SOMETIMES THE SILENCE CAN BE LIKE THE THUNDER:[1] ACCESS TO PHARMACEUTICAL DATA AT THE FDA

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I
INTRODUCTION

According to the advocates of greater corporate involvement in clinical science, the increasingly entwined relationship between corporations, academia and government is the very definition of a "win–win" situation. Corporations can benefit from the knowledge of scientists in academia or government, and the public benefits from the more rapid movement of beneficial products into commerce.

That argument, however, ignores a fundamental clash of cultures. Progress in science is based on the free publication of study results and on the public release of data, allowing scientists to build on the experiences of others. In contrast, the governing ethic in the corporate sector is secrecy—the withholding of any information from which a competitor might benefit. There is perhaps no realm in which these competing viewpoints are presented more starkly than in the area of access to pharmaceutical data at the Food and Drug Administration (FDA).

Those committed to the free exchange of scientific information have long complained about various restrictions on access to these pharmaceutical data and the resultant restrictions on open discourse. Such restrictions include the selective publication of favorable results,[2] gag orders on corporate-funded research,[3] and misleading presentations of data.[4] Only in the last several years have these concerns penetrated public consciousness. Two recent examples demonstrate the problems these restrictions create:

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1. BOB DYLAN, *Lovesick, on* TIME OUT OF MIND (Columbia Records 1997).

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2. An-Wen Chan et al., *Empirical Evidence for Selective Reporting of Outcomes in Randomized Trials: Comparison of Protocols to Published Articles*, 291 J. AM. MED. ASS'N 2457, 2462–64 (2004); An-Wen Chan & Douglas G. Altman, *Identifying Outcome Reporting Bias in Randomized Trials on PubMed: Review of Publications and Survey of Authors*, 330 BRIT. MED. J. 753, 756–57 (2005).

3. Drummond Rennie, *Thyroid Storm*, 277 J. AM. MED. ASS'N 1238, 1239–40 (1997).

4. Elizabeth Barbehenn et al., *Alosetron for Irritable Bowel Syndrome*, 356 LANCET 2009 (2000).

The first example involves the selective publication of data on the efficacy of selective serotonin reuptake inhibitor (SSRI) antidepressants in children. Despite objective evidence demonstrating that SSRI's are, at best, moderately effective in children,[5] published studies generally exaggerated the benefits of these drugs, while certain negative studies provided to FDA were never published. Industry-funded academic scientists withheld from publication some studies that failed to demonstrate drug efficacy,[6] the inclusion of which would have altered the risk–benefit profile of the drugs.[7] Despite these efforts, an FDA analysis of published and unpublished pediatric SSRI trials ultimately led to the addition of a black box to the FDA-approved label that warned of the increased risk of suicidal ideation in children and adolescents.[8]

In another revealing example, the Journal of the American Medical Association published a report in 2001 claiming that, after six months of therapy, the COX-2 inhibitor celecoxib (Celebrex) was associated with a reduced incidence of gastrointestinal ulcers compared to two other pain medications.[9] If true, this outcome would have represented a significant advantage over other approved pain medications. However, the authors of the study failed to disclose that at the time of publication they had already received data for the full twelve-month period for which the study was originally designed.[10] The twelve-month data showed no advantage for Celebrex over other drugs. Although the FDA, armed with the twelve-month data, has never allowed the company to claim reduced ulcer incidence, the published study helped drive the massive Celebrex market.

Together, these two cases underscore the harms resulting from the ability of pharmaceutical companies to withhold data from the view of physicians and patients. Moreover, even when such data are available to the FDA, for reasons described below, the agency may fail to disclose the data publicly, further limiting the public's access to accurate information.

Some observers have suggested that a registry of clinical trials would shed more light on the drug-approval process. In theory, companies (or others) forced to register their studies at the point-of-study initiation and ultimately to disclose their results would be more accountable to regulators, researchers, and patients. However, a review of open-government procedures and litigation at the FDA demonstrates that the need for transparency at the agency extends

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5. Jon N. Jureidini et al., *Efficacy and Safety of Antidepressants for Children and Adolescents*, 328 BRIT. MED. J. 879, 882 (2004).

6. Barry Meier, *Contracts Keep Drug Research Out of Reach*, N.Y. TIMES, Nov. 29, 2004, at A1.

7. Craig J. Whittington et al., *Selective Serotonin Reuptake Inhibitors in Childhood Depression: Systematic Review of Published versus Unpublished Data*, 363 LANCET 1341, 1344–45 (2004).

