 340 BMJ 698, 698 (2010), <http://www.consort-statement.org/Media/Default/Downloads/CONSORT%202010%20Statement/CONSORT%202010%20Statement%20-%20BMJ.pdf>.

4. *The Declaration of Helsinki*, World Medical Association (WMA), <http://www.wma.net/en/30publications/10policies/b3/> (last updated in October 2013). The Declaration of Helsinki states that “[r]esearchers have a duty to make publicly available the results of their research on human subjects and are accountable for the completeness and accuracy of their reports.” *Id.* ¶ 36.

5. Leonard A. Levin & Julie G. Palmer, *Institutional Review Boards Should Require Clinical Trial Registration*, 167 JAMA 1576, 1577 (2007) (citing *The Belmont Report* (1979), Part A, available at <http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.html>). This report differentiates “. . . clinical practice and research: ‘[P]ractice’ refers to interventions that are designed solely to enhance the well-being of an individual patient . . . ‘[R]esearch’ designates an activity designed to test an hypothesis . . . and . . . develop[s] or contribute[s] to *generalizable* knowledge . . .” *Id.*

6. Kathy L. Hudson & Francis S. Collins, *Sharing and Reporting the Results of Clinical Trials*, 313 JAMA 355, 355–56 (2015). In 2003, the National Institutes of Health (NIH) expressed support for the concept of data sharing. *Id.* The NIH said data sharing was “essential for expedited translation of research results into knowledge, products, and procedures to improve human health.” Elizabeth Loder,

repeat mistakes, and potentially cause avoidable injuries or deaths to research subjects.”⁷ Changes in the administration of clinical trials is necessary to safeguard public health and maximize effective use of clinical trial data.⁸ A possible reform is inclusion of independent entities in the process currently dominated by pharmaceutical companies who sponsor, fund, and conduct their own clinical trials.⁹ The present arrangement makes it possible for these companies to publish trial results that favor the company’s product and suppress results that are unfavorable.¹⁰ Glenis Willmott, an advocate of the new European Union (EU) clinical trials legislation, contends, “When a patient makes the decision to take part in a clinical trial, they do so to help advance medicine, to improve treatment . . . They do not do it to help a particular company promote a particular drug.”¹¹ People have a “right to health” and a critical element of the right to health is “shared public access to clinical trials data.”¹²

Since the funds for many clinical trials are supplied by drug manufacturers, who in turn receive large public subsidies, clinical trial data should be considered a “public good”¹³ Yet drug manufacturers continue to assert ownership and proprietary rights to clinical trial data including clinical study reports (CSRs). They classify CSRs as a trade

Sharing Data From Clinical Trials: Where We Are and What Lies Ahead, 347 *BMJ* (2013), available at <http://www.bmj.com/content/347/bmj.f4794>.

7. Levin & Palmer, *supra* note 5, at 1577.

8. Marc A. Rodwin, *Independent Clinical Trials to Test Drugs: The Neglected Reform*, 6 *ST. LOUIS U. J. HEALTH L. & POL’Y* 113 (2013). Hans-Georg Eichler et al., *Access to Patient-Level Trial Data—A Boon to Drug Developers*, 369 *N. ENGL. J. MED.* 1577, 1578 (2013).

9. Rodwin, *supra* note 8. An-Wen Chan et al., *SPIRIT 2013 Explanation and Elaboration: Guidance for Protocols of Clinical Trials*, 346 *BMJ* 6 (2013), <http://www.bmj.com/content/346/bmj.e7586>.

10. Thomas Bodenheimer, *Conflict of Interest in Clinical Drug Trials: A Risk Factor for Scientific Misconduct* (Aug. 15, 2000), <http://archive.hhs.gov/ohrp/coi/bodenheimer.htm>. Therefore, “most journals insist on any declaration of conflict of interest—financial or otherwise.” Peter Fayers and David Machin, *Randomized Clinical Trials Design, Practice and Reporting* (2010), 205. For further discussion, see Gisela Schott et al., *The Financing of Drug Trials by Pharmaceutical Companies and its Consequences*, 107 *DTSCH. ARZTEBL. INT.* (2010), <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2868984/>.

11. Press Release, Glenis Willmott, *Local MEP Leads Drug Trial Transparency Drive* (Apr. 2, 2013), <http://www.gleniswillmott.eu/local-mep-leads-drug-trial-transparency-drive/>.

12. 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.* 65, 89 (2012). “The public needs the information to hold federal authorities accountable for regulatory decisions, and patients need access to the data to help make informed decisions.” Marc A. Rodwin & John D. Abramson, *Clinical Trial Data as a Public Good*, 308 *JAMA* 871, 872 (2012), <http://jama.jamanetwork.com/article.aspx?articleid=1356362&resultClick=3>.

13. Rodwin & Abramson, *supra* note 12, at 872. See generally Jerome H. Reichman, *Rethinking the Role of Clinical Trial Data in International Intellectual Property Law: The Case for a Public Goods Approach*, 13 *MARQ. INTELL. PROP. L. REV.* 1 (2009).

secret¹⁴ and argue a policy of CSR release advantages the competition.¹⁵ Even if this was the case, “patent laws and exclusive marketing periods protect the sponsor’s investment.”¹⁶ In fact, such protections may have a detrimental impact on consumers by placing affordable drugs beyond their reach.¹⁷ More openness could help improve the image of drug companies; there have been calls to ban industry-sponsored research.¹⁸

14. Rodwin & Abramson, *supra* note 12, at 872. Though manufacturers argue CSRs are proprietary, “[p]hysicians need access to such data to practice evidence-based medicine. Medical facilities and insurers need complete trial data to decide whether . . . to include a drug in their formularies.” *Id.* CSRs are “documents produced by study sponsors primarily for drug regulators. They run to many hundreds or thousands of pages, comprising substantially more information about a trial than journal articles and providing relatively unbiased material for evidence synthesis.” Peter Doshi et al., *Clinical Trial Data: Get Them While You Can*, 348 *BMJ* (2014), <http://www.bmj.com/content/348/bmj.g63>.

15. Rodwin & Abramson, *supra* note 12, at 872. Competitors do, in fact, make up a majority of CSR requests to the EMA, which suggests that CSRs may contain proprietary information. Michelle Mello et al., *Preparing for Responsible Sharing of Clinical Trial Data*, 369 *N. ENGL. J. MED.* 1651, 1653–54 (2013), <http://www.nejm.org/doi/full/10.1056/NEJMh1309073>.

16. Rodwin & Abramson, *supra* note 12, at 872. Patent protection covers the development period of new drugs and “when the patents or other periods of exclusivity on brand-name drugs expire, manufacturers can apply to the FDA to sell generic versions.” *How Drugs are Developed and Approved*, FDA (last updated in Nov. 2014), <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/>. Mello observes that early disclosure of clinical trial data could result in patent law issues including a “prior art” barrier, a “shorter exclusivity period,” competitors filing a patent application before the inventor, or “higher risk of denial” of a patent application. Mello et al., *supra* note 15, at 1654.

17. Dean Baker, *The Benefits and Savings From Publicly Funded Clinical Trials of Prescription Drugs*, Center for Economic and Policy Research (2008), http://www.cepr.net/documents/publications/clinicaltrials_2008_03.pdf. Drug companies argue current patent protection and exclusivity periods are not sufficient to boost drug development as the process of “drug discovery [is] difficult, expensive and time consuming.” Josh Bloom & Els Torrelee, *Should Patents on Pharmaceuticals Be Extended to Encourage Innovation?* *WALL ST. J.* (Jan. 23, 2012), <http://www.wsj.com/articles/SB10001424052970204542404577156993191655000>. See generally Dana Goldman et al., *The Benefits from Giving Makers of Conventional ‘Small Molecule’ Drugs Longer Exclusivity Over Clinical Trial Data*, 30 *HEALTH AFFAIRS* 84–90 (2011), <http://content.healthaffairs.org/content/30/1/84.full.html>. Avik Roy also sees the need for change in the system, stating the “nation’s system for drug approval discourages innovation and investment . . . [due to] the high cost of Phase III clinical trials, which are required for FDA approval of most drugs.” Avik S.A. Roy, *Stifling New Cures: The True Cost of Lengthy Clinical Drug Trials*, Manhattan Institute for Policy Research (Apr. 2012), http://www.manhattan-institute.org/html/fda_05.htm.

18. Richard Smith et al., *Should Journals Stop Publishing Research Funded by the Drug Industry?*, 348 *BMJ* (2014), <http://www.bmj.com/content/348/bmj.g171>. Trish Groves notes that *BMJ* “recently banned submissions of research partly or wholly funded by the tobacco industry.” *Id.* However, she points out, “[t]he drug and tobacco industries, notwithstanding the inescapable fact that both are out to make money, have very different aims. The drug industry makes and sells products aimed at improving health . . . The tobacco industry, meanwhile, makes and sells products that harm health.” *Id.*

Given the climate of public distrust toward “Big Pharma,”¹⁹ clinical data transparency is becoming a higher priority item on the agenda of the international community.²⁰ Part II of this Note provides specifics on the recent developments propelling clinical trial registration and reporting. Part III covers the FDA’s stance on clinical trial disclosure in the U.S. Part IV explains the EMA’s initiative to increase transparency in the EU’s newly passed Clinical Trials Regulation. Part V focuses on public release of CSRs. Part VI sets forth proposed models for access to clinical trial data that address issues of patient privacy and proprietary information. Part VII discusses the need to strike a balance between the conflicting interests of drug manufacturers and public health proponents.

II. REPORTING AND REGISTRATION OF CLINICAL TRIALS

Access to health data, clinical trials in particular, is a growing concern among consumers since some pharmaceutical companies develop drugs with no more benefit than drugs currently on the market and even fail to adequately disclose drug use risks.²¹ Big Pharma has faced hefty fines for withholding negative findings from clinical trials, but the fines imposed do not seem to constitute sufficient deterrence.²² Such incidents indicate a more exacting framework is needed to discourage selective reporting.

In 2006, international attention centered on trial registration when the World Health Organization (WHO) established the International Clinical Trial Registry Platform (ICTRP).²³ Regrettably, the ICTRP did not include

19. Big Pharma refers to “the world’s vast and influential pharmaceutical industry and its trade and lobbying group, the Pharmaceutical Research and Manufacturers of America or PhRMA.” Drug Watch, *Big Pharma*, <http://www.drugwatch.com/manufacturer/>. For the purposes of this Note, the European Federation of Pharmaceutical Industries and Associations (EFPIA) is included.

20. Erosion of public trust is one of the common reasons cited in support of transparency. Judy Stone, *Why Transparency and Data Sharing in Clinical Trials Matters*, FORBES (Jan. 15, 2015), <http://www.forbes.com/sites/judystone/2015/01/15/why-transparency-and-data-sharing-in-clinical-trials-matters/>.

