

## NOTE

## IT IS TIME: WHY THE FDA SHOULD START DISCLOSING DRUG TRIAL DATA

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DO NOT INITIATE DISCUSSIONS ON THE RESULTS OF THE VIOXX GI OUTCOMES RESEARCH (VIGOR) STUDY, OR ANY OF THE RECENT ARTICLES IN THE PRESS ABOUT VIOXX. YOU MAY RESPOND . . . ONLY AS OUTLINED BELOW . . .

If the doctor asks you further [about the incidence of myocardial infarction] tell them:

“In the clinical OA trials . . . the incidence of [myocardial infarction] was less than 0.1% with VIOXX.”

“Doctor, As [sic] you can see, Cardiovascular Mortality as reported in over 6,000 patients was Vioxx .1 vs. NSAIDS .8 vs. Placebo 0.”<sup>1</sup>

## INTRODUCTION

Drug manufacturers (“manufacturers”) must obtain regulatory approval from the Food and Drug Administration (“FDA”) in order to market their products in the United States.<sup>2</sup> The FDA’s statutory mandate

1. Merck, Bulletin for Vioxx: Action Required: Response to New York Times article (May 23, 2001), <http://dida.library.ucsf.edu/pdf/uib00a10>. This and similar documents directed Merck sales staff to downplay and even obscure Vioxx’s cardiovascular risks, even after trial results indicated such risks were substantial. The excerpt above directs sales staff to inform doctors that Vioxx was eight times less likely to cause cardiovascular mortality compared to competing drugs, a misleading statement based on Merck’s own interpretation of incomplete and irrelevant trial results. See Memorandum from Rep. Henry A. Waxman, The Roles of FDA and Pharmaceutical Companies in Ensuring the Safety of Approved Drugs, Like Vioxx, at 2–3 (May 5, 2005), <http://waxman.house.gov/UploadedFiles/merck.pdf>. See also Ronald M. Green, *Direct-to-consumer Advertising and Pharmaceutical Ethics: The Case of Vioxx*, 35 HOFSTRA L. REV. 749, 752–53 (2006) (detailing Merck’s aggressive marketing efforts for Vioxx).

2. See FDA, Frequently Asked Questions on Drug Development and Investigational New Drug Applications, <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/ucm069898.htm> (last visited Apr. 30, 2009) (“[C]urrent Federal law requires that a drug be the subject of an approved marketing application before it is transported or distributed across state lines.”). See also James T. O’Reilly, *Knowledge is*

charges it with the duty to protect the public health by ascertaining the risks and benefits of exposing human bodies to drug molecules before certifying these chemicals as safe and effective for their marketed indications.<sup>3</sup> Accordingly, the FDA requires drug candidates to undergo a long, costly, multi-step testing process, which may take many years and include several pre-clinical studies on model organisms, as well as up to three clinical studies on human subjects.<sup>4</sup> Briefly, a manufacturer first files an Investigational New Drug (“IND”) application with the FDA after concluding pre-clinical animal trials and other toxicity studies on a drug candidate.<sup>5</sup> After the FDA approves the IND, the manufacturer may commence human trials, at the conclusion of which the manufacturer may file a New Drug Application (“NDA”). A drug may only be marketed after the FDA approves the NDA.<sup>6</sup> Scientific and clinical data generated during the approval process (“research data”) are what distinguish “the products we call ‘drugs’ from similar products sold in minimally regulated markets.”<sup>7</sup> Although manufacturers bear the cost of research data generation, it is oftentimes a worthwhile investment that also confers significant commercial advantages. Consequently, they have argued that research data should be considered a trade secret and kept confidential. The FDA’s longstanding position has been to accept this proposition.<sup>8</sup> Even when Congress appeared to mandate disclosure or

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*Power: Legislative Control of Drug Industry Trade Secrets*, 54 U. CIN. L. REV. 1, 6 (1985) (describing the regulatory framework from an industry perspective).

3. 21 U.S.C. § 321(p)(1) (2006) (defining a new drug as “[a]ny drug . . . the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the condition prescribed, recommended, or suggested in the labeling thereof. . . .”); see Margaret A. Hamburg & Joshua M. Sharfstein, *FDA as a Public Health Agency*, 360 NEW ENG. J. MED. 2493 (2009) (citing *United States v. Bacto-Unidisk*, 394 U.S. 784 (1969) (emphasizing FDA’s “overriding purpose” is to protect the public health)).

4. See Bruce N. Kuhlik, *The Assault on Pharmaceutical Intellectual Property*, 71 U. CHI. L. REV. 93, 94 (2004) (claiming that obtaining FDA approval may take up to fifteen years and cost an estimated \$802 million).

5. Frequently Asked Questions on Drug Development and Investigational New Drug Applications, *supra* note 2.

6. For a simplified version of the drug development process prepared for lay audiences, see The FDA’s Drug Review Process: Ensuring Drugs Are Safe and Effective, <http://www.fda.gov/Drugs/ResourcesForYou/Consumers/ucm143534.htm> (last visited Aug. 8, 2009).

7. Rebecca S. Eisenberg, *The Role of FDA in Innovation Policy*, 13 MICH. TELECOMM. TECH. L. REV. 345, 347 (2007).

8. Jane A. Fisher, *Disclosure of Safety and Effectiveness Data under the Drug Price Competition and Patent Term Restoration Act*, 41 FOOD, DRUG COSM. L.J. 268, 270 (1986) (setting down the historical basis of FDA’s interpretation and implementation of the trade secrets doctrine to data) (“Since 1938, FDA has consistently interpreted section 301(j) of the FDCA as encompassing animal and human test data in an NDA, in spite of the law’s literal limitation to ‘methods and processes.’”).

weaken the underlying rationale for secrecy,<sup>9</sup> the FDA has continued to treat research data as confidential.<sup>10</sup>

A strong argument against a default posture of confidentiality is that research data disclosure would promote broad public interests by eliminating the societal costs brought about by keeping research data out of the reach of the public. Merck's eventual withdrawal of Vioxx implicates secrecy as a major factor in the failure of the regulatory process to protect the public health. Civil action plaintiffs in Vioxx cases have demonstrated the detrimental impact of a lack of public access to research data about Vioxx's side-effects.<sup>11</sup> Substantial evidence shows that the public health debacle in the Vioxx cases resulted from a combination of failures—Merck's inadequate dissemination and misleading interpretation of Vioxx trial results, the FDA's decision to grant Vioxx "fast-track" approval without a complete and full study of phase III trials, and post-approval delays in communicating the drug's cardiovascular risks to health care providers and consumers.<sup>12</sup>

The Vioxx incident is not the only example of the costs of a blanket policy of secrecy.<sup>13</sup> Nor is preventing a public health disaster the only (or even the most significant) goal a policy of disclosure would serve. Research data, due to rapid and far-reaching advances in the life sciences, has grown exponentially more complex and information-rich in the last two decades. So, too, has data analysis methodology, giving rise to a brand new field—bioinformatics. The tremendous increases in the size and information content of research data, coupled with recent breakthroughs in bioinformatics, present a chance to capture innovation efficiencies that were previously impossible. These efficiencies will largely remain uncaptured under a policy of secrecy that prevents informatics based analyses of increasingly large datasets submitted to the FDA. Public access to research data could therefore potentially yield much valuable new information, aid the development of new products

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9. See Drug Price Competition and Patent Term Restoration Act of 1984, Pub L. No. 98-417, 98 Stat. 1585 (1984) [hereinafter Hatch-Waxman Act]. The Hatch-Waxman Act radically changed the drug certification process by allowing manufacturers of generic drugs to gain FDA approval without having to conduct separate tests. Generic drugs may now rely on an innovator drug's previously approved application and the data submitted in support of that application to gain marketing approval for a "bioequivalent" product.

10. See *supra* note 8 and accompanying text.

11. Proof of Injury Resulting From Prescription Medication Vioxx, 87 AM. JUR. 3D *Proof of Facts* §§ 2-3 (2008).

12. *Id.* See also *id.* § 19 (reciting evidence presented at trials against Merck).

13. See Sidney A. Shapiro, *Divorcing Profit from New Drug Research: A Consideration of Proposals to Provide FDA with Reliable Test Data*, 1978 DUKE L. J. 155, 166-68 (1978) (describing several earlier incidents where trial results were manufactured or misrepresented).

and greatly increase the quality of available information on existing products.<sup>14</sup>

Congress weakened the legitimacy of the nondisclosure argument by enacting the Hatch-Waxman Act.<sup>15</sup> Thus, after the Hatch-Waxman Act, the justification for continued secrecy based on the residual commercial value of research data is substantially weaker. The FDA may and should take into account the realignment of interests to revise its confidentiality policy to a default position of disclosure as a matter of public policy. If the FDA fails to act, Congress should explicitly require the agency to make research data publicly accessible, notwithstanding any residual value of the data or its status as confidential business information.

This Note proceeds in six parts. Part I begins by first analyzing the theoretical underpinnings of pro-disclosure and pro-secrecy arguments. The problems raised by a policy of research data confidentiality in drug regulation are complex and located within the larger doctrinal question posed by interjecting trade secrets into regulatory frameworks—a “big picture” topic on which a substantial body of scholarship already exists.<sup>16</sup> Here, I do not elaborate on these larger topics, except to summarize existing literature and highlight its relevance to this Note. Part II explores the FDA’s evaluation of pro-disclosure and pro-secrecy arguments, its basis for preferring a pro-secrecy stance in its rules implementing the Freedom of Information Act (“FOIA”), as well as its response to the Hatch-Waxman Act’s research data disclosure provisions. Part III switches to a survey of the current state of research data confidentiality by discussing how courts have analyzed and evaluated disclosure requests under the FOIA. Part IV concludes the survey of the legal regime of disclosure by briefly exploring statutory and constitutional restraints in addition to the FOIA. Part V reveals the increasing costs of keeping research data confidential by highlighting the heretofore unachievable innovation efficiencies that would become possible under a regime of

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14. See *infra* Part IV.

15. See discussion of the Hatch-Waxman Act’s effect, or lack thereof, on data disclosure *infra* Part II.B.

16. Trade secrets, with their origins in and emphasis on interactions between private parties, provoke an inherent incongruity in regulatory contexts, where the relevant interests and motivations are of a decidedly public nature. *E.g.*, David S. Levine, *Secrecy and Unaccountability: Trade Secrets in our Public Infrastructure*, 59 FLA. L. REV. 135, 136–37, 148–50, 162–63 (2007); Mary L. Lyndon, *Secrecy and Access in an Innovation Intensive Economy: Reordering Information Privileges in Environmental, Health, and Safety Law*, 78 U. COLO. L. REV. 465, 491–93, 496 (2007). Scholars have already identified data disclosure as a means to promoting goals such as managing the health risks of drugs, preventing costly repetitions of failed drug trials, and allowing better oversight of agency regulation. See Shapiro, *supra* note 13, at 156–58 (providing background on the problems caused by treating research data as trade secrets and the salutary effects of data disclosure).

public access. It focuses on the public interest in ensuring a high standard of scientific quality and integrity in research data, and on the benefits of maximizing our understanding of a drug's mechanism of action and side effects. Finally, Part VI briefly sketches current efforts to achieve full research data disclosure by both private parties and legislatures and points out some means of obtaining that goal.

