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PREDICTABLE MATERIALITY: A NEED FOR COMMON CRITERIA GOVERNING THE DISCLOSURE OF CLINICAL TRIAL RESULTS BY PUBLICLY-TRADED PHARMACEUTICAL COMPANIES

*Katherine Cohen, Joseph W. Cormier, and Mahnu V. Davar**

Pharmaceutical companies are among the most heavily regulated industries in the world.¹ Successfully navigating the United States' regulatory framework comprised of numerous state and federal agencies, while also meeting the expectations of patients, shareholders, employees, and other stakeholders, is a constant challenge. For publicly-traded companies regulated by both the Securities and Exchange Commission ("SEC") and Food and Drug Administration ("FDA"), this challenge is particularly acute with respect to disclosure of clinical trial information.

Publicly-traded pharmaceutical companies are required to make certain information about themselves available to investors and regulators when that information would be material to the decision of the average shareholder to buy or sell shares. At a minimum, compliance with securities laws requires public companies to make such information available in periodic (*e.g.*

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1. *Career Overview: Pharmaceuticals*, WETFEET (Dec. 3, 2012), <https://www.wetfeet.com/articles/career-overview-pharmaceuticals>; *see also* Peter Stonier, *An Insight into Careers for Doctors with the UK Pharmaceutical Industry 3*, APBI (Aug. 2011), <http://www.abpi.org.uk/our-work/library/industry/Documents/careers-doctors.pdf>.

annual and quarterly) reports.² Such reports must be truthful, accurate, and not omit material information.

Publicly-traded pharmaceutical companies are also required to make certain information available under the Federal Food, Drug, and Cosmetic Act ("FDCA") and FDA's implementing regulations and guidance documents. Under the applicable legal principles, labeling and advertising describing a medical product must be truthful and non-misleading,³ which also requires that any facts about the product which are material to safe or effective use are disclosed.⁴ Similar to the SEC, regulated companies must also make a certain minimum amount of information available to FDA in specific reports such as annual reports and adverse event reports.⁵

The type of information that ought to be disclosed under the FDA and SEC regimes appears to be different, i.e., information that is potentially misleading to the average investor may be different for a consumer or a doctor. In a series of warning letters, FDA has taken issue with medical product company press releases that include potentially misleading claims of safety or efficacy, even when the intent behind these releases may have been SEC compliance.⁶ And, most problematically, DOJ has indicated an interest in pursuing omissions of material clinical trial information under expansive criminal enforcement theories.⁷ The threat of enforcement has generally

2. See generally, e.g., *Form 10-K*, SEC. AND EXCH. COMM'N, <http://www.sec.gov/answers/form10k.htm> (last modified Jun. 26, 2009); *Form 10-Q*, SEC. AND EXCH. COMM'N, <http://www.sec.gov/answers/form10q.htm> (last modified Sept. 2, 2011).

3. See 21 U.S.C. § 352(a) (2006); Federal Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. § 502(a) (2006).

4. See 21 U.S.C. § 352(n)(3); FDCA, 21 U.S.C. § 502(n)(3).

5. See generally, e.g., 21 C.F.R. § 314.80 (2006) (postmarketing reporting of adverse drug experiences); 21 C.F.R. § 314.81(b)(2)(i) (postmarketing annual report summaries).

6. See, e.g., *Erchonia Corp. Warning Letter*, FOOD AND DRUG ADMIN. (Jan. 21, 2011), <http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/ucm256890.htm> (discussing, among other things, company's press releases regarding clinical study results); *Glyco-Meds.com Warning Letter*, FOOD AND DRUG ADMIN. (May 19, 2009), <http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/ucm161269.htm>. (citing a press release that discusses clinical trial results supporting efficacy).

arisen in one key area of medical product company activity—clinical research.

What appears to be a “big picture” policy problem actually has some very real consequences for the legal department of a publicly-traded pharmaceutical company. If a company makes a decision not to make public the results of a clinical study because it is deemed “immaterial” under the securities laws, can it also avoid disclosure under the FDCA? Does an FDCA-mandated disclosure always trigger a requirement to disclose under securities laws? Section I of this Note details the specific clinical trial disclosure requirements of US federal agencies. Section II briefly considers international and pharmaceutical industry disclosure standards. Finally, in Section III, this Note discusses the interplay between these requirements and calls for clarification by both agencies under the principle of fairness, i.e., the relevant federal agencies should provide greater regulatory certainty to the pharmaceutical industry, especially when the stakes are so high.

I. FEDERAL ADMINISTRATIVE AGENCY CLINICAL TRIAL DISCLOSURE REQUIREMENTS

Several administrative agencies play a role in determining requirements for the disclosure of clinical trial results by publicly-traded pharmaceutical companies. Relevant regulations promulgated by the Department of Health and Human Services (“HHS”), the National Institutes of Health (“NIH”), the FDA, and the SEC are detailed below.

A. HHS, NIH, and FDA Clinical Trial Disclosure Requirements

Since 1997, federal agencies tasked with regulating drugs, devices, biologics, and public health have incrementally increased requirements for clinical trial registry and results reporting by pharmaceutical companies. The evolution of the rules governing clinical trial disclosure, the current

7. See, e.g., *Information, United States v. GlaxoSmithKline LLC*, C.A. No. 11-10398-RWZ (D. Mass. filed July 2, 2012), available at <http://www.justice.gov/opa/gsk-docs.html> (charging GSK with misbranding Paxil based on, *inter alia*, promoting the drug to doctors for use in children and adolescents without disclosing to safety issues in these populations revealed during internal GSK clinical studies); see also *Agreed Statement of Facts, United States v. Abbott Laboratories*, Crim. No. 1:12-CR-26 (W.D. Va. Filed May 7, 2012) (requiring Abbott Labs to accept certain facts as true as part of a criminal misbranding plea deal, including failing to disclose material safety and efficacy limitations of Depakote learned through internal clinical studies, during product promotion to doctors).

state of these requirements, and possible future developments are outlined herein.

1. *Food and Drug Administration Modernization Act of 1997*
(“FDAMA”) and *ClinicalTrials.gov*

Section 113 of the FDAMA amended the Public Health Service Act (“PHS Act”) to add section 402, which directs the Secretary of HHS, acting through the Director of the NIH, to establish, maintain, and operate a data bank of information on clinical trials for drugs to treat serious or life-threatening diseases and conditions.⁸ Under the FDAMA, this data bank would serve as a central resource for current information on clinical trials that individuals with serious diseases, health care providers, and researchers could access.⁹ To fulfill this mandate, FDA and NIH launched the *ClinicalTrials.gov* website in February 2000 and established a web-based protocol registration system sponsors could use to submit required information.¹⁰

Under section 113 of the FDAMA, pharmaceutical companies are required to submit information regarding federally or privately funded clinical trials if the studies met the following conditions: (1) the trial was conducted under an investigational new drug (“IND”) application, (2) the drug was designed to treat a serious or life threatening disease,¹¹ and (3) the

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

9. *Guidance for Industry: Information Program on Clinical Trials for Serious or Life-Threatening Diseases and Conditions*, FOOD AND DRUG ADMIN., 1 (2002), <http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126838.pdf> [hereinafter *Clinical Trials Guidance*].

10. Christine D. Galbraith, *Dying to Know: A Demand for Genuine Public Access to Clinical Trial Results Data*, 78 MISS. L.J. 705, 736 (2009); *Clinical Trials Guidance*, *supra* note 9, at 6.