21. Baker, *supra* note 17.

22. Patricia M. Tereskerz, *Clinical Research and the Law* (2012), 87. For instance, in 2004, Merck recalled Vioxx after it was revealed it downplayed cardiovascular risks discovered during clinical trials. Merck and other Big Pharma companies have faced lawsuits and reached high dollar settlements. Tereskerz, *supra* note 21, at 94–95. Pfizer was tagged with a \$1.2 billion criminal fine when it tried to shift liability for fraud to its shell company. Tereskerz, *supra* note 21, at 89. Pharmaceutical companies are unfazed by such fines because they “view such fines as merely a cost of doing business. . . .” Kevin Outterson, *Punishing Health Care Fraud—Is the GSK Settlement Sufficient?*, 367 NEW ENGL. J. MED. 1082–85 (2012). For more information on this issue, see Drug Watch, *supra* note 19.

23. Kay Dickersin & Drummond Rennie, *The Evolution of Trial Registries and Their Use to Assess the Clinical Trial Enterprise*, 307 JAMA 1861 (2012), <http://jama.jamanetwork.com/article>.

a means of enforcement.²⁴ Not long afterward, improvements in trial protocols and design were considered to address “biased reporting of outcomes within studies,” a correlative problem to “biased reporting of whole studies.”²⁵

The U.S. was the first to enact clinical trials transparency legislation and Europe followed shortly thereafter.²⁶ Congress mandated trial registration on a public database (ClinicalTrials.gov)²⁷ in the Food and Drug Administration Modernization Act of 1997 (FDAMA).²⁸ The European Parliament required registration on a European database (European Union Drug Regulating Authorities Clinical Trials (EudraCT))²⁹ in the Clinical Trials Directive (Directive 2001/20/EC).³⁰ In 2009, the move toward transparency accelerated when Peter Doshi uncovered data on the limited efficacy of the anti-flu drug Tamiflu and began pushing for release of clinical trial data.³¹

In order to ensure published clinical trials contain correct and updated information, health care professionals need direct access to CSRs, not

aspx?articleid=1150078. See generally World Health Organization (WHO), *About Registries*, <http://www.who.int/ictip/network/trds/en/index.html>.

24. Lemmens & Telfer, *supra* note 12, at 73.

25. Silvio Garattini & Iain Chalmers, *Patients and the Public Deserve Big Changes in Evaluation of Drugs*, 338 *BMJ* 804, 805 (2009). See An-Wen Chan et al., *supra* note 9. See generally Heidi Ledford, *Translational Research: 4 Ways to Fix the Clinical Trial*, 477 *NATURE* 526–28 (2011), <http://www.nature.com/news/2011/110928/full/477526a.html>.

26. Lemmens & Telfer, *supra* note 12, at 71.

27. Kathy Thomas et al., *Clinical Trial Disclosure: Global Overview and Implications of New Laws and Guidelines*, 44 *DRUG INFO. J.* 213, 214 (2010), <http://dij.sagepub.com/content/44/3/213.full.pdf+html>.

28. Pub. L. No. 105–115, 111 Stat 2296 (1997). FDA, *Guidance for Industry, Information Program on Clinical Trials for Serious or Life-Threatening Diseases and Conditions* (2002), <http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126838.pdf>.

29. Charlotte Haug et al., *Registries and Registration of Clinical Trials*, 353 *N. ENGL. J. MED.* 2811 (2005), <http://www.nejm.org/doi/full/10.1056/NEJMe058280>.

30. Thomas et al., *supra* note 27, at 213. See generally European Commission, *Directive 2001/20/EC* (“Clinical Trials Directive”) (Apr. 4, 2001), <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2001:121:0034:0044:en:PDF>.

31. Katie Thomas, *Breaking the Seal on Drug Research*, *N.Y. TIMES* (June 29, 2013), http://www.nytimes.com/2013/06/30/business/breaking-the-seal-on-drug-research.html?_r=0&pagewanted=all. In 2009, the Cochrane Collaboration, working with Peter Doshi, began investigating the efficacy of Tamiflu. *Id.* While they were investigating, Keiji Hayashi, an outside party, discovered that “only two of [the ten clinical trials in the Kaiser study] had been fully published in medical journals.” *Id.* The British Medical Journal conducted their own investigation, which showed that Roche used ghostwriters to portray positive data about Tamiflu. *Id.* Following the Tamiflu controversy, Roche pledged to “release detailed clinical data to outside researchers, upon request.” *Id.* See generally Laurent Kaiser et al., *Impact of oseltamivir Treatment on Influenza-Related Lower Respiratory Tract Complications and Hospitalizations*, 163 *JAMA* 1667 (2003), <http://archinte.jamanetwork.com/article.aspx?articleid=215903>.

merely the filtered data of CSRs presented in journal articles;³² however, transparency presents risks when taken to the extreme and should be pursued in a balanced manner.³³ If transparency is taken to the extreme, the “‘seen’ error of approving new medicines” may result in the “‘unseen’ error of blocking new medicines.”³⁴

Drug manufacturers present the greatest opposition to registration and reporting of clinical trials data.³⁵ They argue trial registration may provide competitors access to confidential information.³⁶ Therefore, some drug manufacturers argue that incentives, such as protection from mass tort litigation, should be exchanged for disclosure.³⁷ Though the need to foster a competitive environment in science is important, it is equally important to hold trial sponsors accountable for the accuracy of their clinical research in order to promote public confidence in drugs based on that research.

32. Peter Doshi et al., *Restoring Invisible and Abandoned Trials: A Call for People to Publish the Findings*, 346 *BMJ* (2013), <http://www.bmj.com/content/346/bmj.f2865>. Peter Doshi calls for correction and republication of abandoned trials. *Id.* at 2. He calls this concept “restoring invisible and abandoned trials (RIAT).” *Id.*

33. Scott Lassman, *Sequestered Science: The Consequences of Undisclosed Knowledge, Transparency and Innuendo: An Alternative to Reactive Overdisclosure*, 69 *LAW & CONTEMP. PROB.* 69, 70 (2006).

The problem of too little transparency—failure to communicate known risks about a drug product—can cause serious harm to the public health... However, the premature communication of “preliminary” safety information also entails serious public health risks, since physicians and patients may make health care decisions based upon information that later turns out to be wrong. This is the problem of too much transparency.

Id. at 76. Too much transparency may also result in unnecessary litigation and jeopardize proprietary information. Mark J. Scheineson and M. Lynn Sykes, *Major New Initiatives Require Increased Disclosure of Clinical Trial Information*, 60 *FOOD & DRUG L.J.* 525, 525 (2005).

34. Roy, *supra* note 17.

35. Lemmens & Telfer, *supra* note 12, at 77. See generally Drummond Rennie, *Trial Registration: A Great Idea Switches from Ignored to Irresistible*, 292 *JAMA* 1359 (2004).

36. Lemmens & Telfer, *supra* note 12, at 79–81. Lemmens and Telfer argue that there are other ways this confidential information could be obtained such as “[s]creening patent applications” and “general competitive intelligence.” *Id.* at 81. The data required to be posted in a clinical trial registry may be voluntarily disclosed by the research subjects. Levin and Palmer, *supra* note 7, at 1579. See generally Trudo Lemmens & Ron Bouchard, *Mandatory Clinical Trial Registration: Rebuilding Trust in Medical Research*, 4 *GLOBAL FORUM UPDATE ON RESEARCH FOR HEALTH* 40–42 (2007).

37. DrugBaron, *Clinical Trial Transparency: Time for Some Carrot as Well as More Stick* (2013), <http://www.tcpiinnovations.com/drugbaron/clinical-trial-transparency/>. DrugBaron suggests that the state should take on some responsibility for potential damage caused by a drug if drug companies voluntarily disclose data. *Id.* While this is not a practicable solution, examples like Medtronic shed light on why drug companies are reluctant to embrace transparency. See generally discussion of Medtronic in Laura DeFrancesco, *Behind Closed Doors*, 32 *NATURE BIOTECHNOLOGY* 528, 529 (2014).

III. CLINICAL DRUG TRIALS IN THE UNITED STATES: THE FDA'S STANCE ON DISCLOSURE OF CLINICAL TRIAL DATA

Many drug manufacturers tend to selectively disclose data to ensure the commercial success of their drugs, resulting in drug scandals.³⁸ These scandals are complicated by the fact that some of the research studies relied upon are, in fact, “seeding trials.”³⁹ Such studies “endanger human subjects” but fly under the radar of public knowledge.⁴⁰ Though institutional review boards (IRBs) serve as a safeguard, they do not check whether the studies they evaluate are seeding trials and their financial ties to the pharmaceutical industry may affect their evaluations.⁴¹ The conflicts of interest manifest in clinical research and drug development bring to mind “the ancient question ‘Who guards the guardians?’”⁴²

Independent scrutiny of clinical trials is critical and must be paired with legislation that promotes transparency of such trials and access to the drugs tested by those trials. To facilitate access, Congress passed the Improving Access to Clinical Trials Act in 2010⁴³ and introduced in 2012 the Transforming the Regulatory Environment to Accelerate Access to Treatments (TREAT) Act, which was ultimately not enacted.⁴⁴ To

38. Brandon Powell, *Silence is Not the Best Medicine: Requiring Disclosure of Clinical Trial Data for Abandoned Drugs*, 33 J. LEGAL MED. 571, 586–87 (2012). The profit motive of pharma companies creates inefficiencies as more money is allocated to developing lifestyle drugs rather than drugs like antibiotics. *Id.*

39. Carl Elliott, *Useless Studies, Real Harm*, N.Y. TIMES (July 28, 2011), http://www.nytimes.com/2011/07/29/opinion/useless-pharmaceutical-studies-real-harm.html?_r=0. “The purpose of seeding trials is not to advance research but to make doctors familiar with a new drug.” *Id.* Such trials are not subject to strict regulation by the FDA as “seeding trials are not illegal, and the drugs in question have already received F.D.A. approval.” *Id.*

40. *Id.*

41. *Id.* “[M]any I.R.B.’s are now themselves for-profit businesses, paid directly by the sponsors of the studies they evaluate . . . If one I.R.B. gets a reputation for being too strict, a pharmaceutical company can simply go elsewhere for its review.” *Id.* See generally Ezekiel J. Emanuel et al., *Should Society Allow Research Ethics Boards to Be Run As For-Profit Enterprises?*, 3 PLOS MED (2006), <http://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.0030309>. Drug Watch, *supra* note 19. Like I.R.B.s, the FDA’s budget derives largely from user fees paid by drug manufacturers. *Cozy Deal*, N.Y. TIMES (Apr. 28, 2012), http://www.nytimes.com/2012/04/29/opinion/sunday/cozy-deal.html?_r=0. Perhaps “the best approach would be for the government to fully finance the FDA.” *Id.*

42. Richard A. Epstein, *How Conflict-of-Interest Rules Endanger Medical Progress and Cures*, Manhattan Institute for Policy Research (2010), http://www.manhattan-institute.org/html/fda_03.htm.

43. Rare Diseases Clinical Research Network, *President Signs “Improving Access to Clinical Trials Act” into Law*, (2010), <https://www.rarediseasesnetwork.org/spotlight/december2010/clinical-trialsact.htm>. This Act “enable[d] patients with rare diseases to participate in clinical trials without losing eligibility for public healthcare benefits.” *Id.* S. 1674 (2010).