8. Food & Drug Admin., *Patient Information Sheet: Celecoxib* (Apr. 7, 2005), http://www.fda.gov/cder/drug/infopage/celebrex/Celebrex-ptsk.pdf.

9. Fred E. Silverstein et al., *Gastrointestinal Toxicity with Celecoxib vs Nonsteroidal Anti-Inflammatory Drugs for Osteoarthritis and Rheumatoid Arthritis: The CLASS Study: A Randomized Controlled Trial*, 284 J. AM. MED. ASS'N 1247 (2000).

10. Susan Okie, *Missing Data on Celebrex; Full Study Altered Picture of Drug*, WASH. POST, Aug. 5, 2001, at A11.

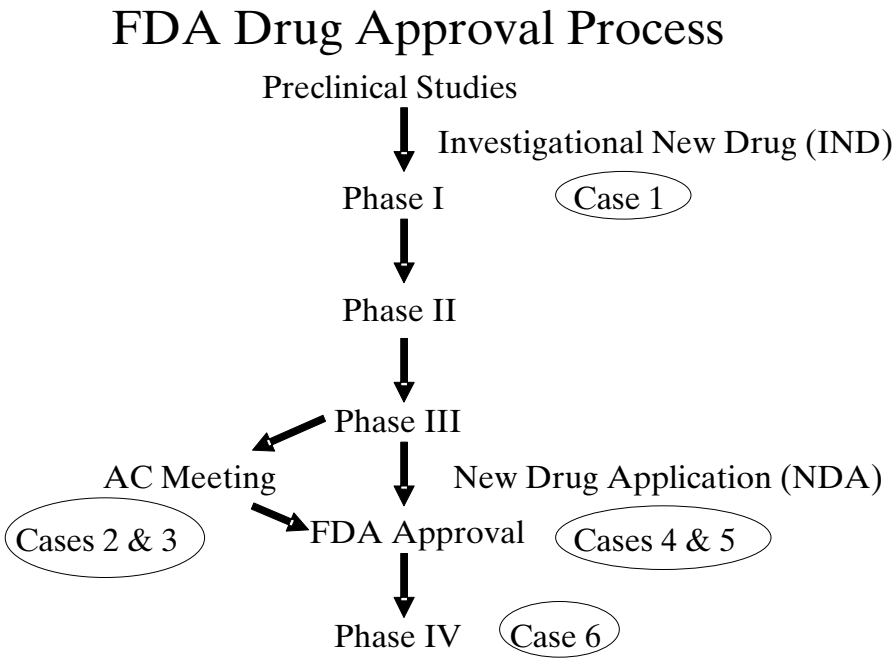
well beyond the reach of any clinical trial registry. Accordingly, efforts to expand openness and accountability must view trial registries as only one component of a broader open-government strategy. This article will confine itself to the approval of drugs at the FDA; the approval process for devices and biologics is similar.

II

THE FDA DRUG APPROVAL PROCESS

For most drugs, the journey toward potential FDA approval begins with preclinical animal testing. Assuming that the results of such testing provide sufficient hints of drug efficacy to merit testing in humans, the company will complete an Investigational New Drug (IND) application and submit it to the FDA (see Figure 1). Upon approval of that application, the company can begin Phase I studies in humans. These studies typically focus on assessing drug safety in relatively crude terms; typically, only a few dozen patients or normal volunteers are included. If the drug does not prove to be inordinately toxic, the sponsor may elect to proceed to Phase II. Such trials, which normally include a few hundred patients, seek to define drug toxicity more closely by examining a variety of doses and to provide some indications of drug efficacy. If the drug passes that hurdle, the company may proceed to Phase III, in which large-scale, randomized clinical trials are conducted, and both safety and efficacy are assessed. These trials are usually the principal ones upon which the FDA bases its decision whether to approve a new drug.

Figure 1:



To obtain permission to market a new drug, the sponsor must submit a New Drug Application (NDA), which includes all the results of pre-clinical and clinical trials, as well as additional studies evaluating the chemical properties of the drug and pharmacokinetic studies of the dosage form. Since the early 1990s, the FDA has followed a bifurcated process for NDAs. Those deemed to be a "significant improvement compared to marketed products" are considered priority applications. The agency seeks to make a decision regarding approval of those drugs within six months. For other drugs, which generally do not represent significant therapeutic advances over existing therapies, the agency generally completes review in one year.