## I. WHY SECRECY, WHEREFORE DISCLOSURE?

Data disclosure is a discretionary function of all agencies.<sup>17</sup> In responding to disclosure requests, the FDA must balance the private, commercial needs of drug manufacturers with the public interest in vigorous and accurate safety and efficacy research.<sup>18</sup> Therefore, understanding the underlying interests that drive the debate is essential in order to properly evaluate the arguments for and against research data disclosure.<sup>19</sup>

### A. *The Nature of Manufacturers' Interests*

Manufacturers have legitimate commercial interests in research data secrecy. As drug development cycles have lengthened, the patent exclusivity term has become increasingly inadequate<sup>20</sup> and less able to provide monopoly profits. Moreover, increasing numbers of drugs lack patent protection because of expired or invalidated patents.<sup>21</sup> Manufacturers have responded to eroding patent protection by expanding their patents to new uses of older compounds or for newer versions of patent-expired drugs under various "evergreening" strategies.<sup>22</sup> In general, these solu-

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17. *See* *Chrysler Corp. v. Brown*, 441 U.S. 281, 290–94 (1979) (holding that the Freedom of Information Act disclosure exemptions do not impose a duty to withhold information regarding a government agency).

18. *See, e.g.*, Shapiro, *supra* note 13, at 156–57 (raising ethical and accuracy concerns with sponsor produced research data). *But see* Kuhlik, *supra* note 4, at 96–97 (“The prospect of earning substantial revenues for successful drugs is a necessary incentive to encourage [research and development] investments.”).

19. The FDA's data disclosure policy is necessarily located within the larger general debate between trade secrets in regulatory frameworks. Though I focus only on the narrower and more specific public interest in data accessibility here, I have organized this Note around the existing theoretical basis of the larger debate. *See supra* note 16 and associated text.

20. *See* Kuhlik, *supra* note 4, at 96–97 (comparing the effective life of pharmaceutical patents with patents in other industries and claiming that pharmaceutical patents' effective lives are shorter by 6.5–7.5 years on average).

21. Many drug patents fail the high bars of nonobviousness and novelty. *See* 35 U.S.C. §§ 101–103 (2006).

22. JOHN R. THOMAS, CONG. RESEARCH SERV., PATENT “EVERGREENING”: ISSUES IN INNOVATION AND COMPETITION, 1 (2009) (defining “evergreening” as generally “obtaining

tions have not fared well in courts and may not provide as rigorous protection as the patentee would like.<sup>23</sup> Moreover, even effective patents may not offer complete protection since they are subject to competition from non-infringing substitutes. One survey found that the mean time to market for substitutes of seven therapeutic drugs was only three years.<sup>24</sup> While the patent system has arguably lost its position as the driving force behind pharmaceutical innovation,<sup>25</sup> the FDA's regulatory framework has taken on a larger role in allowing manufacturers to maintain their competitiveness.

Regulatory burdens delay competing and generic products from entering the market. Lead time to market can provide a substantial commercial advantage. Federal Trade Commission studies show that doctors continue to prefer pioneer drugs even after substitutes become available.<sup>26</sup> Studies also show that the availability of new risk information about an existing drug may have "no [discernible] effect on prescribing behavior."<sup>27</sup> To generate market lead time for a pioneer drug with a long development cycle, or a variant of a drug which is about to lose patent protection, manufacturers may resort to FDA-administered exclusivity.<sup>28</sup> Research data secrecy may delay or even prevent competitors from obtaining marketing approval during the long development phase. For approved products, unavailability of research data still delays competing generic products from entering the market. Thus, manufacturers value research data to the extent that it enables first-to-market products and delays the entry of competing generics.

Even if the domestic regulatory burden for new entries may have arguably decreased following the Hatch-Waxman Act, research data generated domestically may still retain anti-competitive value in other markets. For example, research data may be used to obtain regulatory approval in foreign applications. It may be even more valuable in markets where regulators do not permit generics to be marketed without separate trials.<sup>29</sup> Therefore, in a regime that favors disclosure, competitors may still

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multiple patents that cover different aspects of the same product" that critics charge may "effectively extend[] the term of exclusivity that the patent holder obtains").

23. Eisenberg, *supra* note 7, at 349.

24. Thomas O. McGarity, *The Trade Secret Status of Health and Safety Testing Information: Reforming Agency Disclosure Policies*, 93 HARV. L. REV. 837, 851 (1980).

25. Eisenberg, *supra* note 7, at 347 ("Framing the relationship between patents and drug regulation in this manner is seriously incomplete and out of date.").

26. McGarity, *supra* note 24, at 852.

27. LARS NOAH, LAW, MEDICINE, AND MEDICAL TECHNOLOGY: CASES AND MATERIALS 339 (Robert C. Clark et al. eds., 2nd ed. 2007).

28. See Eisenberg, *supra* note 7, at 359–62 (detailing the role of FDA-administered "pseudo-patents" in delaying market entry for competing drugs).

29. See O'Reilly, *supra* note 2, at 23.

be able to free ride on a manufacturer's U.S. research data in order to gain approval in foreign markets.

Manufacturers also value research data secrecy as a way to minimize third-party scrutiny of the side effects and risks of their products. A manufacturer may even consider secrecy as a necessary means to reduce their exposure to liability.<sup>30</sup> Moreover, competitors may benefit from access when it enables them to gather information about a manufacturer's drug in order to highlight the weaknesses of that product and "the relative virtues of [their] competing products."<sup>31</sup>

Finally, research data is valuable from a purely scientific perspective. Such data from current studies contains information useful for designing future studies and channeling future development of improved versions of the same drug, or even new drugs in the same class of compound.<sup>32</sup> Thus, manufacturers prize research data secrecy even after it loses its "commercial utility . . . as a means of excluding competitors [from U.S. markets]."<sup>33</sup>

#### B. *The Nature of the Public Interest*<sup>34</sup>

Existing scholarship frames the public interest in disclosure as centering on the need to ensure and maintain data integrity and quality.

The FDA is not able to carry out perfect audits.<sup>35</sup> Time pressures and lack of resources often prevent a thorough review of agency decisions, even when existing research data could probably benefit from a reevaluation in light of new scientific information or emerging methodologies.<sup>36</sup> Moreover, research data may not always meet the objectivity standards of the scientific process, while still "falling short of being clearly fraudulent or dishonest."<sup>37</sup> Even when manufacturers employ outside academic researchers to test drugs, neither the impartiality of the research nor an

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30. See Lyndon, *supra* note 16, at 520–21.

31. See Eisenberg, *supra* note 7, at 383.

32. O'Reilly, *supra* note 2, at 24.

33. *Id.* at 21–25.

34. This section briefly summarizes the nature of the public interest and is only meant to introduce and frame the issue that is the focus of this Note. I fully explore the recent expansion of the need for disclosure in light of recent scientific breakthroughs in Part V.

35. Shapiro, *supra* note 13, at 158 ("[FDA reviewers] find it impossible . . . to review every page of the submitted information.").

36. McGarity, *supra* note 24, at 841.

37. See Wendy Wagner & David Michaels, *Equal Treatment for Regulatory Science: Extending the Controls Governing the Quality of Public Research to Private Research*, 30 AM. J.L. & MED. 119, 122–25 (2004).



objective review of the process is guaranteed.<sup>38</sup> In fact, manufacturers are able to influence the results of academic studies in many ways.<sup>39</sup>

Manufacturers are also able to suppress adverse results. For example, a comparison study of trials published in peer-reviewed journals and actual trial results revealed a clear publication bias, with positive results more likely to be published.<sup>40</sup> When negative results were included in published peer-reviewed articles, they were still presented in ways to highlight positive outcomes.<sup>41</sup> Since withholding results is almost always at the discretion of the manufacturer, it is difficult to detect the prevalence of “ends-oriented bias”<sup>42</sup> in publications except through similar serendipitous comparative studies. Proposals addressing this problem have ranged from limited or complete third party testing, to government sponsored testing,<sup>43</sup> to full and public disclosure. Many scholars agree that public disclosure would be the best means to improve research data integrity and quality.<sup>44</sup>

Just as manufacturers are increasingly turning to secrecy in order to protect their commercial interests, the need for disclosure is growing concomitantly.<sup>45</sup> As tension mounts between the commercial interests for secrecy and the need for public disclosure because the intellectual foundation on which the confidentiality discourse has been based is increasingly becoming outdated,<sup>46</sup> it is helpful to understand the currently fragmented and confusing research data disclosure regime resulting from historical interactions regarding disclosure and secrecy between the FDA, courts, and Congress.

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38. *Id.* at 120 (“As long as sponsors control the research at some or all points in the process . . . experiments can be biased in ways that support the sponsor’s interests.”).

39. Shapiro, *supra* note 13, at 164 (describing how academic clinical research is influenced by industry, and quoting an industry person who “spent 6 years influencing clinical investigators” as saying that “objectivity can be destroyed more frequently and effectively by the soft sell than by the bribe.”).

40. Erick H. Turner, et al., *Selective Publication of Antidepressant Trials and Its Influence on Apparent Efficacy*, 358 NEW ENG. J. MED. 252, 256–57 (2008).

41. *Id.*

42. Wagner & Michaels, *supra* note 37, at 123–25.

43. Shapiro, *supra* note 13, at 175–77. According to Professor Shapiro, the FDA has at least once required testing by third parties and public review of the results in the past because of public “sharp [scrutiny]” of a product (Aspartame). *Id.* at 175.

44. *E.g.*, Eisenberg, *supra* note 7, at 383; Lyndon, *supra* note 16, at 523; McGarity, *supra* note 24, at 840.

45. Lyndon, *supra* note 16, at 480–81. (“Commercial interests in controlling information seem to be growing at the same time [data] access is becoming both more necessary and more productive.”)

46. *See infra* Part V.