11. The term life-threatening is defined as: “(1) diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and (2) diseases or conditions with potentially fatal outcomes, where the endpoint of clinical trial analysis is survival.” 21 C.F.R. § 312.81(a) (1999). The seriousness of a disease is a matter of judgment, but is generally based on such factors as survival, day-to-day functioning, and the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one. *Clinical Trials Guidance*, *supra* note 9, at 5.

trial was designed to test effectiveness.¹² If these criteria were met, sponsors were required to register the following information no later than twenty-one days after the trial opened for enrollment:¹³ “[a] description of the purpose of each experimental drug; [e]ligibility criteria for clinical trial participants; [d]escription of the location of trial sites; and [a] point of contact for those wanting to enroll in the trial.”¹⁴

Despite these explicit requirements, section 113 also contained a notable exemption, allowing clinical trial information to be omitted from the data bank if the sponsor provided a detailed certification to the Secretary of HHS, and the Secretary agreed, that such disclosure would substantially interfere with timely enrollment of subjects in the clinical trial.¹⁵ Moreover, because no negative consequences were associated with a trial sponsor’s violation of the FDAMA,¹⁶ many pharmaceutical companies ignored its mandates and refused to comply with the law.¹⁷

12. FDA considers all Phase 2, Phase 3 and Phase 4 trials with efficacy endpoints as trials to test effectiveness. *Clinical Trials Guidance*, *supra* note 9, at 5.

13. *Food and Drug Administration*, *supra* note 8, at 2310. It reads: “not later than 21 days after the approval of the protocol,” but because FDA does not approve protocols, the Agency interpreted this provision to mean twenty-one days after the trial opened for enrollment. Further, because the text did not specify when sponsors of existing or ongoing clinical trials would be required to submit information, FDA asked such sponsors to submit this information within forty-five days after this guidance was made available through the Federal Register. *Clinical Trials Guidance*, *supra* note 9, at 4.

14. 42 U.S.C. § 282(j)(3)(A) (2006).

15. 42 U.S.C. § 282(i)(4). FDA did note, however, that it had not identified specific instances when disclosure of information would substantially interfere with enrollment of subjects in a clinical investigation. *Clinical Trials Guidance*, *supra* note 9, at 8.

16. Galbraith, *supra* note 10, at 737. FDA did not require companies to register their clinical studies in order to utilize data from the investigations for regulatory approval, and refusal to submit information to the registry did not lead to any monetary penalties. *Id.*

17. Galbraith, *supra* note 10, at 737 (noting that studies showed inclusion rates were low, information was inadequate when it was offered).

2. *The Food and Drug Administration Amendments Act of 2007 (“FDAAA”) and the Expanded Clinical Trial Registry*

The FDAAA was enacted on September 27, 2007, expanding the types of clinical trials that must be registered on *ClinicalTrials.gov*, increasing the number of data elements required for each submission, providing for the submission of results data, and establishing penalties for non-compliance.¹⁸ Generally, FDAAA section 801 required a “responsible party” to register “applicable clinical trials.”¹⁹ This “responsible party” was required to submit certain specified data elements following a specified timeline, or be subject to penalties.²⁰ The details of this law are outlined in Table 1, below:

18. Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, 121 Stat. 823 (2007).

19. *Id.* at 121 Stat. 904.

20. FDAAA 801 Requirements, CLINICALTRIALS.GOV, <http://clinicaltrials.gov/ctz/magage-recs/fdaaa> (last visited Apr. 10, 2013) [hereinafter FDAAA Fact Sheet].

TABLE 1: FDAAA SECTION 801 CLINICAL TRIAL REGISTRY AND RESULTS REPORTING REQUIREMENTS

<p>CLINICAL TRIALS THAT MUST BE REGISTERED AT <i>CLINICAL TRIALS.GOV</i></p>	<ul style="list-style-type: none"> ▪ “Applicable Clinical Trials” are controlled interventional studies of drugs, biological products, or devices that are subject to FDA regulation, i.e., the trial has one or more sites in the United States, involves a drug, product, or device that is manufactured in the United States, or is conducted under an investigational new application (IND) or investigational device exemption (“IDE”).²¹ ▪ “Applicable Clinical Device Trials” are controlled trials that prospectively compare a device-based intervention subject to FDA regulation against a control in human subjects and pediatric post-market surveillance.²² ▪ “Applicable Clinical Drug Trials” are controlled clinical investigations other than Phase 1 trials.²³
<p>WHO IS RESPONSIBLE FOR TRIAL REGISTRATION?</p>	<ul style="list-style-type: none"> ▪ “Responsible Party” is the sponsor of the clinical trial or the principal investigator (“PI”) of such clinical trial if so designated by a sponsor, as long as the PI is responsible for conducting the trial and has sufficient data rights.²⁴

21. *Guidance for Sponsors, Investigators, and Institutional Review Boards: Questions and Answers on Informed Consent Elements*, 21 C.F.R. § 50.25(c) 2, FOOD AND DRUG ADMIN. (2012), <http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM291085.pdf>.

22. *Id.*

23. *Id.*

24. FDAAA Fact Sheet, *supra* note 20.

<p style="text-align: center;">REQUIRED DATA ELEMENTS</p>	<ul style="list-style-type: none"> ▪ For registry of new studies, the responsible party must submit descriptive,²⁵ recruitment,²⁶ location/contact,²⁷ and administrative information.²⁸ ▪ For results of completed studies, the responsible party must submit demographic characteristics, number of dropouts, primary and secondary outcome measures, point of contact, and certain agreements between the sponsor and the PI.²⁹
<p style="text-align: center;">TIMING OF REGISTRATION AT <i>CLINICALTRIALS.GOV</i></p>	<ul style="list-style-type: none"> ▪ New studies must be registered within twenty-one days of first patient enrollment. ▪ Ongoing studies must update the registry every twelve months. ▪ Recruitment status must be updated within thirty days of any change. ▪ Results must be registered within one year of the estimated or actual date of last patient's last visit (whichever is earlier), and adverse events data collected and reported within two years.³⁰
<p style="text-align: center;">PENALTIES FOR FAILING TO REGISTER</p>	<ul style="list-style-type: none"> ▪ Civil monetary penalties. ▪ Withholding or recovery of NIH grant funds.

25. *Clinical Trials Disclosure and Reporting Compliance: Navigating Overlapping and Evolving Federal and State Transparency Requirements*, STRAFFORD 9 (2011), <http://media.straffordpub.com/products/clinical-trials-disclosure-and-reporting-compliance-2011-02-03/presentation.pdf> [hereinafter FDAAA Deck]. The term descriptive includes information such as title, trial design, and primary and secondary outcome measures. *Id.*

26. FDAAA Deck, *supra* note 25. This includes patient eligibility and recruitment status. *Id.*

27. *Id.* This must be site-specific information. *Id.*

28. *Id.* This includes the protocol number and IND/IDE information. *Id.*

29. FDAAA Deck, *supra* note 25, at 10.

30. *Id.* at 11.

	<ul style="list-style-type: none"> ▪ Any application or report submitted to FDA under sections 505, 510(k), 515, or 520(m) of the Federal Food, Drug, and Cosmetic Act (“FDCA”) or under section 351 of the PHS Act must include a certification of compliance.³¹
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While the FDAAA remedied several of the major shortcomings associated with the FDAMA by adding monetary penalties and expanding the registry to clinical trials related to all conditions, it also contained some significant limitations. For example, submissions were not required for Phase 1 trials, observational trials, or older trials of drugs approved before the FDAAA was enacted and no longer the subject of ongoing trials.³² Further, although the FDAAA required the Secretary of HHS to expand the clinical trials registry to include results of clinical trials, the only explicit provisions requiring results disclosure in the initial amendment were relatively narrow.