As part of its consideration of an NDA, the FDA sometimes refers the application to one of the FDA's advisory committees. An advisory committee is a group of outside experts chosen by the FDA to provide advice and non-binding recommendations to the agency on topics such as drug approval. Of late, because of the rigid approval deadlines imposed upon the agency by Congress, a declining fraction of new drugs has been subject to this additional stratum of review. In 2001, the approval of only twenty-one percent of new molecular entities was preceded by an advisory committee meeting.[11]

11. DEP'T OF HEALTH AND HUMAN SERVS., OFFICE OF INSPECTOR GENERAL, REPORT NO. OEI-01-01-00590, FDA'S REVIEW PROCESS FOR NEW DRUG APPLICATIONS: A MANAGEMENT REVIEW 42 (2003).

Even if the drug meets with the FDA's approval, the agency still has the authority to make that approval contingent upon the sponsor's conducting of post-marketing studies, often referred to as Phase IV studies. These studies usually focus on safety issues and may take the form of registries, studies in special populations, or full clinical trials. The evidence to date is that companies often do not complete Phase IV studies.[12] The FDA, unsure of its authority to enforce the post-approval requirement, has made little if any effort to ensure that the studies are conducted.

III

OPEN GOVERNMENT STATUTES

Generally, the FDA's approach to data disclosure has been that no public disclosure of information will take place until (and unless) a drug is approved.[13] Indeed, the agency will not even acknowledge that an IND or an NDA has been filed, although companies filing with the Securities and Exchange Commission report such information and often ensure that positive findings from their studies receive media coverage. For those drugs that are evaluated by FDA advisory committees, there is an additional, brief window in which the NDA is formally acknowledged and the data supporting the application are disclosed.

The two statutes that have provided the greatest access to pharmaceutical data are the Federal Advisory Committee Act (FACA)[14] and the Freedom of Information Act (FOIA).[15] FACA ensures that advisory committees are subject to transparency requirements such as advance notice of upcoming meetings, opportunities for public attendance and input, and the preparation of transcripts.[16] FOIA requires public disclosure, upon request by any individual, of agency documents that do not fall into one of nine specific exemptions from disclosure.[17]

In 2004, the FDA processed a total of 18,540 FOIA requests at a cost of $12.8 million.[18] By permitting the online posting of certain frequently requested documents, the Internet has eased the agency's workload somewhat. But the backlog has nevertheless continued to grow and stood at 16,671 pending requests at the end of 2004.

The agency processes requests in two tracks: simple and complex. The latter category applies to requests seeking a voluminous number of records or records from which the agency will want to redact information that falls under one of

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12. Larry D. Sasich et al., The Drug Industry's Performance in Finishing Postmarketing Research (Phase IV) Studies (Apr. 13, 2000), http://www.citizen.org/publications/release.cfm?ID=6721.

13. *See* 21 C.F.R. § 314.430(b)–(d).

14. Federal Advisory Committee Act, 5 U.S.C. app. II §§ 1–15 (2000).

15. Freedom of Information Act, 5 U.S.C. § 552 (2000).

16. 5 U.S.C. app. II §§ 10–11.

17. 5 U.S.C. § 552(b) (2000).

18. FOOD AND DRUG ADMINISTRATION. ANNUAL FREEDOM OF INFORMATION ACT (FOIA) REPORT, FISCAL YEAR (FY) 2004, *available at* http://www.fda.gov/foi/annual2004.html.

the FOIA exemptions. For 2004, the agency reported that eighty-nine percent of the requests it received were simple and usually processed in a median of twenty-five days. Eleven percent were considered complex and were processed in a median of 325 days. In no instance did the FDA expedite processing in repsonse to a requester's assertion of "an exceptional need or urgency,"[19] the standard for expediting.

In 2004, the majority (67.6%) of the FOIA requests processed by the FDA were granted in full. A further 31.9% resulted in nondisclosure—most commonly because there were either no relevant agency records or because the request was withdrawn. Partial satisfaction of the request occurred in forty-five instances, while complete denials ensued in thirty-seven. These two categories of responses are the ones that may lead to litigation.