## II. THE STATE OF THE LAW WITH RESPECT TO RESEARCH DATA DISCLOSURE—THE FREEDOM OF INFORMATION ACT

Current laws governing research data disclosure are a “tangle” that “both encourage and discourage disclosure.”<sup>47</sup> Applicable provisions are scattered throughout the FOIA, the Federal Food, Drug and Cosmetics Act (“FDCA”) and the Federal Trade Secrets Act (“FTSA”), as well as in state trade secret law based on common law, constitutional takings doctrine, and agency regulations.<sup>48</sup> This confusing, complicated, and sometimes contradictory regime contributes to the creation of legal bottlenecks. It allows manufacturers to successfully resist disclosure by arguing for a narrow interpretation of conflicting statutory provisions and unclear terminology.<sup>49</sup> On the whole, this strategy has succeeded and disclosure efforts have been severely curtailed by restrictive judicial interpretation, as well as by consistently pro-secrecy agency regulations. Perhaps because disclosure controversies have been raised as FOIA requests,<sup>50</sup> courts have not been able to consider the rationale behind the drug regulatory regime properly. They have concentrated excessively on the potential harm to private interests and insufficiently on the public interest in disclosure.<sup>51</sup>

### A. *The FDA’s Implementation of the Freedom of Information Act*

The FDA’s application of the trade secret doctrine is “derived from its interpretation of the interaction of three separate statutory provisions;”<sup>52</sup> however, almost all controversies over research data disclosure have turned on the FDA’s construction of the FOIA. When the FDA first published regulations on its FOIA policy, it concluded that “it [was] not practical or feasible to determine the differences, if any, between the confidentiality provisions [in the different statutes].”<sup>53</sup> Arguing that “to

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47. McGarity, *supra* note 24, at 858.

48. See Stanley S. Wang & John J. Smith, *Potential Legal Barriers to Increasing CMS/FDA Collaboration: The Law of Trade Secrets and Related Considerations*, 58 *FOOD & DRUG L.J.* 613, 620–24 (2004).

49. See *infra* Part III.B for an example where drug manufacturer Schering successfully resisted disclosure by arguing for a narrow interpretation of otherwise facially pro-disclosure statutory provisions.

50. See *infra* notes 53, 62.

51. See *infra* Part III.

52. Fisher, *supra* note 8, at 270 (setting down the historical basis of the FDA’s trade secrets doctrine).

53. Food and Drug Administration, Public Information, 39 Fed. Reg. 44,602, 44,612, ¶ 78 (Dec. 24, 1974) [hereinafter FDA Regulations]. Note that this could possibly be an improper construction of the statutory provision in Section 301(j) of the FDCA, which imposes criminal penalties for “revealing . . . any method or process which as a trade secret is entitled

do otherwise would invite confusion [and] lead to arbitrary decisions,” the FDA decided to treat all three statutes as coextensive and base all its future disclosure decisions on its construction of the FOIA.<sup>54</sup>

Designed to “pierce the veil of administrative secrecy and to open agency action to the light of public scrutiny,”<sup>55</sup> the FOIA imposes a general obligation for information disclosure on federal agencies. As a result, the FOIA caused a radical increase in transparency at the FDA.<sup>56</sup> The FDA Commissioner concluded that the new, disclosure-friendly regime had “a beneficial rather than a detrimental effect” and “fostered greater public accountability.”<sup>57</sup> Despite its otherwise pro-disclosure effect, the FOIA has not increased access to research data due to the FDA’s determination to treat such data as private, trade secret, and confidential, and thus exempt from disclosure.<sup>58</sup> While it noted that research data disclosure and trade secrets were the most contentious issues raised by its proposed FOIA regulations,<sup>59</sup> the FDA decided that the contents of NDAs were “private” rather than “public” records<sup>60</sup> and would therefore be exempt from disclosure under the trade secret exemption of the FOIA (“Exemption 4”)<sup>61</sup>. The FDA eventually promulgated this policy under several rules.<sup>62</sup>

The FDA’s reason for arriving at this conclusion has shaped the development and application of the trade secret doctrine within the context of the drug regulatory regime. The agency’s responses to the various

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to protection.” 21 U.S.C. § 331(j). There is at least a colorable argument that data do not constitute “a method or process.”

54. *Id.*

55. *Dep’t of Air Force v. Rose*, 425 U.S. 352, 361 (1976).

56. In the two years after it implemented regulations complying with the FOIA amendments, the proportion of records that the FDA treated as confidential decreased from 90 to 10 percent. FDA Regulations, *supra* note 53, at 44,602, ¶ 1.

57. *Id.*

58. 5 U.S.C. § 552(b)(4) provides that the FOIA disclosure requirement does not extend to “trade secrets and commercial or financial information obtained from a person and privileged or confidential.” *Id.*

59. FDA Regulations, *supra* note 53, at 44,611 (“By far the most extensive comment on the proposed regulations related to the definitions of ‘trade secret’ and ‘confidential data or information’ ”); *id.* at 44,635 (“Undoubtedly the most persistent issue raised in the comments relates to the disclosure of safety and effectiveness data in IND and NDA files.”).

60. *Id.* at 44,633, ¶ 238 (“[T]hese applications, and the notices relating to investigational use of new drugs, result in private licenses rather than public regulations. Accordingly, it was concluded that the safety and effectiveness data for new drugs and new animal drugs, including antibiotic drugs for veterinary use, fall within the trade secrets exemption and thus are not available for public disclosure.”).

61. The trade secret exemption is usually referred to as “Exemption 4” since it is subclause 4 of 5 U.S.C. § 552(b).

62. 21 C.F.R. § 20.60 (2010) (FOIA exemptions control all other disclosure rules); 21 C.F.R. § 20.61 (2010) (data which fall under FOIA exemptions are not available for public disclosure); 21 C.F.R. § 314.430 (2010) (setting forth conditions under which information in new drug applications becomes available for public disclosure).

comments it received during its FOIA rulemaking illustrate the tensions the doctrine raises in a public disclosure context. On the one hand, the agency claimed that research data contained economic value, which would be endangered if disclosed.<sup>63</sup> In responding to a comment which emphasized the safety of human test subjects in clinical trials, the FDA stated that “[t]he remedy for the individual who has participated in the testing of a new drug is to obtain information about the drug from the drug company involved.”<sup>64</sup> In responding to requests that INDs not be terminated, specifically in order to prevent disclosure following such termination, the FDA advised manufacturers that “the termination of an IND is not dispositive with respect to the availability of information contained therein. If the company can demonstrate that the matter is still under active development, such information will retain its trade secret status.”<sup>65</sup> These comments are consistent with a purely commercial and private reading of the interests involved.

On the other hand, the FDA Commissioner praised the FOIA’s open disclosure policy and went on to recommend that “greater use should be made in the future of the Commissioner’s discretionary authority to release agency records which, under the strict terms of the statute, could be retained as confidential.”<sup>66</sup> While the agency appeared to confirm that public policy favored research data disclosure,<sup>67</sup> it refused to do so, arguing that disclosure would harm pharmaceutical innovation by allowing free riders to obtain approval of identical products after an innovator has shouldered the regulatory burden.<sup>68</sup> This is a privately oriented policy and conflates private interests (competition between drug manufacturers) with several public interests (research data access and maintaining the correct incentives for pharmaceutical innovation). Acknowledging the conflicting forces it had to accommodate, the FDA argued that this issue was too important to be addressed by the agency’s rulemaking powers

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63. FDA Regulations, *supra* note 53, at 44,634, ¶ 252 (“[T]here can be no question, under present law, about the tremendous economic value of the full reports of the safety and effectiveness data contained in an IND [or] NDA . . . If a manufacturer’s safety and effectiveness data are to be released upon request, thus permitting ‘me-too’ drugs to be marketed immediately, it is entirely possible that the incentive for private pharmaceutical research will be adversely affected.”).

64. *Id.* at 44,633.

65. *Id.*

66. *Id.* at 44,402.

67. *Id.* at 44,635 (“The Commissioner agrees that public policy supports release of all safety and effectiveness data, but points out that present statutory law, 18 U.S.C. 1905 and 21 U.S.C. 331(j), prohibits such release.”).

68. *See* FDA Regulations, *supra* note 53, at 44,634, ¶ 252.

and pleaded with Congress to remedy the situation.<sup>69</sup> Congress heard; and, ten years later, it attempted to answer.

*B. The Hatch-Waxman Act's Apparent Attempt to  
Authorize Research Data Disclosure*

In 1984, Congress passed the Hatch-Waxman Act, significantly changing the relationship between pioneer drugs, generics, patents and FDA regulation.<sup>70</sup> Fully exploring the contours of the compromise that animated the Hatch-Waxman Act, and its impact, is a task beyond the scope of this Note.<sup>71</sup> For the present, it is sufficient to note that the Hatch-Waxman Act created an abbreviated approval process for generic drugs which explicitly allowed them to rely on research data generated by another manufacturer for a bioequivalent pioneer drug.<sup>72</sup> Thus, the Hatch-Waxman Act removed one of the main objections against disclosure by reducing the value of research data as a means to gain regulatory approval.<sup>73</sup> In addition, the Hatch-Waxman Act took another reasonable step: it made research data explicitly available to the public after the need for secrecy had disappeared. The Hatch-Waxman Act amended Section 505 of the FDCA to add the following provision:

Safety and effectiveness data and information which has been submitted in an application under subsection (b) . . . *shall be made available to the public, upon request*, unless extraordinary circumstances are shown—

(A) if no work is being or will be undertaken to have the application approved,

(B) if the Secretary has determined that the application is not approvable and all legal appeals have been exhausted,

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69. *Id.* at 44,612, ¶ 78 (“The [FDA] has on numerous occasions testified before Congress that current statutory provisions prevent disclosure of useful information . . . The [FDA] cannot change the law, and thus is bound by the present provisions until Congress acts.”); *id.* at 44,614, ¶ 90 (“The Commissioner concludes that it is Congress which weighs the need for the release of certain information against the need for retaining it as confidential.”).

70. See Hatch-Waxman Act, *supra* note 9.

71. Extensive scholarship covers this topic. For a competent summary, see Holly Soehnge, *The Drug Price Competition and Patent Term Restoration Act of 1984: Fine-Tuning the Balance Between the Interests of Pioneer and Generic Drug Manufacturers*, 58 FOOD & DRUG L.J. 51 (2003) (explaining the purpose of the Hatch-Waxman Act as an attempt to correct the perceived imbalances between brand name manufacturers and generics while decrying the abilities of both sides to bypass the Act’s strictures).

72. See 21 U.S.C. § 355(j) (2006).

73. O’Reilly, *supra* note 2, at 21; Eisenberg, *supra* note 7, at 381.

(C) if approval of the application . . . is withdrawn and all legal appeals have been exhausted,

(D) if the Secretary has determined that such drug is not a new drug, or

(E) upon the effective date of the approval of the first application under subsection (j) of this section which refers to such drug or upon the date upon which the approval of an application under subsection (j) of this section which refers to such drug could be made effective if such an application had been submitted.<sup>74</sup>

These provisions require the disclosure of research data when an NDA is not approvable<sup>75</sup> or becomes abandoned,<sup>76</sup> or upon the approval of a generic drug which depended on original research data, or at the earliest date such a generic could have been approved.<sup>77</sup> In other words, research data must be disclosed when it no longer constitutes an anti-competitive barrier. On the face of the legislative language, one might have thought that Congress had solved the problem—as soon as there was no longer any commercial need for secrecy, all research data would be publicly available. Especially in light of the FDA's previous request that Congress “weigh the need for [research data disclosure],”<sup>78</sup> it seemed that Congress had decided in favor of disclosure. The manufacturers viewed the Hatch-Waxman Act as an underhanded attempt to implement disclosure regime by “disclosure advocates.”<sup>79</sup> Despite admittedly acting with that goal, Congress was not as clear about disclosure as it could have been. At the last moment, the sponsors of the Hatch-Waxman Act, perhaps due to a fundamental disagreement about the nature and role of trade secrets in disclosure policy,<sup>80</sup> inserted an exception to the general rule of disclosure.<sup>81</sup> Secrecy would continue to operate if a manufacturer could show that “extraordinary circumstances” applied to the release of research data. This

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74. 21 U.S.C. § 355(l)(1) (2006) (emphasis added).