44. Roy, *supra* note 17. The lengthy FDA drug approval process is problematic for patients seeking “access to new medical treatments.” *Id.* TREAT allows drugs to reach the market faster but

encourage transparency, Congress required posting of summary trial results on the Clinicaltrials.gov database in the 2007 Food and Drug Administration Amendment Acts (FDAAA);⁴⁵ however, the FDAAA contained exemptions for trials of drugs based on phase and approval status.⁴⁶ Its effect in increasing reporting was short-term,⁴⁷ resulting in efforts to pass the 2012 Trial and Experimental Studies (TEST) Act.⁴⁸ The TEST Act was more expansive in scope,⁴⁹ but the bill was not enacted and was reintroduced as H.R. 2031 in 2013 to bring “the U.S. closer toward reforms now underway in the EU.”⁵⁰

Though the TEST Act stalled, transparency remained at the forefront of the FDA’s agenda as seen in its actions in 2014 to make available

whether the faster approval times meet requisite safety criteria is another issue. Avik Roy, *How Big Pharma Undermined Medical Innovation for Financial Gain*, FORBES (Feb. 15, 2012), <http://www.forbes.com/sites/aroy/2012/02/15/how-big-pharma-undermined-medical-innovation-for-financial-gain/>. S.2113 is available at <https://www.govtrack.us/congress/bills/112/s2113>. Another bill, H.R. 6, which addresses accelerates drug approval, is currently being considered. Adam Schank, *BGOV Bill Summary: H.R. 6, FDA Treatment Approvals and NIH Policy*, 13 PLIR 1000 (2015). On a related note, patients with life-threatening diseases can use the “Compassionate Use” or “Expanded Access” exemption to access new drugs that have not yet been approved. William Hudson, *In Cancer Drug Battle, Both Sides Appeal to Ethics*, CNN (Sept. 28, 2013), <http://www.cnn.com/2013/09/28/health/compassionate-drug-use/>. See also Kate Whitfield et al., *Compassionate Use of Interventions: Results of A European Clinical Research Infrastructures Network (ECRIN) Survey Of Ten European Countries*, 11 TRIALS (2010), <http://www.trialsjournal.com/content/11/1/104>.

45. FDA, *FDA’s Role: ClinicalTrials.gov Information*, <http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/FDAsRoleClinicalTrials.govInformation/default.htm>. 42 U.S.C. § 282(j) (2007). *FDAAA 801 Requirements*, <http://clinicaltrials.gov/ct2/manage-recs/fdaaa>. Thomas, *supra* note 27, at 214. Deborah Zarin et al., *The Proposed Rule for U.S. Clinical Trial Registration and Results Submission*, 372 N. ENGL. J. MED. 174, 177 (2015), <http://www.nejm.org/doi/full/10.1056/NEJMs1414226#t=article>.

46. Thomas et al., *supra* note 27, at 217. Hudson & Collins, *supra* note 6. Specifically, Phase I drugs, unapproved drugs, and drugs on the market before 2007 were exempted. *Id.* Erick Turner et al., *Closing a Loophole in the FDA Amendments Act*, 322 SCI 44–46 (2008), <http://www.sciencemag.org/content/322/5898/44.3.full>.

47. Michael R. Law et al., *Despite Law, Fewer Than One in Eight Completed Studies of Drugs and Biologics Are Reported on Time on ClinicalTrials.gov*, 30 HEALTH AFFAIRS 2338 (2011), <http://content.healthaffairs.org/content/30/12/2338.full.html>.

48. Jeffrey M. Drazen, *Transparency for Clinical Trials—The TEST Act*, 367 N. ENGL. J. MED. 863 (2012), <http://www.nejm.org/doi/full/10.1056/NEJMe1209433>.

49. *Id.* at 863. The TEST Act mandated reporting for “[trials]. . . , regardless of phase . . . or approval status” and for “trial(s) that could be used to support an application for FDA approval.” *Id.* H.R. 6272 is available at <http://www.gpo.gov/fdsys/pkg/BILLS-112hr6272ih/pdf/BILLS-112hr6272ih.pdf>.

50. Alexander Gaffney, *US Would See Clinical Trials Reporting Transparency Under New Legislation*, RAPS (May 17, 2013). “The bill has . . . only 1% chance of being enacted most likely because there are not enough active supporters” Ilana Logvinov, *Clinical trials transparency and the Trial and Experimental Studies Transparency (TEST) Act*, 27 CONTEMP. CLINICAL TRIALS 219, 220 (2014). H.R. 2031 is available at <https://www.congress.gov/113/bills/hr2031/BILLS-113hr2031ih.pdf>.

“demographic subgroup data[.]”⁵¹ The Department of Health and Human Services (HHS) continued the transparency initiative by issuing a “Notice of Proposed Rulemaking (NPRM).”⁵² The most significant change proposed in the NPRM is the requirement “to submit summary results to include trials of unapproved . . . products.”⁵³ A secondary proposal by the NIH suggests registration and reporting for all NIH-funded trials “regardless of study phase, type of intervention, or whether they are subject to the FDAAA requirements;”⁵⁴ however, as Jennifer Miller, a fellow at the Kenan Institute for Ethics at Duke University, observes, the impact of these initiatives may be limited since “oversight and enforcement by the FDA . . . is weak.”⁵⁵

Moreover, in the drug evaluation process, the FDA gives drug manufacturers great leeway when it comes to determining the parameters of release for “confidential commercial information (CCI),”⁵⁶ which is often “information relating to risk and benefit” of a new drug.⁵⁷ Currently, the FDA approval process includes safeguards such as advisory committees and “approval contingent upon the sponsor’s conducting of post-marketing studies.”⁵⁸ Even with these measures in place, it remains difficult to ascertain the risks and actual clinical efficacy of drugs in

51. FDA Report, *FDA Action Plan To Enhance The Collection And Availability Of Demographic Subgroup Data* (Aug. 2014), <http://www.fda.gov/downloads/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCA/SignificantAmendmentstotheFDCA/FDASIA/UCM410474.pdf>. This initiative is in response to “Section 907 of the 2012 Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA).” *Id.* at 1.

52. NIH News Release, *HHS and NIH Take Steps to Enhance Transparency of Clinical Trial Results* (2014), <http://www.nih.gov/news/health/nov2014/od-19.htm>.

53. NIH News Release, *supra* note 52. Sara Reardon, *U.S. Government Cracks Down on Clinical Trials Reporting*, NATURE (2014).

54. Zarin, *supra* note 45, at 175. See generally Hudson & Collins, *supra* note 6.

55. Ed Silverman, *What Happens When Results Data From Clinical Trials Goes Missing?* WALL ST. J. (Dec. 4, 2014). The NIH and FDA have the power to impose penalties for noncompliance (for example, the NIH “can withhold grant money, while the FDA can levy a \$10,000-a-day civil penalty for trials that aren’t registered or results that aren’t reported”) but they rarely exercise such authority *Id.*

56. DeFrancesco, *supra* note 37, at 528. DeFrancesco refers to CCI as CBI (confidential business information) but I will use CCI. Drug manufacturers often argue that clinical trial data constitutes CCI. *Id.* at 529. Indefiniteness as to what constitutes CCI has made data release difficult even with “challenge[s] from Public Citizen.” *Id.* at 535. The recalcitrance of the pharmaceutical industry in withholding clinical trial data leads to “incomplete, biased . . . clinical evidence,” which, in turn, leads to doctors “mak[ing] misguided prescription decisions;” the need for this data in medical literature is paramount but it should be weighed against the threat of competitive harm that accompanies data release. *Id.*

57. *Id.* at 529.

58. Peter Lurie & Allison Zieve, *Sometimes the Silence Can Be Like the Thunder: Access to Pharmaceutical Data at the FDA*, 69 LAW & CONTEMPORARY PROBLEMS 85, 88–89 (2006).

clinical trials due to sponsor control. Should the industry retain input in the process, independent experts must be given the dominant role.⁵⁹ Alternatively, in order to ensure drugs meet the requisite criteria before approval, the federal government can sponsor its own independent clinical trials⁶⁰ or Congress can pass legislation that requires independent contractors in the private sector to carry out clinical trials testing (that encompasses New Drug Applications (NDAs), post-marketing trials, and seeding trials) and submit those results to the FDA for further review.⁶¹ The past record on expansive transparency legislation suggests it would face difficulties in passage. Still, such measures may help reverse the current retreat from transparency.⁶²

IV. REFORMING CLINICAL DRUG TRIAL LEGISLATION IN THE EUROPEAN UNION: THE EMA'S NEW POLICY ON TRANSPARENCY

Like the FDA, the European Medicine Agency (EMA)⁶³ expressed commitment to trial transparency but has been mired in issues relating to drug access, lack of compliance with trial reporting requirements, sponsor control of trial data, and conflicts of interest. The EU experiences longer delays in drug approval than the U.S. due to the separation of “the scientific approval process” (handled by the EMA) and “the marketing approval process” (handled by the European Commission (EC)).⁶⁴ Also, the EMA prioritizes market considerations over scientific criteria like safety and efficacy during the evaluation process,⁶⁵ since it “is answerable

59. Independent experts would be ideal but the FDA does sometimes waive conflict of interest issues to obtain individuals with the necessary expertise for its advisory committees. Epstein, *supra* note 42.

60. Rodwin, *supra* note 8, at 162. To avoid the problem of “having the same agency both conduct . . . and evaluate . . . trials,” the NIH and FDA could take on the separate functions or “the FDA [could] evaluate research conducted by private contractors,” which have been carefully chosen by a separate agency. *Id.*

61. *Id.* at 164–65.

62. DeFrancesco, *supra* note 37, at 529. In recent years, there has been increased CCI protection of trial data in regulatory documents, which can be attributed to the increased pressure on the FDA by brand manufacturers seeking to protect their trial data from “generic and biosimilar competition.” *Id.*

63. European Medicines Agency (EMA), *Central Authorization of Medicines*, http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/general/general_content_000109.jsp&mid=WC0b01ac0580028a47. The EMA reviews applications for marketing authorization in the EU and European Economic Area, which is granted or denied by the European Commission. *Id.*

64. Lynn J. Howie et al., *A Comparison of FDA and EMA Drug Approval: Implications for Drug Development and Cost of Care*, ONCOLOGY J. (2013), <http://www.cancernetwork.com/oncology-journal/comparison-fda-and-ema-drug-approval-implications-drug-development-and-cost-care#sthash.CAp0f6HQ.dpuf>.