The FDAAA provides for disclosure of particular categories of information in three successive stages. In the first stage, FDA links *ClinicalTrials.gov* registry entries to a limited group of result information, including FDA public health advisories, as well as any summary documents detailing FDA advisory committee meetings that considered a drug subject to a Phase 3 or 4 trial.³³ The second stage of disclosure involves expanding the clinical trial results database to reflect the data elements listed in the table above, including demographic characteristics of patients participating in the study and the number of participant withdrawals. Additionally, while this second stage of implementation provides for the disclosure of any agreements restricting a PI’s ability to publicly discuss the results of a trial, this provision excludes agreements with entities other than PIs, such as medical school academic scientists and PIs employed by the sponsor.³⁴ Even more limiting, these second stage disclosure requirements excluded Phase 1 trials and trials for drugs that ultimately failed to receive FDA approval.³⁵

31. FDAAA Fact Sheet, *supra* note 20.

32. FDAAA Deck, *supra* note 25, at 13.

33. Galbraith, *supra* note 10, at 742.

34. *Id.* at 743.

35. *Id.* at 744.

The final stage results disclosure requirements remain largely undetermined. The FDAAA only requires that, “to provide more complete results information and to enhance patient access to and understanding of the results of clinical trials, not later than 3 years after the date of the enactment of the [FDAAA], the Secretary shall by regulation expand the registry and results data bank.”³⁶ The statute requires NIH to hold a public meeting to obtain input from interested parties before additional regulations are promulgated.³⁷ Although this meeting was held in April 2009, the Secretary has not issued a rule expanding registration and results reporting at *ClinicalTrials.gov*. Section 3 below addresses possible provisions that may be included in these third stage disclosure requirements based on the topics discussed during the 2009 meeting.

In addition to these limitations, the FDAAA also permits the Director of the NIH to grant extensions of second and third stage data submission requirements.³⁸ The Director is authorized to provide relief from disclosure obligations if a request demonstrates “good cause;” further, there is no explicit time limitation on such extensions, if granted.³⁹ In a different vein, because the FDAAA preempted state provisions relating to the registration of clinical trials or disclosure of study results in a database, states such as Maine that introduced legislation concerning clinical trials are now foreclosed from correcting deficiencies in the federal law through state legislation.⁴⁰

3. *The Future of FDA, HHS, and NIH Clinical Trial Registry and Reporting Requirements*

As noted above, the Secretary of HHS has not yet fulfilled FDAAA’s mandate to clarify and expand registration and results reporting requirements. During the 2009 public meeting, representatives from

36. 42 U.S.C. § 282(j)(3)(D)(i) (2006).

37. 42 U.S.C. § 282(j)(3)(D)(vii).

38. Galbraith, *supra* note 10, at 749.

39. *Id.*

40. *Id.* at 750. It should be noted, however, that while Maine acknowledges federal preemption of some of its reporting requirements, it emphasizes the need for compliance with state law pending the issuance of the final federal regulations implementing FDAAA stage three disclosure requirements. FDAAA Deck, *supra* note 25, at 22.

physician, disease-related advocacy, consumer, and pharmaceutical industry groups discussed a variety of topics. Following the meeting, many stakeholder groups also submitted written comments containing more detailed responses to the specific questions posed by the NIH in its Federal Register notice for the 2009 meeting.⁴¹ Topics and themes raised in representative pre-registered speeches and submitted comments are outlined below:

PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA (“PhRMA”)—Generally, PhRMA noted a need to balance increased transparency with respect for the protection of intellectual property and proprietary business information. Therefore, PhRMA supported a requirement that results information for clinical trials of approved and unapproved medicines, for which research programs are discontinued⁴² be provided when those trials involve patients (rather than healthy volunteers).⁴³ PhRMA’s comments also touched on the following specific issues:

NARRATIVE SUMMARIES: PhRMA felt that narrative summaries of trial results written in technical language for a medical or scientific audience could be included in the results data bank without being misleading or promotional.⁴⁴ Nevertheless, PhRMA asked NIH to work with the International Committee of Medical Journal Editors (“ICMJE”)

41. See HHS, *NLM Public Meeting on Expansion of the Clinical Trials Registry and Results Data Bank*, REGULATIONS.GOV 48 (2009), <http://www.regulations.gov/#!docketDetail;dt=SR;rpp=25;po=0;D=NIH-2009-0002> [hereinafter *Public Meeting*].

42. PhRMA defined discontinued as: the company is no longer studying the molecule, does not expect to resume studying it, and has no plans for the molecule on its own or through collaboration or out-licensing. PhRMA also noted that, because FDA monitors the use and safety of products during IND phase, there is no safety reason for public disclosure of research results before FDA approval or the discontinuation of research. PhRMA, Docket No. NIH-2009-0002, 4 *Public Meeting on Expansion of the Clinical Trial Registry and Results Data Bank* (Jun. 23, 2009) [hereinafter PhRMA Comments].

43. *Id.* at 3-4.

44. *Id.* at 5. More research and consideration needed before including narrative summaries in nontechnical language since those would be more susceptible to being considered misleading or promotional. It is hard to translate trial results and those scientific documents into lay language, especially if the results are inconclusive or have statistical limitations. *Id.* at 8.

to ensure that posting these summaries would not interfere with a sponsor's ability to publish study results in journals; it also asked FDA to issue final guidance defining what would be considered unlawful promotion in the context of the trial results data bank, since many trials involve off-label uses of approved drug products.⁴⁵

ADDITIONAL NONTECHNICAL INFORMATION: PhRMA requested that NIH create a standardized glossary defining technical terms that appear frequently in the data bank.⁴⁶ PhRMA also suggested that *ClinicalTrials.gov* inform patients that information in the registry should not replace appropriate consultation with healthcare professionals for treatment.⁴⁷

VOLUNTARY DISCLOSURES: PhRMA objected to NIH's current treatment of voluntary submissions as if they were required, i.e., refusing to post information if one or more of the mandatory data elements are missing. PhRMA asserted that sponsors may wish to provide early information while protecting confidential information that risks a competitive disadvantage.⁴⁸

CONSUMERS UNION—This organization expressed concern with the overall integrity of the clinical trial process and questioned audit and oversight levels.⁴⁹ Specifically, the Consumers Union felt that the results of all clinical trials, including Phase I trials and unsuccessful trials, should be made available one or two years after the trial's conclusion.⁵⁰ Finally, it asserted that narrative summaries were inherently misleading, could not be trusted, and should not be included in the data bank.⁵¹

45. *Id.* at 6-7.

46. *Id.* at 10.

47. *Id.*

48. *Id.* at 18-19.

49. *Prescription Drug User Fee Act: Hearing on H.R. 6181 Before the Subcomm. on Health and Comm. on Commerce, 110th Cong. 1 (2007)* (statement of Jim Guest, President of the Consumers Union, on Risk Evaluation, Mitigation Strategies and Clinical Trials).

50. *Id.* at 98-99.

51. *Public Meeting, supra* note 41.

COLORECTAL CANCER COALITION (“C3”)—C3 expressed a commitment to providing clinical trial results fairly and honestly, including negative conclusions. The coalition also felt strongly that the results data bank should be presented in a simple and straightforward way, noting that patients have had difficulty navigating the current version of *ClinicalTrials.gov*.⁵²

After reviewing submitted comments, NIH issued a notice of proposed rulemaking in the Fall of 2011. In this notice, NIH expressed its intent to enhance clinical trial and adverse event reporting requirements pursuant to FDAAA section 801. The Agency noted that the regulations would be crafted to fulfill the following objectives:⁵³ identify the trials subject to results reporting requirements; determine the specific information and format for submission to *ClinicalTrials.gov*; create deadlines for registering and reporting results; outline procedures for extending deadlines and waiving submission requirements; and provide for agency review and public posting of submitted information.

There have also been legislative efforts to increase the clinical trial results reporting commitments of pharmaceutical companies. In April 2012, Representative Tom Reed (R-NY) introduced H.R. 5283, a bill to amend the PHS Act to enhance clinical trial registry data bank reporting requirements and enforcement measures.⁵⁴ Specifically, this legislation would amend the definition of “applicable clinical trial” to clarify that results reporting requirements apply to trials with both positive and negative outcomes.⁵⁵ H.R. 5283 would also broaden the scope of FDAAA, including clinical trials funded by the Department of Defense, in addition to those funded by HHS agencies. Further, the bill would enhance enforcement provisions,

52. *Id.*

53. HHS/NIH, *Expanded Registration and Results Reporting at ClinicalTrials.gov*, REGINFO.GOV (2011), <http://www.reginfo.gov/public/do/eAgendaViewRule?pubId=201110&RIN=0925-AA55>.