75. *Id.* at § 355(l)(1)(B), § 355(l)(1)(D).

76. *Id.* at § 355(l)(1)(A), § 355(l)(1)(C).

77. *Id.* at § 355(l)(1)(E).

78. FDA Regulations, *supra* note 53, at 44,614, ¶ 90.

79. *See* O'Reilly, *supra* note 2, at 16 (“Advocates of drug data disclosure acted quietly in attaching a full disclosure provision, buried amidst many unrelated and controversial provisions, to the pending legislation.”).

80. *Id.* at 18 (“Maneuvering in a field of ambiguity and mutual mistrust, the drafters of the 1984 Act settled upon the term ‘extraordinary circumstances’ on the false impression that it represented current FDA policy on data disclosure of live data.”).

81. 21 U.S.C. § 355(l)(1) (2006) (Data “shall be made available to the public, upon request, *unless extraordinary circumstances are shown.*”) (emphasis added).

language was “unexpected and ambiguous.”<sup>82</sup> The ambiguity allowed the argument that *any* residual value a manufacturer could derive from research data, even *after* the FDA approved a generic version of a drug, constituted extraordinary circumstances. Senator Hatch bolstered this argument by noting that this reading of “extraordinary circumstances” simply recapitulated long-standing FDA policy.<sup>83</sup> The FDA confirmed this position. The FDA Commissioner declared that the “extraordinary circumstances” standard was identical to that for Exemption 4.<sup>84</sup> Thus the exception swallowed the rule.

The current state of the law rests on what “trade secrets” and “confidential information” mean within the context of FOIA Exemption 4. Therefore, I turn to the courts’ contribution to our understanding of these terms.

### III. COURTS’ STRUGGLE TO ELUCIDATE THE SCOPE OF TRADE SECRETS UNDER THE FOIA

#### A. A Trade Secret by Any Other Name Would Smell Just as Sweet

The Supreme Court has held that Exemption 4 is not an absolute bar to disclosure.<sup>85</sup> Rather, it only limits an agency’s obligation to disclose.<sup>86</sup> The Court instructed lower courts to balance the private and public interest in determining whether disclosure is appropriate under the FOIA exemptions.<sup>87</sup> In spite of *Chrysler Corp.*’s balancing approach, lower

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82. O’Reilly, *supra* note 2, at 17.

83. *Id.* at 19–22. Interestingly, this colloquy seems to have taken place after the Senate voted on and approved the final version of the Act.

84. 130 CONG. REC. S10981–90 (daily ed. Sept. 12, 1984) (letter from Frank Young, FDA Commissioner to Senator Orrin Hatch.) (“[T]he meaning of ‘extraordinary circumstances’ in the bill . . . is meant to conform the agency’s disclosure standard with that of exemption (4).”) Part III.A, *infra*, investigates how courts have contributed to the development of the agency’s disclosure standard for confidential information.

85. See *Chrysler Corp. v. Brown*, 441 U.S. 281, 291 (1979) (“Chrysler contends that the nine exemptions in general, and Exemption 4 in particular, reflect a sensitivity to the privacy interests of private individuals and nongovernmental entities. That contention may be conceded without inexorably requiring the conclusion that the exemptions impose affirmative duties on an agency to withhold information sought. In fact, that conclusion is not supported by the language, logic, or history of the Act.”).

86. *Id.* at 293 (“[T]he FOIA by itself protects the submitters’ interest in confidentiality only to the extent that this interest is endorsed by the agency collecting the information.”).

87. *Id.* (“Enlarged access to governmental information undoubtedly cuts against the privacy concerns of nongovernmental entities, and as a matter of policy some balancing and accommodation may well be desirable.”) This conclusion is also supported by the Court’s approach in evaluating other FOIA exemptions. See, e.g., *Nat’l Archives & Records Admin. v. Favish*, 541 U.S. 157, 172 (2004) (“The statutory direction that the information not be

courts have not adequately considered the public interest in disclosure when considering attempts to access research data held by the FDA.<sup>88</sup> Courts have been willing to compel disclosure only for records that are directly relevant to opening governmental actions to public scrutiny. Since research data is inextricably linked with private parties' interests, courts have failed to undertake the balancing of interests that a plausible reading of *Chrysler Corp.* would suggest.<sup>89</sup>

Part of the difficulty in correctly gauging the proper scope of Exemption 4 begins with the fact that the statute does not define the term "trade secret." The lack of a definition of "trade secret" was the central dispute in a case involving a FOIA request that the nonprofit consumer advocacy group Public Citizen submitted to the FDA for research data concerning intraocular lenses ("IOL").<sup>90</sup> Noting that the common law supplied two different definitions for "trade secret," the D.C. Circuit rejected the broader of the two definitions set forth by the Restatement of Torts, adopted by the FDA,<sup>91</sup> and sanctioned by the district court.<sup>92</sup> To the D.C. Circuit, this broad definition, where "a trade secret can be any information used in a business which gives competitive advantage," meant that "there is little or no information left that could qualify as commercial or financial information under the second category of the exemption without also qualifying as a trade secret."<sup>93</sup> The court instead adopted a narrower definition of a trade secret.<sup>94</sup> In doing so, it focused on the private law context in which the broader definition evolved, correctly noting that "the *Restatement* definition, tailored as it is to protecting

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released if the invasion of personal privacy could reasonably be expected to be unwarranted requires the courts to balance the competing interests in privacy and disclosure.").

88. See Janene Boyce, *Disclosure of Clinical Trial Data: Why Exemption 4 of the Freedom of Information Act Should Be Restored*, 2005 DUKE L. & TECH. REV. 3, 16–18 (2005).

89. Peter Lurie & Allison Zieve, *Sometimes the Silence can be Like the Thunder: Access to Pharmaceutical Data at FDA*, 69 LAW & CONTEMP. PROBS. 85, 91 (2006) ("The confidential commercial exemption does not authorize the courts to weigh the public interest in disclosure against the potential competitive harm that disclosure may cause.").

90. Pub. Citizen Health Research Group v. Food & Drug Admin., 704 F.2d 1280, 1282–86 (D.C. Cir. 1983) [hereinafter *Public Citizen I*].

91. *Id.* at 1284 n.7 (citing 4 RESTATEMENT (FIRST) OF TORTS § 757 cmt. b (1939)) (defining a trade secret as information that may "consist of any formula, pattern, device or compilation of information which is used in one's business, and which gives him an opportunity to obtain an advantage over competitors who do not know or use it.").

92. *Id.* at 1287–88.

93. *Id.* at 1289 (quoting the House Comm. on Government Operations, *Freedom of Information Act Requests for Business Data and Reverse-FOIA Lawsuits*, H.R. REP. NO. 95-1382, 95th Cong., 2d Sess. 16 (1978)).

94. *Id.* at 1288 ("[A] secret, commercially valuable plan, formula, process, or device that is used for the making, preparing, compounding, or processing of trade commodities and that can be said to be the end product of either innovation or substantial effort."). The court apparently adopted this view of a trade secret from Canadian law. O'Reilly, *supra* note 2, at n.69.



businesses from breaches of contract and confidence by departing employees and others under fiduciary obligations is ill-suited for the public law context in which FOIA determinations must be made.”<sup>95</sup> In a footnote, the court further elaborated on balancing the public need for disclosure with private interests, concluding that “lumping health and safety testing data with all other types of proprietary information is inherently suspect.”<sup>96</sup>

After holding that research data were not “trade secrets” within the meaning of Exemption 4, the court evaluated whether such data were “commercial or financial . . . and privileged or confidential.”<sup>97</sup> The court rejected Public Citizen’s argument that the exemption for commercial or financial information should be limited to information which in fact revealed commercial operations, holding that “commercial,” within its ordinary meaning, extended to “documentation of the health and safety experience of [manufacturers’] products.”<sup>98</sup> The relevant question then became “whether the commercial information submitted to the FDA by the IOL manufacturers [was] ‘confidential’ within the meaning of Exemption 4.”<sup>99</sup> In deciding this issue, the court noted that case law has developed a two-prong test, based on whether disclosure is likely either: “(1) to impair the government’s ability to obtain necessary information in the future, or (2) to cause substantial harm to the competitive position of the person from whom the information was obtained.”<sup>100</sup> Only the second prong of the test applies with respect to research data since manufacturers must disclose such data in order to obtain marketing approval. The court held that because the manufacturers had provided depositions which documented potential competitive injury, testimony which Public Citizen was not able to refute, Exemption 4 still applied. Therefore, summary judgment in favor of the manufacturers was appropriate.<sup>101</sup>

With the *Public Citizen I* decision, the D.C. Circuit adopted a definition of confidentiality very close, if not identical, to the broader definition of trade secret that it had just rejected in the same opinion. Under this standard, manufacturers should almost always be able to show that release of research data will cause them competitive harm. The court qualified its definition of substantial harm as “harm flowing from

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95. *Public Citizen I*, *supra* note 90, at 1289.

96. *Id.* at 1288 n.25.

97. *Id.* at 1290.

98. *Id.*

99. *Id.*

100. *Id.* at 1290–91.

101. *Id.* at 1291.

the affirmative use of proprietary information *by competitors*,<sup>102</sup> which is arguably somewhat narrower than the Restatement definition of a trade secret. In the context of research data, however, this is a distinction without a difference, since existence of competitors who can derive some commercial benefit from data access is a given in the pharmaceutical industry. The court had started its inquiry with the question of whether the trade secret definition was too broad.<sup>103</sup> The question after *Public Citizen I* is whether there is any research data left that could qualify neither as “commercial or financial information” nor as “a trade secret.” Under the confidentiality standard the court adopted, the answer appears to be no.

Lower court decisions applying the confidentiality standard illustrate the ease with which manufacturers can meet the competitive harm requirement. In one such decision, the district court, following *Public Citizen I*, held that research data was exempt from a FOIA request under the second prong of Exemption 4.<sup>104</sup> The court had no difficulty in concluding that “actual competition in the drug business is evident,” because “only a small fraction” of drug applications would “ultimately receive approval from the FDA,” and that “actual competition [existed] among manufacturers seeking approval to market the drug in ‘generic’ form” even after approval.<sup>105</sup> The court based its refusal on the FDA’s declaration that a competitor in possession of raw research data and results “could also use the information to submit its own NDA to FDA for the same or similar drug product. This would therefore likely cause substantial competitive harm to Lilly.”<sup>106</sup> Since these set of circumstances describe almost every pending IND or NDA, any manufacturer should be able to resist disclosure by asserting that some competitor can derive some benefit from accessing its research data. Thus, research data easily becomes confidential and therefore exempt from disclosure.