Over the course of 2004, the FDA claimed a FOIA exemption 114 times; some cases included claims for multiple exemptions. By far the most common exemptions claimed were the exemptions for confidential commercial information (fifty-three exemptions) and investigatory records (twenty-eight exemptions). The remaining claims were based on exemptions for internal agency rules, material for which disclosure is prohibited by another statute, internal agency memoranda, and personal privacy.

IV

CASES RESULTING FROM FOIA REQUESTS: A REVIEW[20]

A. Case 1: Abandoned Investigational New Drug Applications

In *Public Citizen Health Research Group v. Food & Drug Administration (Schering)*,[21] Public Citizen submitted a FOIA request to the FDA requesting copies of IND submissions for five drugs that had been effectively abandoned by their manufacturers for safety reasons. The FDA denied the request, claiming that the records fell under the FOIA exemption for confidential commercial information. Public Citizen then sued to compel disclosure. In the first prong of its argument, Public Citizen contended that the requirement of 21 U.S.C § 355(l)—that "safety and effectiveness data" for a drug abandoned by its sponsor must be disclosed "unless extraordinary circumstances are shown"—

19. *Id.* at III(B)(6).

20. The cases reviewed below were obtained by searching the Westlaw database for published cases and from unpublished cases litigated by the Public Citizen Litigation Group. The timeframe of each case relative to the FDA review process described above is indicated in Figure 1.

The authors also reviewed law review articles regarding FDA and the Freedom of Information Act (FOIA). The most relevant article mounts a general critique of the trade secret status of health and safety information and suggests that FDA has erred in its nearly unlimited granting of trade secret status to such information. *See* Thomas O. McGarity & Sidney A. Shapiro, *The Trade Secret Status of Health and Safety Testing Information: Reforming Agency Disclosure Policies*, 93 HARV. L. REV. 837 (1980).

21. Pub. Citizen Health Research Group v. Food & Drug Admin. (Schering), 185 F.3d 898 (D.C. Cir. 1999).

applied to INDs as well as to NDAs.[22] The court ruled, however, that the relevant section applies to NDAs only.[23]

In arguing that the IND submissions were not protected under the confidential commercial information exemption, Public Citizen contended that they should be released to determine whether the FDA was adequately protecting trial subjects and to allow competitors to avert potentially risky trials of related drugs. This argument, too, failed to convince the court, which held that the bulk of the IND material did fall within the scope of that exemption. The court further stated that the purpose of FOIA is merely to monitor "what the government is up to", and thus that any other benefits of disclosure are not relevant to analysis under that exemption.[24] In other words, 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. The court ordered the release of the one IND application for which it found that disclosure was not likely to cause substantial competitive harm, as required for protection under that exemption.[25]

In a similar, earlier case, Public Citizen sought records regarding preclinical and clinical testing of fialuridine, a drug that had caused the deaths of five patients in clinical trials for Hepatitis B infection at the National Institutes of Health.[26] Despite this striking toxicity, the drug's sponsor, Eli Lilly, claimed that it would continue to develop the drug.[27] The FDA and the drug's sponsor argued that the materials sought were subject to the confidential commercial information exemption. The court agreed, noting in an unreported decision that the records fell within the scope of that exemption because the information they contained might save Lilly's competitors both time and money in doing their own research. Again, under this ruling, such public health concerns as avoiding the exposure of clinical-trial subjects (or patients in general after the drug's approval) to drugs closely related to fialuridine were not factors in the FOIA analysis.

B. Case 2: Advisory Committee Materials

In *Public Citizen Health Research Group v. Food & Drug Administration (Searle)*,[28] Public Citizen sought access under both FOIA and FACA to materials provided to the members of the Arthritis Drugs Advisory Committee prior to the committee's meeting on the drug Celebrex. The FDA eventually provided the material, but not until well after the advisory committee meeting

22. 21 U.S.C. § 355(l) (2000)
23. *Schering*, 185 F.3d at 901.
24. *Id.* at 904.
25. *Id.* at 906.
26. Pub. Citizen Health Research Group v. Food & Drug Admin. (Searle), Civ. A. No. 94-0017(RMU) (D.D.C. April 10, 1995)
27. The drug had never been approved for use in any condition.
28. Pub. Citizen Health Research Group v. FDA, 2000 WL 34262802 (D.D.C. 2000).

had taken place. Public Citizen sued the agency, complaining both about the redaction of specific types of information from the material and about the FDA's continuing failure to make advisory committee materials available to the public prior to meetings.