54. H.R. 5283, 112th Cong. (2012).

55. Kurt R. Karst, *New Bill Would Change Clinical Trial Registry Reporting Requirements and Enforcement Measures for Studies Supported by Federal Grants*, FDA LAW BLOG, (May 3, 2012), http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2012/05/new-bill-would-change-clinical-trial-registry-reporting-requirements-and-enforcement-measures-for-st.html.

mandating the revocation of federal grant funding if pharmaceutical companies failed to report required trial information.⁵⁶

Finally, certain provisions of recent Corporate Integrity Agreements (“CIAs”) entered into between the HHS Office of the Inspector General (“OIG”) and pharmaceutical companies represent an additional signal that the government intends to enhance industry compliance with results reporting requirements. Agreements made with Forest Laboratories and Novartis, for example, included requirements that these companies would publish information about clinical trial outcomes and results.⁵⁷ Thus, given the confluence of amplified activity and attention on the part of NIH, Congress, and OIG to enhancing clinical trial results reporting requirements, it is likely that pharmaceutical companies’ duties to disclose testing outcomes will increase in the coming years.

B. SEC Clinical Trial Disclosure Requirements

Publicly-traded pharmaceutical companies, like all other public companies, are subject to regulation by the SEC. Pursuant to the Securities Act of 1933 (“1933 Act”) and the Securities Exchange Act of 1934 (“1934 Act”), the SEC regulates company disclosures relevant to the purchase or sale of securities on the nation’s public exchanges.⁵⁸ In recent years, the SEC has increasingly pursued enforcement actions against publicly-traded pharmaceutical companies related to allegedly improper disclosures of company information. Furthermore, because the forecast results for publicly-traded pharmaceutical companies are volatile due to the complexities of research and development and the FDA approval process, these companies are especially vulnerable to private shareholder suits alleging violations of federal securities laws.⁵⁹ Despite these high stakes,

56. *Id.*

57. See FDAAA Deck, *supra* note 25, at 61-68 (describing CIA between OIG and Forest Laboratories requiring the company to publish information regarding clinical trial outcomes following an investigation of the company’s concealment of negative pediatric studies for Celexa and Lexapro, as well as the 2010 Novartis CIA that required the company to register all clinical studies and report results on *ClinicalTrials.gov*).

58. See General Rules and Regulations, Securities Exchange Act of 1934, 17 C.F.R. § 240 (2000).

59. See Stuart R. Cohn & Erin M. Swick, *The Sitting Ducks of Securities Class Action Litigation: Bio-Pharmas and the Need for Improved Evaluation of Scientific Data*, 35 DEL. J. CORP. L. 911, 911-14 (2010).

however, SEC laws and regulations provide little guidance to manufacturers that seek to comply with public disclosure requirements.⁶⁰ Thus, this section first details the various rules governing the information disclosures of public companies, then examines relevant case law to glean conclusions regarding how these rules are typically applied to publicly-traded companies.

1. Information Disclosure Requirements for Public Companies

A general lesson that can be gathered from the following discussion of SEC disclosure requirements is that “companies can control what they have to disclose under [federal securities laws] by controlling what they say to the market.”⁶¹ This may involve giving serious thought and consideration to statements made to investors, consumers, and doctors, as well as ensuring that disclosures that are made are accurate and complete. The disclosure obligations of public companies are detailed below.

a. Forms 10-K and 10-Q

The SEC requires publicly-listed companies to submit a Form 10-K annually and a Form 10-Q quarterly. Both forms require submission of “Management’s Discussion and Analysis of Financial Condition and Results of Operations.”⁶² Specifically, Instruction 3 to Item 303(a) requires a focus “on material events and uncertainties known to management that would cause reported financial information not to be necessarily indicative of future operating results or of future financial condition.”⁶³ The type of forward-looking information a pharmaceutical company may maintain regarding products in the development stage, such as negative or inconclusive clinical trial results, may be subject to disclosure pursuant to this instruction.⁶⁴

60. Stephanie A. Scharf, et al., *Failure to Disclose Material Clinical Trial Results: Securities Claims*, PROD. LIAB. LIT. § 10:3, § 10:3:1 (2011).

61. Press Release, Morrison Foerster LLP, *In Matrixx Initiatives, Inc. v. Siracusano, the U.S. Supreme Court Reaffirms that Materiality Depends on a Contextual Analysis of What a Defendant Says* (Mar. 22, 2011), <http://www.mofo.com/files/Uploads/Images/110322-Securities-Fraud.pdf>.

62. See 17 C.F.R. § 229.303 (2010).

63. *Id.* at Instruction 3.

64. See Cohn & Swick, *supra* note 59, at 925.

b. *Form 8-K*

In addition to these annual and quarterly reports, a Form 8-K is a report filed with the SEC by public companies to publicly disclose recent material events. The obligation to file a Form 8-K arises upon the occurrence of “reportable events,” e.g., “includ[ing] entering into material agreements, taking material actions, or when other types of material events occur that an investor would find it important to know about.”⁶⁵ The materiality of a triggering event will be determined by the facts and circumstances surrounding the event, including the size of the company, the nature of the business, or the customs of the industry; generally, however, SEC considers material “matters about which an average prudent investor ought to be reasonably informed.”⁶⁶ In the pharmaceutical companies context, the announcement of a positive business development, such as FDA approval of a new drug, or of a negative business development, such as a recall of an existing product or the denial of FDA approval for a new drug, should be reported on a Form 8-K.⁶⁷

c. *Regulation FD*

SEC’s Regulation FD was designed to prevent public companies from selectively disclosing market-sensitive information. Pursuant to Regulation FD, when a public company or any person acting on its behalf discloses “material nonpublic information” regarding the company to an investment advisor, a broker or dealer, an investment company, or a holder of the company’s securities who plans to purchase or sell those securities on the basis of such information, the company must also make a public disclosure of that information.⁶⁸ The public disclosure must be simultaneous in the case of an intentional disclosure, or made promptly in the case of a non-intentional disclosure.⁶⁹ Public disclosures must take the form of a Form 8-

65. PLC Corporate & Securities, *Form 8-K*, PRACTICAL LAW COMPANY, <http://uslf.practicallaw.com> (last visited Apr. 17, 2013).

66. *Id.*

67. PLC Corporate & Securities, *Events and Transactions Triggering a Form 8-K Filing Chart*, PRACTICAL LAW COMPANY, <http://uslf.practicallaw.com> (last visited Apr. 17, 2013).

68. 17 C.F.R. §§ 243.100(a)-(b) (2000).

69. 17 C.F.R. §§ 243.100(a)(1)-(2). A disclosure is intentional when the person making the disclosure knows, or is reckless in not knowing, that the information he or she

K or other method of disseminating the information “reasonably designed to provide broad, non-exclusionary distribution of the information to the public.”⁷⁰ Thus, publicly-traded pharmaceutical companies must remain aware that answers to market analyst inquiries regarding non-public information may reveal material information and trigger a requirement to publicly disseminate the information.⁷¹

d. Rule 10b-5

Section 10(b) of the 1934 Act makes it unlawful for any person offering securities to use “any manipulative or deceptive device or contrivance in contravention of such rules and regulations as the [SEC] may prescribe as necessary or appropriate in the public interest or for the protection of investors.”⁷² This provision was further codified by SEC Rule 10b-5, which makes it unlawful to “make any untrue statement of a material fact or to omit to state a material fact necessary in order to make the statements made, in the light of the circumstances under which they were made, not misleading.”⁷³ The Court has implied a private cause of action from the purpose and text of the 1934 Act.⁷⁴ Under this rule, plaintiffs asserting a section 10(b) claim must prove “(1) a material misrepresentation or omission by the defendant; (2) scienter; (3) a connection between the misrepresentation or omission and the purchase or sale of a security; (4)

is communicating is both material and nonpublic. 17 C.F.R. § 243.101(a). Promptly is defined as being “as soon as reasonably practicable (but in no event after the later of 24 hours or the commencement of the next day’s trading on the New York Stock Exchange). 17 C.F.R. § 243.101(d).