65. Ernst R. Berndt et al., *Opportunities for Improving the Drug Development Process: Results from a Survey of Industry and the FDA*, 6 INNOVATION POLICY AND THE ECONOMY 91, 101 (2006).

to the [EU] Directorate General for Enterprise and Industry” and this department promotes the view that “drugs should be seen as consumer goods rather than as agents for promoting and protecting health.”⁶⁶ Such a structure has helped drug companies exercise great control “in evaluating [their] own products.”⁶⁷

Recognizing the drawbacks of the system, the EMA implemented measures for increased transparency, including making clinical trial data more readily available in the EU by introducing EudraCT, the counterpart to ClinicalTrials.gov, in 2004.⁶⁸ The EudraCT database includes trials with “at least one site in the EU or EEA” although participants are typically recruited outside this area.⁶⁹ In November 2013, the EMA updated EudraCT, allowing sponsors to upload summary results that would “be made publicly available through the EU Clinical Trials Register (EU CTR).”⁷⁰ The change in EudraCT’s results reporting approach brings

However, recent data shows that the EMA is approving drug applications at a higher rate and may even start outpacing the U.S. Hamilton Moses III et al., *The Anatomy of Medical Research: U.S. and International Comparisons*, 313 JAMA 174, 181 (2015)

66. Garratini & Chalmers, *supra* note 25, at 804. A solution they propose to make the process more transparent and beneficial for patients is to “transfer. . . responsibility for drug licensing and evaluation to the EU Directorate General for Health and Consumers Affairs.” *Id.* at 805.

67. Garratini & Chalmers, *supra* note 25, at 805. They argue that there should be more “[i]ndependent clinical research to evaluate new drugs” so drug companies cannot hide negative results. *Id.*

68. Thomas, *supra* note 27, at 214. See generally European Commission (EC), *Clinical Trials*, <http://ec.europa.eu/health/human-use/clinical-trials/>.

69. Thomas, *supra* note 27, at 214. According to an EMA-conduct analysis, “[a]most 62% of the patients in pivotal trials submitted in marketing-[authorization] applications (MAAs) to the European Medicines Agency between January 2005 and December 2011 were recruited outside of the European Economic Area (EEA) and Switzerland . . .” EMA, *European Medicines Agency Publishes Report on Patient Recruitment and Geographical Location of Clinical Trials* (Sept. 4, 2013), http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2013/04/news_detail_001758.jsp&mid=WC0b01ac058004d5c1. This is significant because:

Failure to recruit sufficient participants is a common reason for stopping a clinical trial. The struggle to find enough people is also one reason that companies are increasingly performing clinical trials in developing nations where infrastructure and [labor] is cheaper, and patients with limited resources are more willing to sign on to a trial as a way to access expensive drugs.

Heidi Ledford, *Therapeutic Success Stifles Medical Progress*, 473 NATURE 433 (May 24, 2011), <http://www.nature.com/news/2011/110524/full/473433a.html>.

70. Press Release, EMA, *European Medicines Agency Launches a New Version of EudraCT* (“New Version of EudraCT”) (Nov. 11, 2013), http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2013/10/news_detail_001918.jsp&mid=WC0b01ac058004d5c1. “The end goal is to move beyond having just basic protocol information in the registry, and toward a system that allows the public to track the end results of trials, including those with negative results.” Alexander Gaffney, *New Updates to EMA Database Will Soon Make Summary Results of Clinical Trials Public*, RAPS (Oct. 11, 2013), <http://www.raps.org/focus-online/news/news-article-view/article/4177/new-updates-to-ema-database-will-soon-make-summary-results-of-clinical-trials-p.aspx>.

it in line with ClinicalTrials.gov; this reflects the fact that the EMA and the NIH, which is in charge of ClinicalTrials.gov, are partners when it comes to promoting transparency.⁷¹ Also, the EMA requires even unapproved clinical trials of drugs to be posted within a year of completion, a move being considered in the U.S. Notice of Proposed Rulemaking.⁷² These changes are important, especially since the EU CTR is “a primary registry in the WHO’s registry network;”⁷³ however, like the U.S., there remain exemptions for certain trials including Phase I trials.⁷⁴

The impetus for EudraCT’s formation, the Clinical Trials Directive,⁷⁵ was intended to establish uniformity among clinical trials in EU member states and thereby increase the quality of research done in the EU.⁷⁶ Ultimately, the Directive created a byzantine bureaucracy that was difficult for clinical researchers to navigate.⁷⁷ Due to these problems, “the number of clinical trials conducted in Europe between 2007 and 2011” fell by 25%.⁷⁸

See generally Roy Watson, *EU Nations Approve Law to Overhaul Clinical Trials*, 347 *BMJ* (2013), <http://www.bmj.com/content/347/bmj.f7682>.

71. New Version of EudraCT, *supra* note 70.

72. Zarin, *supra* note 45, at 178. See generally European Commission, *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*, Official Journal of the European Union (June 10, 2012), http://ec.europa.eu/health/files/eudralex/vol-10/2012_302-03/2012_302-03_en.pdf.

73. EU Clinical Trials Register, *About the EU Clinical Trials Register*, <https://www.clinicaltrialsregister.eu/about.html>. EMA, *EU Clinical Trials Register information now available through WHO’s International Clinical Trials Registry Platform* (2012), http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2012/03/news_detail_001477.jsp&mid=WC0b01ac058004d5c1.

74. *Id.* Trials outside the EU/EEA are only included if they form “part of a [pediatric] investigation plan (PIP), or . . . are sponsored by a marketing [authorization] holder . . .” *Id.* This suggests that companies can get around the disclosure requirements if they conduct trials outside the EU/EEA.

75. EudraCT, *Purpose of EudraCT and the Clinical Trial Application*, https://eudract.ema.europa.eu/help/content/eudract/purpose_cta_ov.htm. The requirements of the EU Directive seems to place at risk trials with non-commercial sponsors (public agencies and nonprofits) rather than those with commercial sponsors, because the directive has a “requirement that each trial have a single sponsor that . . . would be ‘legally liable for failures.’” *Clinical Trials Face European Directive*. 300 *SCI*. 1353 (2003), <http://www.sciencemag.org/content/300/5624/1353.2.full?sid=ed88db8a-a894-4272-9c02-f8fb5c210c65>.

76. Daniel Cressey, *Europe Sets Out to Reform Its Clinical Trial Rules*, 11 *NATURE REVIEWS DRUG DISCOVERY* 660 (2012), available at <http://www.nature.com/nrd/journal/v11/n9/full/nrd3843.html>.

77. *Id.* at 660. The structure of the current system creates unnecessary delay, costs, and paperwork. *Id.*

78. *Id.* at 660.

The Proposal for a Regulation of the European Parliament and of the Council on Clinical Trials on Medicinal Products for Human Use and Repealing Directive 2001/20/EC (Clinical Trials Regulation Proposal) attempted to eliminate the Directive's bureaucratic provisions.⁷⁹ The proposal suggested replacing the directive with a regulation.⁸⁰ Giving the new law the status of a regulation meant EU member states would no longer have to "integrate [it] into [their] own laws" and it would instead "automatically become law in all member states," imposing the uniformity envisioned in but unrealized by the directive.⁸¹ The proposal further streamlined the process for conducting clinical trials by allowing sponsors of EU and EEA clinical trials to submit one application for multi-country trials rather than separate applications for each country.⁸² "One state would be designated as the 'reference' state . . . [to] lead a coordinated assessment."⁸³

The EMA consulted various clinical-trial advisory groups on the proposed regulation,⁸⁴ but the draft legislation did not escape criticism. Some researchers believed that the system should be operated by the EMA rather than the European Commission (EC) since the EMA has experience handling data requests.⁸⁵ According to Mike Clarke, director of the All-Ireland Hub for Trials Methodology Research at Queen's University Belfast, neither the EMA or EC should assume full control; instead,

79. European Commission, *Proposal for a Regulation of the European Parliament and of the Council on Clinical Trials on Medicinal Products for Human Use, and Repealing Directive 2001/20/EC* ("Clinical Trials Regulation Proposal") (2012), 16, http://ec.europa.eu/health/files/clinicaltrials/2012_07/proposal/2012_07_proposal_en.pdf.

80. Christina Reith et al., *Randomized Clinical Trials—Removing Unnecessary Obstacles*, 369 *NEW ENGL. J. MED.* 1061, 1061–62 (2013), <http://www.nejm.org/doi/full/10.1056/NEJMs1300760#t=article>. The proposal the European Commission issued in July 2012 does not address some problems: "[I]ts changes are directed chiefly toward expediting trial initiation [approval processes]," and "there is still inappropriate emphasis on safety assessments that rely on reports of individual adverse events . . ." *Id.* at 1062.

81. Cressey, *supra* note 76, at 660.

82. *Id.* at 660. A single submission portal for multinational trials would benefit, in particular, researchers of rare conditions. *Id.*

83. *Id.* at 660. This particular provision has been criticized because it allows "trial sponsors to choose which member state they want to lead the assessment" and "[allows] the reference member state . . . to decide everything itself." *Id.* Such a system may put a heavy burden on the reference state and does not foster scientific discussion between member states. *Id.* at 660–61.

84. News and Press Release Archive, *European Medicines Agency Publishes Final Advice from Clinical-Trial Advisory Groups*, *EUR. MED. AGENCY* (Apr. 30, 2013), http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2013/04/news_detail_001778.jsp&mid=WC0b01ac058004d5c1.

85. Cressey, *supra* note 76, at 660.

“[t]here should be a mix of academics, nonacademics, and regulators [assessing data requests]”⁸⁶

The European Commission’s proposed regulation was criticized for not explicitly mentioning ethics committees, instead providing that “applications should be evaluated by ‘a reasonable number of persons who collectively have the necessary qualifications and experience.’”⁸⁷ Leaving the provision as-is would permit researchers to “shop around for loose oversight.”⁸⁸ The loosely worded phrasing particularly concerned “Germany, where ethics committees play a powerful role in reviewing trial applications.”⁸⁹

In May 2013, the proposal overcame a major obstacle when it was approved by the European Parliament Environment, Public Health, and Food Safety (ENVI) Committee.⁹⁰ The ENVI Committee considered various transparency amendments to the proposed Clinical Trial Regulation.⁹¹ A controversial amendment stated that the data in CSRs “should not be considered commercially confidential once a marketing [authorization] has been granted or the decision-making process on an application for a marketing [authorization] has been completed.”⁹² Another amendment that drew considerable scrutiny required the

86. Tania Rabesandratana, *Drug Watchdog Ponders How to Open Clinical Trial Data Vault*, 339 SCI. 1369, 1370 (2013), <http://www.sciencemag.org/content/339/6126/1369.full?sid=ed88db8a-a894-4272-9c02-f8fb5c210c65>. This would be the ideal situation. In reality, “[c]ompanies must share their data with regulatory agencies such as [the] EMA or [the] FDA, but they aren’t obliged to publish them in a journal . . . [S]ome negative trials never see the light of day . . . [T]here can be discrepancies between CSRs and published papers” *Id.* at 1369.

87. Gretchen Vogel & Jennifer Couzin-Frankel, *Europe Debates Ethics Reviews, Data Release*, 339 SCI 1024 (2013), <http://www.sciencemag.org/content/339/6123/1024.full?sid=ed88db8a-a894-4272-9c02-f8fb5c210c65>. The ethics committee is the EU equivalent to IRBs in the U.S. Eve M. Brunts et al., *The International Clinical Trials Roadmap: Steering Clear of Legal and Practical Roadblocks*, 5 J. HEALTH & LIFE SCI. L. 1, 6 (2012). According to the EU Directive, only one opinion governs in an EU country even if multiple opinions are provided, which differs from U.S. policy. *Id.* at 7.