The FACA portion of the case, which the parties settled, is probably the more significant. Under FACA, the FDA is required to provide to the public—at or before each advisory committee meeting—the materials provided to the advisory committee members in connection with each meeting. These materials consist of FDA reviews of an NDA, which generally include one or more medical officer's reviews, a pharmacologist's review, and a statistical review, as well as materials provided by the drug's sponsor. The documents are crucial to the public's ability to participate meaningfully in advisory committee meetings because, as discussed above, the FDA generally does not even acknowledge the existence of an NDA, let alone make any of its contents public, prior to the meeting. Thus, the advisory committee briefing materials are often the first glimpse the public has of the data underlying the NDA. The FDA agreed to settle this portion of the case by promising to place the materials provided to advisory committee members on the FDA's website twenty-four hours before each advisory committee meeting.[29] These often extensive materials are now downloaded before the meeting by people seeking to comment in the public session and by stock analysts and the media. The availability of this material has revolutionized the quality of public comment and media coverage. Frequently, the stock market will react to the release of these documents, even prior to the meeting.

The parties litigated the FOIA part of the case, which resulted in disclosure of certain types of information that the FDA had redacted from the medical officer's review of the Celebrex NDA. This aspect of the case involved fact-specific issues and so is not described here.

C. Case 3: FDA Advisory Committee Member Conflict-of-Interest Statements

In 1997, Congress passed the Food and Drug Administration Modernization Act.[30] A little-noticed portion of the Act required the FDA to make a more comprehensive disclosure of the potential conflicts of interest of its advisory committee members and FDA-invited voting consultants.[31] By September 2001, FDA had done little to expand such disclosures, and Public Citizen threatened the agency with a lawsuit for noncompliance. To avert such a lawsuit, the agency drafted a compliance document that required more detailed conflict-of-

29. These same materials are often provided to the drug's sponsor well before the advisory committee meeting, but the FDA says that additional time is needed to redact exempted material before disclosure to the public.

30. Food and Drug Administration Modernization Act of 1997, Pub. L. No. 105-115, 111 Stat. 2296 (1997).

31. 21 U.S.C. § 355 (n)(4) (2000).

interest disclosure.[32] For example, advisory committee members must now disclose the ranges of remuneration by the particular companies with whom they have associations in the form of honoraria, contracts, expert testimony in product liability cases, and stock holdings. These disclosures are now announced in detail by the committee's executive secretary before each advisory committee meeting at which a specific product is being discussed. Such disclosures are not made public at meetings that concern general scientific issues, and the FDA still does not require the disclosure of the names of competing companies with whom an advisory committee member has an association.

D. Case 4: Data about Disapproved Uses

In November 2001, the FDA granted approval to Pfizer for its COX-2 inhibitor valdecoxib (Bextra) for three uses (menstrual pain, rheumatoid arthritis, and osteoarthritis), but rejected its application for acute pain. In accordance with its standard practice, the FDA then posted on its website the FDA medical officers' reviews and other material related to the agency's evaluation of the drug for all four uses. Within a few days, Pfizer complained to the FDA that the agency's posting included material about acute pain, the use rejected by FDA. At Pfizer's request, FDA then took the Bextra material off its website and reposted it several months later, after redacting information about use of the drug for acute pain. In the meantime, an article by Pfizer-sponsored researchers appeared in the Journal of the American Dental Association (JADA)[33] touting the drug for acute pain. The conclusions of the article were reiterated in an accompanying press release.[34] However, neither the article nor the press release mentioned the FDA's rejection of the NDA with respect to acute pain. Due to the FDA's treatment of the acute pain material as confidential commercial information, the assertions of the journal article and the press release went unrefuted, resulting in an incomplete and biased public record.[35] According to a New York Times investigation, the JADA study "helped light a fire under Bextra," which experienced a sixty percent increase in sales in the three months following the article's publication.

Public Citizen later made a FOIA request for complete, unredacted copies of the medical officers' reviews of the Bextra NDA and in 2004 sued to obtain

32. FOOD AND DRUG ADMINISTRATION. DRAFT GUIDANCE ON DISCLOSURE OF CONFLICTS OF INTEREST FOR SPECIAL GOVERNMENT EMPLOYEES PARTICIPATING IN FDA PRODUCT SPECIFIC ADVISORY COMMITTEES (2002), *available at* http://www.fda.gov/oc/guidance/advisorycommittee.html.