70. 17 C.F.R. §§ 243.101(e)(1)-(2).

71. See Cohn & Swick, *supra* note 59, at 927. This scenario may arise, for example, following the issuance of a press release. Although the company may have carefully crafted the release in a manner that couched the information with cautionary language, an answer to an analyst’s subsequent inquiry could trigger a requirement to disclose additional information to the public that the company had not originally intended to reveal.

72. 15 U.S.C. § 78j(b) (1994 & Supp. III 1997).

73. 17 C.F.R. § 240.10b-5(b).

74. See *Tellabs, Inc. v. Makor Issues & Rights, Ltd.*, 551 U.S. 308, 318 (2007).

reliance upon the misrepresentation or omission; (5) economic loss; and (6) loss causation.”⁷⁵ Often, the most critical element of a section 10(b) claim against a pharmaceutical company is the requirement that the plaintiff shows that defendant made a statement that was “misleading as to a material fact.”⁷⁶ The Supreme Court has held that the materiality element is satisfied when there is “a substantial likelihood that the disclosure of the omitted fact would have been viewed by the reasonable investor as having significantly altered the ‘total mix’ of information made available.”⁷⁷

*i. Private Securities Litigation Reform Act (“Reform Act”)
Safe Harbor for Predictions*

The Reform Act added sections to the 1933 Act and the 1934 Act providing a “safe harbor” for forward-looking statements made by public companies.⁷⁸ Under this safe harbor, a company is not liable for forward-looking statements that are identified as such and accompanied by meaningful cautionary statements indicating explicit factors that could cause actual results to differ materially from those predicted.⁷⁹ Additionally, the safe harbor provides that only companies and executives that meet a high level of culpability will be liable for predictions. This requires plaintiffs to plead and prove actual knowledge that the forward-looking statement was false or misleading.⁸⁰ On the other hand, many courts have held that some form of extreme recklessness will satisfy the scienter element of a §10(b)

75. *Stoneridge Investment Partners, LLC v. Scientific-Atlanta, Inc.*, 552 U.S. 148, 157 (2008).

76. *Basic, Inc. v. Levinson*, 485 U.S. 224, 238 (1988).

77. *Id.* at 231-232.

78. 15 U.S.C. §§ 77z-2, 78u-5 (1994 & Supp. III 1997).

79. 15 U.S.C. §§ 77z-2(c)(1)(A)(i), 78u-5(c)(1)(A)(i).

80. 15 U.S.C. § 77z-2(c)(1)(B) (If the statement is made by a natural person, a plaintiff must prove that that individual had actual knowledge that the statement was false or misleading; if made by a business entity, a plaintiff must prove that it was made with the approval of an executive officer who had actual knowledge that the statement was false or misleading.).

claim.⁸¹ Therefore, it is quite unclear what practical effect the Reform Act will have on private shareholder suits.

In addition to these open questions regarding the requisite level of scienter, the definition of a “meaningful cautionary statement” also remains undefined. While the House conference report accompanying the Reform Act noted that boilerplate warnings would not be considered sufficient, as “cautionary statements must convey substantive information about factors that realistically could cause results to differ materially from those projected in the forward-looking statement,” it is difficult to predict what sorts of cautionary language courts would consider merely boilerplate.⁸² Further complicating any potential reliance on this statutory safe harbor, projections tend to be accompanied by the hard, factual information on which they were based. Because “hard information is not within the statutory protection and is subject to the standard objections of being misleading or incomplete,” if a question from a market analyst causes a company to offer the hard information on which predictions were based, the statements are no longer immune.⁸³

e. Exchange Disclosure Requirements

Finally, beyond the disclosure obligations to the SEC or a company’s shareholders, publicly-listed companies must also provide investors with continuous disclosures of material information pursuant to the rules of the various securities exchanges. For example, the New York Stock Exchange (“NYSE”) Manual requires companies listed on the exchange to “release quickly to the public any news or information which might reasonably be expected to materially affect the market for its securities.”⁸⁴ It is possible that clinical trial test results for drugs and devices could be considered material “given the enormous costs sunk into research and the high market interest in potential outcomes.”⁸⁵

81. William O. Fisher, *Key Disclosure Issues for Life Sciences Companies: FDA Product Approval, Clinical Test Results, and Government Inspections*, 8 MICH. TELECOMM. & TECH. L. REV. 115, 120 (2002).

82. H.R. Rep. No. 104-369, at 43 (1995) (Conf. Rep.).

83. Cohn & Swick, *supra* note 59, at 938-40.

84. NYSE, *New York Stock Exchange Manual* § 202.5 (last visited May 11, 2013), <http://nysemanual.nyse.com/lcm/>.

85. Cohn & Swick, *supra* note 59, at 926.

2. *Guidelines from Case Law Applying Securities Information Disclosure Requirements to Publicly-Traded Pharmaceutical Companies*

a. *Disclosing Positive Test Results*

When publicly-traded pharmaceutical companies receive trial results that contain some positive information, they may wish to emphasize the good news in public disclosures. If the product later turns out to be unsuccessful, however, shareholders may question the company's decision to disclose the favorable data. Cases arising from disclosures of positive test results typically arise in three circumstances. In the first scenario, a company discloses only selected information about tests or trials. Given the volume of information amassed during the course of a clinical trial, "[a]bsent publication of virtually all documents created in a clinical trial, every disclosure about such a trial will be limited to the pieces of information that management elects to disclose."⁸⁶ In *In re PLC Systems, Inc. Securities Litigation*, PLC reported positive results from trials of its Heart Laser device in Transmyocardial Revascularization ("TMR"). Plaintiffs criticized a PLC press release that stated that the trial data confirmed that TMR might be an effective therapy, without disclosing the fact that TMR appeared to hasten death for terminal patients suffering from unstable angina.⁸⁷ The court dismissed this claim as immaterial, as a reasonable investor would be primarily interested in whether TMR might prove to be an effective therapy for the majority of patients, rather than for a very small subset.⁸⁸

Padnes v. Scios Nova Inc., another example of this first kind of scenario, involved a press release and a statement in Scios Nova's annual report representing that Phase 2 clinical trials demonstrated that the drug, Auriculín, provided a statistically significant reduction in the need for dialysis in acute renal failure patients.⁸⁹ One year later, however, the company announced that preliminary Phase 3 results failed to show that Auriculín reduced the need for dialysis.⁹⁰ The plaintiff shareholders asserted

86. Fisher, *supra* note 81, at 145.

87. *In re PLC Systems, Inc. Sec. Litig.*, 41 F. Supp.2d 106, 119 (D. Mass 1999).

88. *See id.* at 119-20.

89. *Padnes v. Scios Nova Inc.*, No. C 95-1693 MHP, 1996 WL 539711 at *1-2.