But what of the balancing of interests encouraged by the Court in *Chrysler Corp.*? Courts applying the confidentiality standard will often stop after competitive harm in disclosure has been established for the manufacturer. The magnitude of that harm against the weight of the pub-

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102. *Id.* at 1291, n.30.

103. *Id.* at 1289 (“[T]here is little or no information left that could qualify as commercial or financial information under the second category of the exemption without also qualifying as a trade secret.”) (quoting the House Comm. on Government Operations, *Freedom of Information Act Requests for Business Data and Reverse-FOIA Lawsuits*, H.R. REP. NO. 95-1382, 95th Cong., 2d Sess. 16 (1978)).

104. *Citizens Comm’n on Human Rights v. FDA*, 1993 WL 1610471, at \*9, ¶¶ 59–60 (C.D. Cal. 1993).

105. *Id.* at \*8, ¶ 55.

106. *Id.* at \*9, ¶ 59.

lic interest in disclosure is therefore often not considered by courts. Even when they purport to balance it against private interests, courts fail to consider the magnitude of the public interest. For example, in *Public Citizen Health Research Group v. Nat'l Inst. of Health*, the D.C. District Court refused to uphold the plaintiff's FOIA request for information on royalties the National Institute of Health (NIH) received by licensing its inventions to pharmaceutical companies since disclosing such information would cause competitive harm to the companies.<sup>107</sup> Disclosing royalty information may indeed have caused competitive harm to the companies that licensed technology from the NIH. The court, despite claiming that it was engaging in "a rough balancing . . . between private and public interests,"<sup>108</sup> nonetheless failed to consider whether the plaintiff's asserted interest in "evaluat[ing] whether the government is receiving a reasonable rate of return on the taxpayers' investment in the valuable research done by the NIH"<sup>109</sup> would be a sufficient counterargument to the private interest in secrecy. Moreover, the court ruled that the private interests prevailed on its conclusion that "the agency has substantially demonstrated that the effectiveness of the licensing program would be critically impaired if the royalty information was released."<sup>110</sup> The effectiveness of the NIH's licensing program implicates public as well as private interests, a point which the court did not address. The court ultimately failed to explain how this complex set of interests—the NIH's interest in maintaining its licensing program, pharmaceutical companies' interests in keeping the amount of royalties they pay to the NIH secret, and the public interest in ensuring a fair return for taxpayer financed technologies licensed to private companies—interacted or balanced with each other. The confidentiality test thus appears to be incapable of balancing interests because it focuses extensively on the nature and magnitude of competitive harm to private interests and fails to consider the extent or magnitude of the public interest.<sup>111</sup>

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107. *Pub. Citizen Health Research Group v. Nat'l Inst. of Health*, 209 F.Supp. 2d 37, 51 (D.D.C. 2002) ("[T]he release of negotiated royalty terms of contracts . . . would cause substantial competitive harm to submitting companies.")

108. *Id.* at 45.

109. *Id.* at 41.

110. *Id.* at 54.

111. *See supra* note 85. *See also* Margaret Witherup Tindall, *Breast Implant Information as Trade Secrets: Another Look at FOIA's Fourth Exemption*, 7 ADMIN. L.J. AM. U. 213, 221–31 (1993) (detailing the role of the trade secrets doctrine in preventing safety information on breast implants from reaching the public, even after the FDA received thousands of complaints about the implants).

B. Courts' Construction of the Hatch-Waxman  
Act's Disclosure Requirement

The arguably independent mandate for disclosure in the Hatch-Waxman Act has become entangled with the FOIA and Exemption 4,<sup>112</sup> but the “extraordinary circumstances” exception, though asserted, has not been judicially tested.<sup>113</sup> Moreover, the FDA does not apply the extraordinary circumstances exception evenly. For example, the Hatch-Waxman Act mandates disclosure of “abandoned NDAs,”<sup>114</sup> as well as NDAs for which a generic substitute has been or could theoretically be approved.<sup>115</sup> The FDA takes the position that the latter are not disclosable because access to approved or pending NDAs constitutes competitive harm and thus is an extraordinary circumstance. But in *Davis v. Food and Drug Administration*, the FDA “conceded the disclosability of [abandoned NDAs],”<sup>116</sup> and settled the case without arguing that abandoned NDAs contained residual value. This result may well be due to the ability of a manufacturer “to make broad claims that it has not abandoned its efforts with respect to an NDA and thereby to thwart disclosure.”<sup>117</sup> NDA approval statistics support this observation. Only 97 of 1393 total NDA applications between FY 1993 and FY 2005, or less than 7%, were withdrawn NDAs.<sup>118</sup> For comparison, there were 265 non-approvable NDAs in the same period, about 19%.<sup>119</sup> Since the decision to withdraw is at the discretion of the manufacturer, an NDA is likely to be abandoned only when the manufacturer has presumably decided that its research data content has no residual value. A manufacturer therefore sends a strong signal that they will be unlikely to contest the disclosure of research data from abandoned NDAs.

On the other hand, the FDA resisted Public Citizen’s attempt to rely on the disclosure provisions of section 355(l) to compel the FDA to release “documents concerning pre-clinical and clinical studies for all prescription drugs which had a discontinuance of the clinical trials because of death or serious injury of patients or because of safety concerns

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112. See *supra* Part II.B.

113. O’Reilly, *supra* note 2, at 24.

114. 21 U.S.C. § 355(l)(1)(A)–(D) (2006).

115. *Id.* at § 355(l)(1)(E).

116. Lurie & Zieve, *supra* note 89, at 94.

117. *Id.*

118. CDER, CDER First Action Performance for Original NDAs, <http://www.fda.gov/CDER/rdm/histnda.htm> (last visited Jan. 17, 2007).

119. Of those, 165 (11.8% of total applications) cluster in the time period between FY 1993 and 1998.

from pre-clinical studies.”<sup>120</sup> The FDA first refused to even acknowledge whether it had any such records,<sup>121</sup> and Public Citizen sued.<sup>122</sup> After the district court ordered the FDA to “retrieve the INDs identified and review them for responsiveness,”<sup>123</sup> the agency found only fourteen out of the 230 INDs filed within the requested time frame as responsive, but it denied the request under Exemption 4.<sup>124</sup> The FDA asserted that “certain information consisted of confidential commercial and/or trade secret data and information, the public release of which would cause substantial competitive harm to the sponsors of these INDs.”<sup>125</sup> The district court held that the FDA and the remaining two manufacturers had established that disclosure “would likely cause substantial competitive harm,” but it also held that the manufacturers had abandoned the INDs.<sup>126</sup> After engaging in a lengthy analysis and concluding that the Hatch-Waxman Act amendments required disclosure of research data contained in abandoned INDs, the district court ordered their release.<sup>127</sup>

After losing in the district court, the FDA and Schering, one of the manufacturers, appealed to the D.C. Circuit. The FDA argued that Schering had provided evidence that it was using the research data contained in the abandoned IND for a subsequent drug application. The FDA took the position that Schering had proved competitive harm, which in turn triggered the “extraordinary circumstances” exception<sup>128</sup> and prevented the FDA from releasing the INDs. Public Citizen asserted a public interest in preventing re-testing of a drug “that had previously been found harmful to human health.”<sup>129</sup> Public Citizen also argued that Schering’s assertion of competitive harm would apply to “any drug sponsor who discloses research on an abandoned drug,”<sup>130</sup> and thus there was nothing extraordinary about Schering’s circumstances. The court did not reach

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120. Pub. Citizen Health Research Group v. Food & Drug Admin., 185 F.3d 898, 901 (D.C. Cir. 1999) [hereinafter *Public Citizen II*].

121. Brief of Appellee Public Citizen Health Research Group at 7, Public Citizen Health Res. Group v. Food & Drug Admin., 185 F.3d 898 (D.C. Cir. 1999) (Nos. 98-5161, 98-5162) [hereinafter Public Citizen Brief].

122. *Pub. Citizen Health Research Group v. Food & Drug Admin.*, 997 F. Supp. 56, 59 (D.D.C. 1998). Subsequently, four of the six manufacturers who had responsive INDs settled with Public Citizen and agreed to release their research data.

123. Public Citizen Brief, *supra* note 121, at 7.

124. Final Brief for Appellant Food and Drug Administration at 4, Public Citizen Health Research Group v. Food & Drug Admin., 185 F.3d 898 (D.C. Cir. 1999) (Nos. 98-5161, 98-5162), 1999 WL 34833581 [hereinafter FDA Brief].

125. *Id.*

126. *Pub. Citizen Health Research Group*, *supra* note 122, at 65–66.

127. *See id.* at 66–70.

128. FDA Brief, *supra* note 124, at 4.

129. Public Citizen Brief, *supra* note 121, at 9.

130. *Id.*

the question of what Congress meant by “extraordinary circumstances” because Schering made the threshold argument that an IND should be distinguished from an NDA and that Section 355(l) applied only to NDAs.<sup>131</sup> Interestingly, even though the FDA did not agree,<sup>132</sup> the court engaged in a “plain meaning” construction of Section 355(l), accepted Schering’s argument, and proceeded to distinguish INDs from NDAs because “an IND . . . is submitted under subsection (i), not subsection (b).” The court thus limited the application of Section 355(l) disclosure to NDAs.<sup>133</sup>

Public Citizen also argued that the FOIA trade secret exemption should not apply to abandoned INDs and attempted to convince the court to balance the public interest “to determine whether the FDA was adequately protecting trial subjects and to allow competitors to avert potentially risky trials of related drugs.”<sup>134</sup> The court rejected that argument as well and adhered to a narrow construction of public interest.<sup>135</sup> The court disallowed disclosure of all INDs except for one, holding that there is no public interest in releasing Schering’s research data so that “other drug companies will not conduct risky clinical trials of the drugs that Schering has abandoned,” and because release of such data was not “related to ‘what the government is up to.’”<sup>136</sup> The court flatly refused to “consider Public Citizen’s assertion that disclosure would in fact prevent the exposure of human beings to a health risk.”<sup>137</sup>

*Public Citizen II* exemplifies the burden confidentiality places on the FDA, tasked with guarding the public interest, and courts that are supposed to interpret that interest’s scope in reference to private interests

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131. Final Brief of Appellant Schering Corporation at 13, *Pub. Citizen Health Research Group v. Food & Drug Admin.*, 185 F.3d 898 (D.C. Cir. 1999) (Nos. 98-5161, 98-5162), 1999 WL 34833585.