33. Stephen E. Daniels et al., *The Analgesic Efficacy of Valdecoxib vs. Oxycodone/Acetaminophen After Oral Surgery*, 133 J. AM. DENTAL ASS'N 611 (2002).

34. Melody Petersen, *Madison Ave. Has Growing Role in the Business of Drug Research*, N.Y. TIMES, Nov. 22, 2002, at A1.

35. Companies, particularly start-ups hungry for venture capital, now use their mandatory reports to the Securities and Exchange Commission to tout each step in the drug development process, further distorting the public record.

the information.[36] In response, the FDA released most of the information sought, and Public Citizen then dismissed the case. The released information showed an increased risk of serious thromboembolic events in patients using Bextra and undergoing coronary artery bypass grafts—the same adverse effect subsequently reported in another study of Bextra.[37] Similar toxicity has been documented for the other COX-2 inhibitors, rofecoxib (Vioxx) and Celebrex.[38] Bextra and Vioxx have since been removed from the market.

E. Case 5: Abandoned NDAs

As noted above, court rulings had previously held that abandoned INDs are not automatically disclosable. In *Davis v. Food and Drug Administration*,[39] the plaintiff sought the release of information related to abandoned NDAs—those submitted to the FDA for approval but never approved. The case was settled because the FDA conceded the disclosability of such information. However, because of the size of the materials requested, the litigants entered into a compromise as to which materials would be disclosed. Importantly, the FDA agreed not to assert the FOIA exemption protecting from disclosure agency deliberative material with respect to abandoned NDAs. Unfortunately, because the decision whether to abandon efforts to develop a drug is entirely up to the company and because a statement about its plans in this regard is not verifiable, any company is free to make broad claims that it has not abandoned its efforts with respect to an NDA and thereby to thwart disclosure.

F. Case 6: Phase IV Protocols

The FDA sometimes makes approval of an NDA conditional upon the company's conducting certain post-marketing or Phase IV studies. In *Public Citizen Health Research Group v. Food & Drug Administration (Glucophage Study),*[40] Public Citizen sought the protocol for a Phase IV study of metformin (Glucophage). The FDA had required the study to establish the incidence of a drug-induced metabolic disorder called lactic acidosis. The protocol would provide a detailed description of the study design, including its inclusion criteria, length of follow-up, outcome measures and statistical procedures.

Bristol-Myers Squibb, the drug's manufacturer, intervened in the lawsuit. Both Bristol-Myers and FDA argued that the protocols were properly withheld

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36. Public Citizen Health Research Group v. Food & Drug Admin., No. 04-304 (D.D.C. filed Feb. 26, 2004); *See* Public Citizen Health Research Group, Complaint for Declaratory and Injunctive Relief (Feb. 26, 2004), *available at* http://www.citizen.org/documents/ACF5CF.pdf.

37. Bextra package insert, Pfizer, Inc. (2004), *available at* http://www.pfizer.com/download/uspi_bextra.pdf.

38. Dawn Jennings-Peterson & Sidney M. Wolfe, *Petition to Remove the Cox-2 Inhibitors Celecoxib (Celebrex) and Valdecoxib (Bextra) from the Market* (Jan. 24, 2005), http://www.citizen.org/publications/release.cfm?ID=7358.

39. Davis v. Food & Drug Admin., No. 01-982 (D.D.C. filed May 9, 2001).

40. Pub. Citizen Health Research Group v. Food & Drug Admin. (Glucophage Study), 964 F. Supp. 413 (D.D.C. 1997).

under the confidential commercial information FOIA exemption.[41] The court applied the two-pronged test first enunciated in *National Parks & Conservation Association v. Morton*.[42] Under that test, material falls within the scope of the confidential commercial information exemption only if disclosure is likely to (1) impair the government's ability to obtain information in the future; or (2) cause substantial competitive harm to the person who had submitted the information. The FDA and the company argued that both requirements were satisfied with respect to the Glucophage protocol.[43]

Regarding the first element, the court held that the agency's "argument is unsupported, even by an assertion of agency experience on the point."[44] For the second element, the likelihood of substantial competitive harm, the company argued that disclosure would cause patient drop-out and bias and that competitors would raise "alarmist" safety concerns, learn the results of pre-approval testing, and gain insight into Bristol-Myers Squibb's future marketing strategy. The court sought the input of two independent experts, and both agreed that release of the protocol would not be likely to harm the company at all. The court then ordered the agency to release the protocol.