90. *Id.* at *1.

that the company should have included different measurements of the Phase 2 study's outcome than those performed by that trial's researchers. The court dismissed the complaint, noting that, while reasonable minds could differ with respect to the value of the Phase 2 study in determining the therapeutic effects of Auriculin, reasonable minds could not conclude that Scios Nova's failure to exhaustively catalogue those possibilities was fraudulent.⁹¹

The second category of cases that involves the disclosure of positive test results arises when there are internal disagreements within a company regarding the interpretation of trial outcomes. In an analogous circumstance, courts typically recognize that the financial forecasting process within a company involves the comparison of different projections, an exercise of company judgment, and then a corporate decision on the specific forecast to use for planning purposes or to release to the public. As long as the company had a reasonable basis for its forecast, it is not liable for publishing the one it selects simply because there were also other forecasts that were proposed within the company.⁹² This principle could logically extend to the interpretation of clinical trial results. Even if there is internal debate within a pharmaceutical company regarding test results, if the company has a procedure or process in place to reach an ultimate corporate view, it should not be held liable for ultimately and thoughtfully discarding one possible interpretation.⁹³

The third and final scenario that arises in litigation regarding the disclosure of positive test results occurs when companies release data and statistics for groups of patients and trial protocols that the financial community does not fully understand. In *In re Synergen, Inc. Securities Litigation*, Synergen issued a media advisory on Phase 2 results for its drug stating it "reduces mortality in patients with sepsis syndrome."⁹⁴ The subsequent securities lawsuit turned on the meaning of "mortality." One

91. *Id.* at *5.

92. See *Wielgos v. Commonwealth Edison Co.*, 892 F.2d 509, 516 (7th Cir. 1989) ("Any firm generates a range of estimates internally or through consultants. It may reveal the projection it thinks best while withholding others, so long as the one revealed has a 'reasonable basis'—a question on which other estimates may reflect without automatically depriving the published one of foundation.").

93. See *Fisher*, *supra* note 81, at 153-54.

94. *In re Synergen, Inc. Sec. Litig.*, 863 F. Supp. 1409, 1418 (D. Colo. 1994).

mortality measure is a “survival curve,” which measures the number of days a patient lives during a twenty-eight day trial. This is the meaning of mortality that Synergen used as the basis for its advisory. On the other hand, “twenty-eight day mortality” refers to the percentage of patients who are dead on the twenty-eighth day of the trial.⁹⁵ Although Synergen argued that the investment community understood that the advisory was based on survival curves, the court denied the defendants’ motion for summary judgment on the grounds that there remained a triable issue as to the market’s understanding of Synergen’s “mortality” data.⁹⁶

b. Disclosing Negative Test Results

In addition to issues related to publicizing favorable clinical trial results, publicly-traded pharmaceutical companies also confront significant dilemmas when deciding whether negative trial outcomes are material subject to disclosure requirements. Courts have deemed materiality “one of the most unpredictable and elusive concepts of the federal securities laws.”⁹⁷ These questions are particularly difficult for two critical reasons. First, if materiality is judged by what a reasonable person would consider important when making an investment decision, the general public’s intolerance to adverse health reports may give rise to a materiality issue before sufficient data is collected.⁹⁸ Second, although pharmaceutical companies use clinical trials to produce “statistically significant” evidence that a drug or product is responsible for desired outcomes, the securities law standard of materiality relies on an entirely different determination.⁹⁹

The statistical significance-materiality dichotomy has evolved through case law over time. The Supreme Court first addressed the standard for Rule 10b-5 materiality in *Basic, Inc. v. Levinson*. In *Basic*, plaintiffs alleged that the target company made material misrepresentations in publicly denying its participation in merger negotiations during the timeframe when it was actually participating in these discussions. The Court held that in order to “fulfill the materiality requirement there must be a substantial likelihood that

95. *Id.* at 1418-19.

96. *Id.* at 1419.

97. *SEC v. Bausch & Lomb Inc.*, 565 F.2d 8, 10 (2d Cir. 1997).

98. Cohn & Swick, *supra* note 59, at 929.

99. *Id.* at 929-30.

the disclosure of the omitted fact would have been viewed by the reasonable investor as having significantly altered the ‘total mix’ of information made available.”¹⁰⁰ Following *Basic*, however, circuit courts split on the law of materiality in various §10(b) suits involving pharmaceutical companies. The First, Second, and Third Circuit courts established a distinct materiality standard for pharmaceutical companies, requiring plaintiffs to allege “that the claimed adverse event is statistically significant to the use of the drug in question.”¹⁰¹

This rift was settled in 2011 with the Supreme Court’s decision in *Matrixx Initiatives, Inc. v. Siracusano*. In *Matrixx*, the Court rejected a bright-line rule requiring that results of a clinical trial be statistically significant in order to be considered “material” for purposes of disclosure.¹⁰² The Court categorized the “premise that statistical significance is the only reliable indication of causation” as flawed, given the fact that “medical experts and the [FDA] rely on evidence other than statistically significant data to establish an inference of causation.”¹⁰³ Further, the Court insisted that “materiality is a fact-specific inquiry, requiring consideration of [the] source, content, and context [of adverse reports].”¹⁰⁴ While the Court held that “something more than the mere existence of adverse event reports is needed to satisfy” the standard of what a reasonable investor would have viewed as significantly altering the “total mix” of information made available, “that something more is not limited to statistical significance.”¹⁰⁵ Because the Court refused to adopt a bright-line rule regarding materiality, going forward the assessment of whether an adverse event or trial outcome is material will be decided on a case-by-case basis. This may make it harder for publicly-traded pharmaceutical companies to dispose of securities class action

100. *Basic, Inc. v. Levinson*, 485 U.S. 224, 231-32 (1988).

101. Benjamin Shook, *The Materiality Standard After Matrixx Initiatives, Inc. v. Siracusano*, 12 N.C. J. L. & TECH. 369, 377 (2011).

102. *Matrixx Initiatives, Inc. v. Siracusano*, 131 S. Ct. 1309, 1313-14 (2011).

103. *Id.* at 1319.

104. *Id.* at 1321.

105. *Id.*

lawsuits at the motion to dismiss or summary judgment phases of litigation.¹⁰⁶

While the Court clarified the materiality element of Rule 10b-5 claims, the current status of the rule's scienter element remains uncertain. As mentioned above, the Reform Act appears to have imposed a scienter standard of actual knowledge for plaintiffs suing under 10b-5. In addition, the Reform Act heightened the pleading requirements for plaintiffs, requiring that the complaint "state with particularity facts giving rise to a strong inference that the defendant acted with the required state of mind."¹⁰⁷ Although these appear to be significant obstacles for plaintiffs, most circuit courts have nevertheless adopted recklessness as a substitute for the more demanding intent requirement of scienter. Further, in dicta, the Court in *Matrixx* assumed for the sake of argument that deliberate recklessness would be sufficient to meet the scienter requirement.¹⁰⁸ While recklessness is not an easy allegation to plead and prove, pharmaceutical companies may be particularly vulnerable to liability as the scienter standard shifts from intent to recklessness. This is because the public statements of pharmaceutical companies typically represent only a fraction of the voluminous and detailed results the companies maintain. Once a suit is initiated, however, all of this underlying material will be reviewed with the benefit of hindsight, which may provide plaintiffs with an increased opportunity to "find nuggets that arguably should have been disclosed."¹⁰⁹

Beyond these primary questions of materiality and scienter, it is important to note that a company cannot be liable for failing to publicize a fact, even if the fact is material, unless the company has an obligation to disclose it.¹¹⁰ In the context of disclosures of negative clinical trial results, a duty to disclose a non-public material fact may arise if the company makes statements that will mislead unless the company also reveals the negative test results. This duty arises from sections 11 and 12(a)(2) of the 1933 Act and Rule 10b-5, which expressly impose liability for omitting material facts necessary to

106. Scharf, et al., *supra* note 60, at § 10:3:3.

107. 15 U.S.C. § 78u(b)(2) (2006).