88. Vogel & Couzin-Frankel, *supra* note 87, at 1024.

89. *Id.*

90. Bloomberg BNA, *EU Legislation to Overhaul Regulation of Clinical Drug Trials Clears Key Hurdle*, 12 MED. RES. L. & POL’Y REP. 373 (2013).

91. AllTrials, *Briefing on Transparency Amendments to the Clinical Trials Regulation* (“Transparency Amendments”) (2013), <http://www.alltrials.net/wp-content/uploads/2013/12/Briefing-for-Clinical-Trial-Reg-Dec-2013.pdf>. See also European Parliament, ENVI, *Draft Report on the proposal for a regulation of the European Parliament and of the Council on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC (COM(2012)0369—C7-0194/2012—2012/0192(COD))* (ENVI Draft Report) (2013), <http://www.europarl.europa.eu/sides/getDoc.do?type=COMPARL&reference=PE-504.236&format=PDF&language=EN&secondRef=01>.

92. Transparency Amendments, *supra* note 91, at 5.

publication of CSRs within thirty days of marketing authorization.⁹³ Possible loopholes were considered in amendments that required “data from the clinical trial(s) [to] be submitted . . . even if incomplete”⁹⁴ and explicitly mentioned previously missing language: ethics committees.⁹⁵ These amendments were criticized by the pharmaceutical industry.⁹⁶ In particular, the amendment denying CCI protection to CSRs was of concern to Big Pharma.

V. RELEASING CLINICAL STUDY REPORTS INTO THE PUBLIC DOMAIN

In the transparency debate, access to CSRs is a major issue.⁹⁷ CSRs contain useful data, including adverse events and mortality rates, which is rarely published.⁹⁸ When drug manufacturers submit NDAs to the FDA in the U.S., they are required to submit CSRs and participant-level data.⁹⁹

The EMA “does not routinely request individual participant data or clinical study reports [CSRs]”¹⁰⁰ and receives CSRs when drug companies “apply for licences to sell their products.”¹⁰¹ Though Regulation 726/2004/EC requires that the EMA release documents it receives to the

93. *Id.* at 7. Non-compliant sponsors will face financial penalties. *Id.* at 7–8.

94. *Id.* at 14.

95. ENVI Draft Report, *supra* note 91, at 9.

96. Press Release, EFPIA, *Responsible Sharing of Clinical Trial Information* (May 29, 2013), <http://www.efpia.eu/mediaroom/94/21/EFPIA-Press-Release-on-Responsible-Sharing-of-Clinical-Trial-Information>. The European Federation of Pharmaceutical Industry Association (EFPIA) asserted, “Several of the amendments supported by the European Parliament committee will jeopardize patient privacy, the integrity of regulatory systems and incentives for investment in biomedical research in Europe.” David Holmes, *Transparency Battle Resurfaces as EU Trial Revamp Wraps Up*, 19 NATURE MEDICINE 797, (2013), <http://www.nature.com/nm/journal/v19/n7/full/nm0713-797.html>.

97. Daniel Cressey, *Secrets of Trial Data Revealed*, 502 NATURE 154, 154 (2013), <http://www.nature.com/news/secrets-of-trial-data-revealed-1.13913>.

98. *Id.* at 155. When Wiesler and her team conducted a comparison study of information in CSRs and publicly available information, they found “complete information was available for 86% of these in the CSRs, but only for 39% in the publicly available information.” *Id.* For outcomes related to harm, more information was found in CSRs as well. *Id.* See generally Beate Wieseler et al., *Completeness of Reporting of Patient-Relevant Clinical Trial Outcomes: Comparison of Unpublished Clinical Study Reports with Publicly Available Data*, PLOS MED (2013), <http://www.plosmedicine.org/article/info:doi/10.1371/journal.pmed.1001526>.

99. Doshi et al., *supra* note 32. “The FDA has long treated participant-level data . . . as confidential commercial information” but is currently considering changes in its policy. Mello et al., *supra* note 15, at 1652. See Availability of Masked and De-identified Non-Summary Safety Request for Comments, 78 Fed. Reg. R 33421, (May 29, 2013) (FDA Request for Comment), *available at*, <https://federalregister.gov/a/2013-13083>.

100. Doshi et al., *supra* note 32.

101. Cressey, *supra* note 97, at 154.

public, it contains an exception for CCI (extending to CSRs)¹⁰² and the information provided in European Public Assessment Reports (EPARs), published in accordance with Regulation 726/2004/EC,¹⁰³ is “written under the supervision of the company concerned.”¹⁰⁴

Relying on the CCI exception, the EMA did not “release any original document that the manufacturer submits for the approval process” until 2010.¹⁰⁵ In 2010, a lawsuit was initiated when the EMA refused to release clinical trial data, including CSRs, to Nordic Cochrane Centre researchers.¹⁰⁶ The researchers appealed to the European Ombudsman, who ordered that the CSRs be released.¹⁰⁷ The FDA also disclosed trial data after being sued by Public Citizen; researchers can obtain CSRs through freedom of information requests though it is a lengthy process and CCI is often not released.¹⁰⁸

102. Lincoln Tsang et al., *New Paradigm for Transparency Practice for Greater Openness and Accountability in the Pharmaceutical Sector in Europe*, 8 LSLR 1245, 2 (2014). “Regulation 1049/2001/EC (Public Access Regulation) confers an express legal right to access documents held by European institutions” (with an exception for CCI). *Id.* “Regulation 726/2004/EC . . . requires that the Public Access Regulation should be applied to documents held by the EMA” (including explanations for its recommendations in EPARs). *Id.*

103. *Id.* EMA, *European Public Assessment Reports*, European Medicines Agency, http://www.ema.europa.eu/ema/index.jsp?curl=/pages/medicines/landing/epar_search.jsp&murl=menus/medicines/medicines.jsp.

104. Silvio Garattini & Vittorio Bertele, *How Can We Regulate Medicines Better?* 335 BMJ 804 (2007); *See also* Silvio Garattini & Vittorio Bertele, *Europe’s Opportunity to Open Up Drug Regulation*, 340 BMJ 842 (2010). Likewise, the FDA allows drug manufacturers to “draft the Summary Basis of Approval.” Aaron S. Kesselheim & Michelle M. Mello, *Confidentiality Laws and Secrecy in Medical Research: Improving Public Access to Data on Drug Safety*, 26 HEALTH AFFAIRS 483 (2007), <http://content.healthaffairs.org/content/26/2/483.full.html>. Also, the FDA allows drug manufacturers to write the labels (package inserts) for drugs. Lisa M. Schwartz & Steve Woloshin, *Lost in Transmission—FDA Drug Information that Never Reaches Clinicians*, 361 N. ENGL. J. MED. 1717, 1717, 1720 (2009). “In many cases information [on harms gleaned from trial results] gets lost between FDA review and the approved label.” *Id.* at 1717. Such arrangements, which limit regulators to mere assessment, give drug manufacturers a great degree of discretion over release of trial data.

105. Garattini and Bertele, *Europe’s Opportunity to Open Up Drug Regulation*, *supra* note 104, at 842. Tracy Hampton, *European Drug Agency Under Fire: Critics Charge that Trial Data are too Inaccessible*, 306 JAMA 593–95 (2011).

106. Peter Gøtzsche & Anders Jørgensen, *Opening Up Data at the European Medicines Agency*, 342 BMJ (2011). Gøtzsche and Jørgensen do note that CSRs do not contain any proprietary information. *Id.*

[CSRs] and trial protocols represent the last phase of drug development . . . [o]ther companies could hardly use them as a basis for developing similar drugs. In fact, unpublished trial data are generally less positive than published ones, and competitors would therefore be less likely to start drug development if they had access to the unpublished results.

Id.

107. Hampton, *supra* note 105, at 593. According to the European Ombudsman ruling in 2010, “there were neither commercial data nor confidential patient data in [CSRs].” DeFrancesco, *supra* note 37, at 529.

108. Hampton, *supra* note 105, at 594. Peter Doshi and Tom Jefferson, *Clinical Study Reports of*

The outcomes of the recent cases signal a shift in international policy toward increased transparency but is merely the tip of the iceberg for AllTrials, which been demanding an even higher level of data release including publication of full CSRs¹⁰⁹ and publication of retrospective trials.¹¹⁰ The European Federation of Pharmaceutical Industries and Associations (EFPIA) is not amenable to AllTrials demands, particularly regarding CSR publication,¹¹¹ and the industry has indicated that the EMA, which is rolling out a CSR publication policy, has not implemented sufficient safeguards for protecting the CCI contained in CSRs.¹¹²

Also, the industry steadfastly maintains such a policy benefits competitors.¹¹³ Specifically, the industry has expressed concern that releasing this data makes CCI publicly available and results in freeriding.¹¹⁴ Still, such data should be made accessible to some degree because these investments are also supported by academic studies that rely on public funding.¹¹⁵

The EMA policy of publishing CSRs resulted in lawsuits by two biotechnology companies, AbbVie and InterMune.¹¹⁶ These companies claimed “releasing [CSRs] would compromise ‘CCI’ that would give their

Randomised Controlled Trials: An Exploratory Review Of Previously Confidential Industry Reports, 3 BMJ (2013), <http://bmjopen.bmj.com/content/3/2/e002496.full#ref-31>.

109. AllTrials, *All Trials Registered. All Results Reported* (2013), at 6, <http://www.alltrials.net/wp-content/uploads/2013/09/What-does-all-trials-registered-and-reported-mean.pdf>.

110. *Id.* at 2.

111. Cressey, *supra* note 97, at 155. Richard Bergström, the director-general of the European Federation of Pharmaceutical Industries and Associations (EFPIA), states, “[I]n their current state, CSRs are fundamentally unsuitable for publication.” *Id.*

112. *Id.* at 155. EFPIA insists on redaction of CSRs but the EMA has required only that information be “‘de-identified’ and released only for bona fide research purposes.” *Id.*

113. Rabesandratana, *supra* note 86, at 1369. Bergström says the EFPIA’s concerns about confidentiality are legitimate: “Out of 457 requests for data EMA received between November 2010 and 2012, only 38 came from academics, whereas a majority came from drug companies, lawyers, and consultants.” *Id.* at 1370.

114. Pharmaceutical Research and Manufacturers of America (PhRMA) and European Federation of Pharmaceutical Industries and Associations (EFPIA). *Principles for Responsible Clinical Trial Data Sharing* (“*Principles*”) (2013), 4 <http://www.phrma.org/sites/default/files/pdf/PhRMAPrinciplesForResponsibleClinicalTrialDataSharing.pdf>.

115. Garattini & Bertele, *Europe’s Opportunity to Open Up Drug Regulation*, *supra* note 107, at 842. John Castellani, president and CEO of PhRMA, claims, “No government or academic institution has the resources or multidisciplinary expertise to conduct the clinical trials needed to develop the new medicines patients need.” John Castellani, *Are clinical trial data shared sufficiently today? Yes*, 347 BMJ (2013) <http://www.bmj.com/content/347/bmj.f1881>.