In several instances since then, Public Citizen has submitted FOIA requests for Phase IV study protocols. In the first two instances, the FDA refused to disclose the protocol until Public Citizen filed a lawsuit. The FDA has since begun to release such protocols upon request, in compliance with FOIA and without litigation.

V

CONCLUSION

At each step of the drug approval process, a variety of documents of potential relevance to the public health are generated. Numerous contentious legal battles have been waged to obtain public access to information generated during various stages in this process, with FDA typically weighing in alongside the manufacturer and favoring nondisclosure. Obstacles to the release of information at each of these stages must be addressed if optimal transparency in the drug approval process is to be assured.

Much recent attention has focused on the potential of clinical trial registries to enhance data disclosure.[45] There can be little question that such registries would significantly expand data availability. With such registries, the results of the studies would be disclosed in a more transparent fashion, and the interested community would be able to monitor the registry for the results of studies said to be close to completion. In such circumstances, the kinds of nondisclosure

41. *Id.* at 414.
42. Nat'l Parks & Conservation Ass'n v. Morton, 498 F.2d 765, 770 (D.C. Cir. 1974).
43. *Glucophage Study*, 964 F. Supp. at 415.
44. *Id.*
45. Robert Steinbrook, *Public Registration of Clinical Trials*, 351 NEW ENG. J. MED. 315 (2004).

observed in the Vioxx and SSRI studies would be essentially impossible. In a parallel development, medical journal editors, stung by revelations that the published literature may not fully reflect scientific knowledge and that they have been unable to publish studies in their entirety or even at all, have stated their intention to publish only those studies that are preregistered.[46]

Nonetheless, registries would leave many forms of data-withholding intact. Indeed, of the cases reviewed here, only two would be affected by registries: *Public Citizen Health Research Group v. Food and Drug Administration (Bextra)* (redactions for disapproved uses) and *Davis v. Food and Drug Administration* (abandoned NDAs). In each of these cases, disclosure ultimately took place as part of a settlement, leaving behind no binding precedent. As a result, the FDA could try to withhold similar information in the future. However, a registry requirement would ensure more rapid disclosure, eliminating the need for a FOIA request or litigation.

In our view, a meaningful clinical-trial registry would have to include all efficacy trials for drugs and biologics. The registry would have to include, in abstract and tabular form, the basic elements of each study's design (for example, study arms, sample size, inclusion criteria, planned primary and secondary endpoints) and results as they became available. A short delay, not exceeding twelve months, to permit the publishing of results should be permitted. Unlike the registries or disclosures envisioned by some members of the pharmaceutical industry, registering a trial should be mandatory, and failure to do so should be subject to significant punishments, including financial penalties. Bills that include these basic requirements have been drafted for both the United States Senate and House of Representatives,[47] but face an uphill struggle to passage.

Interestingly, the Department of Health and Human Services, which includes the FDA, does have a tradition of more expansive disclosure than that currently practiced by the FDA. For over twenty years, the National Institutes of Health's Recombinant DNA Advisory Committee has publicly disclosed summary safety and effectiveness data for studies related to human gene therapy and xenotransplantation. As one of its outgoing gestures, the Clinton Administration proposed extending the same level of disclosure to the FDA.[48] That proposal has since been abandoned.[49]

This article has described how small dents have been made in the imposing edifice of the confidential commercial information exemption. The larger

46. Catherine A. De Angelis et al., *Clinical Trial Registration: A Statement from the International Committee of Medical Journal Editors*, 141 ANNALS INTERNAL MED. 477 (2004).

47. Fair Access to Clinical Trials Act, H.R. 5252, 108th Cong. (2004); Fair Access to Clinical Trials Act, S. 2933, 108th Cong. (2004).

48. Availability of Public Disclosure and Submission to FDA for Public Disclosure of Certain Data and Information Related to Human Gene Therapy or Xenotransplantation, 66 Fed. Reg. 4688 (Jan. 18, 2001).

49. Unified Agenda of Federal Regulatory and Deregulatory Actions, 67 Fed. Reg 3304-01 (May 13, 2002).

question remains—why trade secret law should automatically trump public health concerns. If the courts can find no justification in law for balancing private property rights against the public interest, it is time for the Congress to step in and make the need for such a balance explicit.