108. Cohn & Swick, *supra* note 59, at 934.

109. Cohn & Swick, *supra* note 59, at 935-36.

110. *See* Basic, Inc. v. Levinson, 485 U.S. 224, 239 n.17 (1988) ("Silence, absent a duty to disclose, is not misleading under Rule 10b-5.").

make statements made non-misleading. Likewise, section 10(b) cases hold that “when a corporation does make a disclosure—whether it be voluntary or required—there is a duty to make it complete and accurate.”¹¹¹ Applied in the context of pharmaceutical companies, where a drug or device company “has reached a conclusion that test results on a new product are negative, it may, as a practical matter, be difficult to provide any progress report on the product to the investment community that fails to include this ‘bad’ news without the report being arguably incomplete or misleading.”¹¹²

In *Walsingham v. Biocontrol Technology, Inc.*, the court denied Biocontrol’s motion to dismiss claims that it had failed to disclose unfavorable test results while simultaneously touting the effectiveness of and expressing optimism about future FDA approval for its Diasensor 1000 device.¹¹³ In response to a newspaper article raising doubts about FDA approval of the device, Biocontrol stated: “If the device does not work, why struggle so hard to get it to market? Why struggle so hard and long through the FDA approval process and why would eight of the world’s leading endocrinologists have gone to the FDA to support the Diasensor 1000[?]”¹¹⁴ At the time of this statement, however, the company was receiving dismal test results, causing the court to find it “significant that the defendants’ failure to disclose the test results occurred during a time when they were issuing what can only be described as very positive press releases.”¹¹⁵ Even though Biocontrol’s comments were largely phrased as rhetorical questions, this case appears to emphasize that comments implying effective performance may result in litigation if the company does not simultaneously disclose negative test results that have not been superseded by positive ones.¹¹⁶ Thus, to avoid liability for incomplete or inaccurate disclosures,

111. See *Roeder v. Alpha Industries, Inc.*, 814 F.2d 22, 26 (1st Cir. 1987).

112. Fisher, *supra* note 81, at 163.

113. Mem. Op. and Order that Defs. Mot. To Dismiss Pursuant to F.R. Civ. P. 9(b) and 12(b)(6) in Den., *Walsingham v. Biocontrol Tech., Inc.* 66 F. Supp 2d 669 (W.D. Pa. 1998) No. 96-0089.

114. Fisher, *supra* note 81, at 164.

115. *Walsingham v. Biocontrol Tech., Inc.*, 66 F. Supp. 2d 669, 677-78 (W.D. Pa. 1998).

116. Fisher, *supra* note 81, at 164.

publicly-traded pharmaceutical companies would be wise to analyze any disclosures before they are made and consider “whether the information to be disclosed is accurate, complete, and appropriately contextualized within the scope of the company’s overall clinical development program.”¹¹⁷

Similarly, although federal securities laws do not impose an explicit duty to update public disclosures, a duty of this sort may arise in special situations, such as when a later development makes an earlier statement misleading.¹¹⁸ Even in this specific scenario, however, the duty to update appears to be fairly limited. Courts have noted that there is a duty to correct “when a company makes a historical statement that at the time made, the company believed to be true, but as revealed by subsequently discovered information actually was not.”¹¹⁹ By contrast, this duty to correct is quite different from a duty to update “if a prior disclosure becomes materially misleading in light of subsequent events.”¹²⁰ Courts have rejected such a duty. In the first situation, it is possible that a representative from a company could make a disclosure that asserts incorrect financial calculations or inaccurate data; in this case, the company has a duty to correct the original error. In the second situation, courts are unlikely to find an obligation to update soft information that is clearly set forth as a projection.¹²¹

117. Scharf, et al., *supra* note 60, at § 10:3:3.

118. *Id.*

119. *In re Int'l Bus. Machines Corp. Sec. Litig.*, 163 F.3d 102, 109 (2d Cir.1998) (noting the duty to correct arises “if and when a speaker learns that a prior statement was misleading when made.”).

120. *See Stransky v. Cummins Engine Co., Inc.*, 51 F.3d 1329, 1332 (7th Cir. 1995) (amended Apr. 7, 1995) (“Some have argued that a duty to update arises when a company makes a forward-looking statement - a projection - that because of subsequent events becomes untrue. . . . This court has never embraced such a theory, and we decline to do so now.”).

121. Cohn & Swick, *supra* note 59, at 940-41. Notably, however, this issue is not yet fully resolved. Factors that may affect a court’s decision in a particular case may include: 1) the timing of the projection relative to the discovery of its inaccuracy, 2) the type of cautionary statements that may have accompanied the projection, 3) the extent of the discrepancy between the projection and the current information, and 4) a court’s perceived relationship of the statements to attempted stock market manipulation. *Id.*

II. INTERNATIONAL CLINICAL TRIAL DISCLOSURE REQUIREMENTS AND STANDARDS

A. *World Health Organization (WHO)*

WHO, in 2005, began urging research institutions and companies to register all medical studies that test treatments on humans, including the earliest studies.¹²² WHO also created the International Clinical Trial Registry Platform (“ICTRP”)—it is not itself a registry but instead a network of registries.¹²³ Primary registries are WHO-selected and managed by not-for-profit entities. These registries accept any interventional trials and provide the data directly to WHO.¹²⁴ Partner registries are more numerous, and these include registries that submit data to primary registries but limit their own registry to trials in a restricted area (i.e., specific disease, company, academic institution, or geographic region). ICTRP aims to standardize the way information on medical studies is made available to the public. As part of this project, WHO recommends that twenty key details, such as title, funding source, research ethics review, and outcome measures, be disclosed at the time studies are begun and that results of trials are subsequently required.¹²⁵

B. *International Committee of Medical Journal Editors (ICMJE)*

In 2005, ICMJE initiated a policy requiring investigators to deposit information about trial design into an accepted clinical trials registry before the onset of patient enrollment.¹²⁶ Thus, as a condition of consideration for

122. World Health Organization, *Resolution WHA58.34 - Ministerial Summit on Health Research* (May 25, 2005), https://apps.who.int/gb/ebwha/pdf_files/WHA58/WHA58_34-en.pdf.

123. See *About the WHO ICRP*, WORLD HEALTH ORG., <http://www.who.int/ictrp/about/en/> (last visited Apr. 10, 2013).

124. See *About Registries*, WORLD HEALTH ORG., <http://www.who.int/ictrp/network/primary/en/index.html> (last visited Apr. 10, 2013).

125. FDAAA Deck, *supra* note 25, at 78-79.

126. Clinical Trial Registration: A Statement from the International Committee of Medical Journal Editors, Int'l Comm. Of Med. Editors (ICMJE), Editorial (2005), available at http://www.icmje.org/clin_trial.pdf.

publication, ICMJE required registration in a public trials registry.¹²⁷ Although ICMJE did not advocate any particular registry, its member journals required authors to register trials in a registry meeting several criteria, e.g., that it is accessible to the public at no charge, managed by a not-for-profit, and has a mechanism to ensure the validity of the registration data.¹²⁸

Compared to FDAAA requirements, that require registration of “applicable clinical trials,” which excludes Phase 1 trials and trials for unapproved drugs, ICMJE requirements apply to all prospective, interventional human trials.¹²⁹ Further, the ICMJE provisions call for peer review of data, while the FDAAA does not. On the other hand, results disclosure is not stipulated by the ICMJE policy, whereas the FDAAA contains the three various stages of results disclosure outlined earlier.¹³⁰

C. *Bioethics Scholars and Commentators*

Many in the bioethics community make a case for a moral duty to disclose all relevant adverse clinical trial results that involve harms to prospective participants in clinical trials. The typical argument can be summarized as follows: people have a human right not to be placed at risk of harm without their informed consent, and there is a correlative moral duty not to place others at risk of harm without the same consent. It follows that if adverse clinical trial results are not disclosed to prospective participants, then they are placed at risk of harm without their informed consent. Ergo, there is a moral duty to disclose adverse clinical trial results to prospective participants in clinical trials.¹³¹

127. *Id.*

128. *Id.*

129. *Id.*

130. See Laurence Hirsch, *Trial Registration and Results Disclosure: Impact of US Legislation on Sponsors, Investigators, and Medical Journal Editors*, 24 *CURR. MED. RES. & OP.* 1683 (2008).