116. Hester Plumridge, *Proposed Law Would Require More Drug-Trial Transparency*, WALL ST. J. (Mar. 21, 2014), <http://www.wsj.com/articles/SB10001424052702303802104579449160147006896>. See also Phillip Broadwith, *Clinical Trial Data Release Blocked by Companies*, ROYAL SOCIETY OF CHEMISTRY (2013), <http://www.rsc.org/chemistryworld/2013/05/clinical-trial-data-release-blocked-abbvie-intermune>.

competitors an unfair advantage.”¹¹⁷ In April 2013, the two pharmaceutical companies gained a temporary victory when the lower court ruled in their favor and prevented data release by the EMA.¹¹⁸ The Superior European Court of Justice overturned the lower court’s ruling in November 2013.¹¹⁹ These lawsuits “direct[ly] challenge . . . the EMA’s policy of making clinical trial data more accessible.”¹²⁰

In the same year of the AbbVie and InterMune lawsuits, the pharmaceutical industry on both sides of the Atlantic—the Pharmaceutical Research and Manufacturers of America (PhRMA) and EFPIA—took on a leadership role in promoting transparency and vowed to increase access to clinical trial information in the joint *Principles for Responsible Clinical Data Sharing* which took effect in 2014;¹²¹ however, the industry only agreed to release synopses of CSRs, not full CSRs.¹²² The *Principles* state that each company has the right to redact information from CSRs including CCI.¹²³ No discussion of off-label use and retrospective trials appears in the *Principles*.¹²⁴

117. Broadwith, *supra* note 116.

118. Peter Mansell, *EMA Stalls on Data-Disclosure Policy*, PHARMATIMES (2013), http://www.pharmatimes.com/article/13-12-19/EMA_stalls_on_data-disclosure_policy.aspx.

119. *Id.* Court of Justice of the European Union, Order of the Vice-President of the Court, (2013). See *EMA v. AbbVie*, Case C-389/13 P(R), <http://curia.europa.eu/juris/document/document.jsf?text=&docid=145282&pageIndex=0&doclang=en&mode=req&dir=&occ=first&part=1&cid=877340>.

See also *EMA v. Intermune*, Case C-390/13 P(R), <http://curia.europa.eu/juris/document/document.jsf?text=&docid=145281&pageIndex=0&doclang=en&mode=req&dir=&occ=first&part=1&cid=877683>. The Court of Justice of the European Union determined that the General Court had “failed to establish with sufficient weight that the disclosure of commercially confidential information . . . would result in ‘serious and reparable harm’ to the companies.” Mansell, *supra* note 118.

120. Broadwith, *supra* note 116. Peter Doshi states, “If AbbVie and InterMune win their cases, there is a real chance that EMA’s revolution in data transparency will come to an abrupt end, returning us to the old status quo of data secrecy.” All Trials Registered, *Medical Researchers Denied Clinical Trial Information, European Medicines’ Regulator Forced to Withhold Trial Documents* (2013), <http://www.alltrials.net/news/medical-researchers-denied-clinical-trial-information/>.

121. Peter Mansell, *Industry’s Joint Principles on Data-Sharing Take Effect*, PHARMATIMES (2014), http://www.pharmatimes.com/article/14-01-02/Industry_s_joint_principles_on_data-sharing_take_effect.aspx. See also *Principles*, *supra* note 114.

122. *Principles*, *supra* note 114, at 2. The *Principles* state:

[B]iopharmaceutical companies will make publicly available, at a minimum, the synopses of clinical study reports (CSRs) for clinical trials in patients submitted to the Food and Drug Administration (FDA), European Medicines Agency (EMA) . . . Companies will make this information available . . . through appropriate redaction . . . [C]ompanies will evaluate requests for full CSRs. . . .

Id.

123. *Id.* at 5.

124. A Roadmap for Sharing Clinical Trial Data, Vital Transformation (2013), 10, <http://www.efpia.eu/uploads/efpia%20event%2027%20august%2013%20report.pdf>.

Also, the industry drafted the *Principles* so that they control data release, a move mirrored in the Biotechnology Industry Organization (BIO)'s *Principles on Data Sharing* released afterward.¹²⁵ Clearly the pharmaceutical industry prefers a “system of self-regulation” rather than the “open data transparency regime” contemplated in the EMA’s proposal.¹²⁶

The proposal, which promised to undercut trial sponsors control of clinical trial data, was approved by the European Parliament in April 2014; Regulation (EU) No 536/2014, to be applied beginning in 2016, mandates registration of clinical trials and submission of summary results.¹²⁷ The Regulation creates a single submission system, sets up scientific and ethical review,¹²⁸ and mandates submission of CSRs “(thirty) days after the marketing authorization has been granted (or refused or withdrawn).”¹²⁹ That said, it has drawbacks as it makes it easier for trial sponsors to continue off-label use.¹³⁰

125. DeFrancesco, *supra* note 37, at 533. See also Alexander Gaffney, *BIO, Following PhRMA and EFPIA, Releases Clinical Trial Data Transparency Plan*, RAPS (Mar. 26, 2014), <http://www.raps.org/regulatoryDetail.aspx?id=18376>.

126. Vital Transformation, *supra* note 124, at 3. The EMA is already planning to “systematically release the clinical study reports relating [to] all drugs given a marketing [authorization].” *Id.* at 3. The EMA’s stance is that “there is no commercial confidential information in clinical study reports of approved drugs” despite industry claims that “even if the products are patented, information on know-how and trade secrets in CSRs will allow competitors to cut development times.” *Id.* at 6.

127. Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC Text with EEA relevance (“Clinical Trial Regulation”), Official Journal of the European Union, http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1401366187088&uri=OJ:JOL_2014_158_R_0001. The following transparency measures were agreed upon in 2013:

A publicly accessible EU database, set up and run by EMA, containing: . . . [a] summary of results for all trials . . . Clinical Study Reports for all trials used in a marketing [authorization] request, whether it is approved, rejected or withdrawn[;] [a] statement that Clinical Study Reports should . . . not be considered commercially confidential[;] [and] [f]ines to be imposed by Member States for non-compliance . . .

AllTrials, *Clinical Trials Regulation in Europe*, 2013, <http://www.alltrials.net/news/clinical-trials-regulation-europe-breaking-news/>. See also Lincoln Tsang et al., *supra* note 102. For more information, see Viviana Giannuzzi et al., *Clinical Trial Application: What Will Change With the New Regulation?* SCIENCE AND ENGINEERING ETHICS (2015).

128. BEUC, *New European Clinical Trials Regulation: A Major Advance in Transparency, to be Confirmed* (2014), 1, 2, http://www.beuc.org/publications/beuc-x-2014-068_ipa_new_eu_clinical_trials_regulation-joint_letter.pdf.

129. Tsang et al., *supra* note 102.

130. BEUC, *supra* note 128, at 2. “. . . [T]his new regulation considers certain clinical trials in which a drug is used outside its [authorized] indications (off-label use) as ‘low-intervention’ trials which. . . are subject to less stringent regulation.” *Id.* The absence of “a mooted national indemnity [program], in which low-risk trials would have been insured by each member state” is another problem. Daniel Cressey, *Overhaul Complete for EU Clinical Trials*, NATURE, 2014, <http://www.nature.com/news/overhaul-complete-for-eu-clinical-trials-1.15339>. “This could have saved

The EMA decided to go a step further than U.S. transparency legislation (which only requires summary results) by publishing CSRs contained in marketing authorization applications starting from January 2015.¹³¹ This impact of this policy stretches beyond Europe as non-European manufacturers must comply “if they want their products to be marketed in the [EU].”¹³²

Though the Regulation promised transparency measures unprecedented in scope, it was not as far-reaching as anticipated as it reinforced the pharmaceutical industry’s hold on clinical trial data by imposing “Terms of Use” (TOU) and “Redaction Principles” on researchers who seek access to the data.¹³³ The restrictions on data release may be attributed, in part, to the AbbVie and Intermune lawsuits, even though both lawsuits were withdrawn in 2014 after the EMA decided to permit redaction of CCI.¹³⁴

As in the U.S., regulators take into consideration the commercial interests of drug companies, which places trial sponsors in a position of controlling data access.¹³⁵ In January 2015, the EMA defended its decision, stating that there was no “overriding public interest” that

individual researchers from having to obtain their own insurance, which can be expensive.” *Id.*

131. Press Release, EMA, Publication of Clinical Reports, 2014, http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2014/10/news_detail_002181.jsp&mid=WC0b01ac058004d5c1.

132. Alison Abbott, *European Medicines Agency Set to Publish Clinical-trial Reports*, NATURE (2014), <http://www.nature.com/news/european-medicines-agency-set-to-publish-clinical-trial-reports-1.15410>.

133. EMA, European Medicines Agency Policy on Publication of Clinical Data for Medicinal Products for Human Use (2014), http://www.ema.europa.eu/docs/en_GB/document_library/Other/2014/10/WC500174796.pdf. The EMA’s proposed policy included the following provisions: “[CSRs] would only be available for on-screen viewing . . . [;] [s]ubstantial parts of the reports could be redacted . . . [;] [and] [t]rial sponsors could redact their own [CSRs].” AllTrials, *Has the EMA Made a Backroom Deal With Pharma Over Transparency* (2014), <http://www.alltrials.net/news/has-the-ema-made-a-backroom-deal-with-pharma-over-transparency/>. See also European Ombudsman, *Ombudsman Concerned About Change of Policy at Medicines Agency as Regards Clinical Trial Data Transparency*, Press Release No. 13/2014, <http://www.ombudsman.europa.eu/en/press/release.faces/en/54348/html.bookmark>. When its proposed policy faced criticism, the EMA approved an amendment that allows “the public to download, save and print the trial data for academic and non-commercial research purposes.” Alexander Gaffney, *In Landmark Decision, EMA Adopts Clinical Trials Transparency Plan*, RAPS (Oct. 2, 2014), <http://www.raps.org/Regulatory-Focus/News/2014/10/02/20472/In-Landmark-Decision-EMA-Adopts-Clinical-Trials-Transparency-Plan/#sthash.TEUdIJQL.dpuf>.

134. Stephanie Bodoni, *AbbVie Drops EU Court Bid to Block Clinical-Trial Data Release*, BLOOMBERG (2014), <http://www.bloomberg.com/news/2014-04-03/abbvie-drops-eu-court-bid-to-block-clinical-trial-data-release.html>. See also Ben Adams, *Intermune Drops EMA Lawsuit Over Data Release*, PHARMAFILE (2014), <http://www.pharmafile.com/news/187640/intermune-drops-ema-lawsuit-over-data-release>.

135. Ian Bushfield, *The EMA Takes Backward Step in Move Toward Transparency*, THE PHARM. J. (2014), <http://www.pharmaceutical-journal.com/opinion/comment/the-european-medicines-agency-still-has-a-way-to-go-towards-clinical-trial-transparency/20067402.article>.

justified complete information release.¹³⁶ Also, the EMA asserted the right to redact information that is in the process of development and further explained that information redacted in a CSR does not infinitely maintain CCI status and may be released at a later time.¹³⁷

VI. PROPOSED MODELS FOR ACCESS TO CLINICAL TRIAL DATA

The need to share information publicly to further science and promote public health must be balanced with the need to protect proprietary information. The question is: how much transparency is enough?