132. Public Citizen Brief, *supra* note 121, at 12.

133. *Public Citizen II*, *supra* note 120, at 902 (“[Section] 355(l) by its terms applies only to ‘safety and effectiveness data and information’ submitted in an NDA. Therefore, even if the agency had interpreted the phrase ‘subsection (b)’ in § 355 to include information submitted in an IND, we could not defer to that interpretation.”). But when the FDA was formulating its FOIA regulations, manufacturers requested, and the FDA agreed, that INDs should be treated similarly to an NDA, specifically in order to prevent disclosure following IND termination. *See supra* note 65 and accompanying text.

134. Lurie & Zieve, *supra* note 89, at 91.

135. *Public Citizen II*, *supra* note 120, at 904 (“We reject Public Citizen’s proposal because a consequentialist approach to the public interest in disclosure is inconsistent with the ‘balance of private and public interests’ the Congress struck in Exemption 4.” (quoting *Critical Mass Energy Project v. Nuclear Regulatory Comm’n*, 975 F.2d 871, 872 (D.C. Cir. 1992) (en banc)).

136. *Id.* (quoting *Dep’t of Justice v. Reporters Comm. for Freedom of Press*, 489 U.S. 749, 773 (1989)).

137. *Id.* at 905.

and the agency's policies. For example, when the court accepted Schering's argument that an IND is distinct from an NDA because it is filed under a different subsection of Section 355, it did not follow the FDA's long-standing practice, which has been to treat an IND and an NDA incorporating that IND as one continuous document.<sup>138</sup> Moreover, the court was quick to dismiss the public interest in disclosure, perhaps because the agency never articulated the strength of the disclosure interest. The concurring judge emphasized the conclusory nature of the court's dismissal and pointed out that a balancing of interests should have been the appropriate analysis.<sup>139</sup> At the same time, the court accepted another long-standing FDA policy to accord research data confidential status. In fact, this is one FDA policy that no court has been willing to disturb. At least to the extent *Public Citizen II* embodies the courts' approach, it exhibits altogether too high a deference to commercial, private interests at the expense of the public interest.

### C. *The Exceptions Prove the Rule—Instances of Court Ordered Disclosure*

Some courts have compelled the FDA to disclose research data, but have narrowly focused their decisions on a showing of a lack of private harm. The *Public Citizen II* court ordered the release of one IND, which was for “[an] isomer making up a prescription medicine currently marketed by Schering.”<sup>140</sup> The court's cursory conclusion that such disclosure would not result in substantial competitive harm rested on simply rejecting Schering's competitive harm argument. It is not clear why the competitive harm argument failed for this particular IND, since Schering made all of the arguments manufacturers usually make to establish substantial competitive harm.<sup>141</sup> Despite being poorly reasoned,

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138. See FDA Regulations, *supra* note 53, at 44,634, ¶ 248 (responding to a comment that IND data should not be released upon the approval of an NDA application, the FDA stated that “the IND and NDA are regarded as one continuous process. Indeed, the NDA incorporates the IND. Accordingly, upon the filing or approval of an NDA the material in the IND has the same status as the material in the NDA.”)

139. *Public Citizen II*, *supra* note 120, at 908 (Garland, J., concurring) (“Nor is this a case where the legal conclusion the court has reached is indisputable. To the contrary, although no party cited the relevant precedent on this point, we have twice held that Exemption 4 requires a balancing of the interest in nondisclosure ‘against the public interest in disclosure.’”) (citations omitted).

140. *Id.* at 906.

141. See *id.* (Schering argued that “disclosure would reveal substantial basic research, as well as disease models that have been developed by Schering at a great expense, that toxicology data have significant value beyond the compound under investigation, and would be applicable to any drug product any of whose metabolites were identical or similar to those of [their IND] and other drugs of a similar chemical type. [They further argued] that clinical

the court's decision to release that specific IND nevertheless illustrates the general rule: disclosure is only appropriate under a complete lack of competitive harm. It may force disclosure of basic research information from clinical trials of drugs in cases where the drugs' patent terms may have expired or for any other drug for which the market is already competitive. But that opening may also prove too narrow. A party resisting disclosure could plausibly argue that any disclosure under the *Public Citizen II* standard should be limited to the facts of the case, i.e., isomers of currently marketed drugs and only basic research data.

In *Teich*, the court approved the disclosure of animal studies by the manufacturer of silicone gel breast implants.<sup>142</sup> The court reasoned that such disclosure would not cause substantial harm to the competitive position of the manufacturer due to the fact that the plaintiff requested "only protocols and positive results" and "exclude[d] information concerning [the manufacturer's] silicone gel product specifications, marketing strategies, and names of individuals and independent contractors who participated in studies."<sup>143</sup> Moreover, the requested animal studies had been prepared for pre-approval and were twenty years old. The *Teich* court did engage in a more vigorous balancing of the public interest in disclosure with Dow Corning's interest in confidentiality, focusing on the risk to public health posed by the public's inability to access research data.<sup>144</sup> Ultimately, only an understanding that older studies are more likely to be suitable for disclosure allowed the court to broadly construe the public interest.

This Court also notes that most of the studies at issue here were prepared as much as 20 years ago. It can hardly be claimed that Dow Corning's competitors can use this information to any substantial extent in preparing current PMA applications. It is unlikely that competitors would look in any meaningful way to studies undertaken by Dow Corning over 20 years ago in order to satisfy 1990 testing requirements. . . . Given the explosion of technology in recent years, this Court cannot accept, absent sub-

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protocols also have applicability beyond the specific drug being tested and that disclosure would have substantial commercial value to any company attempting to develop cardiovascular therapies generally.") (internal punctuation omitted).

142. *Teich v. Food & Drug Admin.*, 751 F. Supp. 243, 255 (D.D.C. 1990).

143. *Id.* at 253.

144. *Id.* ("To argue that this type of information is confidential suggests that, in order to protect whatever marginal commercial benefit Dow Corning may get from having independently discovered certain risks, other manufacturers be permitted to blindly put out potentially damaging products. Certainly Dow Corning, as a good citizen, would not risk the public health in this manner. The benefit of releasing this type of information far outstrips the negligible competitive harm that defendants allege.")



stantiation, that studies from the 1960's and 1970's are the most productive route for Dow Corning's competitors to pursue.<sup>145</sup>

Similarly, the D.C. District Court, following *Public Citizen II*, concentrated on whether disclosure would “[be] likely to cause substantial harm to Searle’s competitive position,” in ordering the release of underlying raw patient data to a graph about the safety effects of Celebrex.<sup>146</sup> The FDA had already released a graph summarizing the data, including the mean and the standard error, but had withheld the underlying raw data partially on the grounds that it “could help a current or potential competitor to develop a research program or support a competitor’s own NDA for COX-2 Inhibitors.”<sup>147</sup> The court pointed out that Searle, as an intervening defendant, had not offered evidence to rebut Public Citizen’s affidavit that the raw data “would *not* be useful in assisting other drug companies’ product development efforts.”<sup>148</sup> Pointing out that Searle’s “assertions about the harm that could result from disclosing raw patient data supporting its Celebrex NDA are strikingly similar to Schering’s assertions about the fifth IND [in *Public Citizen II*],”<sup>149</sup> the court ordered the release of raw patient data. Once again, the court’s decision seems to have turned entirely on whether Searle would suffer any competitive harm, and not whether the availability of raw data would allow a more sound analysis of the drug’s safety or efficacy.

Research data access is currently possible under the FOIA only if an applicant can show a lack of “competitive harm.” Even where there is no competitive harm, courts have often further limited disclosure to basic research information, positive results, and/or older studies. Limiting disclosure in this way is likely to minimize competitive harms, which aligns with the approach courts have taken so far by concentrating mostly on the private dimension of disclosure. But this type of research data ironically contains little value for advancing the public interests that I have delineated so far. For example, limited access to older research data is unlikely to substantially improve data quality since research data generated several decades ago are likely to be as devoid of current scientific value as they are of the potential to cause competitive harm. Thus, because courts rarely consider the magnitude of the public interest at stake, FOIA requests remain a poor choice by which to obtain disclosure of relevant research data.

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145. *Id.* at 253–54.

146. *Pub. Citizen Health Research Group v. Food & Drug Admin.*, No. Civ.A. 99-0177, 2000 WL 34262802, at \*4 (D.D.C. Jan. 19, 2000).

147. *Id.* at \*2.

148. *Id.* at \*3.

149. *Id.* at \*2.

#### IV. THE STATE OF THE LAW WITH RESPECT TO RESEARCH DATA DISCLOSURE—ADDITIONAL CONSIDERATIONS

##### A. *The FTSA May Constitute a Separate Barrier to Disclosure*

Even when disclosure may be appropriate under the FOIA, persons seeking disclosure have to overcome the FTSA's constraints on disclosure of trade secrets.<sup>150</sup> Unlike Exemption 4, the FTSA affirmatively bars release of information "in a manner not authorized by law."<sup>151</sup> This requirement cannot be overcome by any run-of-the-mill regulation. The Court has held that the FOIA is such a run-of-the-mill regulation.<sup>152</sup> Under this interpretation, the scope of the FTSA is "at least co-extensive with that of Exemption 4 of FOIA, and that, in the absence of a regulation effective to authorize disclosure, the Act prohibits [disclosure that] falls within Exemption 4."<sup>153</sup> In order for a regulation to qualify as authorizing law under the FTSA, the pro-disclosure party must "establish a nexus between the regulations and some delegation of the requisite legislative authority by Congress."<sup>154</sup> In requiring additional specific authority for disclosure under the FTSA, the Court erected another barrier against disclosure even for information disclosure authorized under the FOIA. This barrier may not be quite as high a hurdle as it would seem, however. In a footnote, the *Chrysler Corp.* court stated that the FDCA's labeling requirements contained "explicit" legislative authority for disclosure.<sup>155</sup> Thus, the Court at least acknowledged some recognition for the sufficiency of agency authority under the FDCA in a similar context. Moreover, *Public Citizen I*, by holding that research data were not trade secrets, arguably cabined the FTSA's flat prohibition against disclosing trade secrets in the context of research data disclosure.<sup>156</sup>

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150. McGarity, *supra* note 24, at 859–60.

151. See 18 U.S.C. § 1905 ("Whoever, being an officer or employee of the United States or of any department or agency thereof . . . publishes, divulges, discloses, or makes known in any manner or to any extent *not authorized by law* any information coming to him in the course of his employment or official duties . . . which information concerns or relates to the trade secrets, [etc.] to be seen or examined by any person except *as provided by law*; shall be fined under this title, or imprisoned not more than one year, or both; and shall be removed from office or employment.") (emphasis added).

152. *Chrysler Corp. v. Brown*, 441 U.S. 281, 303–04 (1979) ("Government cannot rely on the FOIA as congressional authorization for disclosure regulations that permit the release of information within [the FTSA].")