131. S. Matthew Lao, et al., *The Duty to Disclose Adverse Clinical Trial Results*, 9 *AM. J. BIOETHICS* 24, 25 (2009).

D. *Pharmaceutical Industry and Related Industry Groups*

The pharmaceutical industry's reaction to clinical trials reporting has been mixed, but some individual manufacturers and groups volunteered to make some clinical trials data public. PhRMA introduced its own clinical trials database in October 2004. In January 2005, the International Federation of Pharmaceutical Manufacturers and Associations ("IFPMA") announced that its members would voluntarily disclose summary results of all industry-sponsored clinical trials. In October 2005, IFPMA announced that it had launched a search portal of clinical trial registries and databases worldwide.

According to recent comments submitted to NIH by PhRMA:

The pharmaceutical industry is firmly committed to the transparency of clinical research and safety information. We recognize that there are important public health benefits associated with making clinical trial information more widely available to healthcare practitioners, patients, and others. Clinical trial registries may assist desperately ill patients and their healthcare providers in identifying ongoing trials of promising new drugs in which patients may be eligible to participate. Moreover, clinical trial results databanks help assure that the results of all meaningful clinical trials—even trials that are not able to be published in peer-reviewed journals—are publicly available for review and consideration by patients, physicians, and others to help inform treatment decisions.¹³²

Additionally, in 2002, PhRMA issued and continues to update its Principles on Conduct of Clinical Trials and Communication of Clinical Trial Results. These Principles include a commitment by the industry to communicate results regardless of whether they were positive, negative, or inconclusive. In 2004, PhRMA "established a free, centralized, publicly-available electronic database at www.ClinicalStudyResults.org."¹³³ In 2009, PhRMA announced it would update its principles to include registering all clinical trials, including Phase 1 trials, and also provide results summaries for all clinical trials involving patients for medicines whose research programs are discontinued.¹³⁴

132. PhRMA Comments, *supra* note 42, at 2.

133. *Id.* at 2-3.

134. *Id.*

III. THE INTERPLAY BETWEEN VARIOUS DISCLOSURE STANDARDS

Before considering how differences among these standards affect real-world outcomes, it is instructive to first evaluate scenarios where there is convergence. One example is when a pharmaceutical company, which has previously discussed its developmental pipeline in its public filings, receives information that suggests that the timing or scope of a drug approval will change. This could take any number of forms: a Phase 1 and 2 study suggests that safety and effectiveness profiles will have the greatest benefit-risk ratio among a disease subpopulation—perhaps only among patients with a specific genetic marker; a co-primary endpoint of a Phase 3 effectiveness study fails to reach statistical significance, forcing the company to consider narrowing the types of indications or claims that are based on the successful endpoint alone; or, in an extreme example, early safety observations force a company to terminate a clinical trial prior to completion and threaten the approvability of the entire compound. In each of these examples, FDA would likely require that a sponsor disclose the clinical trial information, as the data is critical for the evaluation of new or existing claims and indications. Similarly, investors would reasonably view such information as material to the valuation of the company, and, would expect disclosure via a public SEC filing. Here, the public's interests are served by the dual disclosure already a part of the regulatory process.

Although the various disclosure standards can—and do—overlap, those instances when they diverge illustrate particular motivations for harmonization. One example arises where a pharmaceutical company conducts early studies to support a new indication for a drug that does not contain significant safety warnings, but where the new studies in a different patient population give rise to substantial adverse events. In this case, FDA's post-marketing reporting requirements would require the disclosure of these safety findings.¹³⁵ The SEC, however, arguably does not require disclosure if the company has not previously discussed the potential for an expanded indication, though this is not as clear as one would hope given the potential downsides of incorrectly concluding that SEC disclosure is not required.¹³⁶ In this regard, FDA is more restrictive with its requirements, whereas the SEC is more permissive.

135. These negative safety observations would be reported both as adverse drug experiences under 21 C.F.R. § 314.80 as well as results of clinical studies not previously reported to FDA during periodic reporting under 21 C.F.R. § 314.81.

136. Here, arguably, because there was never any "positive" disclosures regarding the possibility of an expanded indication, there is no need to update those disclosures with the new information. A shareholder suit, however, could argue that *any* negative safety

FDA's disclosure requirements, however, are not always the most restrictive. Pharmaceutical companies regularly conduct pharmacoeconomic studies regarding their products. These studies are designed to examine the cost-effectiveness of a therapy; they do not evaluate safety or effectiveness, *per se*. "Positive" pharmacoeconomic information, however, is very valuable when seeking drug formulary access. Hospitals and insurance plans, in an effort to increase cost-efficiencies, seek out interventions that maximize patient benefit while minimizing the overall cost of care. Whether a drug is listed as a preferred intervention drives how much a patient pays for that intervention choice, which, in turn, drives physician prescribing behavior. Pharmacoeconomic study results that are not favorable to a given drug can have substantial impacts on the overall revenues generated from the sale of that drug—information that would be market-driving. FDA, on the other hand, is statutorily antagonistic regarding pharmacoeconomic data.¹³⁷ In these circumstances, the SEC is more restrictive than FDA. It is worth noting, however, that although FDA's approach to pharmacoeconomic data is relatively well-established for drugs, FDAMA section 114 does not apply to medical devices, and FDA's Center for Devices and Radiological Health has not formally stated how it intends to evaluate such data.¹³⁸

As with any regulatory scheme, regulatory uncertainty or divergence results in hesitancy on the part of corporate counsel. Some companies will opt to publicly disclose whenever any regulatory body requires disclosure. Others, however, will use the divergence as a shield to keep information from being disclosed to the public, even when such information would be valuable to patients, consumers, healthcare providers, investors, and regulators. Strategic reasons for non-disclosure are not limited to only self-preservation; information about a company's clinical trials provide a window into its mid- and long-term development concepts. In less-regulated industries, such information would be guarded as trade-secrets. Thus, a

information—and especially such information in the context of a clinical trial—is material information related to the overall safety profile of the drug, as a whole.

137. FDA, however, is concerned about how pharmaceutical companies *use* pharmacoeconomic data in a promotional context. FDAMA amended the FDCA to permit the use of such data only in the very limited context of discussions with formulary committee members acting in their advisory role in making formulary decisions. *See* FDCA § 502(a), 21 U.S.C. § 352(a) (amended by FDAMA § 114 in 1997).

138. FDAMA § 114 modifies FDCA § 505, which applies to new drugs, but not to medical devices.

policy favoring complete disclosure ignores critical intellectual property interests.

Because different companies will take differing approaches to these difficult issues, the public cannot reasonably know what information it can expect from a given company regarding information squarely within the public's interests. Therefore, coordinated efforts to harmonize the various disclosure standards will benefit the public, regulators, and corporate counsel. A single, clear standard levels the playing field and sets expectations in a predictable manner. It will remove uncertainty, which is a barrier to innovation.

IV. CONCLUSION

Although both the FDA and SEC have increased regulatory scrutiny on the clinical trial result disclosures of publicly-traded pharmaceutical companies, whether through the *ClinicalTrials.gov* website or in investor communications, the scope of current disclosure requirements remains largely undefined. While stakeholders within the pharmaceutical industry are generally supportive of efforts to increase the transparency of clinical trials, and recognize the public health benefits associated with making appropriate clinical trial information widely available, an effective regulatory approach to these goals must also include protections for individual privacy, contract rights, and intellectual property.¹³⁹ It is critical, therefore, that the federal agencies involved in regulating the disclosures of clinical trial results work in cooperation toward a comprehensive and comprehensible set of regulations, policies, and guidelines that safeguard patients, investors, and the future of medical and scientific innovation.

139. See PhRMA, *Principles on Conduct of Clinical Trials: Communication of Clinical Trial Results*, 1 (2011), http://www.phrma.org/sites/default/files/105/042009_clinical_trial_principles_final.pdf.