Pharmaceutical and biotechnology companies are often disinclined to include Phase I drug trial data, which are “exploratory . . . or ‘hypothesis-generating’.”¹³⁸ They claim making Phase I trials publicly accessible would probably not result in benefits for patients.¹³⁹ “[A]round [eighty percent] of [drug trials] fail at this stage” and Phase I trials use healthy individuals to obtain safety data rather than testing for efficacy on sick patients.¹⁴⁰ According to these companies, registering early-stage trials could place sensitive information at risk.¹⁴¹

Biotechnology companies also worry that data sharing may stall innovation by deterring potential investors;¹⁴² however, the pharmaceutical and biotechnology sectors will benefit from releasing data about Phase I failures as it would “eliminat[e] the duplication of dead-end

136. EMA, *Letter to Ombudsman* (2015), 7, 9, 10, http://www.ema.europa.eu/docs/en_GB/document_library/Other/2015/02/WC500182064.pdf. Limitations on access and redaction is allowed to protect personal data and CCI “unless there is an overriding public interest.” EMA, *Public consultation on application of transparency rules of EU Clinical Trial Regulation* (2015), http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2015/01/news_detail_002253.jsp. See generally Daniel Strehl & Jasper Littmann, *Lack of Proportionality. Seven Specifications of Public Interest that Override Post-approval Commercial Interests on Limited Access to Clinical Data*, 13 TRIALS (2012).

137. EMA, *EMA Explains its Redaction Rules* (2015), http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2015/02/news_detail_002263.jsp&mid=WC0b01ac058004d5c1.

138. Aaron Bouchie, *Clinical Trial Data: To Disclose or Not to Disclose?*, 24 NATURE BIOTECH 9, 1058 (2006), <http://www.nature.com/nbt/journal/v24/n9/full/nbt0906-1058.html>.

139. *Id.* at 1059. It is true that “early phase I trials often present more risk to research subjects and less or no possibility of individual benefit.” Levin & Palmer, *supra* note 7, at 1579. Therefore, IRBs must ensure that research subjects do not take on too much risk for the sake of “promoting clinical research and motivation.” *Id.*

140. Bouchie, *supra* note 138, at 1059.

141. *Id.* at 1058.

142. *Id.* at 1060. It is crucial to share information to foster scientific advances and protect CCI to encourage the development of innovative products but the difficulty lies in determining how to satisfy the seemingly incompatible objectives and distinguishing how much information should be disclosed. *Id.*

studies” and grow the knowledge base of the drug industry faster.¹⁴³ Merrill Goozner of Washington DC’s Center for Science in the Public Interest states, “Competition in business is understandable, but science doesn’t work that way. Failures advance the field.”¹⁴⁴

Notwithstanding the public health benefit, the industry insists trial data disclosure creates a “risk of jeopardizing the privacy of patients”¹⁴⁵ and has even garnered patient support to lobby against transparency initiatives, particularly the EMA’s proposal for CSR release.¹⁴⁶ Contrary to industry concerns, access to full data sets (including patient-level data) will make the process of developing and researching drugs more efficient.¹⁴⁷ Hans-Georg Eichler, an EMA official, explains that release of clinical trial data will create a “level playing field” as long as the appropriate precautions are taken, including patient data deidentification, data-sharing agreements, and protective measures for proprietary data.¹⁴⁸ Any data-sharing arrangement should also “treat all qualified data requesters and trial sponsors evenhandedly.”¹⁴⁹

Such an arrangement might take the form of a “learned intermediary” model.¹⁵⁰ This model allows a learned intermediary to control and impose

143. *Id.* at 1060.

144. *Id.*

145. Eichler et al., *supra* note 8, at 1578. The laws protecting personal data in the EU tend to be more encompassing than those in the U.S. Eve M. Bruns et al., *supra* note 87, at 23. “[P]ersonal data [a term used by the EU] is defined more broadly than PHI under HIPAA, as EU Directive 95/46/EC defines personal data to include any information relating to a natural person who is identified or identifiable.” *Id.*

146. Ian Sample, *Big Pharma Mobilising Patients in Battle Over Drug Trials Data*, GUARDIAN (July 21, 2013), <http://www.theguardian.com/business/2013/jul/21/big-pharma-secret-drugs-trials>

147. See Eichler et al., *supra* note 8. Eichler and his colleagues predict

[A]ccess to the full data sets of completed studies will lead to improvements in the design and analysis of subsequent trials . . . [L]essons from past trials about the heterogeneity of treatment effects . . . will streamline drug development . . . [W]ider access to patient-level data will allow sponsors to present more robust comparative-effectiveness information about their product soon after licensing . . . [Transparency will prevent] repetition of trials and projects that are doomed from the outset . . .

Id. at 1577–78. For further discussion, see Sabine Azor, et al., Will the EU Clinical Trials Regulation Support the Innovative Industry in Bringing New Medicines Faster to Patients? 27 PHARM MED 75–82 (2013).

148. Eichler et al., *supra* note 8.

149. Mello et al., *supra* note 15, at 1654. See also An-Wen Chan, *Access to Clinical Trial Data*, 342 BMJ (2011).

150. Mello et al., *supra* note 15, at 1656. Mello also discusses the “pure open-access model” and the “database-query model.” *Id.* at 1655–56. Harlan Krumholz and Joseph Ross propose a model in which an “external coordinating organization . . . contracts with the pharmaceutical or medical device manufacturer, which agrees to provide access to all of its [relevant] data . . . [and two] qualified groups to conduct independent reviews of the data . . .” Harlan Krumholz and Joseph Ross, *A Model for Dissemination and Independent Analysis of Industry Data*, 306 JAMA 1593–94, 2011,

conditions on data release.¹⁵¹ The entity would ideally not have conflicts of interest and have the necessary expertise to assess data requests.¹⁵²

This is similar to the EMA's proposed three-category system of data release and includes some of the safeguards mentioned by Eichler.¹⁵³ Category 1 data (CCI) is not to be released into the public domain; Category 2 data (i.e., data "without protection of personal data (PPD)") "will be available [for download] from the [EMA's] website."¹⁵⁴ Category 3 data (i.e., data "with PPD Concerns"), which includes CSRs, is only released upon "appropriate de-identification" and implementation of "controlled access."¹⁵⁵

An alternative is the "sponsor-review" model, which grants the trial sponsor the ultimate authority over whether to grant requests and how much information to release with oversight by an independent board.¹⁵⁶ This is the model favored by the pharmaceutical industry, as seen in PhRMA-EFPIA's *Principles*, which establishes a review board with non-company-affiliated members to review researchers' requests.¹⁵⁷ This model puts in place safeguards for patient-level data and addresses the danger of patient re-identification through "data mining."¹⁵⁸

<http://jama.jamanetwork.com/article.aspx?articleid=1104485>. Medtronic and Yale University are currently implementing this model. *See generally* Yale School of Medicine, Centers for Outcomes Research and Evaluation (CORE), Yale University Open Data Access (YODA) Project, <http://yoda.yale.edu/policies-procedures-guide-external-investigator-access-clinical-trial-data>. Like Medtronic, Johnson & Johnson agreed to share its trial data. Katie Thomas, *Johnson & Johnson Will Make Clinical Data Available to Outside Researchers*, N.Y. TIMES (Jan. 14 2015), <http://www.nytimes.com/2015/01/15/business/johnson-johnson-to-make-clinical-data-available-to-outside-researchers.html>.

151. Mello et al., *supra* note 16, at 1656.

152. *Id.* Perhaps a "body [should] be established at the European level (a Data Access Review Board), which is independent from any of the stakeholders . . ." Rita Banzi et al., *Fostering EMA's Transparency Policy*, 25 EUR. J. INTERN. MED. 681, 683 (2014).

153. EMA, Publication and Access to Clinical Trial Data Draft (EMA/240810/2013) ("CT Data Draft") (2013), http://www.ema.europa.eu/docs/en_GB/document_library/Other/2013/06/WC500144730.pdf. However, the EMA is not necessarily the independent entity envisioned as it has conflict of interest issues. For Overview of Comments Received on Publication of EMA/240810/2013, *see* http://www.ema.europa.eu/docs/en_GB/document_library/Overview_of_comments/2014/09/WC500174224.pdf.

154. CT Data Draft, *supra* note 153, at 4.

155. *Id.* at 5. Researchers must "identify themselves, . . . agree to do only specified studies, . . . not share data or try to identify patients. . . and to make results public within a year." DeFrancesco, *supra* note 37, at 533.

156. Mello et al., *supra* note 16, at 1656. The obvious flaw in this system is that trial sponsors have all the control over release of data, which would not necessarily engender public trust. *Id.* *See also* Zosia Kmiotowicz, *Roche Says It Will Not Relinquish Control Over Access to Clinical Trial Data*, 346 BMJ (2013), <http://www.bmj.com/content/346/bmj.f1374>.

157. *Principles*, *supra* note 114, at 1.

158. *Id.* at 4. The Principles state, "Any patient-level data that is shared will be anonymized to protect personally identifiable information. Companies will not be required to provide access to

Some drug companies are implementing their own “sponsor-review” models.¹⁵⁹ As of 2013, five drugmakers—Boehringer Ingelheim, GlaxoSmithKline (GSK), Roche, Sanofi, and ViiV Healthcare—are participating in an online database called Clinical Study Data Request to provide researchers access to “anonymized, patient-level clinical trial data under a voluntary data-sharing plan.”¹⁶⁰ GSK requires researchers use data only for specified research purposes and sign a contract to that effect; Roche and Pfizer have implemented analogous policies.¹⁶¹ In 2014, other pharmaceutical companies – Eli Lilly, Bayer, and Bristol Myers Squibb (BMS)—also agreed to provide access to their trial data.¹⁶²

The opening of drug company vaults is a step in the right direction, but drug companies have been pushing to be “information gatekeepers” and their commitment to openness contains caveats.¹⁶³ “[GSK], Roche, and Pfizer all largely exclude trials that tested off-label use of their drugs,” which comprises about “[one] fifth of prescription drug use . . . in the [U.S.]”¹⁶⁴ If companies impose their own conditions, “the metaphor for the end state of ‘data transparency’ could easily be a maze.”¹⁶⁵

patient-level data, if there is a reasonable likelihood that individual patients could be re-identified.” *Id.* at 1.

159. Perry Nisen & Frank Rockhold, *Access to Patient-Level Data from GlaxoSmithKline Clinical Trials*, 369 N. ENGL. J. MED. 475–78 (2013), <http://www.nejm.org/doi/full/10.1056/NEJMs1302541>.