153. *CNA Financial Corp. v. Donovan*, 830 F.2d 1132, 1151–52 (D.C. Cir. 1987).

154. *Chrysler Corp.*, 441 U.S. at 304.

155. *Id.* at 306 n.38.

156. *Public Citizen I*, *supra* note 90, at 1289 n.25.

B. *Constitutional Takings Doctrine Has Limited Applicability in Preventing Research Data Disclosure*

Even after arguments for trade secret exemptions and restrictions under federal law fail, research data owners are likely to argue that revelation of such data constitutes a “taking” of their property which justifies compensation.<sup>157</sup> In fact, property arguments have been made frequently in trade secret cases, despite the body of scholarship arguing against according trade secrets all the attributes of property.<sup>158</sup> The Supreme Court confirmed that “trade secrets have many of the characteristics of more tangible forms of property”<sup>159</sup> and “property right is protected by . . . the Fifth Amendment.”<sup>160</sup> At the same time, the Court limited the scope of protection by holding that a taking occurs when the government “interferes with reasonable investment-backed expectations.”<sup>161</sup> With respect to any health, safety, and environmental data, such an expectation is only justified in the presence of an express promise of confidentiality in the regulatory regime.<sup>162</sup> In doing so, the Court rejected Monsanto’s argument that the FTSA constituted a promise of confidentiality. Under the *Ruckelshaus* standard, “as long as [an applicant] is aware of the conditions under which the data are submitted, and the conditions are rationally related to a legitimate government interest, a voluntary submission of data . . . in exchange for the economic advantages of a registration can hardly be called a taking.”<sup>163</sup> The *Ruckelshaus* decision thus undermines the argument that research data disclosure would constitute a taking.

V. SHIFTING THE RATIONALE: THE SCIENTIFIC ARGUMENT FOR DISCLOSURE

A. *Breakthroughs in Biotechnology and Informatics Have Transformed Data Generation and Revolutionized Data Analysis*

Phenomenal paradigmatic shifts have taken place in the life sciences since the FDA promulgated its disclosure regulations in 1974.<sup>164</sup> With

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157. U.S. CONST. amend. V. (“[P]rivate property [shall not] be taken for public use, without just compensation.”).

158. See Lyndon, *supra* note 16, at 496.

159. *Ruckelshaus v. Monsanto Co.*, 467 U.S. 986, 1002 (1984).

160. *Id.* at 1004.

161. *Id.* at 1005 (quoting *Pruneyard Shopping Ctr. v. Robins*, 447 U.S. 74, 83 (1980)).

162. See *id.* at 1008–10.

163. *Id.* at 1007.

164. A very brief, incomplete, and superficial list of some milestone achievements and technological advances behind the paradigm shifts of the last few decades follows. In 1974,

respect to data generation and drug development, all of the relevant life sciences sub-disciplines have undergone significant change. A plethora of theoretical and technological breakthroughs have enabled the genesis and rapid adoption of disciplines such as genomics and proteomics, which have transformed the ways in which scientists generate and analyze data. Biotechnological advances have tremendously increased the size, sophistication, and information content of data. Laboratories across the world are generating even greater quantities of data by conducting large scale expression profiling experiments aimed at simultaneously measuring thousands of molecular species critical to the workings of a cell, such as DNA, RNA and proteins.<sup>165</sup> The life sciences have shifted focus from analyzing single genes to functionally related networks of genes or proteins.<sup>166</sup> Such high throughput experiments can be crucial to our understanding of how drugs interact with our bodies at a molecular level.

The scientific community is also beginning to develop new tools that facilitate comparisons across multiple published studies in order to leverage the added value of comparative data analysis.<sup>167</sup> An entirely new field, bioinformatics, has emerged to meet the challenge of dealing with the burgeoning amount of biological information by coupling “biology, computer science, and information technology,” and “enabl[ing] the discovery of new biological insights as well as to create a global perspective from which unifying principles in biology can be discerned.”<sup>168</sup> Computational biology and data mining technologies now allow “development of new algorithms (mathematical formulas) and statistics with which to assess relationships among members of large data sets,” and ultimately, “a more global perspective in experimental design.”<sup>169</sup>

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the human genome had not yet been sequenced (nor almost any of the other model organisms' genomes), no mammal had been cloned, site specific mutations had not yet been induced, microarray technology did not exist, deoxyribonucleic acid (DNA) and protein sequencing methods were in their infancy, as was the application of robotics to life sciences. Most of the commonly used research tools of today, such as ribonucleic acid (RNA) interference and the polymerase chain reaction (PCR), had not yet been invented. For a timeline of advances in biotechnology, see Biotechnology Industry Organization, Time Line, <http://www.bio.org/speeches/pubs/er/timeline.asp> (last visited Feb. 26, 2009).

165. See, e.g., Mike Tyers & Matthias Mann, *From Genomics to Proteomics*, 422 NATURE 198 (Mar. 13, 2003).

166. E.g., Katherine M. Nolan-Stevaux, *Open Source Biology: A Means to Address the Access & Research Gaps?*, 23 SANTA CLARA COMPUTER & HIGH TECH. L.J. 271, 281–82 (2007).

167. See, e.g., Gong-Hong Wei, et al., *Charting Gene Regulatory Networks: Strategies, Challenges and Perspectives*, 381 BIOCHEM. J. 1, 7–9 (2004).

168. Nat'l Ctr. for Biotechnology Info., *Bioinformatics*, <http://www.ncbi.nlm.nih.gov/About/primer/bioinformatics.html> (last visited Apr. 17, 2010).

169. *Id.*

Bioinformatics applications are not limited to data generated by modern methodology. Meta-analyses and systematic reviews of large datasets, i.e., comparisons of large numbers of datasets for new insights unavailable from analyzing any of them singly, may lead to new discoveries regardless of the type of data. Any research data submitted to the FDA may still be mined for these purposes. For example, in order to uncover the existence of publication bias in drug trial results, the authors of a recent article constructed a database and applied automated data extraction and statistical analysis during a systematic review of 164 efficacy trials found in 33 NDAs and 126 publications derived from these trials in peer-reviewed journals.<sup>170</sup> The authors were able to meta-analyze the limited information currently available from the FDA together with the more complete information from publications in peer-reviewed journals. Their analysis proved that trial results with favorable outcomes were 4.77 times more likely to be published than those with unfavorable results.<sup>171</sup> Even with limited access to information, this study was able to implement sophisticated analysis methods to a large amount of data. With complete access, similar studies could lead to even more important findings with regard to data quality and robustness.

The costs of research data secrecy have also increased in light of technological advances.<sup>172</sup> A few examples will serve to illuminate the increasing importance of open access to research data in this context. Microarray technology can rapidly detect changes in expression levels of a large number of genes, screening for changes associated with, for example, drug treatment or disease progression.<sup>173</sup> Since its inception, microarray technology has been employed to generate enormous amounts of data on “aging, cardiovascular diseases, cancer, and dozens of other diseases” at “enormous cost.”<sup>174</sup> Analysis of multiple microarray datasets can potentially “identify genes that are observed in common between different, independent studies of the same disease or treatment” as well as “identify sets of genes that may be modulated in common

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170. Kristin Rising, Peter Bacchetti & Lisa Bero, *Reporting Bias in Drug Trials Submitted to the Food and Drug Administration: Review of Publication and Presentation*, 5 PLOS MEDICINE 1561, 1563–64 (2008), <http://www.plosmedicine.org/article/info:doi/10.1371/journal.pmed.0050217>.

171. *Id.* at 1566, tbl.2 (this finding had a p-value of 0.018).

172. Eisenberg, *supra* note 7, at 383.

173. See, e.g. Nat'l Center for Biotechnology Info., *Microarrays: Chipping away at the Mysteries of Science and Medicine*, <http://www.ncbi.nlm.nih.gov/About/primer/microarrays.html> (last visited Apr. 17, 2010).

174. Patrick Cahan, et al., *List of lists-annotated (LOLA): A database for annotation and comparison of published microarray gene lists*, 360 GENE 78, 79 (2005).

between different disease states or drug treatments.”<sup>175</sup> Genes changing in a common fashion in multiple studies of the same disease or drug treatment are more likely to be important molecules involved with that disease or drug. A comparison of two different microarray studies of acute myeloid leukemia contained an overlap of only nine common genes, even though each study individually identified over 100 genes as being associated with the disease.<sup>176</sup> Focusing on the small pool of common genes is theoretically more likely to yield useful information about a particular disease, which should increase the efficiency of further studies.

Cross dataset comparisons utilizing larger sample sizes serve another useful purpose by minimizing the impact of statistical insufficiency inherent in single dataset studies. Genomic analyses are often carried out on small numbers of hard to obtain samples. Moreover, the technology is expensive. Thus, it is often not possible to carry out such studies with a sufficient number of replicates to absolutely minimize analytical noise. “Because the cost of generating replicate transcript profiles is high, or because of a limited amount of mRNA, most laboratories do not perform replicate analyses of the same sample to determine the extent of analytical noise.”<sup>177</sup> Cross dataset studies overcome the difficulties of small sample size. Therefore, large-scale comparisons across many studies allow genes implicated weakly by single studies in disease progression to be more significantly correlated with that disease.

Comparisons of larger numbers of microarray datasets can highlight functional relationships between genes. These relationships indicate genes that co-respond to events such as the progression of a disease or the introduction of a drug, in effect forming co-expression pathways or networks. Large-scale comparisons allow aggregation of even low-confidence links between genes in order to determine the functional relationships between those genes. A study comparing sixty published datasets from many different sources allowed the elucidation of hundreds of co-expression networks.<sup>178</sup> Determining which groups of genes respond to a specific disease or treatment focuses drug development and therefore increases innovation efficiency.

Access to raw research data is crucial for conducting meta-analyses. This is especially true for complex data generated by genomic or proteomic studies. As the complexity of data increases, so does the

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175. *Id.* at 79.

176. *Id.* at 81.

177. Stephen Welle, *Gene Transcript Profiling in Aging Research*, 37 EXPERIMENTAL GERONTOLOGY 583, 586 (2002).

178. *Id.* at 1087–89.

complexity of the data analysis, which makes it difficult for third parties to evaluate the findings of a study. One recent study that evaluated gene expression profiling studies published in peer-reviewed journals found the conclusions reached by the original authors difficult to reproduce.<sup>179</sup> The problem was directly linked to data availability; the authors stated that “many, if not most, microarray analyses could potentially be largely reproduced if the data are available and adequately annotated and if the analytic steps and parameters are sufficiently described.”<sup>180</sup> Even in the academic community, with its culture of data accessibility, there is a growing understanding that public access to raw data can bring about increased benefits. Studies with “more transparent availability of data and analyses” tend to be cited by other researchers with greater frequency and have greater impact factors, indicating that scientific value increases with data transparency.<sup>181</sup> Responding to a perceived need, various academic groups are leading the effort to build an infrastructure to enable free public data sharing.<sup>182</sup>

### B. Large Scale Data and the FDA

The FDA itself has recognized the importance of genomics for drug development.<sup>183</sup> In a guidance document for industry, the agency affirmed that it has an important role to play “in the evaluation of pharmacogenomic tests, both to ensure that evolving FDA policies are based on the best science and to provide public confidence in the field.”<sup>184</sup> Importantly,

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179. John P. A. Ioannidis, et al., *Repeatability of published microarray gene expression analyses*, 41 NATURE GENETICS 149, 151 (2009) (“When data analysis steps are very complex and work intensive, it may be difficult or even impossible for even experienced teams of outsiders to reproduce published studies.”).