160. Michael Fitzhugh, *Drugmakers Launch Data-Sharing Site*, THE BURRILL REPORT (2014), http://www.burrillreport.com/article-drugmakers_launch_data_sharing_site.html. AllTrials has been instrumental in bringing about data-sharing sites like ClinicalStudyDataRequest.com. *Id.* Though the five companies have pledged disclosure, study sponsors are not willing to disclose all data. “Most sponsors are excepting clinical studies of rare diseases or single center studies from their data.” *Id.*

161. Nisen & Rockhold, *supra* note 159, at 477. GSK is releasing data to researchers after their research proposals are reviewed by an independent review panel, which will “comprise external experts appointed by GlaxoSmithKline.” *Id.* at 476. Doshi et al., *supra* note 14.

162. Thomas Sullivan, *Clinical Trial Transparency Update: Eli Lilly, Bayer, Boehringer, and BMS Join Pharmaceutical Companies Sharing Patient-Level Clinical Trial Data*, POLICY AND MEDICINE (2014), <http://www.policymed.com/2014/06/clinical-trial-transparency-update-eli-lilly-bayer-boehringer-and-bms-join-pharmaceutical-companies-sharing-patient-level.html>. Eli Lilly and Bayer will be using ClinicalStudyDataRequest.com but BMS will be providing data access separately. *Id.*

163. *Data Sharing Will Pay Dividends*, 505 NATURE 131 (Jan. 9 2014), <http://www.nature.com/news/data-sharing-will-pay-dividends-1.14468>.

164. Doshi et al., *supra* note 14. See also David C. Radley et al. *Off-label Prescribing Among Office-Based Physicians*. 166 JAMA 9, 1021–26 (2006), <http://archinte.jamanetwork.com/article.aspx?articleid=410250>.

165. Doshi et al., *supra* note 14.

VII. TWIN GOALS OF PROTECTING CCI AND PROMOTING PUBLIC HEALTH (OR IS IT JUST ONE?)

Sharing clinical trials data is necessary to foster scientific advances and to promote public health. This means ensuring that trials do not remain unpublished years after they are conducted and ensuring trials that are published do not display a bias toward positive results.¹⁶⁶

Open access to clinical trial results may create risks including possible “misinterpretation of clinical trials due to inappropriate analyses.”¹⁶⁷ This risk is mitigated since patients can discuss information with physicians, who have the expertise to put the information in context.¹⁶⁸

Releasing all clinical trial information, without limitation, is not the answer but neither is redacting all such information. Safety and efficacy data should be released for public health reasons.¹⁶⁹ “Information such as pharmacologic or chemical data about a product’s composition and stability” should be protected if manufacturers can show competitive harm.¹⁷⁰ However, protection for CCI should not be indefinite.¹⁷¹ Also, patient-level data should be de-identified before being published.¹⁷²

Mere disclosure of clinical trials data is not enough. Instead, as Matthew Herder argues, regulatory decisions “whether positive (i.e. product approvals) or negative (i.e. abandoned products, product refusals, and withdrawals)” should be published openly.¹⁷³ The EMA is slowly implementing measures that offer more transparency including publishing

166. Doshi et al., *supra* note 32. See generally UK Parliament, Public Accounts Committee, *Lack of Consensus Over How Well Tamiflu Actually Works* (2014), <http://www.parliament.uk/business/committees/committees-a-z/commons-select/public-accounts-committee/news/tamiflu-report/>. See also Joseph S. Ross et al., *Publication of NIH funded trials registered in ClinicalTrials.gov: cross sectional analysis*, 344 *BMJ* (2012), <http://www.bmj.com/content/344/bmj.d7292>.

167. Eichler et al., *supra* note 8, at 1578.

168. Lemmens & Telfer, *supra* note 12, at 79. “The relative risk of misinterpretation is . . . less threatening to appropriate patient care than selective publication of positive results and hiding of negative data.” *Id.*

169. Kesselheim & Mello, *supra* note 104, at 489.

170. *Id.*

171. Alastair J.J. Wood, *Progress and Deficiencies in the Registration of Clinical Trials*, 360 *N. ENGL. J. MED.* 824, 829 (2009). Wood suggests that the two-year time period should be the standard for Phase 1 trials and the FDA’s “‘negative’ decisions on the [NDA]s.” *Id.* It is also important to distinguish which data should be protected. Data that constitutes CCI is “information relating to trade secrets (formulas, programmes, process, molecules, etc.), not just ambiguous ‘commercial confidences.’” Rita Banzi et al., *supra* note 152, at 682.

172. DeFrancesco, *supra* note 37, at 534. In 2013, the British Medical Journal started requiring release of de-identified data. *BMJ, Open Data*, <http://www.bmj.com/open-data>.

173. Matthew Herder, *Toward a Jurisprudence of Drug Regulation*, 42 *J.L. MED. & ETHICS* 244, 244 (2014).

negative and positive decisions, contrasting the U.S. which “selectively publish[es] their decisions.”¹⁷⁴ The EMA also provides “information about all refusals’ . . . and information pertaining to withdrawn applications” whereas the FDA provides more limited access.¹⁷⁵ Though the FDA and EMA are making more data available, such as providing access to clinical trial summaries through Drugs@FDA and EPARs respectively, gleaned useful information from the summaries is another matter as “the content is not standardised, information deemed to be [CCI] is redacted [and] . . . many trials are not included in regulatory databases.”¹⁷⁶ Therefore, the next step is to disseminate trial data in a manner that allows researchers and other relevant parties to make more efficient use of the data.

Regulators can start by increasing transparency for their decision-making to enhance public trust.¹⁷⁷ They can also solicit data from independent contractors to supplement or even replace industry conducted trials when determining whether to approve drugs.¹⁷⁸ To reduce reliance on industry data, clinical trials can be financed through public funds.¹⁷⁹

While there is greater need for data transparency to protect public health, it is important to note that cooperation from drug companies, health care professionals, researchers, and regulators is key in achieving this goal. The recent changes in FDA and EMA regulations purport to foster information exchange and the two agencies are leading the way to the end goal of transparency, but there is a danger in overregulation, which may have the unintended effect in creating an environment “where [industry and researchers] can[not] collaborate without fear of sanction.”¹⁸⁰ Therefore, regulators should carefully weigh the following considerations: promotion of cooperation for the sake of scientific advances,¹⁸¹ deterrence

174. *Id.* at 244.

175. *Id.* at 246. The FDA has allowed advisory committees, comprised of non-FDA members, to participate in its deliberations. *Id.* at 245. However, Herder questions whether these committee members are disinterested. *Id.* at 250.

176. An-Wen Chan, *Out of Sight but Not Out of Mind: How to Search for Unpublished Clinical Trial Evidence*, 344 *BMJ* (2012), <http://www.bmj.com/content/344/bmj.d8013>.

177. Herder, *supra* note 173, at 249, 256.

178. Rita Banzi et al., *supra* note 152, at 683. Such data includes independently sponsored trials and unpublished results from the scientific community. *Id.* Dean Baker, *supra* note 17, at 11–14.

179. Dean Baker, *supra* note 17. Funding sources include cost reductions for drugs in the Medicare prescription drug plan and decreased pharmaceutical marketing expenditures. *Id.* at 11–14. There is a cost-savings component to publicly funded trials as it cuts downs on duplicative trials and kickbacks. *Id.* at 8.

180. Epstein, *supra* note 42.

181. *Id.* However, while communication and collaboration should be enabled, drug sponsors’ role in evaluating its own drugs should be minimized.

of non-reporting or misreporting of trial results, and the need for health professionals to have access to complete trial information (including adverse events) to ensure that patients do not suffer unnecessary harm.¹⁸² Equally important as data transparency is “market transparency” or pricing regulation to ensure patient access to markets for drugs.¹⁸³

Though progress is slow, the FDA and EMA are working toward a common goal: increasing access to data pertaining to clinical drug trials in a way that ensures patient safety and allows for pharmaceutical innovation.¹⁸⁴ These twin aims are not necessarily incompatible. Transparency of clinical trial data can be realized through enacting legislation to enforce comprehensive registration and standardize trial protocols; providing enforcement for trial registries on national and international levels; adopting policies that allow for release of CSRs and other relevant data; conducting independent testing of clinical trials; imposing greater oversight of studies funded or sponsored by

182. Tsang, *supra* note 102. Health care professionals are the intermediary between the scientific community and the patients. Patients consult health care professionals to figure out what clinical trial information means. Therefore, such information should be posted in online registries or made available through journals and CSRs. A parallel issue is ensuring health care professionals maintain independence in decision-making. In the U.S., the “Sunshine Act,” passed in 2010, requires drug manufacturers “to report payments or transfers of value made to U.S. physicians and teaching hospitals” on a website called Open Payments but there have been many “technical challenges.” *Id.* at 4–5. European pharma decided to implement similar measures as the U.S. when they announced the “EFPIA Disclosure Code” in 2013. *Id.* at 4. In the EU, the law requires that health care professionals make decisions for patient care that are not “influenced by . . . financial inducements.” *Id.* at 2.

183. Markus Hartmann and Florence Hartmann-Vareilles, *Patient Protection and Access to Innovative Medicinal Products in the European Union*, 42 *DRUG INFORMATION JOURNAL* 281, 289–90 (2008). To achieve market transparency, it is critical to increase access to generic drugs, which are cheaper than their brand-name counterparts. Jessica Underwood, *What the EU has that the U.S. Wants: An Analysis of Potential Regulatory Systems for Follow-Up Biologics in the U.S.*, 10 *DEPAUL HEALTH CARE L.* 420–21 (2007). As Donald Light observes, the exorbitant prices the pharmaceutical industry charges for its drugs is unreasonable. Michelle Llamas, *Big Pharma Cashes in on Americans Paying Higher Prices for Prescription Drugs*, *Drug Watch* (2014), <http://www.drugwatch.com/2014/10/15/americans-pay-higher-prices-prescription-drugs/>. Even though drugs have high costs in the initial development phase, the “minor variations [on older drugs]” churned out later have much lower production costs but remain expensive for consumers. *Id.* Pharmaceutical companies continue to find new ways to fund drug development and maximize profits. Llewellyn Hinkes Jones, *Stop Subsidizing Big Pharma*, *N.Y. TIMES* (Jan. 15, 2015), http://www.nytimes.com/2015/01/06/opinion/stop-subsidizing-big-pharma.html?_r=0.

184. The FDA and EMA are collaborating and exchanging information on pharmacovigilance to ensure that drugs that reach the market are safe for consumers. FDA, *FDA and European Medicines Agency Strengthen Collaboration in Pharmacovigilance Area*, <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm386372.htm>. Pharmaceutical companies are working with regulators including the FDA and EMA to standardize clinical trial protocols and increase efficiency in drug development and delivery. Dalvir Gill, *Re-inventing Clinical Trials Through Transcelerate*, 13 *NATURE REVIEWS DRUG DISCOVERY* (2014), <http://www.nature.com/nrd/journal/v13/n11/full/nrd4437.html>.

pharmaceutical companies; and implementing measures for accurate reporting of trial data, particularly safety and efficacy data, on the most popular medium of health information today.¹⁸⁵

*Rebecca Choi**

185. Wood & Gariby, *supra* note 1, at 548. Compliance mechanisms (independent review boards and information gatekeepers) should be put into place to deter trial sponsors from circumventing mandated transparency requirements and regulatory measures. *See infra* Parts III, IV, and V.

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