180. *Id.*

181. *Id.* at 151–52.

182. See Proteomecommons.org, What is the Proteome Commons Tranche repository?, <https://proteomecommons.org/tranche/about.jsp> (last visited Mar. 1, 2009) (providing an example of a peer-to-peer data sharing tool for proteomics). See also Nat’l Institutes of Health, NIH Data Sharing Policy and Implementation Guidance, [http://grants.nih.gov/grants/policy/data\\_sharing/data\\_sharing\\_guidance.htm](http://grants.nih.gov/grants/policy/data_sharing/data_sharing_guidance.htm) (last visited May 10, 2010) (“Data should be made as widely and freely available as possible while safeguarding the privacy of participants, and protecting confidential and proprietary data.”).

183. See FDA, CTR. FOR DRUG EVALUATION AND RESEARCH, MANUAL OF POLICIES AND PROCEDURES: PROCESSING AND REVIEWING VOLUNTARY GENOMIC DATA SUBMISSIONS (2005) <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/StaffPoliciesandProcedures/ucm073575.pdf> (setting forth procedures for genomic data submission to the agency); FDA, Draft Guideline, E15 Terminology in Pharmacogenomics, <http://www.fda.gov/OHRMS/DOCKETS/98fr/06d-0526-gdl0001.pdf> (last visited Aug. 6, 2009) (establishing a common terminology for use in evaluating pharmacogenomic data); FDA, GUIDANCE FOR INDUSTRY, PHARMACOGENOMIC DATA SUBMISSIONS (2005), <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm079849.pdf>.

184. *Id.* at 3.

the FDA stated its goal was to “encourage open and public sharing of data and information on pharmacogenomic test results,”<sup>185</sup> though the field was not yet “well enough established” for the regulatory decision making process.<sup>186</sup> The FDA agrees that it is likely that manufacturers will increasingly turn to the analytical and predictive powers of -omics technologies to generate data.<sup>187</sup> Currently, however, pharmacogenomic data submissions remain voluntary and are not part of the FDA’s regulatory decision making process.<sup>188</sup> The guidance document does not state a clear position on public disclosure other than affirming a desire to encourage sharing.<sup>189</sup>

*C. Scientific Advances Have Radically Transformed the  
Public Interest in Research Data Disclosure*

The public interest in disclosure has grown concomitantly with the rapid advances in life sciences. Bioinformatics methodology allows scientists to perform data mining at a level of sophistication previously impossible to achieve. Data mining has the potential to elucidate results from both legacy data as well as more modern, large-scale pharmacogenomic or proteomic studies. Public availability of existing as well as ongoing pre-clinical experiments and clinical trial results would allow the power of bioinformatic analysis to be brought on drug safety and efficacy determinations. Enabling such analyses across many datasets has utility beyond strengthening statistical relevance. Drug manufacturers may themselves benefit by meta-analyzing pooled research data regarding all other molecules in the same class and by being able to more quickly eliminate potentially troublesome compounds earlier in the drug development process. This should allow them to focus their efforts on more relevant targets, and/or engaging in more targeted drug design. In fact, realizing the potential of large scale informatics, several companies have begun to offer, in addition to analysis software, access to compiled datasets derived from published studies.<sup>190</sup> The appearance of such service-oriented start-ups confirms the notion that there is both a

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185. *Id.*

186. *Id.* at 2.

187. *Id.* at 5 (“As the field of pharmacogenomics advances, it is likely (and desirable) that sponsors will begin to use pharmacogenomic tests to support drug development and/or to guide therapy.”).

188. *Id.* at 14.

189. *Supra* note 184 and accompanying text.

190. *See, e.g.*, Compendia Biosciences, MAPK Pathway Signatures in Oncomine (2008), [http://www.compendiabio.com/pdfs/MAPK\\_Webinar.pdf](http://www.compendiabio.com/pdfs/MAPK_Webinar.pdf).



market advantage and scientific value in applying informatics methodology to large-scale data.

In addition to the usual rationales supporting data disclosure,<sup>191</sup> data has changed fundamentally since the FDA formulated its disclosure policy and chose secrecy over transparency. Even then, the agency acknowledged the precarious balance between private secrecy and public disclosure.<sup>192</sup> Today's data generation and bioinformatics methodologies have transformed the scientific potential of research data and boosted the need to advance the public interest over the private. The balance has firmly swung in favor of disclosure.

### CONCLUSION

The FDA requires that manufacturers study the safety and efficacy of their products. The FDA's goal, in accordance with its mission to protect the public health, is to insure that these studies yield high quality, scientifically rigorous research data.<sup>193</sup> Scientifically sound data is the fulcrum of the approval process. Due to data generation costs, the threat of free-riding by competitors who may use the data to gain approval for their own compounds, and the potential that research data access may reveal information either beneficial to competitors or harmful to the owner, it has value beyond its scientific merits. The FDA has long recognized the manufacturers' interests in secrecy by treating research data as trade secrets and/or confidential business information.

Nevertheless, trade secret doctrine is an ill-fitting restraint within the drug regulatory context. The doctrine developed around the need to protect commercial interests and enable businesses to fully capture the economic benefits of innovation by "keep[ing] secret, for a potentially unlimited time, those formulas, processes and inventions that afford them pecuniary gain."<sup>194</sup> Yet the FDA regulatory framework exists to protect the public health, which necessitates that the nature and magnitude of the public interest in disclosure be taken into account. The agency's cognizance of this conflict has led it to request Congress to intervene in the past.<sup>195</sup>

Overvalued research data has the potential to distort the scientific process by increasing the incentive to achieve positive outcomes.

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191. E.g., Shapiro, *supra* note 13, at 158–61 (ethical considerations); Wagner & Michaels, *supra* note 37, at 122–28 (ends-oriented biases in study design and reporting).

192. See *supra* notes 67–69.

193. Eisenberg, *supra* note 7, at 373.

194. Levine, *supra* note 16, at 136.

195. See *supra* note 69 and accompanying text.

Empirical studies and insider reports verify that secrecy is indeed leading to distortions and loss of data quality. Moreover, advances in data generation methods have resulted in more complex research data content. These incipient attributes have also transformed data analysis. Analyses are more difficult to conduct, complicating third party review of results. One of the most effective ways to overcome these shortcomings is to open research data held by the FDA to public access.

At the same time, progress in informatics technology has reshaped the nature and magnitude of the public interest. Meta-analysis using modern bioinformatics methodologies can increase data quality and yield heretofore inaccessible discoveries. Large scale reviews of publicly available datasets have already produced valuable insights into drug mechanisms of action and advanced our understanding of gene networks. Publicly available research data would constitute a windfall for similar comparative studies. This would not only benefit our general understanding of drugs and their effects, but also help pharmaceutical companies refine and focus their development process, thus leading to cost savings. Continuing to sequester research data as trade secrets or confidential information stunts our ability to achieve these innovation efficiencies.

Because of the conflict between the FDA's mission and its inability to incorporate public interests into its research data confidentiality policy, existing legal mechanisms have failed to enable public access to research data. The agency's insistence on processing disclosure requests via the FOIA mechanism has exacerbated the problem. As a general purpose transparency statute, the FOIA is susceptible to a narrow interpretation where a court can deny data access based on a notion that any involvement of private interests renders disclosure impossible, for example, if it is not directly related to "what the government is up to."<sup>196</sup> Courts' refusal to account for the public interest in research data disclosure make the FOIA an imperfect vehicle to balance valid competing interests.<sup>197</sup>

While the public need for disclosure has grown, part of the rationale for secrecy has disappeared. Free-riding in obtaining regulatory approval

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196. See *supra* notes 135–136 and accompanying text.

197. Each year, the FDA receives more FOIA requests than any other government agency except the Federal Bureau of Investigation. The backlog of FOIA requests at the FDA exceeded that for the Department of Defense and the Justice Department for FY 2006. Justin Blum, *Drug, Food Risks Stay Secret as Inquiries to U.S. FDA Pile Up*, BLOOMBERG.COM, June 19, 2007, <http://www.bloomberg.com/apps/news?pid=20601103&sid=a91FU255oQBM&refer=news>.

became a non-issue in the U.S. after the Hatch-Waxman Act.<sup>198</sup> The remaining private interest in data as a tool to gain foreign regulatory approval is not strong enough to offset the increasing innovation efficiencies disclosure would bring. An overhaul of existing laws is needed in order to enable public access to research data held by the FDA and take advantage of the benefits of such access. Potential solutions include voluntary disclosure by manufacturers, new congressional and/or state legislation with an explicit disclosure mandate, or the FDA acting through its rulemaking powers to mandate disclosure. Both the pharmaceutical industry and the government have created trial registry websites,<sup>199</sup> and Congress has introduced legislation in both houses.<sup>200</sup> Similar bills were also introduced in nine states, with each piece of legislation mandating different levels of disclosure.

The FDA can and should reconsider the tectonic shifts in the interests at stake and revise its research data confidentiality policy. If the FDA cannot, or chooses not to do so, a simple and direct Congressional mandate for full disclosure is the next best remedy, since a state-by-state approach has many shortcomings and may be difficult to implement. Although manufacturers may suffer commercial harm as a result of disclosure, their level of harm is likely to be offset by the potentially enormous scientific gains that are likely to be made possible by a regime of full disclosure. While mandating disclosure, Congress could ameliorate some of the harm to manufacturers by considering a limited period of research data exclusivity. Research data exclusivity would prevent competitors and generic manufacturers from using data access as a means to gain regulatory approval while allowing research data to be mined for maximum benefit.

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198. See *supra* Part II.B.

199. Clinicaltrials.gov contains the NIH's list of clinical trials. Clinicalstudyresults.org is a summary results database organized by Pharmaceutical Research and Manufacturers of America. Neither database contains actual results.

200. See Aneel Damle, Peter Lurie & Sidney M. Wolfe, *A Policy Study of Clinical Trial Registries and Results Databases*, PUBLIC CITIZEN, July 17, 2007, [http://www.citizen.org/publications/release.cfm?ID=7534&secID=1656&catID=126#\\_ednref1](http://www.citizen.org/publications/release.cfm?ID=7534&secID=1656&catID=126#_ednref1) (containing an excellent review of all existing legislation, as well as existing databases).